

**National Cervical Screening Program
Guidelines for the management of
screen-detected abnormalities, screening
in specific populations and investigation of
abnormal vaginal bleeding
(Partial update)**

The updated guidance within this document will take effect on: **1 July 2022**

This PDF has been made available for reference only in advance of this date to allow time for any preparatory activities.

Disclaimer

This document should be read in conjunction with the: Guideline Development Process – 2020 update.

Available online at: cancer.org.au/clinical-guidelines/cervical-cancer-screening

If you have any questions about this document, please email guidelines@cancer.org.au.

Suggested citation: This updated content is not approved until 1 July 2022, therefore there is no recommended citation. A citation will be available from 1 July 2022 on the live guideline pages.

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National Cervical Screening Program Guidelines for the management of screen-detected abnormalities, screening in specific populations and investigation of abnormal vaginal bleeding

Available from: https://wiki.cancer.org.au/australia/Guidelines:Cervical_cancer/Screening.

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Please see the [Australian Department of Health Cancer Screening website](#) for information about the National Cervical Screening Program (NCSP) and policies on transitioning women to the renewed NCSP

Two sections of the guideline, *HPV oncogenic types not 16/18* and *Self-collected vaginal samples* were reviewed and updated and came into effect on 1 February 2021.

Further sections were updated to implement the change in self-collection policy. These were reviewed and will come into effect on 1 July 2022.



Clinical management guidelines for the prevention of cervical cancer

Please see the [Australian Department of Health Cancer Screening website](#) for information about the National Cervical Screening Program (NCSP) and policies on transitioning women to the renewed NCSP.

Resources

[Cervical cancer screening online education modules \(e-learning\)](#)

Foreword

Australia has an excellent record of successful prevention of cervical cancer through routine screening. Conventional cervical cytology (Pap smear), combined with effective screening registries, quality-assured pathology services, well-accepted national screening policy and clear guidelines for the management of screen-detected abnormalities, has served us well for 25 years. The success of the Australian program is demonstrated by annual incidence and mortality rates for cervical cancer that are now amongst the lowest in the world.

Although the National Cervical Screening Program has been very successful, we have some challenges. The significant false-negative rate associated with Pap tests mandates frequent screening to minimise failure to detect disease. However, a newer and more sensitive approach to cervical screening has now been established, which involves testing for the presence of the causal agent for cervical cancer, human papillomavirus (HPV).

In 1984, Professor Harald zur Hausen demonstrated that cervical cancer is due to persisting infection of the cervix with HPV. The knowledge that HPV causes cervical cancer has been further developed through major international epidemiological studies. It is now recognised that HPV comes in many types; some, designated as 'high-risk' or oncogenic types, are associated with a risk of developing cervical cancer in the future if infection persists. The worldwide evidence has also shown that the absence of cervical oncogenic HPV infection is associated with an exceedingly low risk for development of cervical cancer in the next 5 years. The development of automated laboratory tests that enable detection of oncogenic HPV infection in cervical samples thus facilitates the widespread introduction of primary HPV screening. This heralds a new era of more sensitive testing of cervical samples to assess the future risk of cervical cancer.

The discovery of HPV's role in causing cancer has also led to the development a vaccine to prevent cervical cancer. HPV vaccination was introduced into Australia in 2007 and young vaccinated women have already shown a falling rate of cervical abnormalities. These changes make Pap smear-based screening less efficient and the lower incidence of detected cervical abnormalities makes quality control more difficult.

Driven by all these developments, the National Cervical Screening Program has undergone a process of 'renewal' over the last 5 years, and this has resulted in an evidence-based decision to change from 2-yearly Pap smear tests to 5-yearly primary HPV testing. I am confident that the new 5-yearly HPV test based screening policy will provide even greater protection against cervical cancer than the previous program. The renewed program will protect up to 30% more women from cervical cancer, even whilst providing for a later starting age to commence screening and fewer screening tests over a woman's lifetime. HPV-based cervical screening will now provide greater reassurance that all is well, without the need for further investigation in women without detected HPV infection.

This is great news for Australian women, and a testimony to the power of medical research to deliver practical outcomes for Australia. These new guidelines were developed by a team of expert clinicians and scientists. They support the new HPV-based National Cervical Screening Program by providing recommendations for the management of screen-detected abnormalities, symptoms and screening in special circumstances. I commend these guidelines to you and thank, on behalf of all Australians, the team that has evaluated the evidence and put together the recommendations for the benefit of all Australian women.

A handwritten signature in blue ink, appearing to read 'I. Frazer'.

Professor Ian Frazer AC

The University of Queensland

President, Australian Academy of Health and Medical Sciences

FRS, FAA, FTSE, FAHMS

FRCP (Ed) FRACP FRCPA FRCOG FRACGP

MB ChB (Edin) MD (Melb) DSc (Edin)

Introduction

Author(s):

- [Professor Ian Hammond](#) — Author
- [A/Professor Marion Saville](#) — Author
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

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Introduction

The management of screen-detected cervical abnormalities in asymptomatic women, and the care of women presenting with symptoms that may be due to cervical cancer or its precursors, involve health professionals across a broad spectrum of disciplines. These guidelines have been developed to assist women and health professionals to achieve the best outcomes.

The target audience for these guidelines includes all health professionals involved in cervical screening and the clinical care of women presenting with symptoms. It may also be of interest to policy makers and researchers.

In October 2011, the Australian Department of Health announced the renewal of the National Cervical Screening Program (NCSP). In April 2014, following a robust and transparent process involving a commissioned evidence review and health outcome and economic modelling, the Australian Medical Services Advisory Committee (MSAC) made several recommendations for the renewed NCSP. These included 5 yearly primary human papillomavirus (HPV) testing with partial genotyping and liquid-based cytology (LBC) triage, self-collection of an HPV sample for under- or never-screened women, and invitations and reminders to be sent to women aged 25–69 years, with exit testing from age 70–74 years.

In December 2017, the NCSP will change from 2 yearly cervical cytology testing to 5 yearly HPV testing for women aged 25–74 years. An HPV test every 5 years is more effective, just as safe, and is expected to result in a significant reduction (24%-36%) in incidence and mortality from cervical cancer in Australian women, compared with the program it replaces, which is based on 2 yearly Pap smears.

In 2005, the evidence based NHMRC endorsed guidelines *Screening to Prevent Cervical Cancer: Guidelines for the Management of Women with Screen Detected Abnormalities*.^[1] were published and were introduced into practice in 2006. These guidelines were accepted by health professionals as a useful guide to the management of women with cervical abnormalities detected by cervical cytology. With the change to primary HPV testing, it is necessary and

timely to review the 2005 guidelines and to consider recent evidence to formulate guidelines that are relevant to primary HPV testing and triage using LBC.

Following the MSAC recommendations and their acceptance by the Australian Government, the Department of Health requested that the 2005 guidelines be reviewed and updated to assist the implementation of the renewed NCSP. Cancer Council Australia was commissioned and funded by the Department of Health Australia to develop these guidelines with the assistance of an expert clinical management guidelines working party (see [Working party members and contributors](#)) and technical support from Professor Karen Canfell and her Cancer Screening Group at Cancer Council NSW.

These guidelines have been developed and published by Cancer Council Australia in accordance with NHMRC recommended processes (see [Guideline development process](#)). The web-based wiki platform allows for feedback and easy, regular updating in the light of emerging evidence.

These new guidelines offer guidance to health professionals and women as to best practice in the clinical management of women with positive oncogenic HPV test results and abnormalities detected on subsequent LBC. These guidelines address the current epidemiology of cervical cancer in Australia, the benefits and harms of cervical screening, the natural history of cervical HPV infection, the terminology for HPV testing, LBC, cervical histopathology and colposcopy, management of older women and those undergoing exit testing, management of women with positive oncogenic HPV test results, colposcopy, management of histologically confirmed squamous and glandular abnormalities, screening in specific populations, screening for women who are transitioning from the old into the new program, psychosocial issues and economic issues.

For the first time, guidance on the management of symptomatic women has been included, with a particular focus on those with signs or symptoms suggestive of cervical cancer, such as postcoital, intermenstrual and postmenopausal bleeding. These guidelines do not address issues related to the quality control aspects of the cervical screening test or detailed information about the treatment of invasive cervical cancer.

There are specific recommendations regarding the adoption of a new system for reporting cervical histopathology based on the Lower Anogenital Squamous Terminology (LAST) Standardization Project and new terminology recommended by the International Federation for Colposcopy and Cervical Pathology for use in reporting colposcopic findings and treatment.

The development of these guidelines has involved widespread consultation with relevant professional bodies and a wide range of clinicians and consumers. These guidelines have been reviewed and endorsed by The Royal Australian College of General Practitioners (RACGP), The Royal College of Pathologists of Australasia (RCPA), The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG), The Australian Society for Colposcopy and Cervical Pathology (ASCCP) and The Australian Society of Gynaecologic Oncologists (ASGO).

Clinicians must, of course, make individual decisions in consultation with their patients, based on individual clinical circumstances. However, it is anticipated that, in most circumstances, women with screen-detected abnormalities would be managed according to these guidelines. It is important that the NCSP monitors compliance with these guidelines using the [NCSP Quality Framework](#) developed by the Quality and Safety Monitoring Committee.

These guidelines are a distillation of the latest research and data, brought together by some of the leading experts in this field. We commend the guidelines to you in the belief that they will result in further significant improvements in the care and treatment of Australian women.



Professor Ian Hammond

Chair, Cancer Council Australia Cervical Cancer Screening Guidelines Working Party,
Clinical Professor
School of Women's and Infants' Health
University of Western Australia



Associate Professor Marion Saville

Deputy Chair, Cancer Council Australia Cervical Cancer Screening Guidelines Working Party
Cytopathologist and Executive Director, Victorian Cytology Services Ltd.
Melbourne, Victoria
Department of Obstetrics and Gynaecology, University of Melbourne

References

1. ↑ National Health and Medical Research Council. [*Screening to prevent cervical cancer: guidelines for the management of asymptomatic women with screen detected abnormalities*](#). Canberra: NHMRC; 2005.

Summary of recommendations

Author(s):

- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#)
— Author

This guideline contains evidence-based recommendations (EBR), consensus-based recommendations (CBR) and practice points (PP) as defined in [Table B.4 NHMRC approved recommendation types and definitions](#).

[Table B.5. Key to types of recommendations in these guidelines](#) outlines the types of recommendations appearing in these guidelines.

This is a summary of the recommendations in these guidelines, numbered according to chapter to which they relate. Please note that some chapters do not have associated recommendations.

Recommendations

4. Unsatisfactory cervical screening results

Practice point

REC4.1: Attempt adequate repeat preparations for an unsatisfactory LBC test

In the case of unsatisfactory LBC, laboratories should ensure that adequate repeat preparations are attempted, after dealing with potentially remediable technical problems.

Practice point

REC4.2: Report cellular abnormality for LBC specimens with abnormal cells

Any LBC specimen with abnormal cells should **not** be reported as 'Unsatisfactory'. The identified cellular abnormality should be reported.

Practice point

REC4.3: Recall women in 6–12 weeks if they have an unsatisfactory screening report

A woman with an unsatisfactory screening report should have a repeat sample collected in 6–12 weeks. If the reason for the unsatisfactory sample has been identified then this problem should be corrected if possible before the repeat sample is collected.

6. Management of HPV test results

MSAC evidence-based recommendation

REC6.1: Eligibility for screening on a self-collected sample to include all people eligible for cervical screening (people with a cervix aged 25-74 years who have ever been sexually active)

Anyone who is eligible for cervical screening should be offered the choice of HPV testing on a self-collected vaginal sample or on a clinician-collected sample.

Practice point

REC6.2: Clinician-collected cervical samples

A short course of topical oestrogen therapy could be considered in post-menopausal women, people experiencing vaginal dryness, or trans men, prior to collecting the sample, for example daily for a period of at least 2 weeks, ceasing 1-2 days prior to the appointment. The reason for this should be explained (to reduce discomfort from the speculum and to improve the diagnostic accuracy of any associated LBC).

Oncogenic HPV types not detected

MSAC evidence-based recommendation

REC6.3: Oncogenic HPV types not detected at routine screening

Women who have a screening HPV test in which oncogenic HPV types are **not** detected should rescreen in 5 years.

Oncogenic HPV types 16 and/or 18

MSAC evidence-based recommendation

REC6.4: Women with a positive HPV (16/18) test result

Women with a positive oncogenic HPV (16/18) test result should be referred directly for colposcopic assessment, which will be informed by the result of LBC. If the sample has been collected by a healthcare practitioner, then reflex LBC will be performed by the laboratory. If the sample was self-collected, then a sample for LBC should be collected at the time of colposcopy.

Consensus-based recommendation*

REC6.5: Referral of women with a positive HPV (16/18) test result and LBC prediction of invasive cancer to a gynaecological oncologist

Women who have a positive oncogenic HPV (16/18) test result with a reflex LBC report of invasive cancer (squamous, glandular or other) should be referred to a gynaecological oncologist or gynaecological cancer centre for urgent evaluation, ideally within 2 weeks.

Practice point

REC6.6: Referral of women with a positive HPV (16/18) test result and reflex LBC pHSIL/HSIL

Women with a positive oncogenic HPV (16/18) test result and reflex LBC prediction of pHSIL/HSIL should be referred for colposcopic assessment at the earliest opportunity, ideally within 8 weeks.

Practice point

REC6.7: Referral of women with a positive HPV (16/18) test result and unsatisfactory LBC

When HPV 16/18 is detected, colposcopic referral is required regardless of the LBC result and the screening episode should be classified as 'Higher risk for cervical cancer or precursors'. If reflex LBC is unsatisfactory or the screening sample has been self-collected a cervical sample, then LBC should be collected at the time of colposcopy.

Oncogenic HPV types not 16/18

Evidence-based recommendation	Grade
<p>REC6.8: Positive oncogenic HPV (not 16/18) test result at routine screening</p> <ul style="list-style-type: none"> Women with a positive oncogenic HPV (not 16/18) test result, with a LBC report of negative or prediction of pLSIL/LSIL, should have a repeat HPV test in 12 months. When the sample has been collected by a healthcare provider, then the laboratory will perform reflex LBC. When the sample was self-collected, the woman should be advised to return to her healthcare provider so that a cervical sample for LBC can be collected by the healthcare provider. <p><i>Note: It is expected that amendments to relevant Medicare Benefits Schedule items to support testing on a self-collected sample at the follow-up test for people whose initial screening test was done on a clinician-collected sample will be effective from 1 November 2022 pending any external impacts such as upcoming elections and caretaker period.</i></p>	C

Consensus-based recommendation*

REC6.9: Referral to gynaecological oncologist for LBC prediction of invasive disease
 Women who have a positive oncogenic HPV (not 16/18) test result with a LBC report of invasive cancer (squamous, glandular or other) should be referred to a gynaecological oncologist or gynaecological cancer centre for urgent evaluation, ideally within 2 weeks.

Practice point

REC6.10: Referral of women with a positive oncogenic HPV (not 16/18) test result and LBC prediction of pHSIL, HSIL or any glandular abnormality
 Women with a positive oncogenic HPV (not 16/18) test result, with a LBC prediction of pHSIL/HSIL or any glandular abnormality, should be referred for colposcopic assessment at the earliest opportunity, ideally within 8 weeks.

Evidence-based recommendation	Grade
<p>REC6.11: Management after follow-up HPV test at 12 months, following initial positive oncogenic HPV (not 16/18) screening test result</p> <p>At follow-up HPV testing 12 months after a detection of HPV (not 16/18) and LBC results of negative or pLSIL/LSIL:</p> <ul style="list-style-type: none"> if oncogenic HPV is not detected, the woman should be advised to return to routine 5-yearly screening. if HPV (16/18) is detected, then the woman should be referred for colposcopic assessment. If the follow-up sample was collected by a healthcare professional then the laboratory will undertake reflex LBC. If the follow-up sample was self-collected then a sample for LBC should be collected at the time of colposcopy 	C

Practice point

REC6.12: Management after follow-up HPV test at 12 months, following initial positive detection of HPV (not 16/18), for women who:

- were overdue for screening by at least 2 years at the time of their initial positive oncogenic HPV (not 16/18) test result

- identify as Aboriginal and/or Torres Strait Islander
- age 50 years or older.

If oncogenic HPV (any type) is detected at the follow-up HPV test, then the woman should be referred for colposcopic assessment.

If the follow-up sample was collected by a healthcare professional then the laboratory will undertake reflex LBC. If the follow-up sample was self-collected then a sample for LBC should be collected at the time of colposcopy.

Approval: 1-Feb-2021

Consensus-based recommendation

REC6.13: Management after follow-up HPV test at 12 months, following initial positive oncogenic HPV (not 16/18) screening test result: HPV (not 16/18) detected at 12 months

If HPV (not 16/18) is detected again, and the woman does not fall into any of the categories in REC6.12, then LBC should be performed. If the follow-up sample was collected by a healthcare professional then the laboratory will undertake reflex LBC. If the follow-up sample was self-collected then the woman should be advised to return to her healthcare professional so that a sample can be collected for LBC.

- If the LBC is reported as invasive cancer (squamous, glandular or other) the woman should be referred to a gynaecological oncologist or gynaecological cancer centre for urgent evaluation, ideally within 2 weeks.
- If the LBC is reported as pHSIL/HSIL or any glandular abnormality, she should be referred for colposcopic assessment at the earliest opportunity, ideally within 8 weeks

Management of those with HPV (not 16/18) detected at 12 months with negative/ pLSIL/ LSIL LBC is described in REC6.14

Approval: 1-Feb-2021 – 31-Jan-2026

Consensus-based recommendation

REC6.14: Management after follow-up HPV test at 12 months, following an initial positive oncogenic HPV (not 16/18) screening test result

At the follow-up HPV test **12 months** after detection of HPV (not 16/18) with LBC results of negative, pLSIL or LSIL if the woman has a HPV (not 16/18) test result, with an LBC report of negative or prediction of pLSIL/LSIL, and she does not fall into any of the categories in REC6.12, she should have a second follow-up HPV test in a further 12 months.

Approval: 1-Feb-2021

Note: It is expected that amendments to relevant Medicare Benefits Schedule items to support testing on a self-collected sample at the follow-up test for people whose initial screening test was done on a clinician-collected sample will be effective from 1 November 2022 pending any external impacts such as upcoming elections and caretaker period.

Consensus-based recommendation

REC6.15: Management after second follow-up HPV test, following initial detection of HPV (not 16/18) at the baseline screening test

At the second follow-up HPV test, **12 months** after a first follow-up HPV test with HPV (not 16/18) detected and LBC negative or pLSIL/LSIL:

- If HPV (any type) is detected, the woman should be referred for colposcopic assessment, . When the follow-up sample has been collected by a healthcare provider, then the laboratory will perform reflex LBC. When the follow-up sample was self-collected, then a sample should be collected for LBC at the time of colposcopy.
- if HPV is not detected, the woman should be advised to return to routine 5-yearly screening.

Approval: 1-Feb-2021

Self-collected vaginal samples

Practice point

REC6.16: Informed choice for patients about self-collection

When deciding whether to choose self-collection or clinician collection, people must be given clear information by the supervising healthcare professional about the likelihood that HPV may be detected and, if so, what follow-up will be required. If a person chooses self-collection then the healthcare professional should provide information about how to collect the sample and how they will receive the test results.

Among those attending for a routine screening test, approximately 2% have HPV16/18 detected and approximately 6% have HPV (not 16/18) detected, although the latter varies by age.

Practice point

REC6.17: Settings where self-collection can be performed Effective from 1 July 2022

Cervical screening on a self-collected vaginal sample needs to be ordered and overseen by a healthcare professional, but collection of the sample can occur in any setting that the healthcare professional* ordering the test believes is appropriate, including in the context of a telehealth consultation. The healthcare professional is not required to observe the patient collecting their sample unless this is the patient's preference. Patients attending an in-person consultation should be encouraged to collect a sample while they are still at the clinic, as sample collection is considered more likely in this context. The healthcare professional should facilitate access to screening, and the pathology laboratory should deliver the results to the requesting healthcare professional who will be responsible for informing patients of their results and any required follow-up. Within these constraints, healthcare professionals and laboratories have flexibility to develop models of screening that best meet the needs of their communities.

* Only doctors and nurses practitioners can sign the pathology request for tests under current MBS rules.

Practice point

REC6.18 Assistance with sample self-collection

Women who have difficulty collecting a lower vaginal sample by themselves could be assisted to do so by the provider. Alternatively the provider could collect the sample using a self-

collection swab without using a speculum. A sample collected in this way is still classified as self-collection on the pathology request form.

Practice point

REC6.19 Support for underscreened women

Women in whom HPV (any type) is detected in a self-collected sample and who were overdue for screening may require additional and individualised support to progress along the clinical pathway, and access to follow-up services where they will receive sensitive treatment. This additional support may involve, for example, reassurance and explanation of the screening pathway and follow-up procedures, longer appointments, or additional follow-up contact.

Practice point

REC6.20 Indication for genital inspection

Routine genital inspection is not indicated in all people attending for cervical screening, but could still be offered to people who undergo screening on a self-collected sample with any clinical indication that genital inspection is appropriate or who are from populations who are at high risk for vulvar disease

Practice point

REC6.21 Follow-up HPV test after initial self-collected screening sample

When follow-up HPV testing is required after an initial positive oncogenic HPV test result, the sample may be self-collected or collected by a clinician.

The woman's healthcare professional should advise the woman of the follow-up that will be recommended if HPV is detected, and explain that a clinician-collected sample allows for reflex LBC to be performed on the same sample, potentially avoiding the need for an additional visit to collect a cervical sample for LBC. HPV testing is not repeated on the clinician-collected sample in this circumstance.

Approval: 1-Feb-2021

Note: recommendation numbering changed Feb 2021, this was previously 6.14

Women undergoing exit testing

MSAC evidence-based recommendation

REC6:22 Women aged 70–74 years in whom oncogenic HPV is not detected (exit testing)

Women can be discharged from the NCSP if they are aged 70–74 years and have a screening test at which oncogenic HPV is not detected.

Note: recommendation numbering changed Feb 2021, this was previously REC 6.16

Consensus-based recommendation

REC6.23: Referral of women aged 70–74 years with a positive oncogenic HPV test result (exit testing)

Women aged 70–74 who have a positive oncogenic HPV (any type) test result should be referred directly for colposcopic assessment, which should be informed by the result LBC, whether reflex LBC (if the exit test was collection by a healthcare professional or taken at the time of colposcopy if the exit test was self-collected).

Note: recommendation numbering changed Feb 2021, this was previously REC 6.17

Screening in women older than 75

NCSP recommendation

REC6.24 Women aged 75 years or older who request screening

Women who are 75 years or older who have never had a cervical screening test, or have not had one in the previous five years, may request a test and can be screened.

Note: recommendation numbering changed Feb 2021, this was previously REC 6.18

7. Colposcopy

Colposcopy terminology

Practice point

REC7.1: New colposcopy terminology

The new terminology adopted by the IFCPC in 2011 should be incorporated into Australian practice.

History, examination and investigation

Practice point

REC7.2 Preparation for colposcopy: post menopausal women, people experiencing vaginal dryness, or trans men

A short course of topical oestrogen therapy could be considered in post-menopausal women, people experiencing vaginal dryness, or trans men, for example daily for a period of at least 2 weeks, ceasing 1-2 days prior to the appointed reason for this should be explained (to reduce discomfort from the speculum and to improve the diagnostic accuracy of colposcopy and any associated LBC and/or biopsy).

Practice point

REC7.3: Colposcopy and acetic acid

Acetic acid should be applied for 2 minutes to allow sufficient time for aceto-white changes to become apparent. This is especially important when the lesion is low grade as it may take more time to become visible.

Practice point

REC7.4: Colposcopy and VAIN

When the LBC report predicts a squamous abnormality and there is no colposcopically visible cervical lesion, careful colposcopic examination of the vagina should be performed to exclude VAIN, using acetic acid and Lugol's Iodine.

Practice point

REC7.5: Repeat LBC usually not necessary at time of colposcopy

It is not necessary to take a cervical sample for LBC at the time of colposcopy except in the following circumstances:

- delay in attending for colposcopy > 3 months after referral LBC
- referral LBC is unsatisfactory
- referral LBC is negative but lacks an endocervical component
- prior LBC is not available because the HPV test was performed on a self-collected sample
- the woman has developed symptoms suggestive of cervical cancer since undergoing her screening test.

Consensus-based recommendation***REC7.6: Biopsy of high grade lesions**

The cervix should be biopsied when the LBC prediction is pHSIL or HSIL and the colposcopic appearance shows major change (see IFCPC definition above) and the abnormal TZ is visible (Type 1 or Type 2 TZ).

Practice point**REC7.7: Biopsy visible lesion if suspicious for invasion when T3 TZ colposcopy**

In some situations, when there is a visible high-grade lesion on the ectocervix but there is a T3 TZ (lesion extends into canal out of visual range), it may be reasonable to take a cervical biopsy of the visible lesion if there is any suspicion of superficially invasive or invasive carcinoma.

Practice point**REC7.8: Biopsy of low-grade lesions is encouraged but not always necessary**

Women with a LBC prediction of pLSIL or LSIL and a colposcopic impression of low-grade disease or less may not always require a biopsy. However, biopsy is accepted practice for confirmation of the colposcopic impression and exclusion of high-grade disease, and should be encouraged, especially for less experienced colposcopists.

Practice point**REC7.9: Upper genital tract imaging**

Upper genital tract imaging should be considered in cases where no lower genital tract abnormality is detected at colposcopy after referral with abnormal glandular cytology (including atypical glandular cells or endocervical cells of undetermined significance). In some women, further investigation, such as endometrial sampling to exclude an endometrial origin for atypical glandular cells, may be required.

Treatment**Consensus-based recommendation*****REC7.10: Colposcopy prior to treatment**

All women should have an adequate[†] colposcopic assessment prior to treatment.

[†]adequate: the cervix is clearly seen ([IFCPC 2011 terminology](#))

Consensus-based recommendation*

REC7.11: Histopathological confirmation prior to treatment

Treatment should be reserved for women with histologically confirmed HSIL (CIN2/3) or AIS, except for women requiring diagnostic excisional biopsy.

Consensus-based recommendation***REC7.12: Biopsy prior to ablative treatment**

Women should have a cervical biopsy prior to any ablative treatment.

Consensus-based recommendation**REC7.13: Pathology review of discordant test results**

For women who have had a colposcopy with significant discordance between the histopathology and the referral cytology, both specimens should be reviewed by a pathologist from at least one of the reporting laboratories who should then convey the results of the review to the colposcopist in order to inform the management plan.

Practice point**REC7.14: Tertiary referral may be necessary**

In some clinical situations, the woman should be referred to a more experienced colposcopist, a gynaecological oncologist, tertiary colposcopy clinic or gynaecological cancer centre:

- adenocarcinoma in situ
- abnormalities in pregnancy
- immune-deficient women
- women with multifocal lower genital tract disease.

Practice point**REC7.15: Second opinion**

When there is any concern about diagnosis or patient management, a second opinion should be sought and documented.

Practice point**REC7.16: The role of multidisciplinary team review**

It is not always practical for a colposcopist to access a multidisciplinary team review which is usually conducted in a tertiary referral centre. However, a multidisciplinary team review is particularly helpful when:

- dealing with complex cases where there is discordance between histopathology and referral cytology (e.g. LBC prediction of HSIL, with negative or LSIL histology).
- implementation of treatment is not urgent and therefore it is possible to take the required time to review the findings and optimise the management plan.

Practice point**REC7.17: Colposcopy at time of treatment**

All treatments should be performed under colposcopic vision, with the exception of cold-knife cone biopsy.

Consensus-based recommendation*

REC7.18: Criteria for ablative treatment

Ablative therapy should be reserved for women intending to have children, and when the following conditions have all been met:

- TZ is completely visible (Type 1 or Type 2).
- There is no evidence of invasive or glandular disease.
- A biopsy has been performed prior to treatment.
- HSIL (CIN2/3) has been histologically confirmed.
- There is no significant discordance between the histopathology and referral cytology results.

Practice point**REC7.19: Depth of ablation**

A Type 1 TZ with a HSIL (CIN2/3) lesion requires 6–8 mm (and not more than 10 mm) of cervical ablation to be adequately treated.

Consensus-based recommendation***REC7.20: Excision specimen quality and pathology**

Excisional therapy should aim to remove the entire TZ with a pre-determined length of cervical tissue, ideally in one piece, with minimal distortion or artefact to the final histological specimen.[†]

[†]This is critical for management of suspected or histologically confirmed AIS.

Practice point**REC7.21: Excision specimen quality, pathology and very large ectocervical lesion**

A very large ectocervical lesion may require removal in two pieces in order to remove the entire lesion. It is still important that the endocervical and stromal margins are suitable for pathological interpretation and that the specimens are accurately oriented and labelled.

Practice point**REC7.22: Excisional techniques and surgical competency**

Therapeutic colposcopists should use the excisional techniques with which they are comfortable and competent and that produce the best histological specimen.

Practice point**REC7.23: Cold-knife cone biopsy: setting**

Cold-knife cone biopsy should be performed in an operating theatre, under general anaesthesia, by a gynaecological oncologist or gynaecologist competent in the technique.

Practice point**REC7.24: Loop excisional biopsy technique (LEEP/LLETZ)**

A single pass of the loop (side to side or posterior to anterior) to produce a specimen in one piece is optimal.

Practice point**REC7.25: Loop 'top-hat' excisions should be avoided (LEEP/LLETZ)**

The 'top-hat' excision techniques using a wire loop, in which a second piece of endocervical

tissue is removed after the first excision, is not an alternative to a properly performed single-piece Type 3 excision, and should be avoided.

Practice point

REC7.26: Cold-knife cone biopsy and AIS

Predicted or histologically confirmed AIS should be treated by a Type 3 excision (usually a cold-knife cone biopsy) performed in an operating theatre, under general anaesthesia, by a gynaecological oncologist or gynaecologist competent in the technique.

Practice point

REC7.27: Role of repeat excision in management of SISCCA

In the presence of a superficially invasive squamous carcinoma, if HSIL (CIN2/3) extends to any excision margin, a repeat excision (usually by cold-knife cone biopsy) is recommended.

Practice point

REC7.28: Do not treat at first visit with a LBC report of a low-grade lesion

Women who have a LBC prediction of pLSIL/LSIL should **not** be treated at the first visit.

Practice point

REC7.29: Excision required for recurrent disease after ablation

If there is recurrence of high-grade disease after previous ablation, treatment should be by excision.

Practice point

REC7.30: Repeat excision not necessarily required for incomplete excision of high-grade lesions

Women who have incomplete excision of HSIL (CIN2/3) with positive endocervical or stromal margins do not necessarily require immediate repeat excision and could be offered test of cure (HPV and LBC) surveillance, with the exception of:

- women aged 50 years or over
- women who may not be compliant with recommended follow-up
- women in whom subsequent adequate colposcopy and follow-up cytology cannot be guaranteed.

8. Management of discordant colposcopic impression, histopathology and referral LBC prediction

Normal colposcopic findings following LBC prediction of LSIL or HSIL

Consensus-based recommendation

REC8.1: Normal colposcopy following LBC prediction of negative or pLSIL/LSIL

For women with a positive oncogenic HPV (any type) test result, a LBC report of negative or pLSIL/LSIL, and normal colposcopy, the HPV test should be repeated in 12 months:

- If HPV is not detected at 12 months, the woman should return to routine 5-yearly HPV screening.

- If the woman has a positive oncogenic HPV (not 16/18) test result at 12 months and a LBC report of negative or pLSIL/LSIL, the HPV test should be repeated in another 12 months.
- If the woman has a positive oncogenic HPV (any type) test at the 24 month HPV test, she should be referred directly for colposcopic assessment, which will be informed by the result of the reflex LBC.
- If the woman has a positive oncogenic HPV (not 16/18) test result at 12 months and a LBC prediction of pHSIL/HSIL or any glandular abnormality, she should be referred for colposcopic assessment at the earliest opportunity, ideally within 8 weeks.
- If the woman has a positive oncogenic HPV (16/18) test result at 12 months, she should be referred directly for colposcopic assessment at the earliest opportunity, ideally within 8 weeks, and the reflex LBC result will inform the colposcopy.

Practice point

REC8.2: Normal colposcopy following LBC prediction of HSIL: cytopathology review

Cytopathology review is recommended to confirm HSIL before proceeding to excisional treatment for women with a normal colposcopy after a positive oncogenic HPV (any type) test result and an initial LBC prediction of pHSIL/HSIL.

Practice point

REC8.3: Normal colposcopy following LBC prediction of HSIL: exclude VAIN

When colposcopic impression is discordant with a referral LBC prediction of HSIL, colposcopic examination of the vagina is indicated to exclude a vaginal intraepithelial neoplasia **before** diagnostic excisional treatment.

Consensus-based recommendation

REC8.4: Normal colposcopy following LBC prediction of HSIL: diagnostic excision of TZ

For women who have a positive oncogenic HPV (any type) test result, normal colposcopy, and a LBC prediction of HSIL on cytopathology review, diagnostic excision of the TZ should be performed.

Consensus-based recommendation

REC8.5: Normal colposcopy following LBC prediction of pHSIL: consider diagnostic excision of TZ

For women who have a positive oncogenic HPV (any type) test result, normal colposcopy, and a LBC prediction of pHSIL on cytopathology review, diagnostic excision of the TZ should be considered, though observation is an option.

Practice point

REC8.6: Normal colposcopy following LBC prediction of pHSIL: diagnostic excision or observation

Some women with a positive oncogenic HPV test result for whom diagnostic excision of the TZ is recommended due to a confirmed LBC prediction of pHSIL on cytopathology review, despite

normal colposcopic findings, may be concerned about the possibility of having unnecessary treatment. The colposcopist may have similar concerns.

Women who opt to defer treatment, particularly younger women with concerns about fertility, can be offered observation:

- A HPV test and colposcopy should be repeated at 6 months, and a diagnostic excisional procedure should be reconsidered based on the test results (HPV and reflex LBC, if performed) obtained at that time.
- If oncogenic HPV is not detected, and the colposcopic impression is unchanged, the HPV test should be repeated in 12 months and if oncogenic HPV is not detected, the woman can return to routine 5-yearly screening.

Consensus-based recommendation

REC8.7: Downgrading of discordant results

For women who have a positive oncogenic HPV (any type) test result, normal colposcopy, and a subsequent LBC report of pLSIL/LSIL or less on cytopathology review, management should be according to the reviewed cytological report (i.e. repeat HPV test in 12 months).

Practice point

REC8.8: Colposcopist should manage discordant results

Women with discordant colposcopy and LBC results should have their management supervised by the colposcopist until both the colposcopist and the woman are satisfied with the proposed management plan.

Type 3 TZ (previously termed 'unsatisfactory') colposcopy following LBC prediction of LSIL or HSIL

Consensus-based recommendation

REC8.9: Repeat HPV test after Type 3 TZ colposcopy and referral LBC negative or pLSIL/LSIL

For women who have a positive oncogenic HPV (any type) test result with a LBC report of negative or pLSIL/LSIL, and colposcopy is reported as Type 3 TZ,[†] the HPV test should be repeated in 12 months:

- If oncogenic HPV is not detected at 12 months, the HPV test should be repeated 12 months later.
- If oncogenic HPV is not detected again at the second repeat HPV test, the woman should be advised to return to routine 5-yearly screening.
- If the woman has a positive oncogenic HPV (any type) test result at 12 months, she should be referred directly for colposcopic assessment, with the LBC report available to inform the assessment.

[†]Type 3 TZ indicates failure to visualise the upper limit of the TZ, or the entire TZ is within the endocervical canal. It corresponds to 'unsatisfactory' in previous terminology.

Practice point

REC8.10: Cytopathology review prior to observation for pLSIL/LSIL and Type 3 TZ at colposcopy

When observation is advised, cytopathology review is recommended to confirm the low-grade cytological abnormality.

- If pLSIL/LSIL is confirmed, observation is appropriate.
- If pHSIL/HSIL is indicated, then diagnostic excision of the TZ should be considered.

Practice point

REC8.11: Role of ECC in Type 3 TZ colposcopy following LBC prediction of pLSIL/LSIL

Despite a lack of evidence, endocervical curettage can be considered for women who have a positive oncogenic HPV test result (any type) with a LBC report of persistent pLSIL/LSIL and colposcopy reported as Type 3 TZ.[†] A negative ECC may provide additional reassurance for a conservative (observational) approach.

[†]Type 3 TZ indicates failure to visualise the upper limit of the TZ, or the entire TZ is within the endocervical canal. It corresponds to 'unsatisfactory' in previous terminology.

Consensus-based recommendation

REC8.12: Diagnostic excision of the TZ should not be performed if there is no cytological or histological evidence of a high-grade lesion after Type 3 TZ colposcopy

For asymptomatic women who have a positive oncogenic HPV (any type) test result, Type 3 TZ[†] colposcopy, and no cytological, colposcopic or histological evidence of a **high-grade lesion**, further diagnostic procedures (such as diagnostic excision of the transformation zone) should **not** routinely be performed.

[†]Type 3 TZ indicates failure to visualise the upper limit of the TZ, or the entire TZ is within the endocervical canal. It corresponds to 'unsatisfactory' in previous terminology.

Practice point

REC8.13: Role of diagnostic excision: exceptions to recommendation against diagnostic excision of TZ in the absence of high-grade cytology or histology

Diagnostic excision of the TZ can be offered to certain groups of women who have a positive oncogenic HPV test result, a LBC report of negative or pLSIL/LSIL, and colposcopy reported as Type 3 TZ:[†]

- women who have completed childbearing
- women who are anxious about cancer risk
- women aged over 50 years
- women who may not be compliant with recommended surveillance.

[†]Type 3 TZ indicates failure to visualise the upper limit of the TZ, or the entire TZ is within the endocervical canal. It corresponds to 'unsatisfactory' in previous terminology.

Consensus-based recommendation

REC8.14: Diagnostic excision: Type 3 TZ colposcopy after LBC prediction of pHSIL/HSIL

For women who have a positive oncogenic HPV (any type) test result, a LBC prediction of pHSIL/HSIL after cytopathology review, and Type 3 TZ[†] colposcopy, diagnostic excision of the TZ should be performed.

Type 3 TZ indicates failure to visualise the upper limit of the TZ, or the entire TZ is within the endocervical canal. It corresponds to 'unsatisfactory' in previous terminology.

Practice point

REC8.15: Cytopathology review: Type 3 TZ colposcopy following LBC prediction of pHSIL/HSIL

Cytopathology review should be considered to confirm a high-grade cytological abnormality before excision, after a positive oncogenic HPV (any type) test result and an initial LBC prediction of pHSIL/HSIL, when there is a Type 3 TZ colposcopy.

This is particularly important when the LBC prediction is pHSIL because pHSIL has a lower PPV for high-grade disease and the subsequent excision specimens show no evidence of cervical pathology in 45–55% of cases.

Practice point

REC8.16: Deferral of treatment following cytopathology review: Repeat HPV test and colposcopy in 6 months

Following cytopathology review, rarely the woman or the clinician wish to defer treatment. In this situation the woman should have a repeat HPV test and colposcopy in 6 months.

- If HPV detected (any type) and LBC pLSIL/LSIL, repeat HPV test in 12 months.
- If HPV detected (any type) and LBC pHSIL/HSIL, the woman should have diagnostic Type 3 excision of the TZ.

9. Management of histologically confirmed low-grade squamous abnormalities

Consensus-based recommendation

REC9.1: HPV test 12 months after histologically confirmed LSIL (\leq CIN1)

Women who have a positive oncogenic HPV (any type) test result with a LBC report of either negative or pLSIL/LSIL, and histologically confirmed \leq CIN1 on biopsy, should have a repeat HPV test 12 months later:

- If oncogenic HPV is not detected at the repeat HPV test, the woman should return to routine 5 yearly screening.
- If the repeat test is positive for oncogenic HPV (not 16/18) and the LBC report is negative or pLSIL/LSIL, the woman should have a further repeat HPV test in 12 months.
- If the second follow-up HPV test is negative the woman should return to routine 5-yearly screening.
- If the second follow-up test is HPV positive, the woman should be referred for colposcopic assessment informed by reflex LBC.
- If the repeat test is positive for oncogenic HPV (not 16/18) and the LBC report is pHSIL/HSIL, the woman should be referred for colposcopic assessment.
- If the repeat test is positive for oncogenic HPV (16/18), the woman should be referred for colposcopic assessment informed by the reflex LBC.

Consensus-based recommendation

REC9.2: LSIL (\leq CIN1) should not be treated

Women who have a positive oncogenic HPV (any type) test result with a LBC report of negative

or pLSIL/LSIL, who have undergone colposcopy and have a histologically confirmed LSIL (\leq CIN1), should **not** be treated, because these lesions are considered to be an expression of a productive HPV infection.

Consensus-based recommendation

REC9.3: Diagnostic excision when HSIL confirmed on cytopathology review

Women who have a positive oncogenic HPV test result (any type) with a LBC report of HSIL (confirmed after cytopathology review), and who have undergone colposcopy and have a histologically confirmed LSIL (\leq CIN1), should be offered diagnostic excision of the TZ.

Consensus-based recommendation

REC9.4: Option for observation following cytological prediction of pHSIL

Women who have a positive oncogenic HPV (any type) test result with a LBC prediction of pHSIL (confirmed after cytopathology review), and who have undergone colposcopy and have a histologically confirmed LSIL (\leq CIN1), could be offered diagnostic excision of the TZ.

If the colposcopist considers a period of observation is preferable to treatment, or the woman with these findings wishes to defer diagnostic excision, she can be offered observation with a HPV test and colposcopy at 6–12 months:

- If oncogenic HPV is not detected at the repeat test, the HPV test should be repeated again in 12 months.
- If the second follow-up test is negative, the woman should return to routine 5-yearly screening.
- If the woman has a positive oncogenic HPV (any type) test result at the repeat test, her reflex LBC report is negative or pLSIL/LSIL, and her colposcopic impression is normal or LSIL, the HPV test should be repeated annually.
- When oncogenic HPV is not detected at two consecutive annual tests, the woman can return to 5-yearly screening.
- If the woman has a positive oncogenic HPV (any type) test result at the repeat test, and her LBC prediction is pHSIL/HSIL or any glandular abnormality, she should have a diagnostic excision of the TZ.

Practice point

REC9.5: Criteria for observation following cytological prediction of pHSIL

Women should not be offered observation unless the colposcopic assessment meets all the following conditions:

- Colposcopy is adequate.
- TZ is completely visualised (Type 1 or 2 TZ[^]).
- LSIL (\leq CIN1) has been confirmed on histopathological review.

[^]IFCPC: International Federation of Cervical Pathology and Colposcopy 2011

Practice point

REC9.6: Cytology review essential when test results are discordant

For women who have a positive oncogenic HPV (any type) test result with a histologically confirmed LSIL (\leq CIN1) after LBC prediction of pHSIL/HSIL, both the cytology and the histopathology should be reviewed by a pathologist from at least one of the reporting

laboratories, who should then convey the results of the review to the colposcopist in order to inform the management plan.

10. Management of histologically confirmed high-grade squamous abnormalities

Diagnosis of HSIL

Consensus-based recommendation*

REC10.1: Histological diagnosis prior to treatment

For women who have a visible lesion at colposcopy, histological confirmation of HSIL is recommended before undertaking definitive treatment.

Treatment of HSIL

Consensus-based recommendation*

REC10.2: Treatment for HSIL (CIN2)

Women with a histological diagnosis of HSIL (CIN2) should be treated in order to reduce the risk of developing invasive cervical carcinoma.

Practice point

REC10.3: p16 should be used to clarify diagnosis of HSIL (CIN2)

The use of p16 immunohistochemistry is recommended to stratify the management of HSIL (CIN2) into immediate treatment or a period of observation.

Practice point

REC10.4: HSIL (CIN2) and observation

In some circumstances, it may be acceptable to offer a period of observation (generally 6–12 months) to women who have a histological diagnosis of HSIL (CIN2), and this would usually be supervised by an experienced colposcopist or at a tertiary centre. Observation may be considered for:

- women who have not completed childbearing
- women with discordant histology and LBC prediction of pLSIL/LSIL
- women with focal minor changes on colposcopy and HSIL (CIN2) on histology
- women recently treated for HSIL (CIN2).

Consensus-based recommendation*

REC10.5: Treatment of HSIL (CIN3)

Women with a histological diagnosis of HSIL (CIN3) should be treated in order to reduce the risk of developing invasive cervical carcinoma.

Consensus-based recommendation*

REC10.6: Referral of women with invasive disease

A woman with a histologically confirmed diagnosis of invasive or superficially invasive (squamous cell carcinoma) should be referred to a gynaecological oncologist or a gynaecological cancer centre for multidisciplinary team review.

Test of Cure after treatment for HSIL (CIN2/3)

Consensus-based recommendation

REC10.7: Test of Cure after treatment for HSIL (CIN2/3)

A woman who has been treated for HSIL (CIN2/3) should have a co-test[†] performed at 12 months after treatment, and annually thereafter, until she receives a negative co-test on two consecutive occasions, when she can return to routine 5 yearly screening.

[†]Co-testing can be performed by the woman's usual healthcare professional.

Consensus-based recommendation**REC10.8: Abnormal Test of Cure results: positive oncogenic HPV (16/18) test result**

If, at any time post treatment, the woman has a positive oncogenic HPV (16/18) test result, she should be referred for colposcopic assessment (regardless of the reflex LBC result).

Consensus-based recommendation***REC10.9: Abnormal Test of Cure results: LBC pHSIL/HSIL or glandular abnormality**

If, at any time during Test of Cure, the woman has a LBC prediction of pHSIL/HSIL or any glandular abnormality, irrespective of HPV status, she should be referred for colposcopic assessment.

Consensus-based recommendation**REC10.10: Abnormal Test of Cure results: positive oncogenic HPV (not 16/18) test result**

If, at any time post-treatment, the woman has a positive oncogenic HPV (not 16/18) test result and a LBC report of negative or prediction of pLSIL/LSIL, she should continue to have annual co-testing until she has a negative co-test on two consecutive occasions, when she can return to routine 5-yearly screening.

Practice point**REC10.11: Fluctuating Test of Cure results: positive oncogenic HPV (not 16/18) test result and/or pLSIL/LSIL**

Some women may experience fluctuating results with a positive oncogenic HPV (not 16/18) test result and/or LBC prediction of pLSIL/LSIL. These women do not need colposcopic review but, if the woman is anxious, a colposcopic assessment may be appropriate to provide reassurance.

Practice point**REC10.12: Colposcopy is not necessary at the initial post-treatment visit**

A post-treatment colposcopic assessment at 4–6 months has been the usual practice under pre-renewal NCSP guidelines. This practice is not evidence-based, but may provide reassurance to both the patient and clinician regarding the visual appearance of the cervix and allows for the discussion of any other relevant issues (bleeding, fertility, related symptoms etc.) following treatment.

The post-treatment review should:

- include speculum examination of the vagina and cervix (but colposcopy is not considered necessary)
- not involve HPV testing or LBC.

Subsequent post-treatment Test of Cure surveillance should be performed by the woman's GP or health professional, who should follow the recommendations for the management of any abnormal test results.

11. Management of glandular abnormalities

Investigation of cytological glandular abnormalities

Consensus-based recommendation*

REC11.1: Colposcopy referral for atypical glandular/endocervical cells

Women who have a positive oncogenic HPV (any type) test result with a LBC report of atypical glandular/endocervical cells of undetermined significance should be referred to a gynaecologist with expertise in the colposcopic evaluation of suspected malignancies or a gynaecological oncologist.

Consensus-based recommendation*

REC11.2: Follow-up after normal colposcopy and LBC prediction of atypical glandular/endocervical cells

Women who have a positive oncogenic HPV test result (any type) with a LBC prediction of atypical glandular/endocervical cells of undetermined significance and normal colposcopy can be offered repeat co-testing (HPV and LBC) at 6–12 months:

- If the follow-up co-test is negative, co-testing should be repeated annually until the woman has two consecutive negative co-tests, after which she can return to 5-yearly screening.
- If there is either a positive oncogenic HPV (any type) test result or an abnormal LBC (any report other than negative), the woman should be referred for colposcopic assessment, and diagnostic excision of the TZ should be considered.

Practice point

REC11.3: Exclusion of upper genital tract disease before diagnostic excision

For women who have a positive oncogenic HPV test result (any type) and who have atypical glandular/endocervical cells of undetermined significance on cytology, investigation of the upper genital tract (endometrium, fallopian tube or ovary) using endometrial sampling and/or pelvic ultrasound should be considered, before diagnostic excision of the TZ is performed or the woman is advised to return for colposcopy and further tests in 6–12 months, in these groups of women:

- women aged over 45 years
- women aged over 35 years with a BMI greater than 30
- women diagnosed with polycystic ovarian syndrome
- women with abnormal vaginal bleeding.

Practice point

REC11.4: Role of immediate diagnostic excision of TZ versus observation

Immediate diagnostic excision of the TZ can be considered for women with atypical glandular/endocervical cells of undetermined significance if they prefer not to take a conservative observational approach. This might apply to:

- women aged over 45 years
- women who have completed childbearing
- women who are particularly anxious about their cancer risk.

Consensus-based recommendation

REC11.5: Colposcopy for possible high-grade glandular lesions

Women who have a positive oncogenic HPV (any type) test result with a LBC prediction of

possible high-grade glandular lesion should be referred to a gynaecologist with expertise in the colposcopic evaluation of suspected malignancies or a gynaecological oncologist. Diagnostic excision of the endocervical TZ should be performed in most cases.

Practice point

REC11.6: Women who decline treatment for possible high-grade glandular lesions

Women with a LBC prediction of possible high-grade glandular lesion who decline the recommended excision should be offered surveillance with co-testing (HPV and LBC) and colposcopy in 6 months.

- If in 6 months the woman has a positive result, she should be encouraged to have a diagnostic excision of the TZ.
- It is important that the woman understands the potential risk of underlying disease (21.5% risk of AIS and 5.5% risk of invasive cancer).

Consensus-based recommendation*

REC11.7: Colposcopy referral for AIS

Women with a LBC prediction of AIS should be referred to a gynaecologist with expertise in the colposcopic evaluation of suspected malignancies or to a gynaecological oncologist. Diagnostic excision of the endocervical TZ should be performed.

Consensus-based recommendation*

REC11.8: Referral to gynaecological oncologist for LBC prediction of invasive disease

Women who have a positive oncogenic HPV (any type) test result with a LBC prediction of invasive adenocarcinoma should be referred to a gynaecological oncologist or a gynaecological oncology centre for urgent evaluation, ideally within 2 weeks.

Consensus-based recommendation*

REC11.9: Specimen for histological assessment of glandular abnormalities

When diagnostic excision of the TZ is performed in the investigation of glandular abnormalities, the method chosen should ensure that a single, intact specimen with interpretable margins is obtained for histological assessment.

Practice point

REC11.10: Cold-knife cone biopsy is the 'gold standard' for glandular abnormalities

Cold-knife cone biopsy should be considered the 'gold standard' for the diagnostic assessment of glandular lesions. However, a diathermy excisional procedure may be appropriate in some circumstances and could provide an appropriate surgical specimen when performed by a gynaecologist with appropriate training, experience and expertise.

Practice point

REC11.11: Size of cone biopsy

The depth and extent of the cone biopsy should be tailored to the woman's age and fertility requirements. A Type 3 Excision of the TZ is usually required.

Practice point

REC11.12: Cone biopsy excision margins and multifocal AIS

Multifocal disease has been reported in 13–17% of cases of AIS, though the majority of lesions are unifocal. If the margin is close but apparently excised (less than 5 mm), close surveillance by Test of Cure, as recommended in these guidelines, is considered appropriate. In this situation further excision is not considered necessary.

Follow-up after excisional treatment for AIS

Consensus-based recommendation*

REC11.13: Follow-up of completely excised AIS

Women with histologically confirmed AIS who have undergone complete excision with clear margins should have annual co-testing indefinitely.[†]

If any abnormal result is obtained on follow-up co-testing, the woman should be referred for colposcopic assessment.

[†]Until sufficient data become available to support cessation of testing.

Consensus-based recommendation*

REC11.14: Repeat excision for incompletely excised AIS

If AIS is incompletely excised (positive endocervical margin and/or deep stromal margin, not ectocervical margin) or if the margins cannot be assessed, further excision to obtain clear margins should be performed.

Consensus-based recommendation

REC11.15: Role of hysterectomy in AIS

In women who have been treated for AIS by excision, with clear margins, there is no evidence to support completion hysterectomy. In this situation, hysterectomy is not recommended.

12. Screening in Aboriginal and Torres Strait Islander women

Consensus-based recommendation

REC12.1: Cervical Screening for Aboriginal and Torres Strait Islander women

Aboriginal and Torres Strait Islander women should be invited and encouraged to participate in the NCSP and have a 5-yearly HPV test, as recommended for all Australian women.

Practice point

REC12.2: Invitations to screen for Aboriginal and Torres Strait Islander women

Specific efforts should be made to maximise delivery of invitations to Aboriginal and Torres Strait Islander women.

Practice point

REC12.3: Cervical screening services for Aboriginal and Torres Strait Islander women

Specific efforts should be made to provide screening, diagnostic and treatment services that are accessible and culturally appropriate to Aboriginal and Torres Strait Islander women.

Practice point

REC12.4: Eligibility for screening on self-collected sample: Aboriginal and Torres Strait Islander people

All eligible people, including Aboriginal and Torres Strait Islander people, should be offered the choice of HPV testing on a self-collected vaginal sample or on a clinician-collected sample.

Practice point**REC12.5: Data collection and recording Aboriginal and Torres Strait Islander status**

Healthcare professionals should ask all women whether they identify as Aboriginal or Torres Strait Islander, and a woman's Aboriginal and Torres Strait Islander status should be recorded on the pathology request form in accordance with the ABS classification and standards.

13. Screening after total hysterectomy**Consensus-based recommendation*****REC13.1: Total hysterectomy for benign disease**

Women with a normal cervical screening history, who have undergone hysterectomy for benign disease (e.g. menorrhagia, uterine fibroids or utero-vaginal prolapse), and have no cervical pathology at the time of hysterectomy, do not require further screening or follow up.

Consensus-based recommendation***REC13.2: Total hysterectomy after completed Test of Cure**

Women who have had a total hysterectomy with no evidence of cervical pathology, have previously been successfully treated for histologically confirmed HSIL and have completed Test of Cure, do not require further follow-up. These women should be considered as having the same risk for vaginal neoplasia as the general population who have never had histologically confirmed HSIL and have a total hysterectomy.

If unexpected LSIL or HSIL is identified in the cervix at the time of hysterectomy, then these women require follow-up with an annual co-test on a specimen from the vaginal vault until they have a negative co-test on two consecutive occasions.

Consensus-based recommendation**REC13.3: Total hysterectomy after adenocarcinoma in situ (AIS)**

Women who have had a total hysterectomy, have been treated for AIS, and are under surveillance, should have a co-test on a specimen from the vaginal vault at 12 months and annually thereafter, indefinitely.[†]

Women who have a total hysterectomy, as completion therapy or following incomplete excision of AIS at cold-knife cone biopsy or diathermy excision, should have a co-test on a specimen from the vaginal vault at 12 months and annually thereafter, indefinitely.

[†] Until sufficient data become available to support cessation of testing

Consensus-based recommendation***REC13.4: Total hysterectomy for treatment of high-grade CIN in the presence of benign gynaecological disease**

Women who have had a total hysterectomy as definitive treatment for histologically confirmed HSIL in the presence of benign gynaecological disease, irrespective of cervical margins, should have a co-test on a specimen from the vaginal vault at 12 months after treatment and annually thereafter until the woman has tested negative by both tests on two consecutive occasions.

After two annual consecutive negative co-tests, the woman can be advised that no further testing is required.

Consensus-based recommendation*

REC13.5: Total hysterectomy after histologically confirmed HSIL without Test of Cure

Women who have been treated for histologically confirmed HSIL, are under surveillance or have returned to routine screening without Test of Cure, and have had a total hysterectomy with no evidence of cervical pathology, should have a co-test on a specimen from the vaginal vault at 12 months and annually until the woman has tested negative on two consecutive occasions.

After two annual consecutive negative co-tests, the woman can be advised that no further testing is required.

Consensus-based recommendation***REC13.6: Total hysterectomy and no screening history**

Women who have had a total hysterectomy with no evidence of cervical pathology, and whose cervical screening history is not available, should have a HPV test on a specimen from the vaginal vault at 12 months and annually thereafter until they have a negative HPV test on two consecutive occasions.

After two annual consecutive negative HPV tests, women can be advised that no further testing is required.

Note: It is expected that amendments to relevant Medicare Benefits Schedule items to support testing on a self-collected sample for this specific use will be effective from 1 November 2022 pending any external impacts such as upcoming elections and caretaker period.

Practice point**REC13.7: Colposcopy referral for any positive co-test result following total hysterectomy**

Women who have had a total hysterectomy and are under surveillance with co-testing, and have a positive oncogenic HPV (any type) test result and/or any cytological abnormality, should be referred for colposcopic assessment.

Practice point**REC13.8: Vaginal bleeding following total hysterectomy**

Women who have vaginal bleeding[†] following total hysterectomy should be assessed by their GP or gynaecologist, regardless of the results of any surveillance tests.

[†]Vaginal bleeding is quite common in the early weeks following hysterectomy and, where appropriate, should be investigated by the treating gynaecologist.

Practice point**REC13.9: Total hysterectomy after genital tract cancer**

Women who have been treated for cervical or endometrial cancer are at risk of recurrent cancer in the vaginal vault. These women should be under ongoing surveillance from a gynaecological oncologist. Therefore, they will be guided by their specialist regarding appropriate surveillance and this is outside the scope of these guidelines.

Practice point**REC13.10: Subtotal hysterectomy**

Women who have undergone subtotal hysterectomy (the cervix is not removed) should be

invited to have 5-yearly HPV testing in accordance with the recommendation for the general population. Any detected abnormality should be managed according to these guidelines.

14. Screening in pregnancy

Consensus-based recommendation

REC14.1: Positive oncogenic HPV (not 16/18) test result with LBC negative or pLSIL/LSIL in pregnancy

Pregnant women who have a positive oncogenic HPV (not 16/18) test result with a LBC report of negative or prediction of pLSIL/LSIL should have a repeat HPV test in 12 months.

Consensus-based recommendation

REC14.2: Positive oncogenic HPV (not 16/18) test result with LBC pHSIL/HSIL or any glandular abnormality in pregnancy

Pregnant women who have a positive oncogenic HPV (not 16/18) test result with a LBC prediction of pHSIL/HSIL or any glandular abnormality should be referred for early[†] colposcopic assessment.

[†] When practical and not deferred until the postpartum period.

Consensus-based recommendation

REC14.3: Positive HPV (16/18) test result in pregnancy

Pregnant women who have a positive oncogenic HPV (16/18) test result should be referred for early[†] colposcopic assessment regardless of their LBC test result.

[†] When practical and not deferred until the postpartum period.

Consensus-based recommendation*

REC14.4: Referral of pregnant women with invasive disease

Pregnant women should be referred and seen within 2 weeks by a gynaecological oncologist/gynaecological cancer centre for multidisciplinary team review and management in the following situations:

- LBC prediction of invasive disease
- colposcopic impression of invasive or superficially invasive squamous cell carcinoma of the cervix
- histologically confirmed diagnosis of invasive or superficially invasive squamous cell carcinoma of the cervix.

Consensus-based recommendation*

REC14.5: Colposcopy during pregnancy

The aim of colposcopy in pregnant women is to exclude the presence of invasive cancer and to reassure them that their pregnancy will not be affected by the presence of an abnormal cervical screening test result.

Practice point**REC14.6: Colposcopy during pregnancy**

Colposcopy during pregnancy should be undertaken by a colposcopist experienced in assessing women during pregnancy.

Consensus-based recommendation***REC14.7: Cervical biopsy in pregnancy is usually unnecessary**

Biopsy of the cervix is usually unnecessary in pregnancy, unless invasive disease is suspected on colposcopy or reflex LBC predicts invasive disease.

Consensus-based recommendation***REC14.8: Defer treatment until after pregnancy**

Definitive treatment of a suspected high-grade lesion, except invasive cancer, may be safely deferred until after the pregnancy.

Practice point**REC14.9: Follow-up assessment after pregnancy**

If postpartum follow-up assessment (colposcopy and/or HPV test and reflex LBC if necessary) is required, it should be done no less than 6 weeks after delivery and preferably at 3 months. This interval is optimal to reduce the risk of reflex LBC interpretation difficulties or unsatisfactory reflex LBC.

The cervical sample (for HPV test and reflex LBC if necessary) could be collected at the time of postpartum check or at the time of the colposcopic assessment.

Practice point**REC14.10: Vaginal oestrogen prior to postpartum colposcopy**

For women who are breastfeeding, the use of intra-vaginal oestrogen cream or pessary[†] prior to colposcopy may improve visualisation of the cervix and the quality of any cervical sample for LBC.

[†]Daily for two weeks and cease approximately 3 days before colposcopy.

Practice point**REC14.11: Cervical screening in pregnancy**

Routine antenatal and postpartum care should include a review of the woman's cervical screening history. Women who are due or overdue for screening should be screened.

Practice point**REC14.12: Cervical screening in pregnancy**

A woman can be safely screened at any time during pregnancy, provided that the correct sampling equipment is used. A cytobrush or combi-brush should not be inserted into the cervical canal because of the risk of associated bleeding, which may distress women.

Practice point**REC14.13: Self-collection in pregnancy**

* All women who are due for cervical screening during pregnancy may be offered the option of self-collection of a vaginal swab for HPV testing, after counselling by a health care professional about the small risk of bleeding. Women testing positive for HPV (not 16/18) on a self-collected sample should be advised to return so that a cervical sample for LBC can be collected by the healthcare provider.

15. Screening in women who have experienced early sexual activity or have been victims of sexual abuse

MSAC evidence-based recommendation

REC15.1: Routine cervical screening is not recommended in young women

Routine cervical screening is not recommended in women under the age of 25 years.

Consensus-based recommendation

REC15.2: Early sexual activity and cervical screening in young women

Evidence does not support screening for women aged less than 25, even when they have experienced early sexual activity. However, for those who experience their first sexual activity at a young age (<14 years) and who had not received the HPV vaccine before sexual debut, a single HPV test between 20 and 24 years of age could be considered on an individual basis, but is not required.

Note: It is expected that amendments to relevant Medicare Benefits Schedule items to support testing on a self-collected sample for this specific use will be effective from 1 November 2022 pending any external impacts such as upcoming elections and caretaker period.

Consensus-based recommendation

REC15.3: Women with abnormal vaginal bleeding

Women at any age who have signs or symptoms suggestive of cervical cancer or its precursors, should have a co-test[†] and be referred for appropriate investigation to exclude genital tract malignancy.

[†] Co-testing (HPV and LBC) is recommended as the presence of blood has the potential to adversely affect the sensitivity of any of the available tests.

16. Screening in immune-deficient women

Consensus-based recommendation

REC16.1: Immune-deficient women in whom oncogenic HPV is not detected

Immune-deficient women who have a HPV test in which oncogenic HPV types are **not** detected should be screened every 3 years with a HPV test.

Consensus-based recommendation

REC16.2: Colposcopy referral: positive oncogenic HPV test result (any type) in immune-deficient women

Women who are immune-deficient and have a positive oncogenic HPV (any type) test result should be referred for colposcopic assessment informed by the reflex LBC.

Consensus-based recommendation*

REC16.3: Colposcopy assessment and treatment in immune-deficient women

Assessment and treatment of immune-deficient women with screen-detected abnormalities should be by an experienced colposcopist or in a tertiary centre.

Consensus-based recommendation*

REC16.4: Colposcopy of whole lower genital tract in immune-deficient women

The entire lower anogenital tract should be assessed, as the same risk factors apply for cervical, vaginal, vulval, perianal and anal lesions.

Consensus-based recommendation*

REC16.5: Treatment in immune-deficient women

When treatment of the cervix is considered necessary in immune-deficient women, it should be by excisional methods.

Practice point

REC16.6: Histological abnormalities of the cervix in immune-deficient women

Women with histologically confirmed abnormalities should be managed according to the same guidelines as women who are not immune-deficient.

Practice point

REC16.7: Test of Cure for treated immune-deficient women

Women who are immune-deficient and treated for HSIL (CIN2/3) should have follow-up with Test of Cure as recommended in [these guidelines](#). Women who complete Test of Cure should return to routine 3-yearly screening with a HPV test.

Practice point

REC16.8: Screening before solid organ transplantation

Women aged between 25 and 74 years should have a review of cervical screening history when they are added to the organ transplant waiting list and while they remain on the waiting list, to confirm they are up to date with recommended screening for the general population. Women who are overdue for screening, or become due while on the waiting list, should be screened with a HPV test so that any abnormalities can be investigated or treated as necessary prior to transplantation and commencement of immunosuppressive therapy.

Practice point

REC16.9: Screening women with a new diagnosis of HIV

Women aged between 25 and 74 years who have a new diagnosis of HIV should have a review of their cervical screening history to ensure they are up to date with screening in line with the recommended 3-yearly interval for this group.

Practice point

REC16.10: Other groups that may require special consideration

The groups listed below could be considered for screening every 3 years with a HPV test in accordance with the recommendation for HIV-positive women and solid organ transplant recipients:

- women with congenital (primary) immune deficiency
- women who are being treated with immunosuppressant therapy for autoimmune disease (e.g. inflammatory bowel disease, systemic lupus erythematosus, rheumatoid arthritis, neuromyelitis optica, sarcoidosis)
- allogenic bone marrow transplant recipients treated for graft versus host disease.

Practice point

REC16.11: Regular screening for immune-deficient women

Women who are immune deficient should be educated regarding the increased risk from HPV infection and encouraged to attend for regular screening.

Practice point**REC16.12: Young women with long term immune deficiency**

For young women who are sexually active and who have been immune deficient for more than 5 years, a single HPV test between 20 and 24 years of age could be considered on an individual basis (regardless of HPV vaccination status).

Practice point**REC16.13: Guidance for immune-deficient women and their healthcare professionals**

It is important that immune-deficient women and their healthcare professionals are guided by a clinical immunology specialist when using these guidelines.

17. Screening in DES-exposed women

Consensus-based recommendation**REC17.1: Screening in DES-exposed women**

Women exposed to DES in utero should be offered an annual co-test and colposcopic examination of both the cervix and vagina indefinitely.

Consensus-based recommendation***REC17.2: Colposcopy referral for abnormalities in DES-exposed women**

Women exposed to DES in utero who have a screen-detected abnormality should be managed by an experienced colposcopist.

Practice point**REC17.3: Daughters of women exposed to DES**

These women should be screened in accordance with the NCSP policy (5-yearly HPV testing). Evidence of an adverse effect on the daughters of women exposed to DES in utero has not been found.

However, if these women have concerns, testing similar to that recommended for their DES-exposed mothers could be considered on an individual basis. Self-collection for HPV testing is not recommended.

18. Signs and symptoms of cervical cancer

Identification and investigation of abnormal bleeding

Consensus-based recommendation**REC18.1: Postcoital and intermenstrual bleeding and testing for HPV and LBC**

When women present with postcoital or intermenstrual bleeding, appropriate investigations including a clinician-collected cervical sample for a co-test,[†] should be performed and not delayed due to the presence of blood.

[†]The woman's recent cervical screening history should be considered.

Consensus-based recommendation

REC18.2: Postcoital bleeding in pre-menopausal women

Pre-menopausal women who have a **single** episode of postcoital bleeding and a clinically normal cervix do not need to be referred for colposcopy if oncogenic HPV is not detected and LBC is negative.

REC18.3: Persistent or recurrent post coital bleeding in pre-menopausal women

Pre-menopausal women with recurrent or persistent postcoital bleeding, even in the presence of a negative co-test, should be referred to a gynaecologist for appropriate assessment, including colposcopy, to exclude genital tract malignancy.

Practice point

REC18.4: Postcoital bleeding and sexually transmitted infections

Sexually transmitted infections, including chlamydia infection, should be considered in all women presenting with postcoital bleeding. It is necessary to obtain a sexual health history and perform appropriate tests and investigations.

Consensus-based recommendation*

REC18.5: Symptomatic women with LBC prediction of cervical cancer

Women with symptoms and a LBC prediction of invasive cervical cancer should be referred to a gynaecological oncologist or gynaecological cancer centre for assessment, ideally within 2 weeks.

Consensus-based recommendation

REC18.6: Women with intermenstrual bleeding

Women with persistent unexplained intermenstrual bleeding require appropriate investigation and should be referred for gynaecological assessment which may or may not include colposcopy. Common benign causes including a sexually transmitted infection or hormonal contraception-related bleeding should be excluded.

Consensus-based recommendation

REC18.7: Postmenopausal women with vaginal bleeding require specialist referral

Postmenopausal women with any vaginal bleeding, including postcoital bleeding, should be referred for a specialist gynaecological assessment (which may or may not include colposcopy) regardless of test results, to exclude genital tract malignancy.

Practice point

REC18.8 Circumstances that do not require co-testing or referral for colposcopy

The following circumstances do not require co-testing or referral for colposcopy:

- a) Breakthrough or irregular bleeding due to hormonal contraception

Investigations of other symptoms – vaginal discharge and deep dyspareunia

Consensus-based recommendation

REC18.9: Women with abnormal vaginal discharge and/or deep dyspareunia

Almost all women with vaginal discharge and/or deep dyspareunia have benign gynaecological disease. They should be investigated appropriately, and if due for cervical screening a routine CST should be performed (rather than a co-test).

Consensus-based recommendation**REC18.10: Women with unexplained persistent unusual vaginal discharge**

In women of any age, unexplained persistent unusual vaginal discharge, especially if malodorous or blood stained, should be investigated with a co-test (HPV and LBC) and the woman should be referred for gynaecological assessment.

Consensus-based recommendation**REC18.11: Women with unexplained persistent deep dyspareunia**

Women with unexplained persistent deep dyspareunia in the absence of bleeding or vaginal discharge should have a CST if due and referral for gynaecological assessment should be considered.

20. Transition to the renewed National Cervical Screening Program**Practice point****REC20.1: HPV test replaces the Pap test**

All Pap tests are replaced by HPV testing.

Conventional Pap tests are no longer used.

Reflex LBC will be performed on any sample with a positive oncogenic HPV (any type) test result.

Co-testing (HPV and LBC) to be performed only as recommended in these guidelines, in the follow-up of screen-detected abnormalities or the investigation of abnormal vaginal bleeding.

Practice point**REC20.2: HPV testing for women in follow-up after pLSIL/LSIL**

Women who are in follow-up for pLSIL/LSIL cytology in the previous program (pre-renewal NCSP) should have a HPV test at their next scheduled follow-up appointment.

- Women with a positive oncogenic HPV (any type) test result should be referred for colposcopic assessment informed by reflex LBC.
- If oncogenic HPV is not detected, the woman can return to 5-yearly screening.

Practice point**REC20.3: Colposcopic management of a prior screen-detected abnormality should continue**

Women who have been referred for colposcopic assessment following any cytological

abnormality in the pre-renewal NCSP should continue their colposcopic management according to these guidelines.

Practice point

REC20.4: Prior treatment and Test of Cure

Women who have been treated for HSIL (CIN2/3) in the pre-renewal NCSP and are undergoing, or have not yet commenced Test of Cure, should start or continue Test of Cure in accordance with these guidelines.

Women should have an annual co-test (HPV and LBC) performed at 12 months after treatment, and annually thereafter, until both tests are negative on two consecutive occasions, when they can return to routine 5-yearly screening.

Practice point

REC20.5: Prior treatment for AIS

Women who have been treated for AIS in the pre-renewal NCSP, and are undergoing or have not yet commenced surveillance, should have annual co-testing (HPV and LBC) indefinitely.[†]

[†]Until sufficient data become available that may support a policy decision that cessation of testing is appropriate.

1. Cervical Cancer in Australia

Author(s):

- [Dr Alison Budd](#) — Co-author
- [Professor Ian Hammond](#) — Co-author
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

Introduction

Australian rates of cervical cancer incidence and death are among the lowest in the world.^[1] This is largely attributed to the successful introduction in 1991 of the National Cervical Screening Program (NCSP). The NCSP is an organised approach to cervical screening that operates as a joint program of the Australian Government and the state and territory governments. It is implemented by a range of health professionals, including general practitioners, women's health nurses, gynaecologists, gynaecological oncologists, cytologists and pathologists.

In 1982 cervical cancer was the sixth most common cancer in Australian women and by 1991 it had fallen to eighth ranking, presumably related to opportunistic screening for cervical cancer. Following the introduction of the NCSP in 1991 there was a steady fall in the incidence of cervical cancer, and by 2009 it ranked the twelfth most common cancer in Australian women.^[2] Table 1.1 shows the Australian incidence and mortality rates for cervical cancer (age-standardised to the World Standard Population) in comparison with other countries for the period up to and including 2012.

Table 1.1. Incidence and mortality rates for cervical cancer (selected countries), 2012

Country	Incidence (ASRW) ^(a)	Mortality (ASRW) ^(a)
Sweden	7.4	1.9
United Kingdom	7.1	1.8
USA	6.6	2.7
Canada	6.3	1.7
Australia	5.5 (ASR)	1.6 (ASR)
New Zealand	5.3	1.4
Finland	4.3	1.0

ASRW: age-standardised rate (World Standard Population) except for Australia (see note)

ASR: age-standardised rate (Australian population)

Notes:

Incidence is the number of new cases of cervical cancer per 100,000 women, age-standardised to the World Standard Population.

Mortality is the number of deaths from cervical cancer per 100,000 women, age-standardised to the World Standard Population.

While incidence and mortality rates have been age-standardised to the World Standard Population, which is appropriate for international comparisons, the remainder of incidence and mortality rates have been age-standardised to the Australian population at 30 June 2001, which is appropriate for comparisons within Australia (such as over time or across population groups). Source: GLOBOCAN (2012)^[3]

Incidence and mortality from cervical cancer

Since 1991 Australian incidence and mortality rates for cervical cancer have decreased by approximately 50%, and are among the lowest in the world.^[2]

Figure 1.1 shows the time trends in incidence of cervical cancer in Australian women aged 20–69 years. The ASR for cervical cancer incidence fell slowly from 14.2 new cases per 100,000 women in 1982, to 13.3 in 1991,^[2] probably related to uptake of opportunistic screening. The organised approach provided by the NCSP commenced in 1991, following which the rate fell rapidly to reach a plateau of about 7 new cases per 100,000 women between 2002 and 2011.^[2] Overall, the incidence rate fell by 51% between 1982 and 2011. A plateau in incidence rates was evident from about 2004.

The ASR for cervical cancer incidence followed a similar trend when considering only women in the target age group 20–69 years, falling only slightly from 19.0 new cases per 100,000 women in 1982, to 17.2 in 1991, before falling rapidly to reach a plateau of about 9 new cases per 100,000 women between 2002 and 2011 (Figure 1.1).

Figure 1.1. Incidence of cervical cancer in women aged 20–69 years, 1982–2011

Note: Incidence rate is the number of new cases of cervical cancer per 100,000 women, age-standardised to the Australian population at 30 June 2001.

Source: Australian Institute of Health and Welfare (AIHW) analysis of the Australian Cancer Database 2011 ^[2]

In 1982 there were 963 new cases of cervical cancer in Australia, 826 of which occurred in the target age group 20–69 years. By 1994, a few years after the introduction of the NCSP, the number of new cases peaked at 1144 new cases (937 in women 20–69 years). By 2002 this had decreased to 690 new cases and of these 558 occurred in the target age group 20–69 years. In 2011 there were 801 new cases overall, with an ASR of 6.9 per 100,000 women, and 682 occurred in women in the target age group of 20–69 years.^[2]

Figure 1.2 shows the time trends in mortality from cervical cancer in Australian women aged 20–69 years.

Figure 1.2. Mortality from cervical cancer in women aged 20–69 years, 1982–2012

Note: Mortality rate is the number of deaths from cervical cancer per 100,000 women, age-standardised to the Australian population at 30 June 2001.

Source: AIHW analysis of the National Mortality Database^[2]

In 2012 there were 226 deaths from cervical cancer (with an ASR of 1.8 per 100,000 women), and 143 occurred in the target age group of 20–69 years.^[2] A plateau in mortality rates was reached in about 2004.

Incidence rates for cervical cancer by histological type over time

Figure 1.3 shows the time trends between 1989 and 2010 in the incidence of the various histological types of cervical cancer.^[2]

Figure 1.3. Incidence of carcinoma of the cervix (squamous cell carcinoma, adenocarcinoma, adenosquamous carcinoma and other carcinomas) in women aged 20–69 years, 1982–2011

Note: Incidence rate is the number of new cases of cervical cancer per 100,000 women, age-standardised to the Australian population at 30 June 2001.

Source: AIHW analysis of the Australian Cancer Database 2011^[2].

The incidence of squamous cancers fell between 1991 and 2002, with little fall thereafter. In contrast, the incidence of adenocarcinoma has been relatively stable. In 1982 the ASR of adenocarcinoma was 2.1 new cases per 100,000 women; by 1991 it had risen to 2.8, from which it fell to a minimum of 2.0 in 2002 and thereafter rose again to nearly reach the levels of the early 1990s.^[2] Incidence rates of adenosquamous carcinoma and of other and unspecified carcinoma appear to have fallen by about 50% since the early 1990s.

The glandular cancers now comprise a quarter of all cervical cancers, whereas in 1991 they accounted for 5–10% of cervical cancers.^[2] The failure to reduce the incidence of adenocarcinoma is usually attributed to difficulties in sampling, less effective identification and more difficult interpretation of abnormal glandular cells.^{[3][4]}

The incidence of glandular cancers has not changed significantly since the inception of the NCSP. Glandular cancers are less frequent than squamous cancers, which the original NCSP was designed to detect. Improvement of the rate of detection of glandular precursor lesions was one aspect considered in the strategy for renewal of the NCSP, to ensure that Australian women are offered optimal cervical screening.

Incidence and mortality for different age groups between 1982 and 2011

Incident cancers decreased over time in each age group from 25–29 years to 85+ years (Figure 1.4). Before the introduction of the NCSP there was a clear second (and higher) peak in the graph of incidence with age in women from 60 years onwards. This peak appears to have reduced substantially over time, possibly because of increased uptake of screening by older women in the organised program. There is also some suggestion that this peak has moved to women in their late seventies and eighties.

Figure 1.4. Incidence of cervical cancer in women by 5-year age group, 1982–1991, 1992–2001, and 2002–2011

Note: Incidence rate is the number of new cases of cervical cancer per 100,000 women.

Source: Australian Cancer Incidence and Mortality^[5].

Similarly, reductions in mortality has been recorded over the same period. Figure 1.5 shows the reduction in the number of deaths during the period 1982–2011 and the variation among women of different age groups. The major reduction in mortality occurred after the introduction of the organised approach to cervical screening in 1991, with the greatest absolute reduction in women in their late sixties and early seventies. This effect is most notable in the period 2002–2012, which does not show the small rise in mortality for women around the age of 65–69 years that is apparent in both the 1982–1991 and 1992–2001 periods.

Figure 1.5. Mortality from cervical cancer in women by 5-year age group, 1982–1991, 1992–2001, and 2002–2012

Note: Mortality rate is the number of deaths from cervical cancer per 100,000 women. Source: Australian Cancer Incidence and Mortality^[5].

Cervical cancer screening across specific groups

Since 1991 cervical screening, using a Pap smear every 2 years, has been recommended for all Australian women aged 20–69 years.

General population

Around 6 in 10 women participate in the NCSP every 2 years. In 2012–2013 (and in preliminary data available for 2013–2014), more than 3.8 million women participated in the NCSP. This was 58% of women aged 20–69 years, and is similar to the 2010–2011 and 2011–2012 periods, for which participation rates were 57% and 58%, respectively. Women under 25 years have the lowest participation rates. Figure 1.6 shows the participation in the NCSP by age over intervals of 2, 3 and 5 years. Five-year participation is more than 80%.

Figure 1.6. Participation of women aged 20–69 years, by age, over 2 years (2012–2013), 3 years (2011–2013), and 5 years (2009–2013)

Participation rate is the number of women screened as a percentage of the resident population (Australian Bureau of Statistics estimates) adjusted to include only women with an intact cervix (using hysterectomy fractions derived from the National Hospital Morbidity Database).

Source: AIHW analysis of state and territory cervical screening register data^[2]

Remoteness and socioeconomic status

Participation differed little across remoteness areas. ASRs range between 58% and 60% in all areas except for very remote areas (55%). However, there is a clear trend of increasing participation with increasing socioeconomic status of residence, from 52% in areas of lowest socioeconomic status to 64% in areas of highest socioeconomic status.

Figure 1.7. Participation of women aged 20–69, by remoteness area and by socioeconomic status, 2012–2013

Notes: Participation rate is the number of women screened as a percentage of the resident population (Australian Bureau of Statistics estimates), adjusted to include only women with an intact cervix (using hysterectomy fractions derived from the National Hospital Morbidity Database), age-standardised to the Australian population at 30 June 2001.

Source: AIHW analysis of state and territory cervical screening register data^[2]

Cervical cancer across specific groups

Women who do not participate as recommended in the NCSP

Failure to participate in the NCSP is related to increased incidence of cervical cancer.

Fifty per cent of cervical cancers occur in women who have never been screened and a further 28% occur in women who do not screen regularly or are lapsed screening participants. This finding suggests that cancer incidence patterns do follow rates of participation in the NCSP.^[6]

Socioeconomic status

Figure 1.8 shows the incidence of cervical cancer in women according to socioeconomic status in 2006–2009. This would appear to reflect the different participation rates related to

socioeconomic status as shown in Figure 1.7. In particular, the incidence of cervical cancer was lowest for women living in areas of highest socioeconomic status (ASR 7.4 new cases per 100,000 women) and it was this group that has the highest participation rate. The four lowest socioeconomic groups had similar rates, with an ASR of 9–10 new cases per 100,000 women. Figure 1.8. Incidence of cervical cancer in women aged 20–69, by socioeconomic status, 2006–2009

Note: Incidence rate is the number of new cases of cervical cancer per 100,000 women, age-standardised to the Australian population at 30 June 2001.

Source: AIHW analysis of the Australian Cancer Database 2011^[2]

Figure 1.9 shows mortality from cervical cancer in women according to socioeconomic status in 2007–2011. This would again appear to reflect the different participation rates related to socioeconomic status as shown in Figure 1.7, and incidence shown in Figure 1.8. Mortality from cervical cancer was lowest for women living in areas of highest socioeconomic status (ASR 1.2 deaths per 100,000 women), broadly increased with decreasing socioeconomic status, and was highest in the lowest socioeconomic group (ASR 2.8 deaths per 100,000 women). The variation of mortality with socioeconomic status was somewhat greater than for incidence, however, suggesting that treatment factors and variations in survival also play a role in the difference. Figure 1.9. Mortality from cervical cancer in women aged 20–69 years, by socioeconomic status, 2007–2011

Note: Mortality rate is the number of deaths from cervical cancer per 100,000 women, age-standardised to the Australian population at 30 June 2001. Source: AIHW National Mortality Database.

Source: AIHW analysis of the National Mortality Database ^[7]

Geographical variation

The incidence and mortality of cervical cancer shows some geographical variation within Australia. This is most noticeable when comparing data from major cities, and inner and outer regional areas, with remote and very remote areas, as shown in Figure 1.10.

During the period 2005–2009 major cities and inner and outer regional areas had incidence rates of 9.0 and 9.3 new cases per 100,000 women, respectively. The incidence in remote and very remote areas was significantly higher, at 12.7 new cases per 100,000 women.^[2]

Figure 1.10. Incidence of cervical cancer in women aged 20–69, by remoteness area, 2005–2009

Note: Incidence rate is the number of new cases of cervical cancer per 100,000 women, age-standardised to the Australian population at 30 June 2001. Source: AIHW analysis of the AIHW Australian Cancer Database 2011^[2]

Figure 1.11 shows that mortality was similar in major cities (1.8 deaths per 100,000 women) and inner and outer regional areas (2.2 deaths per 100,000 women), but mortality in remote and very remote areas was significantly higher (3.4 deaths per 100,000 women). A higher proportion of Aboriginal and Torres Strait Islander women live in remote and very remote areas, and Aboriginal and Torres Strait Islander women experience higher incidence and mortality from cervical cancer.^[2]

Figure 1.11. Mortality from cervical cancer in women aged 20–69 years, by remoteness area, 2008–2012

Note: Mortality rate is the number of deaths from cervical cancer per 100,000 women, age-standardised to the Australian population at 30 June 2001. Source: AIHW analysis of the AIHW National Mortality Database^[2]

Aboriginal and Torres Strait Islander women

Indigenous status has not been recorded in cancer and mortality registers by all jurisdictions for all time periods. Data from those jurisdictions with adequate reporting of cervical cancer by Indigenous status show a significantly higher incidence among Aboriginal and Torres Strait Islander women during 2005–2009, with an ASR of 19.5 new cases per 100,000 women, compared with 8.7 among non-Aboriginal and Torres Strait Islander women (Figure 1.12). Similarly, available data show a significantly higher mortality rate among Aboriginal and Torres Strait Islander women during 2008–2012, at 7.7 deaths per 100,000 women, compared with 1.9 deaths per 100,000 women among non-Aboriginal and Torres Strait Islander women (Figure 1.13).

Figure 1.12. Incidence of cervical cancer in women aged 20–69 years (NSW, QLD, WA, NT) by Indigenous status, 2005–2009

Notes: Incidence rate is the number of new cases of cervical cancer per 100,000 women, age-standardised to the Australian population at 30 June 2001.

Only data from New South Wales, Queensland, Western Australia and the Northern Territory only were considered to have adequate levels of Indigenous identification in cancer registration data. Source: AIHW analysis of the Australian Cancer Database 2011^[2]

Figure 1.13. Mortality from cervical cancer in women aged 20–69 years (NSW, QLD, WA, SA and NT), by Indigenous status, 2008–2012

Notes: Mortality rate is the number of deaths from cervical cancer per 100,000 women, age-standardised to the Australian population at 30 June 2001.

Only data from New South Wales, Queensland, Western Australia, South Australia and the Northern Territory were considered to have adequate levels of Indigenous identification in cancer mortality data.

Source: AIHW analysis of the National Mortality Database^[2]

NCSP participation rates for Aboriginal and Torres Strait Islander women are not available because information on Indigenous status is not collected on pathology forms in all jurisdictions. However, there is evidence that Aboriginal and Torres Strait Islander women are under-screened, and that this contributes to their higher cervical cancer incidence and mortality.^{[8][9][10]}

Cervical cancer control in Australia: now and in the future

Survival

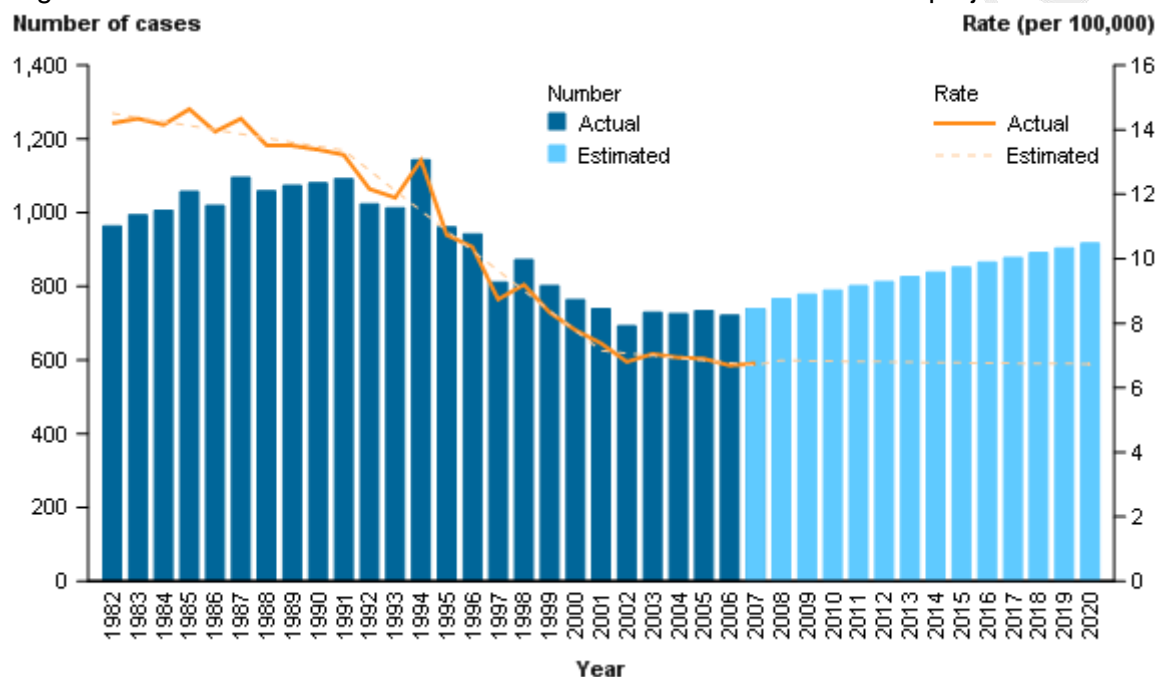
Improvements in speed of referral, investigation, diagnosis, staging of disease, treatment efficacy and availability, subspecialist care, multidisciplinary team management and patient quality of life, have translated into a modest increase in 5-year relative survival for women diagnosed with cervical cancer. Between time periods 1982–1987 and 2006–2010, the 5-year

relative survival (the ratio of observed survival to expected survival) for cervical cancer rose substantially, from 68% in 1982–1987 to 71% in 1988–1993, and to 71.9% in 2007–2011.^{[11][12]}

Incidence

In the absence of any change to the screening program, and assuming that the ASR of 6.7 new cases per 100,000 women will remain constant, the actual number of cases of cervical cancer will rise slowly over the next few years due to population growth and ageing (Figure 1.14). However these projections are not forecasts; they do not allow for future changes in methods of cancer detection or prevention, nor the likely impact of vaccination against human papillomavirus (HPV) in reducing the incidence of cervical cancer in young women.

Figure 1.14. Incidence of cervical cancer observed for 1982–2007 and projected to 2020



Note: Incidence rate is the number of new cases of cervical cancer per 100,000 women, age-standardised to the Australian population at 30 June 2001.

Source: AIHW analysis of the AIHW Australian Cancer Database 2007^[13].

The future of cervical cancer control is in prevention of the disease. Australia has a two-pronged approach: the primary prevention strategy is school-based HPV vaccination, and the secondary prevention strategy is HPV screening (replacing the Pap smear) commencing in December 2017.

National HPV Vaccination Program

The National HPV Vaccination Program commenced for girls in 2007 and for boys in 2013, using a quadrivalent vaccine against HPV types 6, 11, 16 and 18 (Gardasil). This vaccine is effective in preventing infection with the oncogenic HPV types (16 and 18) that cause 70–80% of cervical cancer in Australia.

The National HPV Vaccination Program Register has reported an initial vaccination uptake of 73% for the full course of three doses among eligible girls aged 12–13 years nationally. Reductions in the prevalence of infections with vaccine-included oncogenic HPV types, anogenital warts and histologically confirmed HSIL have already been documented in young women, including a reduction in vaccine-included type infections in unvaccinated young women.^{[7][14][15][16][17]}

A next-generation 9-valent vaccine, with the capacity to prevent up to 90% of cervical cancers in effectively vaccinated females, is expected to be considered for inclusion in the National HPV Vaccination Program. However, this is not expected to have an immediate effect on cervical screening because the new vaccine would be delivered to girls aged 12–13 years, who would not be eligible for screening for a number of years.

Renewal of the National Cervical Screening Program

[Renewal of the NCSP](#) commenced in late 2011, to ensure the continuing success of the program and to ensure that all Australian women – HPV vaccinated and unvaccinated – have access to a cervical screening program that is based on current evidence and best practice.

Factors stimulating the renewal include:

- a plateau in the incidence of cervical squamous cell carcinoma since 2002
- lack of significant reduction in glandular carcinomas since the introduction of the NCSP
- new knowledge about the natural history of cervical cancer (see [Chapter 2. The rationale for primary HPV testing](#))
- new evidence about the optimal screening age range and interval
- new tests, such as liquid based cytology (LBC) and HPV testing
- the National Human Papillomavirus Vaccination Program, which commenced in 2007 for girls and in 2013 for boys.

After a rigorous and transparent process involving an external evidence review^[18] and economic modelling^[19], the Australian Medical Services Advisory Committee (MSAC) released its recommendations in April 2014.

In December 2017 Australia is changing to a renewed NCSP based on 5-yearly cervical screening using a primary HPV test with partial genotyping and reflex LBC triage, for women aged 25–69 years, with exit testing up to age 74 years. Invitations and reminders will be sent to women, and a provision has been made for self-collection of a HPV sample for an under-screened or never-screened woman. The modelled evaluation performed for the MSAC evaluation of the renewed program estimated that the new program will deliver a further 15–22% reduction in incidence and mortality from cervical cancer in Australian women.^[19]

Subsequent modelling, taking into account post-colposcopy management as recommended in these guidelines, has predicted reductions of 31–36% in cervical cancer incidence and mortality in unvaccinated cohorts, and reductions of 24–29% in cohorts offered vaccination (see [Appendix A. Modelled evaluation of the predicted benefits, harms and cost-effectiveness of the renewed National Cervical Screening Program \(NCSP\)](#) in conjunction with these guideline recommendations).

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2. [Rationale for primary HPV screening](#)

Author(s):

- [Professor Karen Canfell](#) — Co-author
- [A/Professor Marion Saville](#) — Co-author
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

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[Cervical cancer](#). Chapter in: [National Cancer Prevention Policy](#), Cancer Council Australia.

[Chapter revised in March/April 2012 in consultation with Professor Karen Canfell (now Director Research Cancer Council NSW). Kristine Macartney (Deputy Director of Government Programs, National Centre for Immunisation Research & Surveillance) provided advice about HPV immunisation. The chapter was externally reviewed in July 2012 by Professor Ian Frazer, Professor Ian Hammond and Associate Professor Marion Saville].

Canfell K, The Australian example: An integrated approach to HPV vaccination and cervical screening. HPV Today. Vol 34. August 2015. <http://www.hpvtoday.com/revista34/09-The-Australian-Example.html>

HPV infection

Over 100 different types of human papillomavirus (HPV) have been identified and there are more than 40 anogenital HPV types, 15 of which are classified as 'high risk' or oncogenic.^{[1][2]} HPV infections can induce the development of either benign or malignant lesions. Benign lesions (including non-genital and anogenital skin warts, oral and laryngeal papillomas and anogenital mucosal condylomata) are caused by HPV types designated 'low risk' (notably HPV 6 and 11, which cause anogenital warts).^[3] Persistent infection with oncogenic HPV types is generally subclinical, but can result in the development of a range of anogenital tumours including cancers of the cervix, anus, penis, vulva and vagina.^[3] HPV infection is also associated with squamous cell carcinomas of the head and neck, particularly oropharyngeal cancers.^[4]

Anogenital HPV infections are transmitted mainly by skin-to-skin or mucosa-to-mucosa contact.^[5] Penetrative sexual intercourse is not strictly necessary for transmission and HPV can be transferred to the cervix from original infection at the introitus.^[6] Therefore, genital skin-to-skin contact, vaginal sex, oral sex, and anal sex represent types of sexual activity that may facilitate the person-to-person transmission of anogenital types of HPV.

to the implementation of HPV vaccination, cervical HPV infection was common in sexually active women. A study of pre-vaccination cervical HPV prevalence found multiple infections were common in Australian women, with a wide range of HPV types detected (HPV 16 being the most common), and incidence peaking in the years following the start of sexual activity.^[7] International data show prevalence is high even in young women who are with their first partner and are monogamous, with HPV infection rates of 30% within 1 year of becoming sexually active and 48% within 3 years.^[8] HPV prevalence peaks soon after the average age of first sexual intercourse. In Australia the median age of sexual debut is 17 years for females born from 1965 onwards.^[9] Prevalence among women aged over 30 years is much lower than among younger women.^[10] Most infections are cleared by the immune system within 1–2 years.^[11]

HPV, cervical intraepithelial neoplasia, and cancer of the cervix

There is overwhelming evidence that HPV infection is necessary for development of cancer of the cervix. The International Agency for Research on Cancer has classified certain HPV types as Group 1 carcinogens (agents for which there is sufficient evidence that it is carcinogenic to humans).^[12]

While HPV infection is necessary for the development of cervical cancer, it is certainly not sufficient.^[13] Worldwide, it has been estimated that pre-vaccination, there were about 100 million adult women infected with oncogenic HPV types.^[14] This compares with approximately 528,000 new cases of cervical cancer worldwide each year.^[10] However, the risk of developing cancer increases significantly with persistent HPV infection.^[15]

Women with persistent infections, especially with HPV 16, are at significantly higher risk of cervical cancer and its immediate precursor lesion, cervical intraepithelial neoplasia (CIN) grade 3 (CIN3).^{[16][17][18]} However, although a majority of women are infected with HPV within a few years of sexual debut, incidence of cervical cancer peaks at about age 45 years,^[19] which suggests that progression from persistent infection to invasive cervical cancer is generally slow. More than 70% of cervical squamous cell carcinomas and about 78% of cervical adenocarcinomas are caused by oncogenic HPV types 16 and 18.^[20] HPV 16 is the most carcinogenic, accounting for about 55–60% of cervical cancers, while HPV 18 accounts for a further 10–15% of cervical cancers.^{[21][21]}

The four major steps in cervical cancer development are HPV infection/acquisition, viral persistence (versus clearance), progression to cervical pre-cancer, and invasion.^[22] The natural history of HPV and cervical intraepithelial neoplasia (CIN) is summarised in Figure 2.1.. It has been estimated that persistent HPV infections and pre-cancer are established, typically within 5–10 years, from less than 10% of new infections.^[22] However invasive cervical cancer arises only rarely, in a small proportion of women with pre-cancer. If invasive cancer arises, this generally occurs over many years – often decades – with the peak risk occurring after about age 35–55 years.^[22]

Low-grade squamous intraepithelial lesions (LSIL) are manifestations of acute HPV infection with any type (oncogenic types or other types such as 6, 11), rather than cancer precursors,^[23] and most will resolve spontaneously within 12 months.^[24] Some high-grade squamous intraepithelial lesions (HSIL [CIN2]) will regress over time, but these lesions are associated with a higher risk of progression compared with LSIL. At the molecular level, pre-cancerous lesions occur when oncogenic HPV is not cleared, infects immature cells and prevents maturation and differentiation, resulting in the replication of immature cells and the accrual of genetic changes that can lead to cervical cancer (Figure 2.1).^[25] Lesions histologically classified as CIN2 represent a heterogeneous mix of low-grade and high-grade abnormalities at the molecular level. Clinically, however, lesions classified as CIN2 or above (CIN2+) are often termed 'high grade' or 'precancerous' and are treated.

In women with oncogenic HPV infection, current cigarette smoking significantly increases the risk of squamous cell carcinoma, but not of adenocarcinoma.^[26] Other co-factors that increase the risk of progression to cervical cancer in women who have a persistent oncogenic HPV infection includes multiparity (more than five full-term pregnancies),^[27] early age at first full-term pregnancy,^[27] and the use of oral contraceptives.^[28] Immune deficiency (e.g. acquired by HIV infection) contributes significantly to persisting HPV infection and cervical cancer risk.^[29]

Figure 2.1. HPV to cervical cancer

Acknowledgment: Adapted from Schiffman M, 2005.^[30]

HPV vaccination

Since 2007, prophylactic vaccination against HPV in pre-adolescent females has been introduced in most developed countries, supported by modelled evaluations of the cost-effectiveness of this intervention.^[31] Two first-generation vaccines are available: the quadrivalent vaccine (*Gardasil*, CSL/Merck) and the bivalent vaccine (*Cervarix*, GSK). These have been shown to be effective in preventing persistent infection and histologically confirmed HSIL (CIN2/3) in females naïve to HPV vaccine types^{[32][33]} and at preventing persistent infection, external genital lesions and anal intraepithelial neoplasia in males.^[34]

First-generation HPV vaccines protect against oncogenic HPV types 16 and 18, which are together responsible for approximately 70% of invasive cervical cancers.^[2] The quadrivalent vaccine also protects against oncogenic HPV types 6 and 11, which cause more than 90% of anogenital warts. As nearly 80% of adenocarcinomas are associated with the HPV types 16/18,^[35] prophylactic HPV vaccination is also expected to be effective in preventing these cancers.^[36]

Large-scale studies have shown the HPV vaccines to be safe and well tolerated. *Gardasil*, the quadrivalent vaccine distributed via the National Immunisation Program, has been assessed as safe and effective by the Australian Therapeutic Goods Administration, the US Food and Drug Administration and the European Medicines Agency. For further information about HPV vaccine safety and efficacy, as well as dosage and administration, please refer to the [Australian Immunisation Handbook](#).

For maximum efficacy, prophylactic vaccines need to be administered to individuals prior to HPV exposure.^[14] Current vaccines do not have a therapeutic effect in those already infected with HPV. It is recommended that HPV vaccines be provided before sexual activity commences. In Australia, the National Immunisation Program targets ongoing vaccination towards adolescent/pre-adolescent girls, aged 11–13 years. Young males were included on the National HPV Vaccination Program from 2013.^[37] Australia-specific modelling has suggested this will increase the level of 'herd immunity' protection to females.^[38]

In late 2014, the US Food and Drug Administration approved a second-generation 9-valent vaccine, which targets the quadrivalent oncogenic HPV types and five additional oncogenic HPV types (31, 33, 45, 52, and 58). Together, oncogenic HPV types included in the 9-valent vaccine are found in approximately 90% of cervical cancers globally.^[39] Compared with the quadrivalent vaccine, the 9-valent vaccine has been shown to be 97% effective for prevention of high-grade cervical, vulvar, and vaginal disease caused by types 31, 33, 45, 52, and 58 in individuals naïve for these types, and to be associated with non-inferior seroconversion for the oncogenic HPV types included in the current quadrivalent vaccine: 6, 11, 16, and 18.^[40] The Australian Pharmaceutical Benefits Advisory Committee will evaluate the 9-valent vaccine for inclusion in the National Immunisation Program. As of early 2016 this had not yet occurred.

Impact of HPV vaccination in Australia

Australia was the first country to initiate a national public vaccination program, which began in 2007. Female vaccination uptake is approximately 71–72% for three-dose coverage in girls aged 12–13 years, and catch-up in women aged 18–26 years (conducted from 2007–2009) achieved coverage rates of approximately 30–50%.^{[18][41]} From 2013, males aged 12–13 years have also been vaccinated at school with a 2-year catch-up to Year 9 (age approximately 15 years). Via herd immunity, male vaccination will also provide incremental benefits to females, and is expected to lead to further reductions in rates of infection with vaccine-included oncogenic HPV types and high-grade cervical abnormalities in females.^[38]

Several factors have come together to achieve a more rapid impact of vaccination on cervical screening in Australia than in many other countries. These include the early introduction of HPV vaccination, the extended catch-up to age 26 years, the early age of screening commencement at 18–20 years, with the consequent overlap of vaccinated and screened populations from the inception of the vaccination program, and the relatively high coverage rates for vaccination and cervical screening.

After the introduction of vaccination, Australia experienced rapid falls in rates of infections with vaccine-included oncogenic HPV types, in anogenital warts and in histologically confirmed HSIL. These reductions have now been documented extensively in young females and also in heterosexual males due to herd immunity effects.^{[42][43][44][45][46]} Between 2004–2006 and 2012, rates of CIN2/3 among women aged less than 20 years decreased by 53%, while rates of confirmed CIN2/3 among women aged 20–24 years were stable until 2010, then decreased by 21% in the following year.^[42]

It is expected that rates of HSIL (CIN2/3) will continue to decline, and that the decline will extend to older age groups as the cohorts offered vaccination continue to age. As successive cohorts of girls are vaccinated, and the vaccinated cohorts mature, the risk of cervical cancer will continue to fall.

However, cervical screening will remain necessary, since the current vaccine does not cover all oncogenic HPV types that can lead to cervical cancer and may not be effective in women exposed to HPV prior to vaccination. If 9-valent vaccines are introduced, the extent of these reductions in HSIL (CIN2/3) would eventually be expected to increase further, but this is not expected to occur until 2030, since cohorts aged 12–13 years offered next-generation vaccines will not reach the new target age group for cervical screening for some years.

Impact of vaccination on the starting age for cervical screening

Even in completely unvaccinated populations, rates of invasive cervical cancer are low in women younger than 25 years^[42] (see also [Cervical cancer in Australia](#)). A substantial body of evidence has found that cervical screening in this age group has little or no impact on the risk of developing invasive cancer before age 30 years.^[47] Almost all countries with organised programs recommend that cervical screening commences at age 25 or 30 years and the International Agency for Research on Cancer (IARC) recommends regular cervical screening begin at the age of 25.^[48] This starting age achieves the best balance of benefits and harms for cervical screening, as detailed in the report of effectiveness modelling and economic evaluation^[49] undertaken during renewal of the NCSP.^[50]

The evaluation undertaken for renewal of the NCSP considered a range of screening strategies starting at age 25 years.^[50] The evaluation predicted that, compared with pre-renewal NCSP based on cytology screening in sexually active women starting at age 18–20 years, 5-yearly HPV

screening starting at age 25 will be associated with reductions in cervical cancer incidence and mortality rates of at least 15%; this reduction is predicted even if the population had never been offered HPV vaccination. Subsequent modelling, taking into account post-colposcopy management as recommended in these guidelines, has predicted reductions of 31-36% in cervical cancer incidence and mortality in unvaccinated cohorts, and reductions of 24-29% in cohorts offered vaccination (see [Appendix A. Modelled evaluation of the predicted benefits, harms and cost-effectiveness of the renewed National Cervical Screening Program \(NCSP\) in conjunction with these guideline recommendations](#)).

In the post-vaccination era the risk of cervical cancer in women aged 25 years or less has been reduced even further.^[50] In Australia, the prevalence of infections with vaccine-included oncogenic HPV types decreased by 78% among women aged 18-24 years between 2005-2007 (pre-vaccination era) to 2010.^[44] This substantial reduction occurred within a few years after vaccination was introduced. Furthermore, the impact of the vaccination program has not been confined to those who are individually vaccinated. Even prior to the implementation of male vaccination, females showed herd immunity due to the vaccination of other females in the community. The effect has been documented as a fall in the prevalence of infections with vaccine-included oncogenic HPV types in unvaccinated women aged 18-24 years that occurred by 2012; the effect of herd immunity is expected to be even further increased following the implementation of male vaccination in 2013. As detailed above, a dramatic fall in histologically confirmed HSIL (of over 50%) has also been documented in women under 25 years of age in Australia.^[44]

Therefore, several factors have combined to support a starting age of 25 years in the renewed NCSP, including:

- the relatively lower rates of cervical cancer in women less than 25 years of age
- the lack of evidence for the effectiveness of cervical screening in this age group
- the impact of HPV vaccination on further substantially lowering the risks for both vaccinated and unvaccinated young women.

Primary HPV Screening

Due to the relationship between persistent infection with oncogenic HPV types and the development of cervical cancer, testing for the presence of oncogenic HPV DNA in cervical cell specimens has the potential to identify women at increased risk of developing cervical cancer. Women in whom oncogenic HPV types are not detected are at very low risk of CIN3 or cancer for at least 5 years.^{[51][52]}

HPV DNA testing in cervical screening is more sensitive than cytology and detects high-grade lesions earlier, thus preventing more cervical cancers.^{[53][54]} Screening using HPV testing has the potential to improve identification of adenocarcinoma and its precursors.^{[51][55]} A large body of evidence, including data from randomised trials in developed countries, has shown HPV testing in primary screening is superior to cytology.^{[55][56][57]} Analysis of four European randomised controlled trials found that, compared with cytology, HPV-based screening provided greater protection against invasive cervical cancers.^[55]

Using the HPV test as a primary screening tool allows for development of population-based screening recommendations based on individual risk assessment rather than vaccination status, which will change over time as vaccinated cohorts reach screening age.^[58] Given oncogenic HPV

types 16 and 18 account for the greatest proportion of infections causing cervical cancer, screening tests with partial genotyping for oncogenic HPV types 16/18 are expected to improve risk stratification of women with a positive oncogenic HPV test result in cervical screening programs.^[23]

In the renewed NCSP, HPV testing at 5-year intervals from age 25 years has been recommended and adopted as the preferred pathway for screening in Australia.^[59] The review of strategy and policy undertaken for renewal of the NCSP identified options for HPV screening in Australia that were predicted to result in life-year savings, compared with current practice.^[59] The greatest gains in effectiveness were associated with strategies based on primary HPV testing with partial genotyping for HPV 16/18, in which women with these HPV types are referred directly for diagnostic evaluation.^[59]

An Australian trial of HPV screening with partial genotyping, [Compass](#), is providing information on resource use and outcomes of the renewed NCSP in both unvaccinated and vaccinated women. This information has informed the development of these guidelines. Conducted in the state of Victoria by the Victorian Cytology Service Ltd and Cancer Council NSW, Compass has two phases: Phase I (the pilot), which recruited 5000 women, and Phase 2 (the main trial) which is recruiting 121,000 women.

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3. [Terminology](#)

Author(s):

- [A/Prof Lyndal Anderson](#) — Co-author
- [A/Professor Marion Saville](#) — Co-author
- [Professor Gordon Wright](#) — Co-author
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

See the following sections:

- [HPV testing terminology](#)
- [Cytology and AMBS 2004 terminology for reporting cervical cytology](#)
- [Preparation of cervical screening reports](#)

- [Colposcopy](#)
- [Histopathology](#)
- [Supplement. Sample reports](#)

HPV testing terminology

Author(s):

- [A/Prof Lyndal Anderson](#) — Co-author
- [A/Professor Marion Saville](#) — Co-author
- [Professor Gordon Wright](#) — Co-author
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

HPV testing

HPV testing refers to testing for oncogenic human papillomavirus (HPV) types. Oncogenic HPV types are defined as those associated with the development of invasive cervical cancer, and include HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 and 68.^[1] HPV testing can be performed using a range of technologies including DNA PCR, DNA hybridisation, and testing for RNA. Technologies that are to be used in the National Cervical Screening Program (NCSP) will be required to meet performance standards as determined by the National Pathology Accreditation Advisory Council (NPAAC).

The role of partial genotyping

The risk of having, or developing, cervical intraepithelial neoplasia (CIN) grade 3 or higher (CIN3+) can be stratified based on the results of partial genotyping on an HPV test. Several epidemiological analyses have been performed to inform estimates of the longitudinal risk associated with each HPV type. For example, Khan and colleagues^[2] calculated the cumulative incidence rates (CIR) of CIN3+, including cancer, over a 10-year period as follows:

- 17.2% for women with a positive oncogenic HPV test result (type 16)
- 13.6% for women with a positive oncogenic HPV test result (type 18)
- 3% for women with a positive oncogenic HPV test result (not 16/18)
- 0.8% for women in whom oncogenic HPV is not detected.

HPV testing within the NCSP includes partial genotyping for HPV types 16 and 18, as these types are managed differently to other oncogenic HPV types (not 16/18) in the program (see [Oncogenic HPV types 16/18](#) in *Chapter 6. Management of oncogenic test results*).

Some HPV test platforms provide additional channels for reporting HPV 31, 45 and/or other (not 16/18) oncogenic types, as part of their partial genotyping reporting. Some test platforms report HPV 18 and 45 together. For assays that do not distinguish between oncogenic HPV 18 and 45, a woman in whom type 18/45 is detected should be managed as for women with a positive oncogenic HPV (16/18) test result.

HPV results

For the purpose of reporting, this guideline recognises the following categories for HPV test results (see Preparation of cervical screening reports):

- HPV 16/18 detected
- oncogenic HPV (not 16/18) detected
- oncogenic HPV not detected.

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Cytology and AMBS 2004 terminology for reporting

Author(s):

- [A/Prof Lyndal Anderson](#) — Co-author
- [A/Professor Marion Saville](#) — Co-author
- [Professor Gordon Wright](#) — Co-author
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

Cytology

Background

In 1991, the US National Cancer Institute (NCI) sponsored a multidisciplinary meeting in Bethesda, Maryland to consider Pap smear terminology. Participants including pathologists, cytotechnologists, gynaecologists and primary care health professionals (predominantly from the USA, but also from other countries) agreed on a consistent system for reporting Pap smears: *The Bethesda System 1991* (TBS 1991).^[1]

NHMRC Australian terminology, 1994

As part of preparing the first National Health and Medical Research Council (NHMRC) 1994 guidelines for the management of women with screen-detected abnormalities,^[2] the Australian working party considered the Bethesda terminology and recommended a range of modifications that resulted in a unique Australian terminology system.

Revisions of The Bethesda System 2001 (TBS 2001) and 2014 (TBS 2014)

There have been few changes in terminology since 2001.^{[3][4]} In 2014, a smaller working party of cytopathologists, clinicians and epidemiologists reviewed TBS 2001, resulting in the 2014 update of The Bethesda System (TBS 2014) published in 2015.^[5] Changes included additional information on cytology at other anatomical sites, adjunctive HPV testing, immunochemical assays such as dual p16 and Ki67 staining, and computer-assisted interpretation of cytology.

Australian Modified Bethesda System (AMBS 2004): current terminology in Australia

Building on the historical NHMRC Australian terminology from 1994, the Australian Modified Bethesda System (AMBS) was introduced in 2004. AMBS 2004:

- incorporated the separation of suspected from confidently predicted low-grade abnormalities
- reflected a modern understanding of the relationship between HPV infection and cervical cancer and its precursors
- was compatible with terminology systems used internationally
- did not mandate distinctions for which there is poor evidence for reproducibility or clinical significance.

There has been no change to the AMBS since 2004 and it remains the current terminology in Australia. Table 3.1 compares AMBS 2004 with TBS 2001 and TBS 2014.

Table 3.1. Comparison of the Australian Modified Bethesda System (AMBS 2004) and The Bethesda System (TBS 2001/2014)

AMBS 2004	TBS 2001/2014	Incorporates
Squamous abnormalities		
Possible low-grade squamous intraepithelial lesion	Atypical squamous cells, undetermined significance (ASC-US)	Nonspecific minor squamous cell changes. Changes that suggest but fall short of HPV/CIN1
Low-grade squamous intraepithelial lesion	Low-grade squamous intraepithelial lesion	HPV effect, CIN1
Possible high-grade squamous lesion	Atypical squamous cells, possible high-grade lesion (ASC-H)	Changes that suggest, but fall short of, CIN2, CIN3 or SCC
High-grade squamous intraepithelial lesion	High-grade squamous intraepithelial lesion	CIN2, CIN3
Squamous cell carcinoma	Squamous cell carcinoma	Squamous cell carcinoma
Glandular abnormalities		
Atypical endocervical cells of undetermined significance	Atypical endocervical cells, undetermined significance	Nonspecific minor cell changes in endocervical cells
Atypical glandular cells of undetermined significance	Atypical glandular cells, undetermined significance	Nonspecific minor cell changes in glandular cells
Possible high-grade glandular lesion	Atypical endocervical cells, possibly neoplastic	Changes that suggest, but fall short of, AIS or adenocarcinoma
Endocervical adenocarcinoma in situ	Endocervical adenocarcinoma in situ	Adenocarcinoma in situ
Adenocarcinoma	Adenocarcinoma	Adenocarcinoma

Explanation of AMBS 2004 terminology for reporting cervical cytology

Squamous abnormalities

Possible low-grade squamous intraepithelial lesion

The category of possible low-grade squamous intraepithelial lesion (pLSIL) is to be used when the reporting scientist/pathologist observes changes in squamous cells that may represent a low-grade squamous intraepithelial lesion, but the changes are not so clear-cut as to justify a 'definite' diagnosis. This category specifically excludes changes that are within the scope of reactive processes.

Low-grade squamous intraepithelial lesion

The low-grade squamous intraepithelial lesion (LSIL) category is the morphological correlate of productive viral infection. It is to be used when the scientist/pathologist observes changes that, pre-AMBS 2004, would have been described as 'HPV effect' or 'CIN1'.

Possible high-grade squamous intraepithelial lesion

The category of 'possible high-grade squamous intraepithelial lesion' (pHSIL) is to be used when the reporting scientist/pathologist suspects the presence of a high-grade squamous

abnormality, such as CIN2, CIN3 (in the pre-AMBS 2004 system) or squamous cell carcinoma (SCC), but the changes are insufficient to justify a confident cytological prediction of a high-grade lesion.

High-grade squamous intraepithelial lesion

The high-grade squamous intraepithelial lesion (HSIL) category is the morphological correlate of a true preneoplastic change occurring in squamous cells as a result of HPV infection. It is to be used when the scientist/pathologist observes changes that, pre-AMBS 2004, would have been described as CIN2 or CIN3.

If, in addition to the presence of a definite intraepithelial high-grade abnormality, there are features that suggest the presence of an invasive component, this should be noted in the 'specific diagnosis' section of the report.

Squamous cell carcinoma

The SCC category is self-explanatory.

Glandular abnormalities

Atypical endocervical cells of undetermined significance

Atypical glandular cells of undetermined significance

These categories encompass those changes in glandular cells that the reporting scientist/pathologist believes are outside the scope of a definite reactive process.

It has been well documented that productive HPV infection does not exist in glandular cells, and therefore there is no glandular correlate to the low-grade squamous abnormality. Nevertheless, the morphological changes observed in glandular cells encompass a spectrum of changes.

These categories should be used when such changes are insufficient to raise the possibility of a neoplasm, such as AIS, but are beyond those accepted as definitely representing a reactive process.

Cells in this category are to be designated as follows:

- *atypical glandular cells* when the reporting scientist/pathologist is not sure whether the cells are endocervical
- *atypical endocervical cells* when the reporting scientist/pathologist is confident that the cells are endocervical

Possible high-grade glandular lesion

This category is to be used when the reporting scientist/pathologist suspects the presence of a high-grade glandular abnormality such as possible AIS, possible endocervical adenocarcinoma or possible endometrial adenocarcinoma, but is unable to make a confident prediction.

Endocervical adenocarcinoma in situ

The endocervical AIS category is self-explanatory. The diagnosis is to be used when the reporting scientist/pathologist is confident of the presence of AIS.

Adenocarcinoma

The adenocarcinoma category is self-explanatory. The reporting scientist/pathologist has the option of designating whether they believe the adenocarcinoma is endocervical, endometrial or extrauterine in origin.

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Preparation of cervical screening reports

Author(s):

- [A/Prof Lyndal Anderson](#) — Co-author
- [A/Professor Marion Saville](#) — Co-author
- [Professor Gordon Wright](#) — Co-author
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

Preparation of cervical screening reports

Examples of cervical screening reports conforming to the requirements of the renewed NCSP are found in the [Supplement. Sample reports](#).

Cervical screening result

Reported as low, intermediate or higher risk of significant cervical abnormality, or as unsatisfactory for evaluation, based on both the HPV test and (where indicated) reflex LBC (Table 3.2).

Table 3.2. Reporting of cervical screening result

Findings		Report
HPV test result	Reflex LBC	
Oncogenic HPV not detected	N/A	<i>Low risk for significant cervical abnormality</i>
Oncogenic HPV (not 16/18)	Negative or pLSIL/LSIL	<i>Intermediate risk for significant cervical abnormality</i>
HPV 16/18	Any of the following: Unsatisfactory Negative pLSIL/LSIL pHSIL/HSIL+ Any glandular abnormality	<i>Higher risk for significant cervical abnormality</i>
Oncogenic HPV (not 16/18)	pHSIL/HSIL+ Any glandular abnormality	<i>Higher risk for significant cervical abnormality</i>
Oncogenic HPV (any type) persisting at 12 month repeat following initial oncogenic HPV (not 16/18)	Any of the following: Unsatisfactory Negative pLSIL/LSIL	<i>Higher risk for significant cervical abnormality</i>

	pHSIL/HSIL+ Any glandular abnormality	
Test not completed for technical reasons	N/A	<i>Unsatisfactory for evaluation</i>
Oncogenic HPV (not 16/18)	Unsatisfactory	<i>Unsatisfactory for evaluation</i>

LBC: liquid-based cytology

HSIL+: HSIL or higher-grade abnormality

Specimen type

- Indicate sample medium.
- Indicate method of collection:
 - practitioner-collected
 - self-collected.
- Indicate that the specimen is cervical in origin.

Test result(s)

HPV test

- Indicate the test method used.
- Indicate the test result:
 - HPV 16/18 detected. (For test platforms that do not distinguish between HPV 18 and 45, use this category to report HPV 18/45.)
 - oncogenic HPV (not 16/18) detected. (For test platforms that separately identify 45,31,33 or other oncogenic types (not 16/18), include any such types in this category.)
 - oncogenic HPV not detected
 - unsatisfactory.

LBC results

- Indicate method of analysis:
 - image assisted
 - manually screened.
- Report the epithelial cell findings using AMBS terminology.
 - Include a statement on the presence or absence of an endocervical component.
 - Note the presence of organisms when identified:
 - *Trichomonas vaginalis*
 - fungal organisms morphologically consistent with *Candida* spp
 - shift in flora suggestive of bacterial vaginosis
 - bacteria morphologically consistent with *Actinomyces* spp

- cellular changes consistent with herpes simplex virus.
- Note the presence of other non-neoplastic findings when identified (optional):
 - reactive cellular changes associated with:
 - inflammation and repair
 - radiation
 - intrauterine contraceptive device
- glandular cells after hysterectomy
- atrophy.

Recommendation

Concise management recommendations, as set out in these guidelines, should be included in the report.

The recommendation must take account of the woman's screening history as recorded with the National Cancer Screening Register (NCSP).

The management recommendations should align with the cervical screening result as follows:

Cervical screening result	Management recommendation'
Low risk of significant cervical abnormality	Rescreen in 5 years
Intermediate risk of significant cervical abnormality	Repeat HPV test in 12 months
Higher risk of significant cervical abnormality	Refer for colposcopic assessment
Unsatisfactory	Retest in 6 weeks#

#In cases where the HPV test has been performed and reflex LBC is indicated but cannot be performed, the laboratory should not repeat the HPV test on receipt of the repeat sample, but should proceed directly to LBC and then issue a combined report taking account of both tests.

Preparation of stand-alone LBC reports

LBC will be requested without an HPV test in the following circumstances:

- at the time of colposcopy (when indicated)
- where reflex LBC has been reported as 'Unsatisfactory' following the detection of oncogenic HPV (not 16/18)
- following the detection of Oncogenic HPV (not 16/18) in a self-collected sample.

Reporting LBC at the time of colposcopy

LBC on samples taken at the time of colposcopy is not considered a screening test, but rather as part of the assessment process. Accordingly, an over-arching cervical screening report incorporating a risk statement is not required or appropriate in this setting.

- Indicate sample medium.
- Indicate method of analysis:

- image assisted
 - manually screened.
- Report the epithelial cell findings using AMBS terminology (2004).
- Include a statement on the presence or absence of an endocervical component.
- Note the presence of organisms when identified:
 - *Trichomonas vaginalis*
 - fungal organisms morphologically consistent with *Candida* spp
 - shift in flora suggestive of bacterial vaginosis
 - bacteria morphologically consistent with *Actinomyces* spp
 - cellular changes consistent with herpes simplex virus.
- Note the presence of other non-neoplastic findings when identified (optional):
 - reactive cellular changes associated with:
 - inflammation and repair
 - radiation
 - intrauterine contraceptive device
 - glandular cells after hysterectomy
 - atrophy.
- Document that the woman is under gynaecological management and therefore a recommendation is not provided.

Following Unsatisfactory LBC

Where a woman has a positive oncogenic HPV (not 16/18) test result and the reflex LBC was unsatisfactory, she should have a further cervical sample taken for LBC in 6 weeks. The repeat cervical sample should not be tested for HPV. The laboratory should undertake LBC and prepare a cervical screening report (see [Preparation of cervical screening reports](#)), combining the results of the original HPV test and the repeat LBC. It is anticipated that the support of the National Cancer Screening Register will be critical in this circumstance.

Following self-collection

Where a woman has a positive oncogenic HPV (not 16/18) test result on a self-collected sample she should have an LBC sample taken by her health care professional. The LBC specimen should not be tested for HPV. The laboratory should undertake LBC and prepare a cervical screening report (see [Preparation of cervical screening reports](#)), combining the results of the original HPV test result and the LBC. It is anticipated that the support of the National Cancer Screening Register will be critical in this circumstance.

Colposcopy

Author(s):

- [Mr. C. David H. Wrede](#) — Author
- [A/Professor Alison Brand](#) — Co-author
- [Professor Ian Hammond](#) — Co-author
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

Introduction

The aim of diagnostic colposcopy following an abnormal cervical screening test is to assess the nature, severity and extent of the abnormality. This requires the identification of the cervix and external os, the exclusion of invasive disease, the mapping and typing of the transformation zone (TZ), the identification of any visible abnormalities and the targeting of the most abnormal area(s) for biopsy. Systematic examination of the whole lower genital tract and accurate, concise recording of the findings are required to produce the highest sensitivity and best positive predictive value for diagnosing high-grade abnormalities, as well as determining if treatment is required and planning the most appropriate mode, timing and extent of therapy.

In the renewed National Cervical Screening Program (NCSP) colposcopists are required to submit data from diagnostic and therapeutic colposcopy to the National Cancer Screening Register (NCSR). In return, they will receive data directly from the NCSR to enable them to review their own performance against defined benchmarks. These data can then be submitted to fulfil requirements for recertification in colposcopy. The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) will manage the certification and recertification processes for colposcopists. In the renewed program, the annual performance report prepared by the Australian Institute of Health and Welfare (AIHW) will include colposcopy data.

This chapter contains recommendations about the performance of colposcopy and related treatments. It is not intended to replace supervised training in accredited centres, nor attendance at colposcopy training and update courses, but offers guidance as to the minimum standards expected of a colposcopist providing services to the NCSP.

See:

- [Colposcopy terminology](#)

- [Principles of practice](#)
- [History, examination and investigation](#)
- [Treatment](#)
- [Colposcopy data for the National Cancer Screening Register](#)
- [Quality improvement in colposcopy](#)
- [Supplement. Colposcopy information for discussion with patient](#)
- [Supplement. Colposcopy technologies and documentation](#)

Histopathology

Author(s):

- [A/Prof Lyndal Anderson](#) — Co-author
- [A/Professor Marion Saville](#) — Co-author
- [Professor Gordon Wright](#) — Co-author
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

Background

The histopathological classification of HPV-associated disease of the anogenital tract prior to 2012 was complex. Terminology changed for different sites and variable terms such as condyloma, dysplasia, intraepithelial neoplasia and carcinoma in-situ were employed. This was partly due to development of a number of different interest groups including pathologists, dermatologists and gynaecologists using their own version of terminology for similar lesions.

LAST Standardization Project for HPV-associated lesions

To address this problem and to improve communication between the specialties, the Lower Anogenital Squamous Terminology (LAST) Standardization Project for HPV-Associated Lesions was convened, including five major working groups. The findings were first published in June 2012,^[1] with two further publications within the following 12 months in order to reach a broad audience.^{[2][3]}

The LAST Standardization Project working groups recognised a number of general principles:^[1]

- HPV-related squamous disease reflects a unified epithelial biology.
- Each cytological or histological sample provides only a statistical representation of the patient's true biology; the more samples or data points available, the more accurate the assessment of the patient's true biology.
- The true biology represents the risk for cancer at the current time, and the risk for cancer over time.
- Diagnostic variation can be improved by:
 - aligning the number of diagnostic terms with the number of biologically relevant categories
 - the use of biological markers.

The findings of the LAST project have been widely accepted and adopted by members of the Royal College of Pathologists of Australasia (RCPA) and the World Health Organization (WHO)^[4], and have been referenced in the first edition (2013) of the RCPA protocol for structured reporting of cervical carcinoma^[5].

Two tiered nomenclature

A two-tiered nomenclature system has been accepted for non-invasive HPV associated squamous proliferations of cervix and lower anogenital tract. The two groups are LSIL and HSIL. These two groups may be further characterised by the applicable intraepithelial neoplasia or –IN subcategory. The nomenclature addresses pre-invasive mucosal lesions and early invasive mucosal lesions.

Low-grade squamous intraepithelial lesion (LSIL)

LSIL is the morphologic expression of acute HPV infection and is characterised by cells with increased nuclear to cytoplasmic ratios and irregular nuclear membranes. Mitoses are limited to the lowermost third of the epithelium and maturation begins in the middle third. Multi-nucleation and perinuclear halos, characteristic of HPV effect, may be seen. LSIL encompasses changes previously called 'HPV effect' and CIN1 (pre-AMBS 2004). The LAST terminology does not support the distinction between these two categories because of poor inter-observer agreement, lack of clinical significance and the common underpinning biology. In cases with LSIL morphology, p16 staining should not be performed.

High-grade squamous intraepithelial lesion (HSIL)

HSIL is the morphologic expression of persistent HPV infection that has the potential to progress to invasive carcinoma. It is characterised by mitoses seen at any level of the epithelium, little to no cytoplasmic differentiation in the middle third and upper third, increased nuclear size, and irregular nuclear membranes. Where the pathologist is considering a diagnosis of CIN2, p16 staining should be performed.

The result for p16 is reported as positive if there is strong and diffuse block staining for p16. In squamous epithelia, this is defined as continuous strong nuclear, or nuclear plus cytoplasmic, staining of the basal cell layer with extension upward involving at least one-third of the epithelial thickness.^[2] The LAST Standardization Project group notes that this height restriction is somewhat arbitrary but adds specificity, and that full-thickness staining or extension into the upper third or upper half is specifically not required to call a specimen positive.^[2]

When the p16 stain is negative the lesion is either LSIL or a mimic of HSIL and, accordingly, should not be diagnosed as HSIL.

HSIL encompasses lesions previously called 'CIN2' and 'CIN3'. The following subcategories should continue to be used:

- HSIL (CIN2) – used when p16 positive
- HSIL (CIN3).

This practice will enable continued measurement of the prevalence of CIN3 in Australian women during and after transition to the renewed NCSP.

Superficially invasive squamous cell carcinoma (SISCCA)

The term 'microinvasive carcinoma' is no longer recommended, and the term 'superficially invasive squamous cell carcinoma' (SISCCA) should be used instead. It is recognised that SISCCA has a favourable prognosis.

A report including the finding of SISCCA must include a comment on the presence or otherwise of lymphatic invasion and a comment on the number and size of multifocal carcinomas, once the presence of a single carcinoma is excluded. The International Federation of Gynecology and Obstetrics (FIGO) staging should be based on the highest FIGO stage of an individual focus, rather than adding multiple foci together.^[6]

Squamous cell carcinoma (SCC)

Squamous cell carcinoma is an invasive epithelial tumour showing variably differentiated squamous cells.^[2] The majority are of large cell keratinizing type, demonstrating sheet-like growth, with surrounding desmoplastic stromal response. Virtually all SCCs are thought to arise from a pre-cancerous intraepithelial lesion (HSIL).^[2]

Biomarkers

The LAST group assessed data on p16, Ki-67 (Mib1), ProEx C, L1, HPV 16/18 mRNA, telomerase/TERC, and HPV genotyping. It concluded that p16 was the only biomarker for which there was sufficient evidence to recommend its use for distinguishing between types of mucosal pre-cancerous lesions. Staining for p16 is particularly useful for lesions with inflammation or atrophy, lesions affected by diathermy, and thin lesions.

Glandular proliferations

Adenocarcinoma in-situ (AIS)

'Adenocarcinoma in situ' (AIS) is the only currently recommended term in Australasia for glandular mucosal pre-invasive lesions.^[8] The term 'glandular dysplasia' is not currently used in Australia, but has been used historically and is in use in the United Kingdom (where the synonym is 'low grade cervical glandular intraepithelial neoplasia').^[9]

AIS is an intraepithelial lesion containing malignant-appearing glandular epithelium. Nuclei are hyperchromatic and stratified, mitoses are frequently seen towards the apex of the cell, and apoptotic debris may be seen towards the base of the cell. The use of p16 can be very effective in distinguishing AIS from mimics including tubular metaplasia following previous surgical treatment.^[9]

Invasive adenocarcinoma of cervix

Adenocarcinoma of cervix is an invasive epithelial tumour showing glandular differentiation.^[7] There is significant morphological overlap with adenocarcinoma in situ. However, clues to the invasive nature of the lesion include a desmoplastic stromal response, small angulated claw-like glands branching from the areas of AIS and complex architectural proliferations such as solid, papillary cribriform and labyrinthine growth patterns.^[10] Several subtypes are currently recognised.^{[7][11]}

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Supplement: Sample cervical screening reports

CERVICAL SCREENING	LOW RISK FOR SIGNIFICANT CERVICAL ABNORMALITY
SPECIMEN	Cervical – ThinPrep
TEST RESULTS	PCR for Oncogenic HPV and genotype: <ul style="list-style-type: none"> • HPV 16 – Not detected • HPV 18 – Not detected • HPV (not 16/18) – Not detected
RECOMMENDATION	Rescreen in five years.

CERVICAL SCREENING	UNSATISFACTORY
SPECIMEN	Cervical – SurePath
TEST RESULTS	PCR for Oncogenic HPV and genotype: Unsatisfactory
RECOMMENDATION	Retest within six weeks.

CERVICAL SCREENING	UNSATISFACTORY
SPECIMEN	Cervical – ThinPrep
TEST RESULTS	PCR for Oncogenic HPV and genotype: <ul style="list-style-type: none"> • HPV 16 – Not detected • HPV 18 – Not detected • HPV (not 16/18) – Detected Liquid Based Cytology (LBC), Image assisted: Unsatisfactory
RECOMMENDATION	Repeat screening test in six weeks.

CERVICAL SCREENING	INTERMEDIATE RISK FOR SIGNIFICANT CERVICAL ABNORMALITY
SPECIMEN	Cervical – SurePath
TEST RESULTS	PCR for Oncogenic HPV and genotype: <ul style="list-style-type: none"> • HPV 16 – Not detected • HPV 18 – Not detected • HPV (not 16/18) – Detected Liquid Based Cytology (LBC), Manually Read: There is no evidence of a squamous intraepithelial lesion or malignancy Endocervical component: Present
RECOMMENDATION	Repeat test in 12 months.

CERVICAL SCREENING	INTERMEDIATE RISK FOR SIGNIFICANT CERVICAL ABNORMALITY
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SPECIMEN	Cervical – SurePath
TEST RESULTS	PCR for Oncogenic HPV and genotype: <ul style="list-style-type: none"> • HPV 16 – Not detected • HPV 18 – Not detected • HPV (not 16/18) – Detected Liquid Based Cytology (LBC), Image Assisted: Low grade intra-epithelial lesion (LSIL) Endocervical component: Present
RECOMMENDATION	Repeat test in 12 months.

CERVICAL SCREENING	HIGHER RISK FOR SIGNIFICANT CERVICAL ABNORMALITY
SPECIMEN	Cervical – ThinPrep
TEST RESULTS	PCR for Oncogenic HPV and genotype: <ul style="list-style-type: none"> • HPV 16 – Not detected • HPV 18 – Detected • HPV (not 16/18) – Not detected Liquid Based Cytology (LBC), Manually Read: High grade squamous intra-epithelial lesion (HSIL) Endocervical component: Present
RECOMMENDATION	Referral for Colposcopic assessment.

CERVICAL SCREENING	HIGHER RISK FOR SIGNIFICANT CERVICAL ABNORMALITY
SPECIMEN	Cervical – SurePath
TEST RESULTS	PCR for Oncogenic HPV and genotype: <ul style="list-style-type: none"> • HPV 16 – Detected • HPV 18 – Not detected • HPV (not 16/18) – Not detected Liquid Based Cytology (LBC), Manually Read: Unsatisfactory
RECOMMENDATION	Referral for Colposcopic assessment.

CERVICAL SCREENING	HIGHER RISK FOR SIGNIFICANT CERVICAL ABNORMALITY
SPECIMEN	Cervical – ThinPrep
TEST RESULTS	PCR for Oncogenic HPV and genotype: <ul style="list-style-type: none"> • HPV 16 – Not detected • HPV 18 – Not detected • HPV (not 16/18) – Detected Liquid Based Cytology (LBC), Image Assisted: Possible high grade squamous intra-epithelial lesion (pHSIL) Endocervical component: Not identified
RECOMMENDATION	Referral for Colposcopic assessment.

CERVICAL SCREENING	HIGHER RISK FOR SIGNIFICANT CERVICAL ABNORMALITY
SPECIMEN	Cervical – SurePath
TEST RESULTS	PCR for Oncogenic HPV and genotype: <ul style="list-style-type: none"> • HPV 16 – Detected • HPV 18 – Not detected • HPV (not 16/18) – Detected Liquid Based Cytology (LBC), Manually Read: High grade squamous intra-epithelial lesion (HSIL) Endocervical component: Not identified
RECOMMENDATION	Referral for Colposcopic assessment.

CERVICAL SCREENING	HIGHER RISK OF SIGNIFICANT CERVICAL ABNORMALITY
SPECIMEN	Cervical – ThinPrep
TEST RESULTS	PCR for Oncogenic HPV and genotype: <ul style="list-style-type: none"> • HPV 16 – Detected • HPV 18 – Not detected • HPV (not 16/18) – Not detected Liquid Based Cytology (LBC), Image Assisted: There is no evidence of a squamous intraepithelial lesion or malignancy Endocervical component: Present
RECOMMENDATION	Referral for Colposcopic assessment.

CERVICAL SCREENING	HIGHER RISK OF SIGNIFICANT CERVICAL ABNORMALITY
SPECIMEN	Cervical – SurePath
TEST RESULTS	PCR for Oncogenic HPV and genotype: <ul style="list-style-type: none"> • HPV 16 – Not detected • HPV 18 – Not detected • HPV (not 16/18) – Detected Liquid Based Cytology (LBC), Manually Read: There is no evidence of a squamous intraepithelial lesion or malignancy Endocervical component: Present
RECOMMENDATION	In view of the previously reported abnormality referral for colposcopic assessment.

CERVICAL SCREENING	HIGHER RISK OF SIGNIFICANT CERVICAL ABNORMALITY
SPECIMEN	Cervical – ThinPrep
TEST RESULTS	PCR for Oncogenic HPV and genotype: <ul style="list-style-type: none"> • HPV 16 – Not detected • HPV 18 – Not detected • HPV (not 16/18) – Detected

	Liquid Based Cytology (LBC), Image Assisted: Low grade squamous intra-epithelial lesion (LSIL) Endocervical component: Present
RECOMMENDATION	In view of the previously reported abnormality referral for colposcopic assessment.

CERVICAL SCREENING	HIGHER RISK OF SIGNIFICANT CERVICAL ABNORMALITY
SPECIMEN	Cervical – SurePath
TEST RESULTS	PCR for Oncogenic HPV and genotype: <ul style="list-style-type: none"> • HPV 16 – Not detected • HPV 18 – Not detected • HPV (not 16/18) – Detected Liquid Based Cytology (LBC), Manually Read: Atypical endocervical cells of undetermined significance There is no evidence of a squamous intraepithelial lesion or malignancy
RECOMMENDATION	Referral for colposcopic assessment by a gynaecologist with expertise in the evaluation of suspected malignancies or by a gynaecological oncologist.

CERVICAL SCREENING	HIGHER RISK OF SIGNIFICANT CERVICAL ABNORMALITY
SPECIMEN	Cervical – ThinPrep
TEST RESULTS	PCR for Oncogenic HPV and genotype: <ul style="list-style-type: none"> • HPV 16 – Not detected • HPV 18 – Detected • HPV (not 16/18) – Not detected Liquid Based Cytology (LBC), Image Assisted: Possible high grade glandular lesion The findings suggest possible adenocarcinoma-in-situ
RECOMMENDATION	Referral for colposcopic assessment by a gynaecologist with expertise in the evaluation of suspected malignancies or by a gynaecological oncologist.

CERVICAL SCREENING	HIGHER RISK OF SIGNIFICANT CERVICAL ABNORMALITY
SPECIMEN	Cervical – ThinPrep
TEST RESULTS	PCR for Oncogenic HPV and genotype: <ul style="list-style-type: none"> • HPV 16 – Detected • HPV 18 – Not detected • HPV (not 16/18) – Not detected Liquid Based Cytology (LBC) Image Assisted: Squamous cell carcinoma There are abnormal cells that indicate origin from an invasive squamous cell carcinoma Endocervical component: Present

RECOMMENDATION	Colposcopy is recommended. Patient should be referred to a gynaecological oncologist or a gynaecological cancer centre for assessment.
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CERVICAL SCREENING	HIGHER RISK OF SIGNIFICANT CERVICAL ABNORMALITY
SPECIMEN	Cervical – SurePath
TEST RESULTS	PCR for Oncogenic HPV and genotype: <ul style="list-style-type: none"> • HPV 16 – Not detected • HPV 18 – Detected • HPV (not 16/18) – Not detected Liquid Based Cytology (LBC), Manually Read: Endocervical adenocarcinoma
RECOMMENDATION	Colposcopy is recommended. Patient should be referred to a gynaecological oncologist or a gynaecological cancer centre for assessment.

Sample stand alone LBC reports

SPECIMEN	Cervical – SurePath
TEST RESULTS	Liquid Based Cytology (LBC) Manually Read: Low grade squamous intra-epithelial lesion (LSIL) Endocervical component: Present
RECOMMENDATION	This woman is under specialist management, therefore no management recommendation is made.

SPECIMEN	Cervical – ThinPrep
TEST RESULTS	Liquid Based Cytology (LBC) Image assisted: High grade squamous intra-epithelial lesion (HSIL) Endocervical component: Present
RECOMMENDATION	This woman is under specialist management, therefore no management recommendation is made.

Reports for self-collected samples

CERVICAL SCREENING	LOW RISK OF SIGNIFICANT CERVICAL ABNORMALITY
SPECIMEN	Lower vaginal sample – Self-collected
TEST RESULTS	PCR for Oncogenic HPV and genotype: <ul style="list-style-type: none"> • HPV 16 – Not detected • HPV 18 – Not detected • HPV (not 16/18) – Not detected
RECOMMENDATION	Rescreen in five years.

CERVICAL SCREENING	
SPECIMEN	Lower vaginal sample – Self collected
TEST RESULTS	PCR for Oncogenic HPV and genotype: <ul style="list-style-type: none"> • HPV 16 – Not detected • HPV 18 – Not detected • HPV (not 16/18) – Detected
RECOMMENDATION	Collect a cervical sample for LBC within six weeks.

CERVICAL SCREENING	HIGHER RISK OF SIGNIFICANT CERVICAL ABNORMALITY
SPECIMEN	Lower vaginal sample – Self collected
TEST RESULTS	PCR for Oncogenic HPV and genotype: <ul style="list-style-type: none"> • HPV 16 – Detected • HPV 18 – Not detected • HPV (not 16/18) – Not detected
RECOMMENDATION	Refer for colposcopic assessment. Cervical sample for LBC can be obtained at time of that assessment.

CERVICAL SCREENING	UNSATISFACTORY
SPECIMEN	Lower vaginal sample – Self collected
TEST RESULTS	PCR for Oncogenic HPV and genotype: Unsatisfactory
RECOMMENDATION	Retest within six weeks.

4. Unsatisfactory cervical screening results

[Guideline contents](#) > [4. Unsatisfactory cervical screening results](#)

Author(s):

- [A/Professor Marion Saville](#) — Author
- [A/Prof Lyndal Anderson](#) — Co-author
- [Professor Ian Hammond](#) — Co-author
- [Professor Gordon Wright](#) — Co-author
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

In the renewed National Cervical Screening Program (NCSP), unsatisfactory screening results may occur either because the HPV test cannot be performed or because liquid-based cytology (LBC), when indicated, cannot be evaluated.

Unsatisfactory HPV tests

HPV tests can be unsatisfactory because of the effects of inhibition or, in the case of some tests, because the internal control failed to demonstrate the presence of human DNA in the sample. If the HPV test cannot be performed, then the screening episode should be classified and reported as 'Unsatisfactory'.

Unsatisfactory LBC

The Bethesda System 2014 (TBS 2014)^[1] defines an unsatisfactory LBC preparation as one with fewer than 5000 well-visualised, well-preserved squamous or squamous metaplastic cells. TBS 2014 provides extensive practical guidance for laboratories.^[1]

Practice point

REC4.1: Attempt adequate repeat preparations for an unsatisfactory LBC test

In the case of unsatisfactory LBC, laboratories should ensure that adequate repeat preparations are attempted, after dealing with potentially remediable technical problems.

When reflex LBC is unsatisfactory in a case where it was required to determine whether the woman should be referred for colposcopic assessment or should have a repeat test in 12 months, then the screening episode should be classified as 'Unsatisfactory' and retesting in 6 weeks should be recommended.

At retesting, the repeat sample should not be tested for HPV. The laboratory should undertake LBC and then prepare a cervical screening report combining the results of the original HPV test and the repeat LBC (see Preparation of cervical screening reports in [Chapter 3. Terminology](#)). It is anticipated that the support of the NCSR will be critical in this circumstance.

When reflex LBC is unsatisfactory, but the woman requires colposcopic referral regardless of the LBC result, then the screening episode should be reported as 'Higher risk for significant cervical abnormality'. LBC should then be performed at the time of colposcopy.

Application

The laboratory should state why the screening sample is unsatisfactory: either because the HPV test or the LBC could not be completed. In the case of unsatisfactory LBC, the laboratory should report why the sample is unsatisfactory.

Practice point

REC4.2: Report cellular abnormality for LBC specimens with abnormal cells

Any LBC specimen with abnormal cells should not be reported as 'Unsatisfactory'. The identified cellular abnormality should be reported.

Management of Unsatisfactory Screening Samples

Practice point

REC4.3: Recall women in 6–12 weeks if they have an unsatisfactory screening report

A woman with an unsatisfactory screening report should have a repeat sample collected in 6–12 weeks. If the reason for the unsatisfactory sample has been identified then this problem should be corrected if possible before the repeat sample is collected.

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5. Benefits, harms and cost-effectiveness in renewed NCSP

Author(s):

- [Professor Karen Canfell](#) — Author
- [Professor Ian Hammond](#) — Co-author
- [A/Professor Marion Saville](#) — Co-author
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

Introduction

All screening programs involve the balancing of benefits, potential harms and cost-effectiveness considerations.

The benefits of cervical screening include the early detection and treatment of cervical abnormalities, and a reduction in the incidence of invasive cervical cancer and associated mortality.

Potential harms include the psychosocial impact of receiving an abnormal screening result and being referred for subsequent colposcopy and treatment. Treatment of the cervix may be unnecessary for some lesions that would have regressed without treatment. There is some evidence to suggest that treatment may adversely affect obstetric outcomes in a small proportion of women.^{[1][2]} Assessment of the utilisation of health resources considers the impact of cervical screening on clinical services, including colposcopy and treatment. Assessment of the cost-effectiveness of cervical screening considers the total costs of the program and also the benefits in terms of life-years saved in relation to the total costs involved in screening, management of detected abnormalities, and treatment for invasive cervical cancer.

Methods for predicting benefits, harms and cost-effectiveness

A modelling approach was used to predict the impact on the benefits, harms, cost-effectiveness and resource utilisation for the renewed National Cervical Screening Program (NCSP) in conjunction with these guidelines (see [Appendix A. Modelled evaluation of the predicted benefits, harms and cost-effectiveness of the renewed National Cervical Screening Program \(NCSP\) in conjunction with these guideline recommendations](#)). The estimates presented here are an update of predictions that underpinned the Medical Services Advisory Committee (MSAC) recommendations,^[2] revised to take into account the specific recommendations of this guideline.

We have used the same model platform that was used for the MSAC evaluation. This platform has been used for a number of HPV vaccination evaluations as well as screening technology, screening interval and screening management evaluations performed on behalf of national cervical screening programs in Australia, New Zealand and England. Details of the modelling methods, and the updates to model pathways that were made in order to take into account these guideline recommendations, are provided in the [Technical report](#).

The model incorporated assumptions about adherence to screening in the renewed NCSP after taking into account the introduction of a call-and-recall system for screening. The specific assumptions for adherence were described in detail in the MSAC evaluation and are

summarised in the [Technical report](#). The predicted impact of the renewed NCSP, and associated cervical cancer incidence and mortality reductions, are predicated on achieving the level of adherence assumed.

Benefits

The impact of the renewed NCSP on predicted cervical cancer cases, deaths, colposcopies and treatments for cervical intraepithelial neoplasia (CIN) grades 2–3 (CIN2/3) is shown in Table 5.1. Taking into account the recommendations of these guidelines, the model predicts the following outcomes of the renewed NCSP:

- **For unvaccinated cohorts** (i.e. assuming vaccination had not been introduced) the model predicts a 31% reduction in cervical cancer incidence and a 36% reduction in cervical cancer mortality, compared with the pre-renewal NCSP – equivalent to 265 fewer cancer cases and 82 fewer cancer deaths annually.
- **For cohorts offered HPV vaccination as 12-year-olds** the model predicts a 24% reduction in cervical cancer incidence and a 29% reduction in cervical cancer mortality, compared with the pre-renewal NCSP – equivalent to 85 fewer cancer cases and 28 fewer deaths annually.

See also: [Appendix A. Modelled evaluation of the predicted benefits, harms and cost-effectiveness of the renewed National Cervical Screening Program \(NCSP\) in conjunction with these guideline recommendations.](#)

Table 5.1. Predicted annual numbers of cervical cancer cases and deaths for the pre-renewal NCSP and the renewed NCSP (showing differences in case numbers and relative percentage differences)*

	Pre-renewal NCSP		Renewed NCSP	
	If HPV vaccination had not been introduced	For cohorts offered vaccination as 12 year olds	If HPV vaccination had not been introduced	For cohorts offered vaccination as 12 year olds
Cervical cancer cases	850	353	584 (-265; -31%)	267 (-85; -24%)
Cervical cancer deaths	227	94	145 (-82; -36%)	66 (-28; -29%)

Note: Figures are based on* the female Australian population as predicted for 2017.

Potential harms

Model predictions for impact on colposcopies and treatments

The impact of the renewed NCSP on colposcopies and treatments predicted by the model is shown in Table 5.2. Compared with the pre-renewal NCSP, a 36% increase in colposcopies is predicted if HPV vaccination had not been introduced, but a 7% decrease in colposcopies is predicted in cohorts offered vaccination as 12-year-olds. Although there would have been a substantial increase in colposcopies if HPV vaccination had not been introduced, it should be noted that 70% of these additional colposcopies would have occurred in women less than 35 years of age. However, all of these women will have been offered vaccination by 2017, when these new clinical guidelines will be implemented.

Similarly, a 6% increase in treatments is predicted for CIN2/3 in cohorts not offered HPV vaccination, but a 5% decrease in treatments is predicted for CIN2/3 in cohorts offered vaccination.

For cohorts offered HPV vaccination, overall outcomes for colposcopy and treatment-related harms under the renewed NCSP are expected to be as good or better than for cohorts offered vaccination but managed under the pre-renewal NCSP.

See also: [Appendix A. Modelled evaluation of the predicted benefits, harms and cost-effectiveness of the renewed National Cervical Screening Program \(NCSP\) in conjunction with these guideline recommendations.](#)

Table 5.2. Predicted annual numbers of colposcopies and treatments for CIN2/3 for the pre-renewal NCSP and the renewed NCSP (showing differences in case numbers and relative percentage differences)*

	Pre-renewal NCSP		Renewed NCSP	
	If HPV vaccination had not been introduced	For cohorts offered vaccination as 12 year olds	If HPV vaccination had not been introduced	For cohorts offered vaccination as 12 year olds
Colposcopies	85,795	60,995	116,889 (+31,094; +36%)	56,479 (-4,516; -7%)
Treatments for CIN2/3	22,661	13,899	23,963 (+1,302; +6%)	13,240 (-659; -5%)

Note: *Figures are based on the female Australian population as predicted for 2017.

Potential fertility and early pregnancy outcomes

It has been suggested that treatment for CIN2/3 could adversely affect fertility by causing cervical stenosis and a decreased volume of mucus due to the destruction of endocervical glands.^{[3][4]} A systematic review of the literature identified only a few studies, mostly of small size, investigating fertility outcomes in treated women.^[5] Based on a pooled analysis of four studies, the overall pregnancy rate in treated women was reported to be higher than in untreated women although significant heterogeneity was observed between the primary studies.^[6] A Finnish study investigating the use of in-vitro fertilisation (IVF) among women who had undergone treatment for CIN found that the rate of IVF deliveries was not increased after cervical conisation or ablation.^[6] A meta-analysis of studies also reported that treatment did not affect the proportion of women who needed more than 12 months to conceive.^[5]

A meta-analysis also found no effect of treatment on overall rates of miscarriage or of miscarriage during the first trimester.^[5] The risk of miscarriage in the second trimester was found to be higher in treated women, compared with untreated women, with the pooled estimate driven primarily by one large study.^[7] However, the design of these studies cannot establish a causal link between treatment and second trimester miscarriage, because other factors cannot be excluded.^[8]

Potential obstetric complications

Treatment for cervical abnormalities has been associated with subsequent obstetric complications in some studies. A 2006 meta-analysis of observational studies found significantly increased risks of preterm delivery (< 37 weeks), low birth weight (< 2500 g) and preterm premature rupture of membranes among treated women, compared with untreated women.^[9] A subsequent meta-analysis reported that cold-knife cone biopsy and ablation by radical diathermy were associated with significantly higher risks of perinatal mortality, severe preterm

delivery (< 32/34 weeks) and extreme preterm delivery (< 28/30 weeks), unlike other therapies.^[10] The effects of treatment on preterm delivery have been confirmed by some,^{[11][12][7]} but not all^{[13][14]} subsequent studies. A recent study in England reported an increased risk of preterm delivery among first, second and subsequent births with increasing depth of excision (when compared with small excisions of less than 10 mm).^[15]

While the evidence generally suggests an increased risk of obstetric complications following treatment, some evidence suggests that this depends on the depth of excision and amount of cervical tissue removed. Potential confounding factors must also be considered, since even in women with untreated CIN2/3 the risk of preterm delivery may be elevated (possibly due to the presence of risk factors in this group of women that are directly associated with preterm delivery).^{[14][16][17]}

Psychosocial effects

The psychosocial aspects of cervical screening and clinical management of detected abnormalities in the renewed NCSP are discussed in [Chapter 19. Psychosocial issues](#).
Cost-effectiveness

Table 5.3 shows the estimated cost of the NCSP before and after renewal. If HPV vaccination had not been introduced, a 19% reduction in program costs would have been predicted under the renewed NCSP. For cohorts offered vaccination, a 26% reduction in costs is predicted under the renewed NCSP. This is equivalent to a cost saving of \$41 million per annum for unvaccinated cohorts and \$50 million per annum for cohorts offered vaccination. It should be noted that these cost savings may not be fully realised, since they are predicated on the assumption that there will be an overall reduction in GP visits due to a reduced number of screening visits. However, in practice these screening visits may be replaced by routine visits for other conditions with no obvious reduction in costs to the health system.

Since the renewed NCSP is predicted to be both cost saving and life-year saving, it is not possible to calculate an incremental cost-effectiveness ratio compared with the pre-renewal NCSP. Table 5.3 shows the disaggregated discounted costs and life-years predicted for the pre-renewed NCSP and the renewed NCSP.

See also: [Appendix A. Modelled evaluation of the predicted benefits, harms and cost-effectiveness of the renewed National Cervical Screening Program \(NCSP\) in conjunction with these guideline recommendations](#).

Table 5.3. Predicted annual cost of the program and the predicted discounted costs and effects for the pre-renewed NCSP and the renewed NCSP (showing differences in costs and relative percentage differences)*

	Pre-renewal NCSP		Renewed NCSP	
	If HPV vaccination had not been introduced	For cohorts offered vaccination as 12 year olds	If HPV vaccination had not been introduced	For cohorts offered vaccination as 12 year olds
Annual cost* of the screening program	\$223 million	\$192 million	\$182 million	\$142 million
Discounted costs^	\$383	\$325	(\$41 million; – 19%) \$304	(\$50 million; – 26%) \$227
Discounted life-years^	21.6219	21.6239	21.6229	21.6242

Note: Figures are based on* the female Australian population as predicted for 2017.

^Discounting at 5% per annum starting from 12 years of age.

Impact on clinical practice

The rate of detection of CIN grade 2 and higher (CIN2+) lesions has been reported to increase initially after the transition from cytology-based screening to HPV test-based screening.^[18] Accordingly, a transient increase in detected CIN2+ lesions is expected in Australia after the introduction of HPV screening. This may lead to a transient parallel increase in treatments. This increase would be offset later by a lower rate of detection of CIN grade 3 and higher (CIN3+), due to increased detection and treatment of lower-grade lesions.^[19] Direct referral to colposcopy due to a positive oncogenic HPV (16/18) test result is not expected to result in high colposcopy referral rates among Australian women, due to high uptake of HPV 16/18 vaccination in cohorts born in 1981 or later following the National HPV Vaccination Program, which commenced in April 2007.^[20] Overall, colposcopy referrals are expected to fall markedly as the rate of HPV 16/18 infection declines over time.

To minimise potential harms, MSAC recommended that use of the HPV test is limited to use in healthcare settings that can provide patient counselling, clinical interpretation of results, patient follow-up and confirmatory testing for positive results when required, in addition to testing in a safe environment with infection control procedures.^[20] This is important for all women, especially for those who choose to self-collect HPV test samples (see [Self-collected samples](#) in Chapter 6. Management of HPV test results).

Colposcopic assessment and management will be more challenging in the renewed NCSP because there will be a higher proportion of women with a positive oncogenic HPV test result but minimal or no cytological changes.

Barriers to implementation

Education for primary care health professionals and the public will be necessary to support implementation of the renewed NCSP and these clinical management guidelines. It is essential that health professionals have an understanding of the purpose, strategy, benefits and safety of primary HPV screening. If this is not achieved, there may be some resistance to full implementation of these changes.

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6. Management of Oncogenic HPV test results

Author(s):

- [Professor Bruce Armstrong](#) — Co-author
- [A/Professor Alison Brand](#) — Co-author
- [Professor Karen Canfell](#) — Co-author
- [Professor Ian Hammond](#) — Co-author
- [A/Professor Marion Saville](#) — Co-author
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#)
— Co-author

See the following sections:

- [Medical Services Advisory Committee recommendations for HPV testing](#)
- [Oncogenic HPV types not detected](#)
- [Oncogenic HPV types 16 and/or 18](#)
- [Oncogenic HPV types not 16/18](#)
- [Self-collected cervical samples](#)
- [Women undergoing exit testing](#)
- [Screening in women older than 75](#)
- [Discussion: Management of oncogenic HPV test results](#)

Medical Services Advisory Committee recommendations for HPV testing

Author(s):

- [Professor Ian Hammond](#) — Contributor
- [A/Professor Marion Saville](#) — Co-author
- [A/Professor Megan Smith](#) — Co-author
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

In 2014 the Medical Services Advisory Committee (MSAC) recommended that the National Cervical Screening Program (NCSP) adopt human papillomavirus (HPV) testing for cervical screening at 5-yearly intervals.^[1]

After considering the strength of the available evidence in relation to the safety, clinical and cost-effectiveness of a cervical screening pathway for the NCSP, MSAC supported public funding for the following:^[1]

- five-yearly cervical screening using a primary HPV test with partial HPV genotyping and reflex liquid-based cytology (LBC) triage, for HPV vaccinated and unvaccinated women aged 25–69 years, with exit testing of women up to age 74 years
- self-collection of an HPV sample for an under-screened or never-screened woman, facilitated by a medical practitioner, nurse practitioner or other healthcare professional on behalf of a medical practitioner who also offers mainstream cervical screening
- a system of invitations and reminders to be sent to women aged 25–69 years, and exit communications to be sent to women aged 70–74 years of age, to ensure the effectiveness of the program
- de-listing of the existing cervical screening test MBS items over a 6- to 12-month transition period.

See [MSAC outcomes. Application No. 1276 – Renewal of the National Cervical Screening Program](#).

The renewed NCSP applies to both HPV-vaccinated and unvaccinated women. It involves a primary screening test for HPV with partial genotyping (to distinguish HPV types 16 and 18 from other oncogenic types) and reflex LBC testing for all women with a positive oncogenic HPV test result:

- Women who have a positive oncogenic HPV (16/18) test result are referred immediately to colposcopy, with reflex LBC results available to inform the colposcopy examination.
- For women with a positive oncogenic HPV (not 16/18) test result, LBC is used as a triage to determine whether they are referred for colposcopy, or for repeat HPV testing in 12 months.

MSAC advised that this screening strategy was safer, more effective and more cost-effective than the pre-renewal NCSP,^[1] which is based on 2-yearly screening using conventional cytology (the Pap test) in sexually active women between the ages of 18–20 and 69 years.

The MSAC recommendation was based on systematic review of evidence and a comprehensive modelled evaluation.^{[2][3][4]} The modelling for HPV primary screening with partial genotyping for HPV 16/18 indicated an expected reduction in cancer incidence and mortality of over 20% (if women were screened until age 70 years).^[3] Subsequent modelling, taking into account post-colposcopy management as recommended in these guidelines, has predicted that a 31–36%

reduction in incidence and mortality may be achievable in unvaccinated cohorts and a 24–29% reduction may be achievable in cohorts offered vaccination (see [Appendix A. Modelled evaluation of the predicted benefits, harms and cost-effectiveness of the renewed National Cervical Screening Program \(NCSP\) in conjunction with these guideline recommendations](#)).

These recommendations were accepted by the Australian Government in May 2015. [A revised NCSP policy has been developed](#) based on these recommendations and has been endorsed by the Standing Committee on Screening.

NCSP policy summary

Five-yearly cervical screening using a primary HPV test:
partial HPV genotyping and LBC triage
in HPV-vaccinated and unvaccinated women aged 25–69 years
exit testing of women up to age 74 years.
Source: National Cervical Screening Policy (2016)

2021 MSAC review

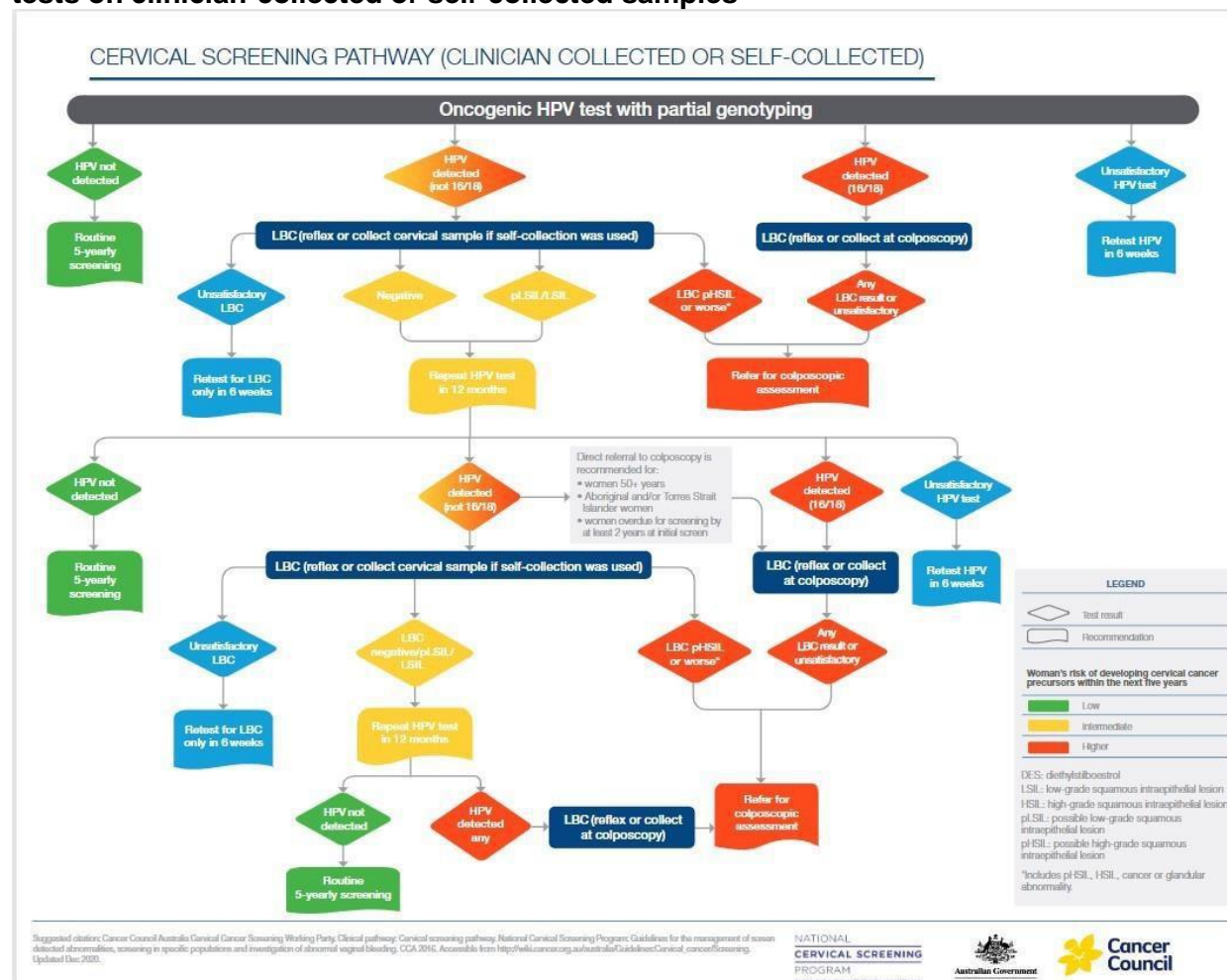
In 2021, the Medical Services Advisory Committee (MSAC) reviewed an application from the National Cervical Screening Program requesting expansion of the eligibility to participate in cervical screening using self-collection.¹ The Self-Collection Expert Advisory Group was convened to guide this review, and to provide advice on policy, implementation and consultation.

MSAC noted the large body of evidence showing no material difference in the diagnostic accuracy of HPV testing between using self-collected and clinician-collected samples (relative sensitivity = 0.98; 95% CI: 0.96 to 1.01; relative specificity = 0.99; 95% CI: 0.98 to 1.01).¹

MSAC concluded that HPV testing using self-collected samples is just as accurate as using clinician-collected samples. MSAC supported expanding access to self-collection to include everyone eligible for cervical screening, giving all eligible people a choice in how their screening sample is collected. MSAC considered self-collection to be safe and effective, and that it would likely increase participation in cervical screening.

MSAC advised that expanding self-collection is an important option to increase access to screening, particularly for people who may feel uncomfortable with a clinician collecting their sample. People who choose to use self-collection would still access cervical screening through their healthcare provider, to allow for education and engagement.

Flowchart 6.1 Cervical screening pathway for primary oncogenic HPV screening (HPV tests on clinician-collected or self-collected samples)



<https://www.cancer.org.au/assets/pdf/cervical-screening-pathway-flowchart-6.1-July-2022>

MSAC evidence-based recommendation

REC6.1: Eligibility for screening on a self-collected sample to include all people eligible for cervical screening (people with a cervix aged 25-74 years who have ever been sexually active)

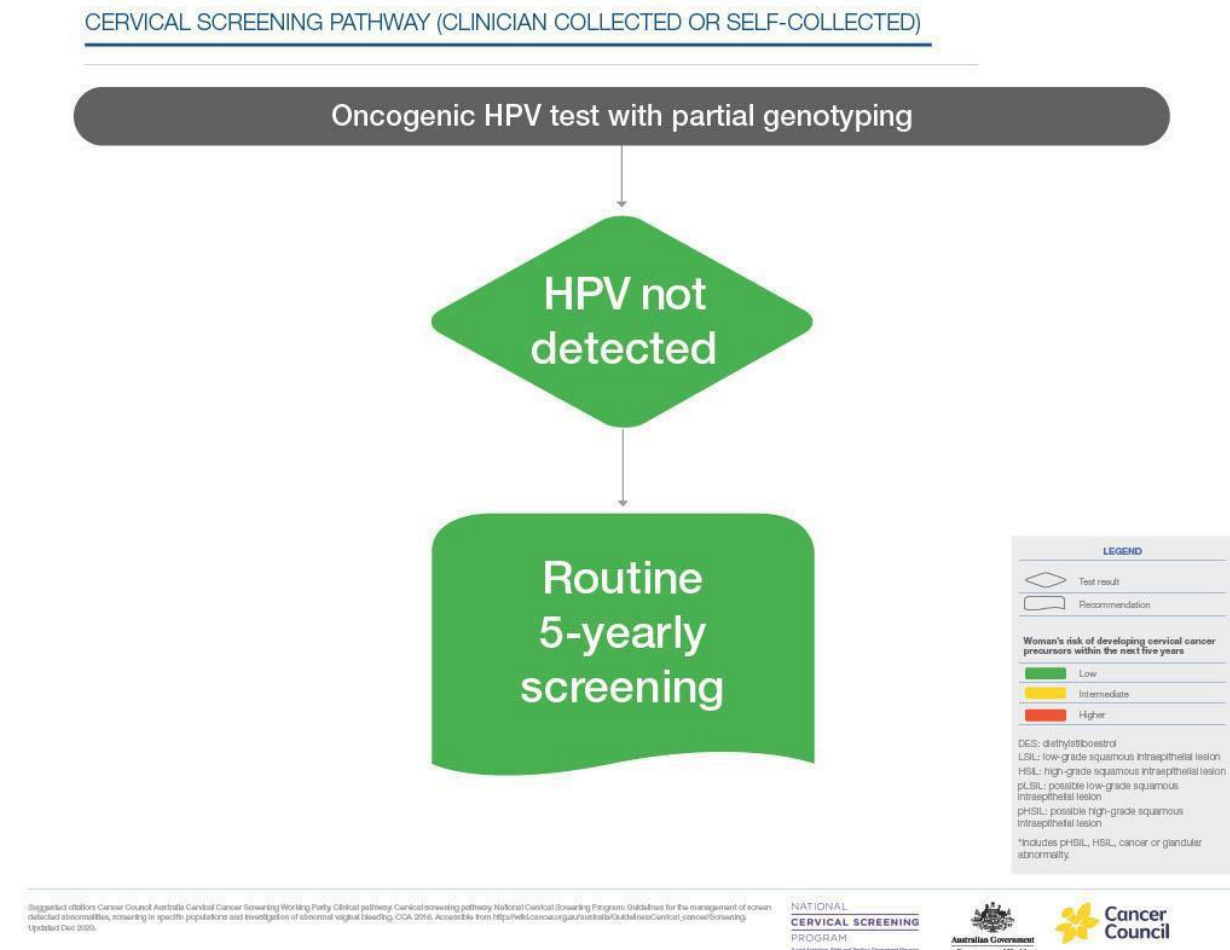
Anyone who is eligible for cervical screening should be offered the choice of HPV testing on a self-collected vaginal sample or on a clinician-collected sample.

Practice point

REC12.5: Data collection and recording Aboriginal and Torres Strait Islander status

Healthcare professionals should ask all patients whether they identify as Aboriginal or Torres Strait Islander, and a person's Aboriginal and Torres Strait Islander status should be recorded on relevant clinical records, including pathology request form in accordance with the Australian Bureau of Statistics classification and standards. Aboriginal and Torres Strait Islander status influences clinical management of tests in some cases.

Flowchart 6.2 Cervical screening pathway for primary oncogenic HPV testing HPV not detected



<https://www.cancer.org.au/assets/pdf/flowchart-6-2-cervical-screening-pathway-for-primary-oncogenic-hpv-testing-hpv-not-detected>

Practice point

REC6.2 Clinician-collected cervical samples

A short course of topical oestrogen therapy could be considered in post-menopausal women, people experiencing vaginal dryness, or trans men, prior to collecting the sample, for example daily for a period of at least 2 weeks, ceasing 1-2 days prior to the appointment. The reason for this should be explained (to reduce discomfort from the speculum and to improve the diagnostic accuracy of any associated LBC).

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Oncogenic HPV types not detected

Author(s):

- [Professor Karen Canfell](#) — Co-author
- [Professor Ian Hammond](#) — Co-author
- [A/Professor Marion Saville](#) — Co-author
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

Canfell,K, Hammond, I, Saville,M, Cancer Council Australia Cervical Cancer Screening Guidelines Working Party. Clinical question:Oncogenic HPV types not detected . In: National Cervical Screening Program: Guidelines for the management of screen-detected abnormalities, screening in specific populations and investigation of abnormal vaginal bleeding.

Women in whom oncogenic HPV types are not detected are at very low risk of cervical intraepithelial neoplasia grade 3 (CIN3) and cervical cancer for at least 5 years (see [Chapter 2. The rationale for primary HPV screening](#)).^{[1][2]} MSAC recommended that these women can continue 5-yearly screening (see [Medical Services Advisory Committee recommendations for HPV testing](#)).^[3]

MSAC evidence-based recommendation

REC6.3: Oncogenic HPV types not detected at routine screening

Women who have a screening HPV test in which oncogenic HPV types are **not** detected should rescreen in 5 years.

References

1. ↑ Katki HA, Kinney WK, Fetterman B, Lorey T, Poitras NE, Cheung L, et al. [Cervical cancer risk for women undergoing concurrent testing for human papillomavirus and cervical cytology: a population-based study in routine clinical practice](#). Lancet Oncol 2011 Jul;12(7):663-72 Available from: <http://www.ncbi.nlm.nih.gov/pubmed/21684207>.
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3. ↑ Medical Services Advisory Committee. [MSAC Outcomes. Application No. 1276 – Renewal of the National Cervical Screening Program](#). [homepage on the internet] Canberra: Australian Government Department of Health; 2014 [updated 2015 Apr]. Available from: [http://www.msac.gov.au/internet/msac/publishing.nsf/Content/FD36D6990FFAA639CA25799200058940/\\$File/1276%20-%20Final%20MSAC%20PSD%20-%20NCSP%20Renewal.pdf](http://www.msac.gov.au/internet/msac/publishing.nsf/Content/FD36D6990FFAA639CA25799200058940/$File/1276%20-%20Final%20MSAC%20PSD%20-%20NCSP%20Renewal.pdf).

Oncogenic HPV types 16 and/or 18

Women who have a positive oncogenic HPV test result indicating the presence of oncogenic HPV types 16 and/or 18, regardless of the presence of any other oncogenic types, should be managed according to the recommendations in this section.

These guidelines incorporate recommended HPV, cytology and histopathology terminology (see [Chapter 3. Terminology](#)).

Background

Cross-sectional and longitudinal follow-up studies have shown that HPV type 16 is associated with a higher cross-sectional and future risk of developing CIN grade 2 or higher (CIN2+) and CIN grade 3 or higher (CIN3+) than other oncogenic HPV types.^[1] Worldwide, oncogenic HPV types 16/18 are detected in approximately 70% of cervical cancers.^[2] Preliminary results from a recent Australian consecutive case series found that HPV types 16 and 18 were detected in 52.3% and 19.4% of cervical cancers, respectively.^[3]

HPV testing without genotyping has a high sensitivity but lower specificity for the detection of CIN2+ compared to cytology,^[4] so referral of all HPV-positive women for colposcopic assessment (especially in unvaccinated populations) would result in a large number of unnecessary colposcopy procedures. However, partial genotyping to detect the highest risk oncogenic HPV types 16/18 can be used to stratify risk after primary HPV screening and thus improve the specificity of the HPV test.

MSAC undertook systematic reviews and modelling analyses to assess the efficacy and safety of the partial genotyping strategy in which women with a positive oncogenic HPV (16/18) test result are referred to colposcopy, and those with a positive oncogenic HPV (not 16/18) test result are triaged by LBC. MSAC compared this and other HPV testing strategies with the cytological screening strategy used in the pre-renewal NCSP.

Evidence

MSAC systematic reviews

The details and results of the systematic reviews are described in the MSAC review of evidence report.^[1] No studies were identified that provided adequate evidence of the effect of HPV partial genotyping screening strategies on cervical cancer incidence or cervical cancer mortality rates in either vaccinated or unvaccinated populations.

See the [MSAC National Cervical Screening Program renewal: evidence review November 2013](#).

MSAC modelling

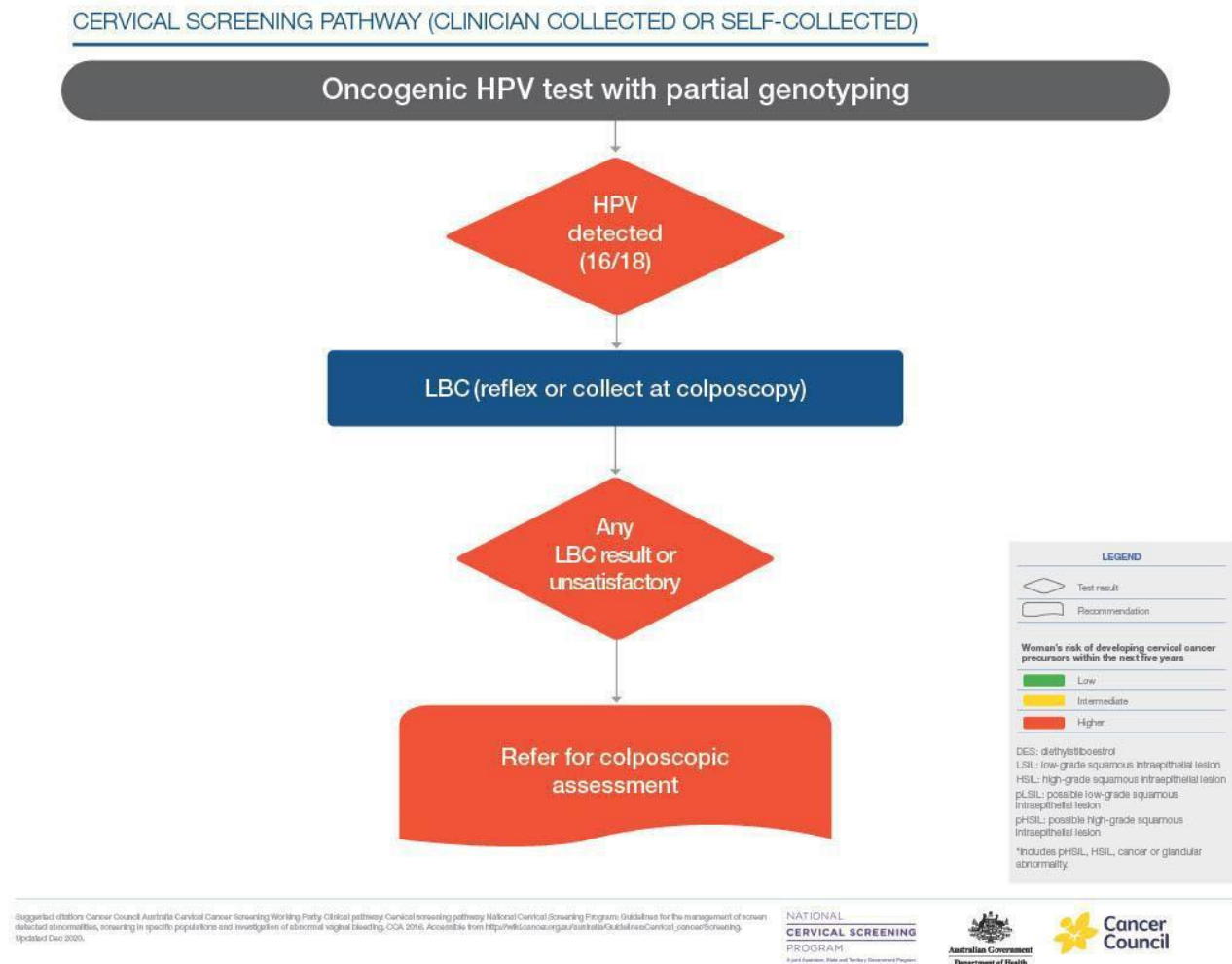
Given the limited evidence from systematic reviews, MSAC evaluated partial genotyping strategies in the Australian context using a comprehensive model to synthesise clinical trial evidence identified through systematic reviews and Australian data for screening participation, HPV vaccine uptake by age, and management practices.^[4]

The modelling approach, assumptions and options are described in the MSAC reports.^{[4][5]} The modelling for HPV primary screening with partial genotyping indicated an expected reduction in cancer incidence and mortality of over 20% (if women were screened until age 70 years).

See [MSAC outcomes. Application No. 1276 – Renewal of the National Cervical Screening Program](#).

Recommendations

Flowchart 6.3. Cervical screening pathway for primary oncogenic HPV screening (HPV tests on clinician-collected or self-collected samples): HPV16/18 detected



<https://www.cancer.org.au/assets/pdf/flowchart-6-3-cervical-screening-pathway-for-primary-oncogenic-hpv-screening-hpv-tests-on-clinician-collected-or-self-collected-samples-hpv16-18-detected>

MSAC evidence-based recommendation

REC6.4: Women with a positive HPV (16/18) test result

Women with a positive oncogenic HPV (16/18) test result should be referred directly for colposcopic assessment, which will be informed by the result of LBC. If the sample has been collected by a healthcare practitioner, then reflex LBC will be performed by the laboratory. If the sample was self-collected, then a sample for LBC should be collected at the time of colposcopy.

Consensus-based recommendation*

REC6.5 Referral of women with a positive HPV (16/18) test result and LBC prediction of invasive cancer to a gynaecological oncologist

Women who have a positive oncogenic HPV (16/18) test result with a reflex LBC report of invasive cancer (squamous, glandular or other) should be referred to a gynaecological oncologist or gynaecological cancer centre for urgent evaluation, ideally within 2 weeks.

Practice point

REC6.6: Referral of women with a positive HPV (16/18) test result and reflex LBC pHSIL/HSIL

Women with a positive oncogenic HPV (16/18) test result and reflex LBC prediction of pHSIL/HSIL should be referred for colposcopic assessment at the earliest opportunity, ideally within 8 weeks.

Practice point

REC6.7: Referral of women with a positive HPV (16/18) test result and unsatisfactory LBC

When HPV 16/18 is detected, colposcopic referral is required regardless of the LBC result and the screening episode should be classified as 'Higher risk for cervical cancer or precursors'. If reflex LBC is unsatisfactory or the screening sample has been self-collected a cervical sample, then LBC should be collected at the time of colposcopy.

Benefits and harms

When making the recommendation to refer women with a positive oncogenic HPV (16/18) test result directly for colposcopic assessment, MSAC took into account the benefits and harms and the health system implications of partial genotyping and immediate colposcopy in this group. Updated modelling, taking into account the recommendations in these guidelines, has informed an assessment of the benefits and harms of partial genotyping. The updated modelling used the same platform as that used for the MSAC evaluation (POLICY1-Cervix),^[5] and took into account the Renewed NCSP screening recommendations and management as specified in these guidelines. The findings are summarised in [Chapter 5. Benefits, harms and cost-effectiveness of cervical screening in the renewed National Cervical Screening Program \(NCSP\)](#).

Health system implications of these recommendations

Clinical practice

The referral of women with a positive oncogenic HPV (16/18) test result for colposcopy, regardless of the LBC prediction, is a major change to clinical practice and requires appropriate education and implementation.

Resourcing

When making this recommendation, MSAC took into account the resourcing issues for partial genotyping and the referral of women with a positive oncogenic HPV (16/18) test result for immediate colposcopy.

Updated modelling, taking into account these detailed Guideline recommendations, and taking into account the reduction in oncogenic HPV 16/18 infections due to vaccination in the population, has informed an assessment of the resourcing associated with partial genotyping strategies (see [Chapter 5. Benefits, harms and cost-effectiveness of cervical screening in the renewed National Cervical Screening Program \(NCSP\)](#)).

Barriers to implementation

A potential barrier is that GPs may not refer women who have a positive oncogenic HPV (16/18) test result to colposcopy, especially if the reflex LBC report is negative. However, the risk of this will be mitigated by the laboratory report to the GP clearly recommending referral and the NCSR follow-up protocols with reminder letters as needed.

A second potential barrier is that the woman may not fully understand the need for colposcopy, especially if the reflex LBC report is negative, and may not attend. NCSR reminder letters will play an important role in this situation.

References

1. ↑ ^{1.0 1.1} Medical Services Advisory Committee. *National Cervical Screening Program renewal: evidence review November 2013. MSAC Application No. 1276*. Canberra: Australian Government Department of Health; 2014 Available from: [http://www.cancerscreening.gov.au/internet/screening/publishing.nsf/Content/E6A211A6FFC29E2CCA257CED007FB678/\\$File/Review%20of%20Evidence%20notated%2013.06.14.pdf](http://www.cancerscreening.gov.au/internet/screening/publishing.nsf/Content/E6A211A6FFC29E2CCA257CED007FB678/$File/Review%20of%20Evidence%20notated%2013.06.14.pdf).
2. ↑ Clifford GM, Smith JS, Plummer M, Muñoz N, Franceschi S. *Human papillomavirus types in invasive cervical cancer worldwide: a meta-analysis*. Br J Cancer 2003 Jan 13;88(1):63-73 Available from: <http://www.ncbi.nlm.nih.gov/pubmed/12556961>.
3. ↑ Tabrizi S, Brotherton J, Saville M, et al. *The Australian Cervical Cancer Study (ACCTS)*. Data presented at HPV2015, Lisbon 2015; Abstract 347.
4. ↑ ^{4.0 4.1 4.2} Medical Services Advisory Committee. *National Cervical Screening Program renewal: executive summary. Report November 2013. MSAC application no. 1276. Assessment report*. Canberra: Australian Government Department of Health; 2014 Available from: [http://www.cancerscreening.gov.au/internet/screening/publishing.nsf/Content/E6A211A6FFC29E2CCA257CED007FB678/\\$File/Executive%20Summary%20notated%2013.6.14.pdf](http://www.cancerscreening.gov.au/internet/screening/publishing.nsf/Content/E6A211A6FFC29E2CCA257CED007FB678/$File/Executive%20Summary%20notated%2013.6.14.pdf).
5. ↑ ^{5.0 5.1} Medical Services Advisory Committee. *National Cervical Screening Program renewal: effectiveness modelling and economic evaluation in the Australian setting. Report November 2013. MSAC application 1276*. Canberra: Australian Government Department of Health; 2014 Available from: [http://www.cancerscreening.gov.au/internet/screening/publishing.nsf/Content/E6A211A6FFC29E2CCA257CED007FB678/\\$File/Renewal%20Economic%20Evaluation.pdf](http://www.cancerscreening.gov.au/internet/screening/publishing.nsf/Content/E6A211A6FFC29E2CCA257CED007FB678/$File/Renewal%20Economic%20Evaluation.pdf).

Oncogenic HPV types not 16/18

Women who have a positive oncogenic human papillomavirus (HPV) test result for which HPV types other than 16 and/or 18 are detected ('HPV not 16/18'), should be managed according to the recommendations in this section.

*Women who have a positive oncogenic HPV test result indicating the presence of **both** HPV type 16 and/or 18 **and** other oncogenic HPV types (**not** 16/18), for example, a woman whose test indicates the presence of types 16 and/or 18 and 31, or 18 and 33), should be managed as for HPV types 16/18 (see [Oncogenic HPV types 16/18](#)).*

Some HPV test platforms may provide additional channels with information on some of the other oncogenic HPV types (e.g. Type 31, 33 and/or 45). For the purposes of these guidelines, these HPV types should be considered as 'oncogenic HPV (not 16/18)' and women with these types should be managed accordingly.

These guidelines incorporate recommended HPV, cytology and histopathology terminology (see [3. Terminology](#)).

Author(s):

- [Professor Karen Canfell](#) — Author
- [A/Professor Marion Saville](#) — Author
- [A/Professor Megan Smith](#) — Author
- Professor Deborah Bateson – Co-author
- [A/Professor Alison Brand](#) — Co-author
- Ms Kirsteen Fleming – Co-author
- Dr Vivienne Milch – Co-author
- Dr Marsali Newman – Co-author
- A/Prof Lisa Whop – Co-author
- [Professor Bruce Armstrong](#) — Contributor
- [Professor Ian Hammond](#) — Contributor
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

Background 2016 analysis

MSAC recommended liquid-based cytology (LBC) triage for women with a positive oncogenic HPV (not 16/18),¹¹ but made no recommendations for subsequent management on the basis of triage LBC.

For some groups of women, it may be safe to delay colposcopy and monitor risk with follow-up surveillance, as distinct from women with a positive oncogenic HPV (16/18) test result, for whom MSAC recommended immediate colposcopy (see [Oncogenic HPV types 16/18](#)).

HPV infections typically clear rapidly. Overall, an estimated 67% of infections resolve by 12 months, although the rate of resolution probably varies between age groups and by HPV type. After viral clearance (i.e. oncogenic HPV is no longer detected), women are at very low risk of significant cervical disease for the next 5 years. Therefore, if women with a positive oncogenic HPV (not 16/18) test result are not referred to colposcopy immediately, 12 months is an appropriate follow-up interval for retesting and allows for viral clearance to occur in a proportion of women.

The modelled MSAC evaluation of partial genotyping strategies made the following assumptions:

- Women with pHSIL or a higher-grade lesion on LBC are referred for immediate colposcopy, irrespective of HPV type. This assumption is standard-of-care because these women are already known to be at risk of a high-grade lesion. Within the pre-renewal National Cervical Screening Program (NCSP), women with pHSIL are referred to immediate colposcopy.
- Women with a positive oncogenic HPV (not 16/18) test result who have negative LBC undergo follow-up surveillance at 12 months rather than immediate colposcopy.

The MSAC evaluation also modelled alternative management options for women with a LBC prediction of possible low-grade intraepithelial lesion (pLSIL) or low-grade intraepithelial lesion (LSIL) and a positive oncogenic HPV (not 16/18) test result. These women are at intermediate risk of significant cervical abnormality (see [Section 3. Terminology](#)). MSAC did not make recommendations for the follow-up of this group of women.^[1] Therefore, further systematic reviews and modelling analyses were undertaken to inform recommendations for this group. The updated modelled analysis considers the management pathways for colposcopy referral, colposcopic management, and post-treatment test-of-cure as specified in these guidelines, some of which differ from the assumptions made in the MSAC modelling. Therefore, the final modelled analysis considers the impact of changing recommendations for this group on outcomes and costs (see [Section 5. Benefits, harms and cost-effectiveness of cervical screening in the renewed NCSP](#) and [Modelling reports.](#))

2020 analysis

In April 2020, the NCSP reviewed program data relating to biopsy outcomes in women referred to colposcopy following persistent detection of oncogenic HPV (not 16/18) at their 12-month follow-up HPV test, where LBC was either negative, pLSIL or LSIL.^[2]

As a result, an update was made to the management of HPV (not 16/18) – such that if HPV (not 16/18) continues to be detected at 12 months and reflex LBC does not predict a possible high-grade squamous intraepithelial lesion (pHSIL), high-grade squamous intraepithelial lesion (HSIL), cancer or a glandular abnormality, women can safely be retested in a further 12 months before being referred to colposcopy if HPV detection persists at that time.

Evidence – sources and methods

Initial evidence review

Systematic reviews and modelling studies were initially undertaken to assess the comparative safety and effectiveness of different strategies based on LBC triage in women with a positive oncogenic HPV (not 16/18) test result.

In the initial evaluation, for women with a positive oncogenic HPV (not 16/18) test result and LBC prediction of pLSIL/LSIL, we compared the following strategies:

- immediate colposcopy
- 12-month follow-up and referral to colposcopy if follow-up HPV testing is positive (regardless of HPV type) at 12 months.

In the initial evaluation, for women with a positive oncogenic HPV (not 16/18) test result who do not undergo immediate colposcopy, we compared the following strategies:

- repeated HPV testing at 12 and 24 months before returning to 5-yearly screening if negative at both follow-up tests
- repeated HPV testing at 12 months only, before returning to 5-yearly screening if negative at 12 months.

Evidence update (non-systematic review)

In a subsequent (April 2020) evaluation of emergent National Cancer Screening Register (NCSR) data from the renewed NCSP, we considered the following modification in management for women with a positive oncogenic HPV (not 16/18) test result who do not undergo immediate colposcopy, and who have a follow-up HPV testing at 12 months where the follow-up HPV test is positive for oncogenic HPV (not 16/18):^[2]

- Where reflex LBC at 12 months predicts pHSIL, HSIL, cancer or a glandular abnormality – colposcopy referral is recommended (no change in management)
- Where reflex LBC at 12 months does not predict pHSIL, HSIL, cancer or a glandular abnormality – a second follow-up HPV test in a further 12 months is recommended (i.e. 24 months after the initial screen). If HPV detection persists at the second follow-up test, it is recommended that women are referred for colposcopy, regardless of the result of reflex LBC.

Women who may be at higher risk of harbouring a high-grade abnormality should be referred to colposcopy if HPV is detected at 12 months, regardless of the result of reflex cytology. This includes the following groups:

- Women two or more years overdue for screening at the time of the initial screen
- Women who identify as Aboriginal or Torres Strait Islander
- Women age 50 years or older

There are other groups of women who fall outside these recommendations with separate guidance, including:

- [Immune-deficient women](#)
- [Women exposed to diethylstilboestrol \(DES\) *in utero*](#)
- [Women currently undergoing Test of Cure following treatment of histological HSIL](#)
- [Women aged 70-74 \(attending for an exit test\)](#)
- [Women aged 75+](#)

Evidence findings

Systematic review

The systematic literature search identified no randomised or pseudo-randomised controlled trials directly addressing either of the following:

- the safety and effectiveness of immediate colposcopy for women with a positive oncogenic HPV (not 16/18) test result and a reflex LBC prediction of pLSIL/LSIL, compared with 12 months' delay.
- the safety and effectiveness of repeating HPV testing after 12 and 24 months for women with a positive oncogenic HPV (not 16/18) test result and LBC reported negative or with a prediction of pLSIL/LSIL, compared with repeating HPV testing at 12 months only, before returning to 5-yearly screening.

The search strategies and inclusion and exclusion criteria are described in detail in the [Technical report](#).

In the absence of studies directly addressing these issues, an indirect approach to the literature review was planned which focussed on benchmarking (i.e. assessing the underlying risk

threshold for abnormalities that may develop into cervical intraepithelial neoplasia grade 3 (CIN3) or invasive cancer, which was accepted in the pre-renewal NCSP as requiring colposcopy referral). Similarly, we sought evidence on the benchmark (lower) risk level for which, in the pre-renewal NCSP, it was accepted that 12-month follow-up was appropriate. These 'benchmark' risks were compared with the risks in women in the renewed NCSP with LBC reported negative or with a prediction of pLSIL/LSIL and a positive oncogenic HPV (not 16/18) test result.

Risk benchmarks were considered for women with a positive oncogenic HPV (not 16/18) test result and a reflex LBC prediction of pLSIL/LSIL:

- **12-month follow-up benchmark:** as recommended for women with LSIL cytology in the pre-renewal NCSP.^[3]
- **Colposcopy referral benchmark 1 (cytology prediction of pHSIL/HSIL):** as recommended (and considered standard-of-care) in the pre-renewal NCSP^[3]
- **Colposcopy referral benchmark 2 (positive oncogenic HPV (16/18) test result):** as recommended by MSAC in the renewed NCSP.

Systematic reviews were performed to identify studies examining the risk for the development of CIN3+ (CIN 3 or invasive cervical cancer) among women with a positive oncogenic HPV (not 16/18) test result and pLSIL/LSIL cytology, compared with each of the following groups:

- women with cytological prediction of pLSIL/LSIL, regardless of HPV status
- women with cytological prediction of pHSIL/HSIL, regardless of HPV status
- women with a positive oncogenic HPV (16/18) test result, regardless of cytology status.

The search strategies and findings are described in detail in the [Technical report](#).

Searches identified six relevant prospective cohort studies (level II evidence): two longitudinal studies^{[4][5]} and four studies that reported results for outcomes on immediate colposcopy.^{[6][7][8][9][10][11][12][13][14]} None of these studies were specifically designed to compare the risks associated with specific oncogenic HPV genotypes and specific cytology findings. As a result, it was not possible to determine whether subgroups with oncogenic HPV types (not 16/18), pLSIL or LSIL were similar to benchmark groups or to control for confounding factors such as smoking. Therefore, all six studies were assessed to have a high risk of bias.

Both longitudinal studies reported CIN3+ risks associated with oncogenic HPV (not 16/18), LSIL cytology and, for the benchmark for 12-month follow-up, all LSIL cytology, regardless of HPV status. In one study women were actively followed up for 2 years and underwent an exit colposcopy,^[4] and in the other women were passively followed-up for a maximum of 18 years.^[5] Two studies^{[6][7][8][9][10][14]} reported CIN3+ risks on immediate colposcopy for women with a positive oncogenic HPV (not 16/18) test result, pLSIL (ASC-US, Bethesda 2001) or LSIL cytology and the benchmarks for immediate colposcopy (pHSIL/HSIL cytology or positive HPV (16/18) test result), as well as the benchmark for 12-month follow-up (all LSIL).

The findings of these studies showed the following:

- For women with a positive oncogenic HPV (not 16/18) test result and a cytological prediction of LSIL, the risk of CIN3+ was lower than that for the 12-month follow-up benchmark (LSIL cytology, regardless of HPV status):
 - over 2 years in cohorts age >18 years or >30 years at baseline
 - after 18 years in a cohort age >16 years at baseline.
- For women with a positive oncogenic HPV (not 16/18) test result and a cytological prediction of pLSIL/LSIL, the risk of CIN3+ diagnosed on immediate colposcopy was consistently less than half the risk for the immediate colposcopy benchmarks (cytological prediction of pHSIL/HSIL or positive oncogenic HPV (16/18))

test result) and similar to (if not less than) the 12-month follow-up benchmark (cytological prediction of LSIL, regardless of HPV status) in cohorts age >25 years, >21 years or >18 years at baseline.

A second systematic review was performed to identify studies examining the risk of CIN3 or higher-grade lesion among women undergoing routine cervical screening with a positive oncogenic HPV (not 16/18) test result and negative cytology, compared with the following groups:

- 12-month follow-up benchmark (women with a cytological prediction of pLSIL/LSIL, regardless of HPV status)
- women with a cytological prediction of pLSIL/LSIL and a positive oncogenic HPV (not 16/18) test result.

No studies that met inclusion criteria were identified. The search strategy and findings are described in detail in the [Technical report](#).

Modelling

The findings of the systematic review confirmed that a modelled analysis was required to assess the safety and effectiveness of immediate colposcopy, compared with returning in 12 months for a repeat HPV test, for women with a positive oncogenic HPV (not 16/18) test result and reflex LBC prediction of pLSIL/LSIL at triage. The modelling study assessed the population-level effects of alternative strategies, within a national program of primary HPV screening with partial genotyping, for women with a positive oncogenic HPV (not 16/18) test result and reflex LBC prediction of pLSIL/LSIL. Modelling was performed for HPV-unvaccinated women and for cohorts offered vaccination.

Options compared in women with a positive oncogenic HPV (not 16/18) test result and reflex LBC prediction of pLSIL/LSIL

Comparison 1:

- (Option A) follow-up with HPV testing in 12 months, followed by colposcopy for those with a positive oncogenic HPV (any type) test result at 12 months, or return to routine 5-yearly screening if oncogenic HPV not detected at 12 months
- (Option B) referral to colposcopy.

Comparison 2:

- (Option A) as above
- (Option C) referral to follow-up with HPV testing in 12 months and 24 months, with immediate colposcopy for those with a positive oncogenic HPV (any type) test result at either follow-up test, or return to routine 5-yearly screening if oncogenic HPV not detected at both follow-up tests.

Summary of findings

The findings are described in detail in the [Modelling reports](#).

Comparison 1: 12-month follow-up versus immediate colposcopy

Modelling comparing 12-month follow-up with immediate referral to colposcopy in **women with a positive oncogenic HPV (not 16/18) test result and reflex LBC prediction of pLSIL/LSIL** predicted the following:

- For women in this group undergoing 12-month follow-up (Option A), the 20-year risk of developing invasive cervical cancer (Figure 6.1) is lower than the risk for women with a screening cytology prediction of LSIL in the pre-renewal NCSP (i.e. lower than the accepted benchmark risk for 12-month follow-up in Australia).
- The renewed NCSP, incorporating **12-month follow-up** for women in this group (and incorporating other recommendations in these guidelines), is predicted to reduce cervical cancer incidence and mortality by 31–36% in unvaccinated cohorts and 24–29% in cohorts offered vaccination, compared with the pre-renewal NCSP.

- The renewed NCSP, incorporating **immediate colposcopy** for women in this group (and incorporating other recommendations in these guidelines), is predicted to reduce cervical cancer incidence and mortality by 32–37% in unvaccinated cohorts and 27–32% in cohorts offered vaccination, compared with the pre-renewal NCSP.
- For women in this group, immediate referral to colposcopy provides an incremental 1–3% reduction in cervical cancer incidence and mortality, compared with 12-month follow-up. However, colposcopy referral for this group substantially increases the number of colposcopies in the renewed NCSP, with more than 650 colposcopies required to avert an additional case of cervical cancer, compared with 12-month follow-up.
- Colposcopy referral for this group would be very cost-ineffective, with an incremental cost-effectiveness ratio of >\$100,000 per life-year saved (LYS), compared with 12-month follow-up.
- Colposcopy referral of only women age >45 years in this group, however, is more cost-effective, with an incremental cost-effectiveness ratio of \$40,000/LYS (95% credible interval (CrI): \$37,000–42,000/LYS) in unvaccinated cohorts, and \$41,000/LYS (95% CrI: \$38,000–44,000/LYS) in cohorts offered vaccination.

Figure 6.1. Predicted 20-year risk of cervical cancer in women with a positive oncogenic HPV (not 16/18) test result and a reflex LBC prediction of pLSIL/LSIL



Figure 6.1

Note: The black horizontal line in each figure indicates the risk under the pre-renewal NCSP for women with a cytological prediction of LSIL at a routine screening visit and a negative cytology test in the previous 2 years.

Comparison 2: follow-up options (12 and 24 months versus 12 months only)

Modelling comparing follow-up at both 12 months and 24 months, with 12-month follow-up only, in **women with a positive oncogenic HPV (not 16/18) test result and reflex LBC prediction of pLSIL/LSIL at index screening visit** predicted the following:

- Performing both 12-month and 24-month follow-up results in <1% difference in cervical cancer incidence and mortality and <1% difference in colposcopies, compared with 12-month follow-up only.
- Performing both 12-month and 24-month follow-up for this group would be very cost-ineffective, with an incremental cost-effectiveness ratio of >\$300,000/LYS, compared with 12-month follow-up only.
- Limiting both 12-month and 24-month follow-up to women over 55 in this group remains cost-ineffective compared with 12-month follow-up only. The incremental cost-effectiveness ratio is >\$65,000/LYS if 12-month and 24-month follow-up is used in women age over 55 years, compared with performing 12-month follow-up only for women of all ages.

The detailed description of the model assumptions, calibration and findings are provided in [the Modelling reports](#).

Although the update to these Guidelines in 2020 for the management of intermediate risk women who remain HPV positive at 12/24 months was not explicitly modelled, based on the 2020 NCSR data analysis (see below), the overall population-level benefits modelled for the renewed NCSP compared with the pre-renewed NCSP, are likely to be similar to those originally modelled.

Review of NCSP data

In 2020, a review of the first 2 years of the renewed NCSP was conducted on data for women classified as having higher or intermediate risk of cervical cancer on their baseline Cervical

Screening Test with subsequent colposcopy and/or histology recorded on the NCSR. The following data were included:

- all results for women at higher risk and intermediate risk from 1 December 2017 to 31 December 2019 (data extracted 14 January 2020)
- all colposcopy assessment and MBS forms coded and completed by the NCSR relating to visits up to 16 April 2020 (data extracted 22 September 2020)
- and all histology assessment and MBS forms coded and completed by the NCSR relating to samples collected up to 16 April 2020 (data extracted 22 September 2020).

For benchmarking, the outcomes for intermediate risk women whose follow-up test result is HPV (not 16/18) were compared with outcomes in those women at higher risk at baseline (Tables 6.1, 6.2).^[2]

Table 6.1. Outcomes for higher-risk group according to baseline test (based on April 2020 NCSR data)

Baseline test result	Histologically confirmed CIN2+	Histologically confirmed CIN3+	Invasive cervical cancer
HPV 16/18	17.8–19.5%	12.6–14.0%	0.88–0.96%
HPV (not 16/18) and LBC prediction	55.4–58.6%	35.9–38.5%	0.66–0.76%
pHSIL, HSIL, or glandular			

Source: National Cervical Screening Program^[2]

Ranges reflect variation depending on whether or not histological outcomes are restricted to occurring within 6 months of referral.

Table 6.2. Outcomes for women initially at intermediate risk, whose follow-up test result is HPV (not 16/18), according to LBC prediction at follow-up test (based on April 2020 NCSR data)

LBC prediction	Histologically confirmed CIN2+	Histologically confirmed CIN3+	Invasive cervical cancer
pHSIL, HSIL, or glandular	54.1–55.8%	32.1–33.8%	0.32–0.37%
negative, pLSIL or LSIL	8.1–8.5%	3.1–3.4%	0.01–0.02%

Source: National Cervical Screening Program^[2]

Ranges reflect variation depending on whether or not histological outcomes are restricted to occurring within 6 months of referral.

The analysis shows that, compared with other groups who are referred for colposcopy, the risk of CIN2+, CIN3+ and cervical cancer are much lower for women at intermediate risk whose follow-up test is HPV (not 16/18) and who have an LBC prediction of negative, pLSIL or LSIL. Within this group of women, we compared risks for women age <50 years with those for women age 50 years or older (Table 6.3).^[2]

Table 6.3. Outcomes for women initially at intermediate risk, whose follow-up test result is (HPV (not 16/18), and LBC prediction is negative, pLSIL or LSIL, according to age (based on April 2020 NCSR data)

Age	Histologically confirmed CIN2+	Histologically confirmed CIN3+	Invasive cervical cancer
<50 years	10.08%	4.0%	0.02%
≥50 years	3.4%	1.5%	No cases identified

Source: National Cervical Screening Program^[2]

It should be noted that women 50 years or older who are HPV positive without a visible lesion at colposcopy, are at higher risk of harbouring a covert abnormality in the canal (compared to younger women who are HPV positive). Considering this issue, and applying the precautionary principle, among women at intermediate risk whose follow-up test is HPV (non 16/18), LBC prediction negative, pLSIL or LSIL, direct referral to colposcopy should still be recommended for women 50 years of age or over. It is important to note that older women referred to colposcopy on this basis, who are likely to have a type 3 TZ, not undergo diagnostic excision of the TZ without histological or cytological evidence of a high-grade lesion (see [Recommendation 8.12](#)). Additionally, other groups of women may be at higher risk of harbouring a high-grade abnormality, and again applying the precautionary principle, among women at intermediate risk whose follow-up test is HPV (non 16/18), LBC prediction negative, pLSIL or LSIL, direct referral to colposcopy should still be recommended for:

- Women two or more years overdue for screening at the time of the initial Cervical Screening Test
- Women who identify as Aboriginal or Torres Strait Islander

Women who identify as Aboriginal or Torres Strait Islander are known to have higher rates of cervical cancer incidence and mortality. There is a paucity of program-wide data on risk of high-grade abnormalities in Aboriginal or Torres Strait Islander women, due to a historical lack of data on Indigenous status in screening registers and continuing low levels of completeness of this information on the National Cancer Screening Register. Data from population-based linked health records in Queensland, however, document a higher risk of high-grade histological abnormalities among Aboriginal or Torres Strait Islander women (OR 2.0, 95% CI 1.9–2.1).^[15] Note that there are other groups of women who fall outside these recommendations as there are separate guidelines specifically for them, including:

- [Immune deficient women](#)
- [Women exposed to diethylstilboestrol \(DES\) *in utero*](#)
- [Women currently undergoing Test of Cure following treatment of histological HSIL](#)
- [Women aged 70+ \(attending for an exit test\)](#)

Evidence summary and recommendations

Level References

Evidence summary

Data from two prospective cohort studies indicate that women with a cytological prediction of LSIL in whom HPV 16/18 is not detected, but have a positive oncogenic HPV (not 16/18) test result at lower risk for CIN3+ over 2 years (and for up to approximately 18 years) than women with a cytology prediction of LSIL, regardless of HPV status (who are referred to 12-month follow-up within the pre-renewal NCSP).

II [4], [5]

No longitudinal studies were found that reported the subsequent risks of CIN3+ for women with normal cytology in whom HPV 16/18 is not detected, have a positive oncogenic HPV (not 16/18) test result, compared with either of the following groups:

- women with a cytological prediction of pLSIL/LSIL, regardless of HPV status
- women with a cytological prediction of pLSIL/LSIL and a positive oncogenic HPV (not 16/18) test result.

Modelling study findings

N/A

For women with a positive oncogenic HPV (not 16/18) test result and reflex LBC prediction of pLSIL/LSIL:

- modelling comparing 12-month follow-up with immediate colposcopy predicted that the 20-year risk of developing invasive cervical cancer for those who have 12-month follow-up surveillance is lower than the risk in women with a screening cytology result of LSIL in the pre-renewal NCSP (i.e. lower than the accepted benchmark risk for 12-month follow-up in Australia).
- performing both 12-month and 24-month follow-up results in <1% difference in cervical cancer incidence and mortality and <1% difference in colposcopies, compared with 12-month follow-up only.

Based on data for first 2 years of the renewed NCSP, risks are low for women at intermediate risk whose follow-up test is HPV (not 16/18) and LBC prediction negative, pLSIL or LSIL: N/A ^[2]

- The likelihood of histologically confirmed CIN2+ is approximately 8.1–8.5%.
- The likelihood of histologically confirmed CIN3+ is approximately 3.1–3.4%.
- The risk of invasive cervical cancer is extremely low (0.02%).

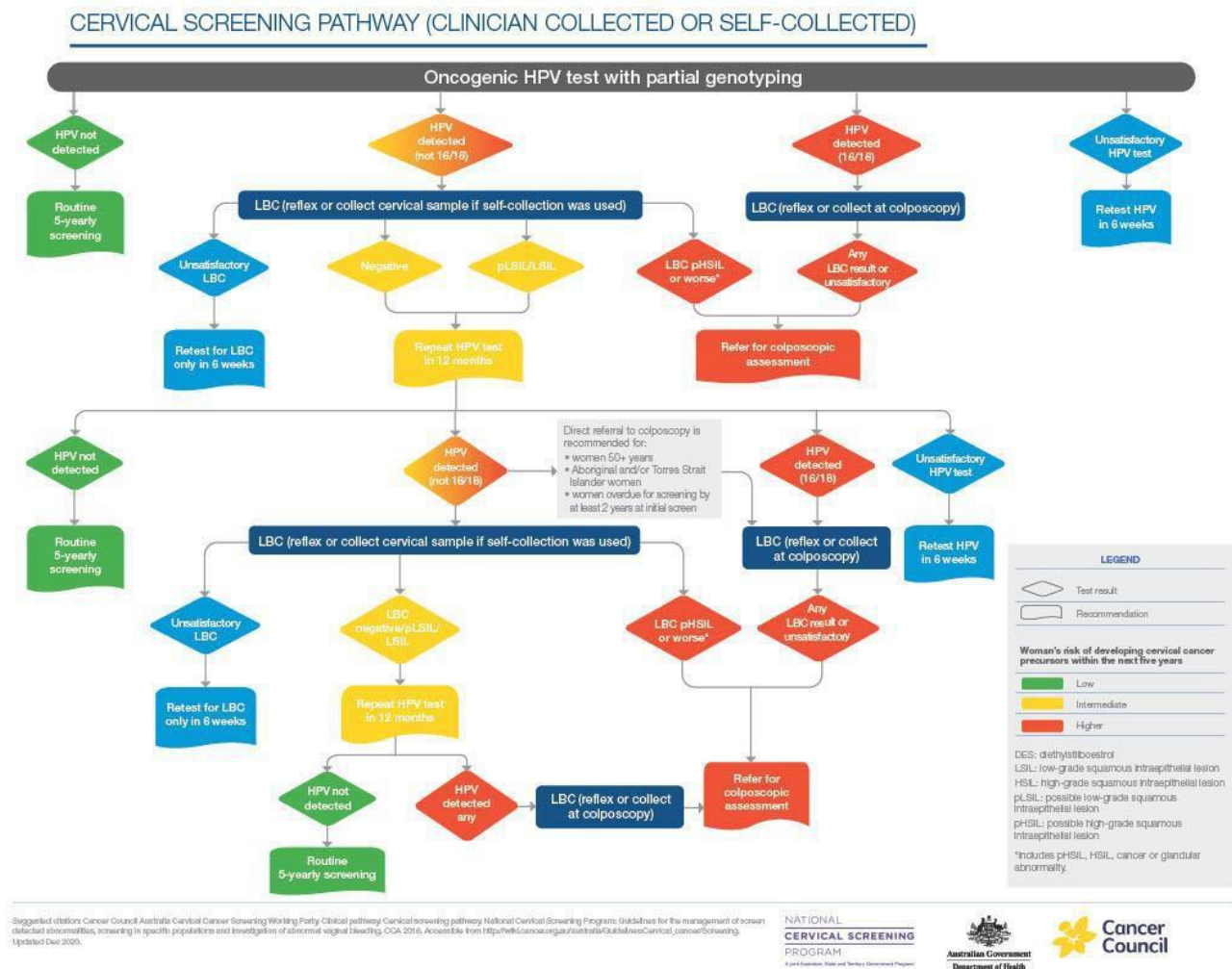
Ranges reflect variation depending on whether or not histological outcomes are restricted to occurring within 6 months of referral.

*Note that grading of the evidence was performed according the NHMRC guidelines in place at the time of the original development of these guidelines (for consistency).

**2020 review of NCSP data.

Flowchart 6.4. Recommendations

Flowchart 6.4. Cervical screening pathway for primary oncogenic HPV screening HPV tests on clinician collected or self-collected samples HPV detected not 16/18



<https://staging.cancer.org.au/assets/pdf/flowchart-6-4-cervical-screening-pathway-for-primary-oncogenic-hpv-screening-hpv-tests-on-clinician-collected-or-self-collected-samples-hpv-detected-not-16-18>

Evidence-based recommendation

REC6.8: Positive oncogenic HPV (not 16/18) test result at routine screening C

- Women with a positive oncogenic HPV (not 16/18) test result, with a LBC report of negative or prediction of pLSIL/LSIL, should have a repeat HPV test in 12 months.
- When the sample has been collected by a healthcare provider, then the laboratory will perform reflex LBC. When the sample was self-collected, the woman should be advised to return to her healthcare provider so that a cervical sample for LBC can be collected by the healthcare provider.

Note: It is expected that amendments to relevant Medicare Benefits Schedule items to support testing on a self-collected sample at the follow-up test for people whose initial screening test was done on a clinician-collected sample will be effective from 1 November 2022 pending any external impacts such as upcoming elections and caretaker period.

Consensus-based recommendation

REC6.9: Referral to gynaecological oncologist for LBC prediction of invasive disease

Women who have a positive oncogenic HPV (not 16/18) test result with a LBC report of invasive cancer (squamous, glandular or other) should be referred to a gynaecological oncologist or gynaecological cancer centre for urgent evaluation, ideally within 2 weeks.

Practice point

REC6.10: Referral of women with a positive oncogenic HPV (not 16/18) test result and LBC prediction of pHSIL, HSIL or any glandular abnormality

Women with a positive oncogenic HPV (not 16/18) test result, with a LBC prediction of pHSIL/HSIL or any glandular abnormality, should be referred for colposcopic assessment at the earliest opportunity, ideally within 8 weeks.

Evidence-based recommendation

Grade

REC6.11: Management after follow-up HPV test at 12 months, following initial positive oncogenic HPV (not 16/18) screening test result

At follow-up HPV testing 12 months after a detection of HPV (not 16/18) and LBC results of negative or pLSIL/LSIL:

- if oncogenic HPV is not detected, the woman should be advised to return to routine 5-yearly screening.
- if HPV (16/18) is detected, then the woman should be referred for colposcopic assessment. If the follow-up sample was collected by a healthcare professional then the laboratory will undertake reflex LBC. If the follow-up sample was self-collected then a sample for LBC should be collected at the time of colposcopy.

Management of those with HPV (not 16/18) detected at 12 months is described in REC6.12 - 6.14

Practice point

REC6.12: Management after follow-up HPV test at 12 months, following initial positive detection of HPV (not 16/18), for women who:

- were overdue for screening by at least 2 years at the time of their initial positive oncogenic HPV (not 16/18) test result
- identify as Aboriginal and/or Torres Strait Islander
- age 50 years or older.

If oncogenic HPV (any type) is detected at the follow-up HPV test, then the woman should be referred for colposcopic assessment.

If the follow-up sample was collected by a healthcare professional then the laboratory will undertake reflex LBC. If the follow-up sample was self-collected then a sample for LBC should be collected at the time of colposcopy.

Approval: 1-Feb-2021

Evidence based recommendation

REC6.13 Management after follow-up HPV test at 12 months, following initial positive oncogenic HPV (not 16/18) screening test result: HPV (not 16/18) detected at 12 months

If HPV (not 16/18) is detected again, and the woman does not fall into any of the categories in REC6.12, then LBC should be performed. If the follow-up sample was collected by a healthcare professional then the laboratory will undertake reflex LBC. If the follow-up sample was self-collected then the woman should be advised to return to her healthcare professional so that a sample can be collected for LBC.

- If the LBC is reported as invasive cancer (squamous, glandular or other) the woman should be referred to a gynaecological oncologist or gynaecological cancer centre for urgent evaluation, ideally within 2 weeks.
- If the LBC is reported as pHSIL/HSIL or any glandular abnormality, she should be referred for colposcopic assessment at the earliest opportunity, ideally within 8 weeks

Management of those with HPV (not 16/18) detected at 12 months with negative/ pLSIL/ LSIL LBC is described in REC6.14

Approval: 1-Feb-2021

Consensus-based recommendation

REC6.14: Management after follow-up HPV test at 12 months, following an initial positive oncogenic HPV (not 16/18) screening test result

At the follow-up HPV test **12 months** after detection of HPV (not 16/18) with LBC results of negative, pLSIL or LSIL if the woman has a HPV (not 16/18) test result, with an LBC report of negative or prediction of pLSIL/LSIL, and she does not fall into any of the categories in REC6.12, she should have a second follow-up HPV test in a further 12 months.

Approval: 1-Feb-2021

Note: It is expected that amendments to relevant Medicare Benefits Schedule items to support testing on a self-collected sample at the follow-up test for people whose initial screening test was done on a clinician-collected sample will be effective from 1 November 2022 pending any external impacts such as upcoming elections and caretaker period.

Consensus-based recommendation

REC6.15: Management after second follow-up HPV test, following initial detection of HPV (not 16/18) at the baseline screening test

At the second follow-up HPV test, **12 months** after a first follow-up HPV test with HPV (not 16/18) detected and LBC negative or pLSIL/LSIL:

- If HPV (any type) is detected, the woman should be referred for colposcopic assessment, . When the follow-up sample has been collected by a healthcare provider, then the laboratory will perform reflex LBC. When the follow-up sample was self-collected, then a sample should be collected for LBC at the time of colposcopy.
- if HPV is not detected, the woman should be advised to return to routine 5-yearly screening.

Approval: 1-Feb-2021

Benefits and harms

While all screening programs will fail to detect some cases, implementation of these recommendations does not present any significant concern about the potential for missed cancers. Rates of cervical cancer are low in Australia, compared with international rates.^[16] Modelling, taking into account post-colposcopy management as recommended in these guidelines, has predicted that a 31–36% reduction in incidence and mortality may be achievable in unvaccinated cohorts and a 24–29% reduction may be achievable in cohorts offered vaccination ([Section 2. The rationale for primary HPV screening](#) and [Section 5. Benefits, harms and cost-effectiveness of cervical screening in the renewed NCSP](#)).^[17] In 2005, the NCSP adopted a policy of 12-month follow-up for women with a cytological prediction of pLSIL/LSIL, replacing the previous policy of immediate referral to colposcopy. A recent evaluation by the NCSP Quality and Safety Monitoring Committee found that this policy was not associated with an increase in the incidence of cervical cancer in women age 20–69 years.^[18]

Within the renewed NCSP, the policy of 12-month follow-up for women with a LBC prediction of pLSIL/LSIL would apply only to the subgroup of women at intermediate risk of significant cervical abnormality based on HPV testing with partial genotyping, in contrast to the pre-Renewal program in which the policy applies to an undifferentiated group of women with either high or intermediate risk. Accordingly, modelled results suggest that the risk for women with a positive oncogenic HPV (not 16/18) test result and a reflex LBC prediction of pLSIL/LSIL who have 12-month follow-up surveillance, is lower than the risk in women with a screening cytological prediction of LSIL in the pre-Renewal NCSP (i.e. the risk in this group is lower than the accepted benchmark risk for 12-month follow-up in Australia).

More than half of women with an oncogenic HPV infection are expected to clear the infection within 12 months.^[19] Those with persistent infection (or with an HPV infection detected on repeat testing) would be identified at the 12-month HPV repeat test.

The original prediction of low risk among women with oncogenic HPV (not 16/18) and a reflex LBC prediction of pLSIL/LSIL has been borne out by a 2020 review of NCSP data from the first 2 years of the renewed program. In fact, the risk of CIN2+ among women presenting for colposcopy following persistent detection of HPV (not 16/18), in the absence of pHSIL, HSIL, cancer of glandular abnormality on cytology, is low enough to justify a further 12 months of surveillance prior to referral to colposcopy. This change results in a better balance of benefits and potential harms by allowing women at very low risk of CIN2+ (and based on current data, very low risk of cancer) a further 12 months, by which time many women will have cleared the HPV infection and will then not require colposcopy at all.

Implementation of these recommendations will avoid many unnecessary colposcopies and associated harms (including biopsy, overtreatment, anxiety and financial costs) for women with HPV-related cervical abnormalities that would resolve spontaneously without medical intervention.

Health system implications of these recommendations

Clinical practice

Effective from 1 July 2022

Colposcopic assessment and management will be more challenging in the renewed NCSP because there will be a higher proportion of women with a positive oncogenic HPV test result who have minimal or no cytological changes. Originally, all women with persistent infections with oncogenic HPV (not 16/18) were referred to colposcopy after 12 months and a very large proportion of these will represent HPV infection without neoplastic potential. This has been borne out in practice in the first 2 years of the renewed NCSP, placing considerable pressure on colposcopy services, with some women in this category therefore facing considerable delay in accessing colposcopy. The change, implemented in 2020, to allow a further 12 months of surveillance prior to referral to colposcopy is designed to safely relieve these pressures.

Resourcing

Updated modelling, taking into account these detailed guideline recommendations, and taking into account the reduction in HPV 16/18 infections due to vaccination in the population, has informed an assessment of the resourcing associated with partial genotyping strategies (see [Section 5. Benefits, harms and cost-effectiveness of cervical screening in the renewed NCSP](#)).

Barriers to implementation

Healthcare professionals may be reluctant to delay colposcopy in women who have a positive oncogenic HPV (not 16/18) test result, despite this being their current practice with low-grade cytology. Education of GPs and other healthcare professionals who provide cervical screening services, emphasising the safety of this approach, will be essential to the implementation of this recommendation.

Some women may be reluctant to accept a 12-month delay in referral for colposcopy, especially if they are aware of their HPV test result. Education of women and careful explanation by their healthcare provider will be of paramount importance.

GPs, other healthcare professionals and women participating in screening should understand that the recommendation to defer colposcopy (if needed at all) for 12 months is unchanged from accepted practice for women with an abnormal Pap test result predicting pLSIL/LSIL.

Conversely, GPs may not refer women with a persistent positive oncogenic HPV (not 16/18) test result to colposcopy, but this risk will be mitigated by the laboratory report to the GP clearly recommending referral, and by existing registry follow-up with reminder letters as needed.

Similarly, the women in this situation may not fully understand the need for colposcopy, especially if the reflex LBC result is negative, and may fail to attend. Patient education and registry reminder letters will play an important role in this situation.

Effective communication with health professionals, and with affected women, will be necessary to implement the change in the pathway for women with HPV (not 16/18) detected and negative, pLSIL or LSIL cytology (Flowchart 6.1).

Colposcopy waiting lists will need to be re-prioritised and primary health providers may find that women previously referred to colposcopy are returned to primary care for a further follow-up HPV test. This will require careful communication. Laboratories will need to rework their procedures for reporting recommended management in these cases and for many laboratories a software adjustment will be needed, where decision support software is in place. The NCSR will also need to adjust its follow-up communications accordingly.

Appendices

[PICO questions 1a & View Systematic review report q 1a](#)

[View Systematic review report q 1b](#) [View Evidence Statement q 1a](#)

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Self-collected vaginal samples

Author(s):

- [Professor Karen Canfell](#) — Author
- [A/Professor Marion Saville](#) — Author
- [A/Professor Megan Smith](#) — Author
- Professor Deborah Bateson – Co-author
- [A/Professor Alison Brand](#) — Co-author
- Ms Kirsteen Fleming – Co-author
- Dr Vivienne Milch – Co-author
- Dr Marsali Newman – Co-author
- A/Prof Lisa Whop – Co-author
- [Professor Bruce Armstrong](#) — Contributor
- [Professor Ian Hammond](#) — Contributor
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

Background

Only around five in 10 women participate in the National Cervical Screening Program (NCSP) at the recommended interval.^[1] Participation at the recommended interval is less than 50% in the Northern Territory, and in outer regional, remote, or very remote areas.^[1] Some of the groups of women and other people with a cervix who are underscreened include those who identify as Aboriginal and Torres Strait Islanders, are culturally and linguistically diverse, are socioeconomically disadvantaged, have experienced sexual assault, have a disability, identify as lesbian or bisexual, or are trans men and gender diverse people with a cervix who do not identify as women.

Data from the Victorian Cervical Cytology Register (VCCR) show that 74% of women diagnosed with invasive cervical cancer over 2012-2014 have never been screened or have participated in the screening program but were overdue for a recommended cytology test at the time of their cancer diagnosis.^[2,3,4] Self-collection of human papillomavirus (HPV) test samples has been shown to overcome some of the barriers to undergoing a screening test that some women experience. Providing HPV self-collection kits to never-screened and under-screened women has been shown to improve screening participation in international studies.^[5]

Under the renewed NCSP, HPV testing on self-collected samples with limited eligibility was introduced in December 2017. From 1 July 2022, HPV testing on self-collected samples will be available as a choice to all women eligible for routine screening or for a follow-up HPV test. The clinical guidelines define the pathways for people who have a positive self-collected sample. There are some groups of people who require co-testing and will therefore require a clinician-collected sample.

Evidence

2013 MSAC systematic review

The MSAC evaluation assessed the comparative safety and effectiveness of including self-collected samples for HPV testing for never-screened and under-screened women, to supplement the organised screening program using clinician-collected samples for HPV testing, compared with the existing collection protocol.^[2]

The MSAC assessment of accuracy of self-collected samples was based on 10 level III-2 diagnostic accuracy studies conducted in a screening setting, which were included in a systematic review.^[5] Evidence for adherence rates was obtained from a randomised controlled trial^[8] and two cohort studies.^{[9][10]}

The 2013 MSAC systematic review made the following conclusions:^[7]

- The accuracy of HPV testing using self-collected samples varies between different types of sampling devices and HPV tests.
- HPV tests using self-collected samples have moderate-to-high sensitivity and comparably high specificity for detecting cervical intraepithelial neoplasia grade 2 or higher (CIN2+), compared with clinic HPV testing in nine of 10 studies identified, with a relative sensitivity of 0.62–1.00 and relative specificity of 0.93–1.00.
- High rates of adherence to screening follow-up have been reported among previously unscreened women with a positive HPV test result from a self-collected sample.

Other evidence

A more recent meta-analysis^[11] found that the sensitivity and specificity of HPV testing to detect CIN2+ in self-collected samples were similar to those for clinician-collected samples when using validated PCR-based HPV assays. When using signal amplification-based HPV assays, self-collected samples showed lower sensitivity than clinician-collected samples.^{[11][12]}

Two studies conducted in Victoria suggest that offering self-collection is likely to be acceptable to Australian women who have not been screened recently.^{[13][14]} One of these, a randomised controlled trial, additionally found that offering self-collection was more effective than a reminder letter in encouraging women who were unscreened or overdue for screening to undergo a round of screening.^[15] Overall, 75.7% of women with a positive oncogenic HPV (any type) test result had the appropriate clinical follow-up within 6 months. Among 45 women with a positive oncogenic HPV (16/18) test result, 28 (62.2%) attended for colposcopy within 6 months, and attendance for colposcopy was lower among women with negative or LSIL cytology (18/27 attended) than among women with HSIL cytology (8/8 attended).^[15] The authors suggested that medical practitioners may not have referred women for colposcopy when subsequent cytology was negative.^[15] The trial protocol had recommended colposcopy referral for women with a positive oncogenic HPV (16/18) test result, and did not require or actively recommend that cytology be collected prior to referral (this was at the discretion of the healthcare professional),^[16] however, cytology was collected from 35 of the 37 women who attended for any follow-up.^[15]

A modelled analysis found that undergoing even one round of screening could substantially reduce an unscreened woman's risk of cervical cancer over her lifetime, by around 41% if this occurred at age 30 or 40.^[12] The authors noted that benefits of self-collection would be maximised by using a sufficiently accurate HPV test that had capacity to perform partial genotyping for HPV 16/18.^[12]

2021 MSAC review

In 2021, the Medical Services Advisory Committee (MSAC) reviewed an application from the National Cervical Screening Program requesting expansion of the eligibility to participate in cervical screening using self-collection. The Self-Collection Expert Advisory Group was

convened to guide this review, and to provide advice on policy, implementation and consultation.^[17]

MSAC noted the large body of evidence showing no material difference in the diagnostic accuracy of HPV testing between using self-collected and clinician-collected samples (relative sensitivity = 0.98; 95% CI: 0.96 to 1.01; relative specificity = 0.99; 95% CI: 0.98 to 1.01).^[17]

MSAC concluded that HPV testing using self-collected samples is just as accurate as using clinician-collected samples, provided a PCR based assay was used. MSAC supported expanding access to self-collection to include everyone eligible for cervical screening, giving all eligible people a choice in screening method. MSAC considered self-collection to be safe and effective, and that it would likely increase participation in cervical screening.^[17]

MSAC advised that expanding self-collection is an important option to increase access to screening, particularly for people who may feel uncomfortable with a clinician collecting their sample. People who choose to use self-collection would still access cervical screening through their healthcare provider, to allow for education and engagement.

2021 evidence review

A general review of the literature was undertaken to identify studies in Australia assessing the acceptability to women of screening on a self-collected sample (including uptake of this option) and adherence to follow-up among women in whom HPV is detected. Eight articles assessing acceptability were identified,¹⁸⁻²⁵ six of which reported on findings for women who were under- or never-screened and who had used or been offered self-collection.¹⁸⁻²³ Two other studies were among women with a mix of screening histories who were asked for opinions on self-collection but had not used it,^{24,25} and in one case were asked about home-based self-collection rather than the clinic-based model as has been adopted in Australia.²⁴ In all studies where women had been offered or used self-collection there was a high level of acceptability of self-collection. The two studies among women with a mix of screening histories and who had not used self-collection reported that many women would prefer to continue to be screened on a clinician-collected sample, especially if they were screening regularly, but nevertheless there was high acceptability of self-collection being offered as an alternative option.^{24,25} Women who indicated they would prefer a healthcare professional to collect the sample expressed concerns about performing sample collection correctly. Most women who had used self-collection reported they found it easy to perform, less embarrassing, and a convenient option.

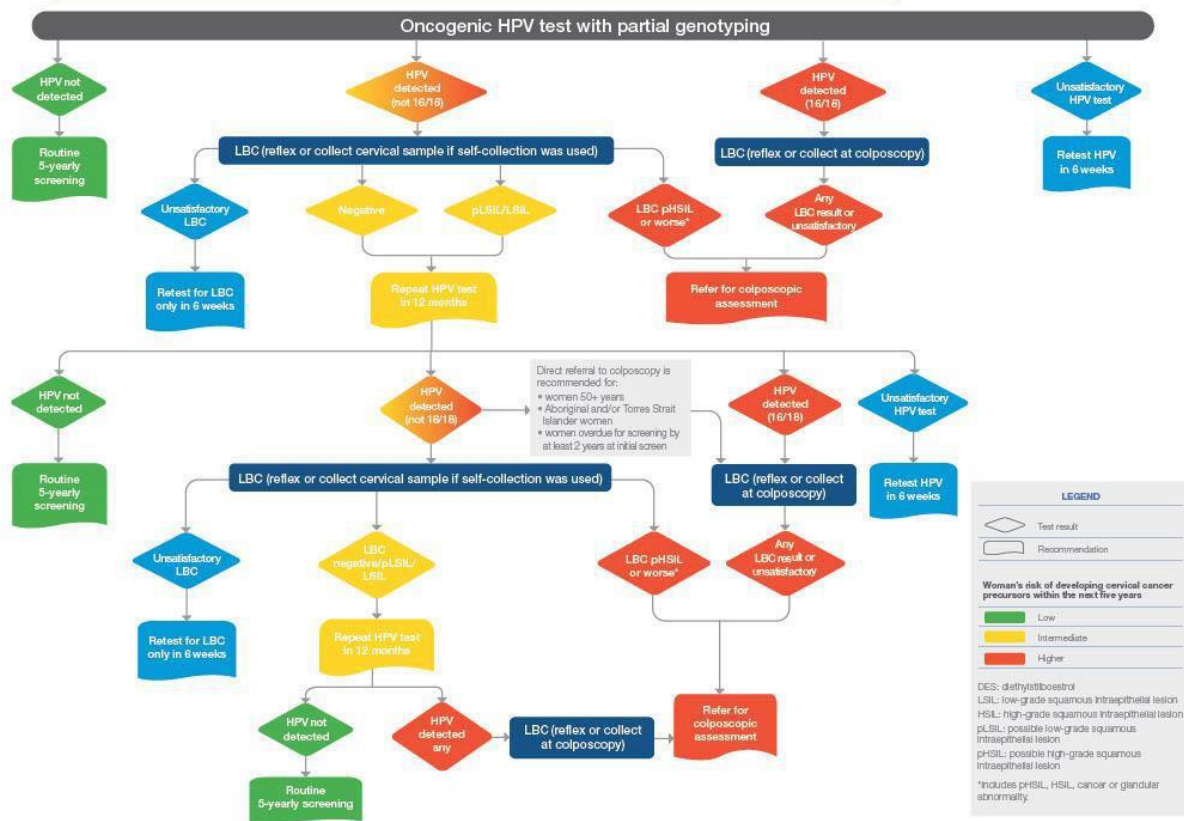
Only three studies provided information about adherence to recommended follow-up after a self-collected sample,^{18,20,21} all of which were undertaken with under-screened women. The findings of these studies may therefore have limited applicability to the general screening population. The number of women requiring follow-up was generally small (range: 14-140). Adherence to follow-up ranged from 52 to 82%. Study findings were inconsistent as to whether women with HPV (16/18) detected (colposcopy recommended) were more or less likely to have completed follow-up than women with HPV (not 16/18) detected.

The eight identified articles were reporting on six different studies or pilot studies of self-collection (for two studies there was both a quantitative and a qualitative paper). Three of these six studies were conducted in, or reported findings specifically for, Aboriginal or Torres Strait Islander women^{18,19, 25} (see [Screening in Aboriginal and Torres Strait Islander women](#)). Each of these studies reported a high level of acceptability of self-collection as an alternative option.

Recommendations

Flowchart 6.1. Cervical screening pathway for primary oncogenic HPV screening (HPV tests on clinician-collected or self-collected samples)

CERVICAL SCREENING PATHWAY (CLINICIAN COLLECTED OR SELF-COLLECTED)



Suggested citation: Cancer Council Australia Cervical Cancer Screening Working Party. Clinical pathway: Cervical screening pathway. National Cervical Screening Program. Guidelines for the management of women detected abnormalities, screening in specific populations and investigations of abnormal vaginal bleeding. CCA 2016. Accessible from http://www.cancer.org.au/australia/outlines/cervical_cancer_screening. Updated Dec 2020.

NATIONAL
CERVICAL SCREENING
PROGRAM
A joint Australian Government and Territory Government Program

Australian Government
Department of Health

Cancer
Council

<https://www.cancer.org.au/assets/pdf/cervical-screening-pathway-flowchart-6.1-July-2022>

MSAC evidence-based recommendation

REC6.1: Eligibility for screening on a self-collected sample to include all people eligible for cervical screening

Anyone who is eligible for cervical screening (people with a cervix aged 25-74 years who have ever been sexually active) should be offered the choice of HPV testing on a self-collected vaginal sample or on a clinician-collected sample.

Practice Point

REC6.16: Informed choice for patients about self-collection

When deciding whether to choose self-collection or clinician collection, people must be given clear information by the supervising healthcare professional about the likelihood that HPV may be detected and, if so, what follow-up will be required. If a person chooses self-collection then the healthcare professional should provide information about how to collect the sample and how they will receive the test results.

Among those attending for a routine screening test, approximately 2% have HPV16/18 detected and approximately 6% have HPV (not 16/18) detected, although the latter varies by age.

Practice Point

REC6.17: Settings where self-collection can be performed

Effective from 1 July 2022

Cervical screening on a self-collected vaginal sample needs to be ordered and overseen by a healthcare professional, but collection of the sample can occur in any setting that the healthcare professional* ordering the test believes is appropriate, including in the context of a telehealth consultation. The healthcare professional is not required to observe the patient collecting their sample unless this is the patient's preference. Patients attending an in-person consultation should be encouraged to collect a sample while they are still at the clinic, as sample collection is considered more likely in this context.

However, [with the aim to maximise participation in cervical screening,] collection of the sample can occur in any setting that the healthcare professional* ordering the test believes is appropriate, including in the context of a telehealth consultation. The healthcare professional should facilitate access to screening, and the pathology laboratory should deliver the results to the requesting healthcare professional who will be responsible for informing patients of their results and any required follow-up. Within these constraints, healthcare professionals and laboratories have flexibility to develop models of screening that best meet the needs of their communities.

* Only doctors and nurses practitioners can sign the pathology request for tests under current MBS rules.

Practice Point

REC6.18 Assistance with sample self-collection

Women who have difficulty collecting a lower vaginal sample by themselves could be assisted to do so by the provider. Alternatively the provider could collect the sample using a self-collection swab without using a speculum. A sample collected in this way is still classified as self-collection on the pathology request form.

Practice Point

REC6.19 Support for underscreened women

Women in whom HPV (any type) is detected in a self-collected sample and who were overdue for screening may require additional and individualised support to progress along the clinical pathway, and access to follow-up services where they will receive sensitive treatment. This additional support may involve, for example, reassurance and explanation of the screening pathway and follow-up procedures, longer appointments, or additional follow-up contact.

Practice point

REC6.20 Indication for genital inspection

Routine genital inspection is not indicated in all people attending for cervical screening, but could still be offered to people who undergo screening on a self-collected sample with any clinical indication that genital inspection is appropriate or who are from populations who are at high risk for vulvar disease.

Practice point

REC6.21 Follow-up HPV test after initial self-collected screening sample

When follow-up HPV testing is required after an initial positive oncogenic HPV test result, the sample may be self-collected or collected by a clinician.

The woman's healthcare professional should advise the woman of the follow-up that will be recommended if HPV is detected, and explain that a clinician-collected sample allows for reflex LBC to be performed on the same sample, potentially avoiding the need for an additional visit to collect a cervical sample for LBC. HPV testing is not repeated on the clinician-collected sample in this circumstance.

Approval: 1-Feb-2021

Note: recommendation numbering changed Feb 2021, this was previously 6.14

Benefits and harms

Women who are eligible for the self-collection pathway will benefit by participation in screening, especially if disease is detected and treated. They will also benefit by being reassured that they are at low risk of cervical cancer if oncogenic HPV is not detected.

Some women who choose to be screened using self-collection may be more anxious about cervical screening than other women and will need special consideration regarding reassurance and explanation of the screening pathway and the procedure. Women in whom HPV is detected will require a clinician-collected cervical sample for LBC and should be guided through this process in a sensitive and culturally appropriate manner. Women in whom HPV (16/18) is detected can have this sample collected at colposcopy. It is also important that health professionals communicate the meaning of HPV test results in a sensitive and culturally appropriate manner.

Providing flexibility for collection of a vaginal sample to occur in any setting the healthcare professional overseeing the test considers to be appropriate could further reduce barriers to cervical screening for under-screened and never-screened groups including rural and remote communities, people from diverse cultural and faith backgrounds, and LGBTIQ communities. See [Section 5. Benefits, harms and cost-effectiveness of cervical screening in the renewed NCSP](#).

Health system implications of these recommendations

Clinical practice

When deciding whether to choose self-collection or clinician collection, people must be given clear information by the supervising healthcare professional about the probability that HPV will be detected and, if so, what follow-up will be required. Among those attending for a routine screening test, approximately 2% have HPV16/18 detected and approximately 6% have HPV (not 16/18) detected, although the latter varies by age. If a person chooses self-collection then the healthcare professional should provide appropriately tailored information about how to collect the sample and how they will receive the test results.

Resourcing

If people who have been regular participants in the NCSP switch to using self-collection, they may require two visits to their healthcare provider, which will increase the costs of the program. However, this is only expected to affect people in whom HPV (not 16/18) is detected, around 6% of all participants attending for routine screening.

Barriers to implementation

Many people may be unaware of the self-collection option. Healthcare professionals who identify individuals who are never-screened or overdue for screening are encouraged to opportunistically offer cervical screening and the choice of self-collection or clinician-collection. Women in whom HPV is detected may not undergo recommended further assessment, which includes taking a cervical sample for LBC and/or colposcopy.

It is possible that some healthcare professionals may choose to delay colposcopy referral for women with a positive oncogenic HPV (16/18) test result until after they have collected a cervical sample for LBC. However, women who have a positive HPV (16/18) test result should be referred directly to colposcopy and the cervical sample for LBC will be collected by the colposcopist.

Key messages to educate women and healthcare professionals about the self-collection option and subsequent management of any abnormalities will be developed as part of implementation planning to support this updated guideline.

See the [National Cervical Screening Program Policy](#).

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Women undergoing exit testing

Background

The HPV test is significantly more sensitive than cytology for the detection of cervical abnormalities caused by HPV infection, and a single HPV test for which oncogenic HPV is not detected is considered sufficient to safely discharge women from the NCSP.^[1]

MSAC has recommended that women between the ages of 70 and 74 years can cease 5 yearly screening after a HPV test at which oncogenic HPV is not detected.^[1]

Recommendations

MSAC evidence-based recommendation

REC6.22: Women aged 70–74 years in whom oncogenic HPV is not detected (exit testing)

Women can be discharged from the NCSP if they are aged 70–74 years and have a screening test at which oncogenic HPV is not detected.

Note: recommendation numbering changed Feb 2021, this was previously REC 6.16

Consensus-based recommendation

REC6.23: Referral of women aged 70–74 years with a positive oncogenic HPV screening test result (exit testing)

Women aged 70–74 who have a positive oncogenic HPV (any type) screening test result should be referred directly for colposcopic assessment, which should be informed by the result of LBC. If the sample was collected by a healthcare provider, then the laboratory will perform reflex LBC. If the sample was self-collected, then a cervical sample for LBC should be collected at the time of colposcopy.

Note: recommendation numbering changed Feb 2021, this was previously REC 6.17

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Screening in women older than 75

Within the renewed NCSP, women aged 75 years and older are eligible to undergo a cervical screening test if they have never participated in screening or have not had a screening test in the past 5 years.^[1]

Recommendations

NCSP recommendation

REC6.24: Women aged 75 years or older who request screening

Women who are 75 years or older who have never had a cervical screening test, or have not had one in the previous five years, may request a test and can be screened. The sample can be clinician-collected or self-collected, according to the woman's choice.

REC6.2 Clinician-collected cervical screening samples

A short course of topical oestrogen therapy could be considered in post-menopausal women, people experiencing vaginal dryness, anyone who has previously had poor sample pickup, or trans men who opt for a clinician-collected sample, prior to collecting the sample, for example daily for a period of at least 2 weeks, ceasing 1-2 days prior to the appointment. The reason for this should be explained (to reduce discomfort from the speculum and to improve the diagnostic accuracy of LBC).

Note: recommendation numbering changed Feb 2021, this was previously REC 6.18

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Unresolved issues

There is uncertainty about participation in the Renewed NCSP over the 5-yearly interval and compliance with the follow-up recommendations for HPV-positive women. There is also uncertainty about the timing of impact of HPV vaccination on the numbers of women referred to colposcopy, and about the transitional aspects of the program and impact on colposcopy volumes. These issues will be informed by modelled analysis (see [Modelling reports](#), [safety monitoring of the Renewed NCSP](#), and by emerging data from the [Compass trials](#).

Women who test positive for HPV 16/18 on a self-collected sample will need further investigation. It is unclear at present whether these women would prefer to visit their usual primary care health professional to have a cervical sample for liquid-based cytology taken by someone they know and trust, or be referred directly to specialist colposcopist and have the sample taken at that time. A stepwise protocol involving primary care would involve an extra examination, but might be perceived as less threatening. Several options might be offered, one of which should be further assessment by a female primary care practitioner or specialist.

Ongoing clinical research

A large RCT ([Compass](#)) is underway comparing 5-yearly HPV testing with 2.5 yearly liquid-based cytology screening in women aged 25–69 years in Victoria.^[1] The primary objectives of Compass are:^[1]

- to confirm that 5.5-year CIN3+-free survival is non-inferior for HPV screening compared with cytology screening in vaccinated and unvaccinated cohorts
- (if HPV screening is not inferior to cytology screening) to determine if 5.5-year CIN3+ free survival is superior among HPV-screened women who were HPV-negative at baseline, compared with cytology-screened women who were cytology-negative at baseline and at 2.5-year follow-up.
- Compass is providing information on colposcopy referral rates and outcomes and is acting as a sentinel experience for the Renewed NCSP.

Initial results have been published from the pilot component of the Compass trial, relating to outcomes at baseline and 12-month follow-up. Results from 5-year follow-up in the pilot and outcomes at baseline and 12-month follow-up in the main trial are forthcoming.

A body of implementation research on universal self-collection is underway in Victoria.

- EASI-C: (Expanding Access to Self-collection to Increase Cervical Screening participation) aims to support and monitor the implementation of universal access to self-collection by working with general practices in Victoria to identify and mitigate the implementation challenges experienced.
- Do it for Yourself is a demonstration project of universal access to self-collection in Victorian Aboriginal Community Controlled Health Services that aims to explore the impact and acceptability of self-collection for Aboriginal women. The project also aims to evaluate rates of follow up for women testing HPV positive and to document implementation challenges experienced at the service level.

Future research priorities

The use of dual-stained cytology for the overexpression of the molecular markers p16 and Ki 67 has been proposed as a strategy for further stratification of risk among HPV-positive women.^{[1][2][3]} In particular, there is a need to determine whether or not dual staining (p16 and Ki67) for women who test positive to HPV (not 16/18) on partial genotyping would materially

improve the prediction of cervical cancer risk. The Compass trial is also assessing the role of this technology and initial results are expected in around 2022.

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7. Colposcopy

Author(s):

- [Mr. C. David H. Wrede](#) — Author
- [A/Professor Alison Brand](#) — Co-author
- [Professor Ian Hammond](#) — Co-author
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

Introduction

The aim of diagnostic colposcopy following an abnormal cervical screening test is to assess the nature, severity and extent of the abnormality. This requires the identification of the cervix and external os, the exclusion of invasive disease, the mapping and typing of the transformation zone (TZ), the identification of any visible abnormalities and the targeting of the most abnormal area(s) for biopsy. Systematic examination of the whole lower genital tract and accurate, concise recording of the findings are required to produce the highest sensitivity and best positive predictive value for diagnosing high-grade abnormalities, as well as determining if treatment is required and planning the most appropriate mode, timing and extent of therapy.

In the renewed National Cervical Screening Program (NCSP) colposcopists are required to submit data from diagnostic and therapeutic colposcopy to the National Cancer Screening Register (NCSR). In return, they will receive data directly from the NCSR to enable them to review their own performance against defined benchmarks. These data can then be submitted to fulfil requirements for recertification in colposcopy. The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) will manage the certification and recertification processes for colposcopists. In the renewed program, the annual performance report prepared by the Australian Institute of Health and Welfare (AIHW) will include colposcopy data.

This chapter contains recommendations about the performance of colposcopy and related treatments. It is not intended to replace supervised training in accredited centres, nor attendance at colposcopy training and update courses, but offers guidance as to the minimum standards expected of a colposcopist providing services to the NCSP.

See:

- [Colposcopy terminology](#)
- [Principles of practice](#)
- [History, examination and investigation](#)
- [Treatment](#)
- [Colposcopy data for the National Cancer Screening Register](#)
- [Quality improvement in colposcopy](#)
- [Supplement. Colposcopy information for discussion with patient](#)
- [Supplement. Colposcopy technologies and documentation](#)

Colposcopy terminology

[Guideline contents](#) > [Colposcopy terminology](#)

Author(s):

- [Mr. C. David H. Wrede](#) — Author
- [A/Professor Alison Brand](#) — Co-author
- [Professor Ian Hammond](#) — Co-author
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

2011 International Federation for Cervical Pathology and Colposcopy (IFCPC) nomenclature
The terminology surrounding the clinical reporting of colposcopic examinations has continued to evolve, reflecting the improved understanding of cervical oncogenesis and the normal and abnormal appearances of the cervix. It is timely to review the current terminology used in Australia and align it to internationally accepted standards.

In Australia, the current commonly used nomenclature is the terminology recommended by the International Federation for Cervical Pathology and Colposcopy (IFCPC) in 2002.^[1] In 2008, IFCPC formed a nomenclature committee to review the previous IFCPC terminologies (1975, 1990 and 2002) and publications that critically analysed each colposcopic sign, aiming to create an evidence-based terminology. The committee, chaired by Jacob Bornstein, was composed of 13 colposcopists from different countries and one pathologist from Australia. After an exhaustive and transparent process the final terminology was reviewed and approved by all committee members, the IFCPC board and the IFCPC general assembly held at the World Congress in Rio de Janeiro in July 2011.^[2]

As the representative body of the national societies for colposcopy and cervical pathology, the IFCPC recommended that the 2011 terminology replace all other terminologies and be implemented without delay for diagnosis, treatment and research. It is recommended that the 2011 IFCPC terminology^{[2][3]} (see the following section) should be used in Australia and replace other terminology.

Practice point

REC7.1: New colposcopy terminology

The new terminology adopted by the IFCPC in 2011 should be incorporated into Australian practice.

Summary of IFCPC colposcopic terminology of the cervix^{[2][3]}

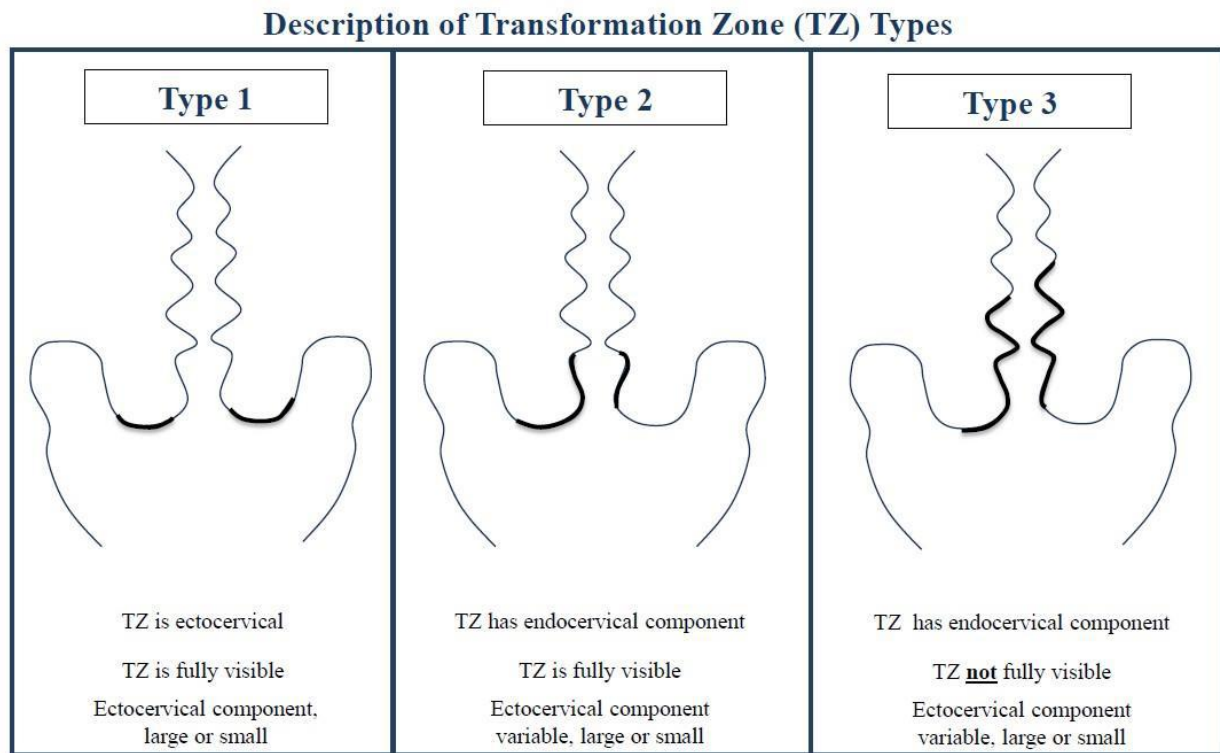
General assessment

The colposcopist should assess and record the following:

- adequate/inadequate: records whether the cervix has been visualised or not and includes the reason if inadequate (e.g. vaginal stenosis, cervix obscured by inflammation, bleeding, scarring)
- squamocolumnar junction visibility: this refers to the internal margin of the TZ that is either completely visible, partially visible, or not visible
- TZ should be classified as Types 1,2,3 according to the visibility of all or part of the upper limit of the squamocolumnar junction:
- **Type I** – the whole TZ including all the upper limit is ectocervical

- **Type 2** – the upper limit of the TZ is partly or wholly visible in the canal and is completely visible around 360 degrees
- **Type 3** – part or the entire upper limit of the TZ cannot be seen in the canal. In Type 3 TZ the outer limit may be visible on the ectocervix, in the canal or also not visible (Figure 7.1).

Figure 7.1. Description of transformation zone (TZ) categories



Description of transformation zone (TZ) categories

Normal colposcopic findings

The colposcopist should assess the following:

- Identify the outer limit of the original squamocolumnar junction.
- Identify the columnar epithelium, and upper limit of the TZ.
- Look for and note the following normal findings: ectopy, metaplastic squamous epithelium (mature or immature), nabothian cysts, crypt (gland) openings, deciduous in pregnancy or atrophy.

Abnormal colposcopic findings (after application of acetic acid)

Aceto-white changes:

- Minor (Grade 1)
 - thin aceto-white epithelium; irregular geographic border
 - fine mosaic, fine punctation
- Major (Grade 2)
 - dense aceto-white epithelium, rapid appearance of aceto-whitening, cuffed crypt (gland) openings
 - coarse mosaic, coarse punctation, sharp border, inner border sign, ridge sign

Suspicious for invasion

Atypical vessels

- additional signs (suspicious for invasion): fragile vessels, irregular surface, exophytic lesion, necrosis, ulceration (necrotic), tumour/gross neoplasm suspicious for invasion

Lugol's staining (Schiller's test) if performed:

- stained/non-stained

Location of the lesion:

- Is this inside or outside the TZ?
- location of the lesion by clock position

Size of the lesion:

- number of cervical quadrants the lesion covers
- size of the lesion (as percentage of cervix)

Miscellaneous findings

- Stenosis (partial or complete), congenital anomaly, post treatment consequences, endometriosis, congenital TZ, condyloma, polyp (ectocervical/endocervical) inflammation.

Excision treatment types

This includes stratification and measurement of treatment excision specimens (Australian modification of IFCPC excision nomenclature).

Excision treatment by whatever mode defined by the length of cervical tissue excised as:

- Type 1 < 10 mm
- Type 2 > 10 mm and < 15 mm
- Type 3 > 15 mm

(See [Treatment](#).)

NB: This stratification is modified from that of the IFCPC (2012) because, traditionally in Australia, excision specimens are measured using two diameters (anterior to posterior; 12 to 6 o'clock, and side to side; 3 to 9 o'clock) and length (external os to endocervical margin).

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Principles of practice

Principles of practice

Colposcopy should be conducted:

- by an adequately trained colposcopist who is registered with c-QUIP and undertakes mandated QA activities
- in appropriate surroundings
- with properly functioning diagnostic and therapeutic equipment

Patient information should be provided (see [Supplement. Colposcopy information for discussion with patient](#)):

- before or during the first colposcopy consultation
- after a treatment
- in a culturally and linguistically appropriate format.

Results of any procedure or treatment should be communicated in a timely fashion. Non-attendance should be documented and minimisation strategies implemented.

The examination of the cervix and vagina with a magnifying instrument called a colposcope, to check for abnormalities.

Page Break

History, examination and investigation

History

History taking at a colposcopy consultation should be relevant, concise and accurately recorded.

Minimum clinical history

The colposcopist should obtain and record the following information:

- primary reason for referral (usually from referring healthcare professional), e.g. abnormal screening test, post-coital bleeding, abnormal cervical appearance or other
- screening history, previous colposcopies and treatments
- parity
- menstrual history or any abnormal bleeding
- past gynaecological history including history of sexually transmitted infections (STIs)
- past medical and surgical history with particular reference to immune-deficiency due to disease or treatment
- current medication and allergies
- smoking/tobacco use, current status
- HPV vaccination status
- relevant family history including diethylstilboestrol (DES) exposure.

Examination

The colposcopist should perform a systematic examination of the lower genital tract, including the cervix, vagina, vulva, perineum and perianal area.

Macroscopic

After visual inspection of the vulva, perineum and perianal skin, the cervix should be identified using a bivalve speculum, and observed with the naked eye and then with the colposcope. The vagina can be inspected through the speculum. Thorough the entire length on slow removal of a partially open speculum.

Colposcopic Cervix

The cervix should be examined under low-power magnification prior to application of acetic acid to:

- exclude clinical invasive disease
- note presence of inflammation, infection or atrophy.

Dilute acetic acid (3–5%) is applied to the cervix allowing for typing of the TZ and to determine the extent and degree of any abnormality.

Practice point

REC7.2 Preparation for colposcopy: post menopausal women, people experiencing vaginal dryness, or trans men

A short course of topical oestrogen therapy could be considered in post-menopausal women, people experiencing vaginal dryness, or trans men, for example daily for a period of at least 2 weeks, ceasing 1-2 days prior to the appointment. Reason for this should be explained (to reduce discomfort from the speculum and to improve the diagnostic accuracy of colposcopy and any associated LBC and/or biopsy).

Practice point

REC7.3: Colposcopy and acetic acid

Acetic acid should be applied for 2 minutes to allow sufficient time for aceto-white changes to become apparent. This is especially important when the lesion is low grade as it may take more time to become visible.

Application of aqueous Iodine (Lugol's or Schiller's solutions) before or after biopsy may assist in defining the external limits of the TZ and any vaginal extension or separate lesions. Iodine can be applied to outline the TZ at the examination preceding therapy, and this is particularly useful when there is vaginal extension of the TZ.

Remainder of lower genital tract (vagina, vulva, perineum & perianal area)

The vulva, perineum and perianal skin should be inspected and any abnormality noted. The upper vagina should be assessed at all colposcopies to avoid missing extension of cervical dysplasia or isolated lesions of vaginal intra-epithelial neoplasia (VAIN).^[1]

Practice point

REC7.4: Colposcopy and VAIN

When the LBC report predicts a squamous abnormality and there is no colposcopically visible cervical lesion, careful colposcopic examination of the vagina should be performed to exclude VAIN, using acetic acid and Lugol's Iodine.

Anus and anal canal

Women who are diagnosed with cervical dysplasia or are immune- deficient are at increased risk of anal intra-epithelial neoplasia (AIN) and anal cancer. Anoscopy, its findings and subsequent management is outside the scope of this document. It is usually practised by specially trained colposcopists, sexual health physicians or colorectal surgeons.^[2]

Investigations

Cytology

It is not necessary to take a cervical sample for LBC at the time of colposcopy, except in exceptional circumstances outlined below.^{[3][4]}

Practice point

REC7.5: Repeat LBC usually not necessary at time of colposcopy

It is not necessary to take a cervical sample for LBC at the time of colposcopy except in the following circumstances:

- delay in attending for colposcopy > 3 months after referral LBC
- referral LBC is unsatisfactory
- referral LBC is negative but lacks an endocervical component
- prior LBC is not available because the HPV test was performed on a self-collected sample
- the woman has developed symptoms suggestive of cervical cancer since undergoing her screening test.

Biopsy

The colposcopically directed biopsy should be taken from the most abnormal area of the cervix. There is evidence that, in larger lesions, the higher-grade abnormality will be more centrally placed, that taking more than one biopsy will detect more high-grade disease and that taking random four-quadrant biopsies has the highest sensitivity for detecting cervical intraepithelial

neoplasia (CIN) grade 2 or higher (CIN2+).^{[5][6][7][8][9]} However, the random four-quadrant biopsy technique will cause more discomfort, is not usual practice and is not acceptable to the majority of women.

In general, biopsy of abnormal areas should be encouraged, but many experienced colposcopists do not always biopsy a lesion that appears to be low-grade, especially in young women, when the referral cytology predicts pLSIL/LSIL. For less experienced colposcopists, biopsy of a suspected low-grade lesion is appropriate to confirm the diagnosis and exclude high-grade abnormalities. Colposcopists should be aware that histologically proven high-grade abnormalities due to non-16/18 HPV types may not have the classic colposcopic appearances of CIN2/3 (Swede scores <7). Adjunctive technologies may assist in identifying the most abnormal areas but these are not widely used in Australia at this time (see [Supplement. Colposcopy technologies and documentation](#)).

Consensus-based recommendation*

REC7.6: Biopsy of high grade lesions

The cervix should be biopsied when the LBC prediction is pHSIL or HSIL and the colposcopic appearance shows major change (see IFCCPC definition above) and the abnormal TZ is visible (Type 1 or Type 2 TZ).

Practice point

REC7.7: Biopsy visible lesion if suspicious for invasion when T3 TZ colposcopy

In some situations, when there is a visible high-grade lesion on the ectocervix but there is a T3 TZ (lesion extends into canal out of visual range), it may be reasonable to take a cervical biopsy of the visible lesion if there is any suspicion of superficially invasive or invasive carcinoma.

Practice point

REC7.8: Biopsy of low-grade lesions is encouraged but not always necessary

Women with a LBC prediction of pLSIL or LSIL and a colposcopic impression of low-grade disease or less may not always require a biopsy. However, biopsy is accepted practice for confirmation of the colposcopic impression and exclusion of high-grade disease, and should be encouraged, especially for less experienced colposcopists.

Endocervical curettage

Endocervical curettage (ECC) as an outpatient investigation is practised frequently in the USA and rarely in Australia. There is a lack of evidence to support its routine use in clinical practice.^[10] There is a lack of prospective studies evaluating the utility of ECC performed at the time of diagnostic colposcopy. However, the findings of a recent retrospective study^[11] suggest that ECC may be useful in predicting cervical cancer. The study included 455 women who had ECC at the time of colposcopy for an incompletely visible endocervical lesion, atypical glandular cells on smear or discrepancy between colposcopic impression and cytological abnormality. The ECC was performed by two expert colposcopists who used a Kevorkian curette to sample four endocervical quadrants. They analysed the reliability of ECC in detecting high-grade CIN (CIN2/3) and cervical cancer, and concluded that ECC had a high sensitivity in the diagnosis of endocervical pre-cancerous lesions and cancer. ECC resulted in a diagnosis of cancer in 96% of cases, either directly from the analysis of ECC tissue or from that of the cone biopsy made necessary by the ECC findings of a pre-cancerous lesion. They also concluded that, in some situations, a negative ECC could safely allow a period of surveillance and reduce the number of

unnecessary treatments. The authors recognised that, because they were very experienced colposcopists, it may not be possible to extrapolate their results to all colposcopists. It is possible, despite a lack of evidence, that ECC could be used in Australian practice, particularly when there is a discrepancy between referral LBC prediction (low-grade squamous intraepithelial lesion (LSIL), possible high-grade squamous intraepithelial lesion (pHSIL), or high-grade squamous intraepithelial lesion (HSIL)) and colposcopy in the presence of a Type 3 TZ. ECC may provide reassurance that there is no significant endocervical lesion and that an immediate diagnostic excision could be deferred and be replaced by short-term surveillance.

Imaging

Women who are referred for evaluation of abnormal glandular cytology, especially those with atypical glandular cells or endocervical cells of undetermined significance, may not always have a detectable lower genital tract abnormality.[12] In this situation, imaging of the upper genital tract could be performed. Imaging may detect gross disease of the fallopian tube, ovary and of the endometrium in postmenopausal women, as these sites may be giving rise to the abnormal glandular cells. Further investigation, such as endometrial sampling, to exclude an endometrial origin for atypical glandular cells, may be required.

However, in the renewed NCSP, LBC is only carried out following a positive oncogenic HPV test result. Therefore, the detection (via the screening episode) of abnormal glandular cells from extra-cervical sites will be reduced, given that endometrial, tubal and ovarian pathology is not HPV-related. However, such abnormal glandular cells could be present coincidentally, unrelated to the positive oncogenic HPV test result (see [Chapter 11. Management of glandular abnormalities](#)).

Practice point

REC7.9: Upper genital tract investigation

Upper genital tract imaging (usually transvaginal ultrasound) should be considered in cases where no lower genital tract abnormality is detected at colposcopy after referral with abnormal glandular cytology (including atypical glandular cells or endocervical cells of undetermined significance). In some women, further investigation, such as endometrial sampling to exclude an endometrial origin for atypical glandular cells, may be required.

Documentation

High-quality patient management requires meticulous documentation of the woman's medical record. The results of consultations, examinations and treatments must be recorded – preferably electronically, as this will facilitate the submission of colposcopy data to the National Cancer Screening Register (see Colposcopy data required for the National Cancer Screening Register). Colposcopy data can be entered into the National Cancer Screening Register using the Healthcare Provider Portal (this requires a Healthcare Provider Individual Identifier (HPI-I) and a [Provider Digital Access \(PRODA\)](#) account). The National Cancer Screening Register [website](#) provides information about how to access and use the Healthcare Provider Portal. Information can also be provided to the NCSR by HL7 direct links with specific clinical software systems or by using the paper form. It is useful to keep an annotated diagram of the cervix and vagina or keep a digitally captured image.

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Colposcopy and treatment

Author(s):

- [Mr. C. David H. Wrede](#) — Author
- [A/Professor Alison Brand](#) — Co-author
- [Professor Ian Hammond](#) — Co-author
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

The decision to treat

Women should understand the indication for treatment. Information regarding the procedure and potential complications should be given and consent obtained.

Most treatments can be completed under local anaesthesia as an outpatient procedure.

Obstetric and neonatal morbidity is associated with some treatment modalities and the aim is to ablate or excise the smallest amount of cervical tissue necessary to achieve clearance of disease.^{[1](#)[1](#)[2](#)[3](#)[4](#)[5](#)[6](#)}

Consensus-based recommendation*

REC7.10: Colposcopy prior to treatment

All women should have an adequate[†] colposcopic assessment prior to treatment.

[†]adequate: the cervix is clearly seen ([IFCPC 2011 terminology](#))

Consensus-based recommendation*

REC7.11: Histopathological confirmation prior to treatment

Treatment should be reserved for women with histologically confirmed HSIL (CIN2/3) or AIS, except for women requiring diagnostic excisional biopsy.

Consensus-based recommendation*

REC7.12: Biopsy prior to ablative treatment

Women should have a cervical biopsy prior to any ablative treatment.

Consensus-based recommendation

REC7.13: Pathology review of discordant test results

For women who have had a colposcopy with significant discordance between the histopathology and the referral cytology, both specimens should be reviewed by a pathologist from at least one of the reporting laboratories who should then convey the results of the review to the colposcopist in order to inform the management plan.

Practice point

REC7.14: Tertiary referral may be necessary

In some clinical situations, the woman should be referred to a more experienced colposcopist, a gynaecological oncologist, tertiary colposcopy clinic or gynaecological cancer centre:

- adenocarcinoma in situ
- abnormalities in pregnancy
- immune-deficient women
- women with multifocal lower genital tract disease.

Multidisciplinary/concordance consultation and meetings

In tertiary centres, a regular 'concordance' or multi-disciplinary team (MDT) meeting may be convened to review the pathology results and discuss the management of cases.^[7]

Practice point

REC7.15: Second opinion

When there is any concern about diagnosis or patient management, a second opinion should be sought and documented.

Practice point

REC7.16: The role of multidisciplinary team review

It is not always practical for a colposcopist to access a multidisciplinary team review which is usually conducted in a tertiary referral centre. However, a multidisciplinary team review is particularly helpful when:

- dealing with complex cases where there is discordance between histopathology and referral cytology (e.g. LBC prediction of HSIL, with negative or LSIL histology).
- implementation of treatment is not urgent and therefore it is possible to take the required time to review the findings and optimise the management plan.

Training

All therapeutic colposcopists should have undergone approved, recognised and supervised training and have demonstrated competence in the therapy/therapies that they use.

Modalities of treatment

Practice point

REC7.17: Colposcopy at time of treatment

All treatments should be performed under colposcopic vision, with the exception of cold-knife cone biopsy.

Treatment is achieved by ablation of the abnormal tissue or the complete excision of the atypical TZ. The modalities currently used in Australia are:

- ablation – tissue destroyed by an energy source
- CO₂ Laser
- excision – tissue excised by surgery using a scalpel or energy source
- cold-knife (scalpel) cone biopsy
- electrosurgery

- large loop diathermy; loop electrosurgical excision procedure (LEEP) or large loop excision of the TZ (LLETZ)
- fixed profile rotating excision (Fisher cone or Utah type)
- fine needle/wire; straight wire excision of the TZ (SWETZ) or needle excision of the TZ (NETZ)
- CO₂ laser cone.

Cryotherapy and thermal coagulation are not currently used in Australia (see [Supplement. Colposcopy technologies and documentation](#)).

The amount of cervical tissue to be ablated or excised should be determined by:^{[8][9]}

- the Type of TZ
- the size and extent of the lesion
- the known or suspected final histology.

Note: ideally, the planned depth of ablation/excision should be recorded and where possible, the extent of the ablation/excision should be measured.

Ablation

Consensus-based recommendation*

REC7.18: Criteria for ablative treatment

Ablative therapy should be reserved for women intending to have children, and when the following conditions have all been met:

- TZ is completely visible (Type 1 or Type 2).
- There is no evidence of invasive or glandular disease.
- A biopsy has been performed prior to treatment.
- HSIL (CIN2/3) has been histologically confirmed.
- There is no significant discordance between the histopathology and referral cytology results.

Practice point

REC7.19: Depth of ablation

A Type 1 TZ with a HSIL (CIN2/3) lesion requires 6–8 mm (and not more than 10 mm) of cervical ablation to be adequately treated.

Carbon dioxide (CO₂) laser ablation

CO₂ laser ablation is usually practised in tertiary centres where a clinical CO₂ laser is available. Laser ablation is usually performed as an outpatient procedure under local anaesthesia.^[10]

Excision

Excisions are stratified as Types 1, 2 or 3, according to the length of cervical tissue excised. It is important to establish the stratification of the excision type and, as Australian pathologists do not routinely use the measurements specified by the IF CPC, a modification of the IF CPC definition has been suggested.

Treatment types are defined below (modified from the IF CPC):^[11]

- **Type 1 excision (for Type 1 TZ):** usually to 8 mm and not more than 10 mm length of cervical tissue excised
- **Type 2 excision (for Type 2 TZ):** not more than 15 mm length of tissue excised

- **Type 3 excisions (for Type 3 TZ):** equivalent to 'cone biopsy' and > 15 mm length. Should be used for women with:
 - suspected invasive disease
 - proven or suspected glandular disease
 - Type 3 TZ with proven or suspected high-grade disease.

The specimen should be removed in **one** piece. Specimens in two or more pieces may create difficulties in histological assessment, particularly in the interpretation of margins, completeness of excision and the evaluation of invasive disease. This is very important if AIS is predicted or histologically confirmed.

However, in women who have a very large ectocervical TZ, it may be necessary to remove the TZ in two pieces. This should rarely be required and is an unusual situation. It is important that the endocervical and stromal margins are suitable for pathological interpretation, that the specimens are accurately orientated and labelled and that the whole lesion is removed.

Consensus-based recommendation*

REC7.20: Excision specimen quality and pathology

Excisional therapy should aim to remove the entire TZ with a pre-determined length of cervical tissue, ideally in one piece, with minimal distortion or artefact to the final histological specimen.[†]

[†]This is critical for management of suspected or histologically confirmed AIS.

Practice point

REC7.21: Excision specimen quality, pathology and very large ectocervical lesion

A very large ectocervical lesion may require removal in two pieces in order to remove the entire lesion. It is still important that the endocervical and stromal margins are suitable for pathological interpretation and that the specimens are accurately oriented and labelled.

Practice point

REC7.22: Excisional techniques and surgical competency

Therapeutic colposcopists should use the excisional techniques with which they are comfortable and competent and that produce the best histological specimen.

Cold-knife cone biopsy

Historically, cold-knife cone biopsy has been the recommended procedure in suspected cases of glandular disease and invasion. Current evidence indicates that it carries the best rates of single specimens and achieved length > 15 mm (Type 3 excision), but it has higher reported rates of short-term and long-term complications including primary haemorrhage and subsequent pre-term labour, when compared with other excisional modalities.^{[3][4][5][6][12][13]} However, a meta-analysis reported that all excisional procedures used to treat cervical intraepithelial neoplasia seem to be associated with adverse obstetric morbidity.^[6] Loop diathermy excisions (LLETZ/LEEP) that remove large amounts of cervical tissue probably have the same effect as cold-knife cone biopsies. Given the design of published observational studies, observed differences in perinatal mortality and severe premature delivery, in treated versus non-treated women, cannot be ascribed solely to treatment.^[6]

Practice point**REC7.23: Cold-knife cone biopsy: setting**

Cold-knife cone biopsy should be performed in an operating theatre, under general anaesthesia, by a gynaecological oncologist or gynaecologist competent in the technique.

Loop diathermy (LEEP or LLETZ)

Loop diathermy (LEEP or LLETZ) is the most commonly used therapy for CIN in resource-rich countries. Disposable loops are available in a wide variety of profiles and sizes (Figure 7.2). The loop should be chosen after colposcopy preceding therapy to meet the width of the TZ and the planned type (length) of excision.

In Australia it has been reported that this technique frequently results in fragmented specimens with excessive thermal artefact.^[4] Published studies from other countries do not report the same rates of problems with loop diathermy, suggesting that this is a local training and performance issue.

Diathermy settings should be significantly higher than used in most open or laparoscopic surgeries to reduce thermal artefact (this should be minimised to 0.2 mm). It is imperative that the clinician obtain the recommended power settings from the electrosurgical system manufacturer. It should be noted that each clinician will have a personal preference (to suit their surgical technique, loop size, speed of excision and other factors) that determine their personal 'best settings' for electrosurgical procedures. Extensive application of coagulation current should be avoided, especially at the endocervical margin, which rarely bleeds.

Figure 7.2. Examples of loops



Examples of loops



Examples of loops

Practice point

REC7.24: Loop excisional biopsy technique (LEEP/LLETZ)

A single pass of the loop (side to side or posterior to anterior) to produce a specimen in one piece is optimal.

Practice point

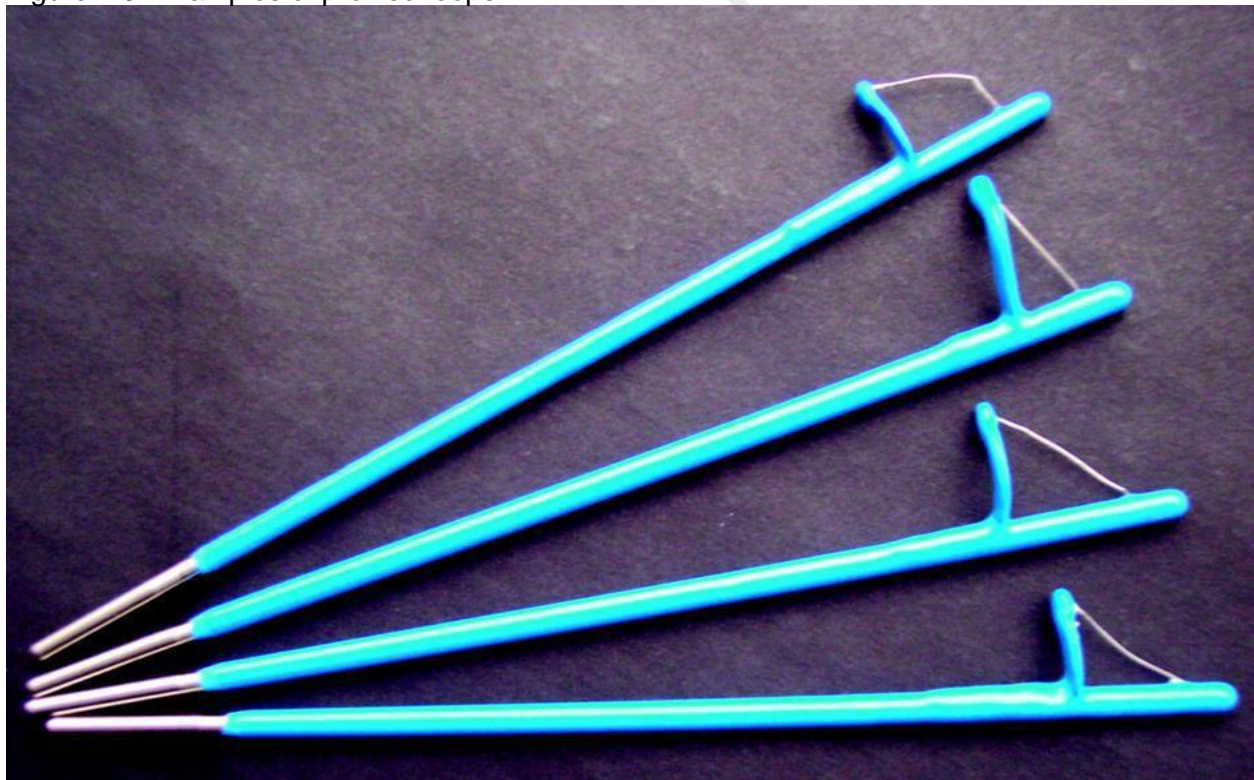
REC7.25: Loop 'top-hat' excisions should be avoided (LEEP/LLETZ)

The 'top-hat' excision techniques using a wire loop, in which a second piece of endocervical tissue is removed after the first excision, is not an alternative to a properly performed single-piece Type 3 excision, and should be avoided.

Profiled electrosurgical excision

There are several patented profiled devices for a rotational excision (Fisher, Utah, etc) that come in different sizes/lengths (Figure 7.3).^[15] These are inserted into the cervix under power, usually anteriorly (12 o'clock) and rotated through 360 degrees. They have the advantage of being easy to use, but have the thermal artefact disadvantage of diathermy-based techniques.^[14] These devices usually provide a one-piece specimen, but the initial entry incision renders an opened cone that may distort during fixation and require a different pathological management to single-piece closed loop and knife cones.

Figure 7.3. Examples of profiled loops



Examples of profiled loops

Diathermy point/needle excision: straight wire excision of the TZ (SWETZ) and needle excision of the TZ (NETZ)

Type 3 excisions can be achieved using cutting diathermy with a straight or angled needle (NETZ)^[16] or straight wire (SWETZ)^[17] in the same fashion as using a scalpel. Bleeding is less

than with cold-knife cone biopsy but thermal artefact can be greater than with loop or profiled excisions. Scarring and the risk of stenosis are greater than with loop diathermy or cold-knife excisions.

Laser cone biopsy

Laser Cone Biopsy was introduced in the 1980's after it was realised that widespread use of laser ablation might be resulting in the under diagnosis of micro-invasive disease. It can be practised under local anaesthesia in adequately equipped rooms or outpatients as well as in operating theatres, but requires considerable skill in balancing the laser's ability to cut and coagulate.^[18] ^[12] It can produce more thermal artefact than correctly set diathermy techniques and takes significantly longer to perform than LEEP/LLETZ. It is rarely performed now.

Special treatment considerations

Treatment of endocervical adenocarcinoma in situ (AIS)

Women with a proven glandular abnormality who wish to retain their fertility should be treated with local excision and some colposcopists will also perform a post-excision endocervical curettage at the time of the excision.^[19] A woman presenting with a definite high-grade glandular abnormality on cytology has a 24% or greater chance of having invasive adenocarcinoma in the excision specimen.

A Type 3 excision is usually performed, most commonly by cold-knife cone biopsy in Australia.^{[20][21][22]} There are recent retrospective reports, including one from Western Australia, showing satisfactory management with large loop diathermy, which is also widely practised overseas.^{[23][24]} However the authors concluded that further prospective studies were needed to confirm their findings.^[24] The shape of the excision is not usually described as a true cone but a cone on top of a cylinder. The initial incision is perpendicular to the external cervical surface to ensure the excision of glands originally exposed in the post-menarche TZ now overlain by mature squamous metaplasia.

There is evidence that in women under 35 years of age a more conservative Type 2 excision can be offered initially, as long as the woman is counselled about the possibility of repeat therapy. Any incomplete margin will require a repeat excision.^{[25][26][27]} Because of the acceptance of the concept of 'skip' lesions it has been practice to try to achieve an endocervical clearance of a minimum of 5 mm.

Practice point

REC7.26: Cold-knife cone biopsy and AIS

Predicted or histologically confirmed AIS should be treated by a Type 3 excision (usually a cold-knife cone biopsy) performed in an operating theatre, under general anaesthesia, by a gynaecological oncologist or gynaecologist competent in the technique.

Superficially invasive squamous cell cancer (SISCCA)[†]

Women diagnosed as FIGO Stage IA1^[28] squamous carcinoma after local excision do not require further excision if the following criteria are satisfied:^{[29][30]}

- The margins are clear of CIN and invasive disease.
- There is no evidence of lymphovascular space invasion.
- The case has been reviewed by a gynaecological pathologist and discussed at a gynaecological oncology multidisciplinary meeting.

[†]Previously called 'micro-invasive'.

Practice point

REC7.27: Role of repeat excision in management of SISCCA

In the presence of a superficially invasive squamous carcinoma, if HSIL (CIN2/3) extends to any excision margin, a repeat excision (usually by cold-knife cone biopsy) is recommended.

Treatment at first visit

There is evidence that treatment at the first visit can reduce overall levels of anxiety in women with cervical abnormalities,^[31] but anxiety may be increased if they are not adequately informed of the potential for treatment at their first visit.

Most women do not need to consider this option. It is recommended that women should have an adequate colposcopic assessment and a colposcopically directed biopsy at the first visit. This will provide histological confirmation of the colposcopic impression and inform the need for definitive treatment that is usually performed at a later date.

The indiscriminate practice of treatment at first visit ('see and treat') has in the past led to an excessive number of unnecessary treatments, especially when the referral cytology is pLSIL/LSIL and the diagnostic colposcopist thought there was a higher grade lesion but this was not confirmed on final histopathology.^[32] This approach should be avoided in light of increased awareness of the potential complications of treatment.^{[5][6]}

A recent systematic review and meta-analysis included 13 studies that considered the rate of 'over-treatment' for women with various referral cytology results. Overall rates of over-treatment were 11.6% in women with high-grade cervical cytology and high-grade colposcopic impression, 29.3% in women with high-grade cervical cytology and low-grade colposcopic impression, 46.4% in women with low-grade cytology and high-grade colposcopic impression, and 72.9% for women with low-grade cytology and low-grade colposcopic impression. The authors recommend that 'see and treat' is reasonable **only** if the referral cytology and the colposcopic impression are both high grade.^[33]

In the Australian context it may be appropriate to consider treatment, which is almost always excisional, at the first visit.^{[34][35][36]} Women may face logistical problems attending for appointments, especially if they live a considerable distance from the colposcopy clinic or private rooms. Some anxious women request that treatment is performed at the first visit so that the diagnostic and treatment process is not prolonged.

Women for whom treatment at the first visit is being considered should satisfy the following criteria:

- Referral cytology predicts HSIL.
- Colposcopic impression is high-grade disease.
- TZ is completely visible (Type 1 or 2).
- Invasive cancer has been excluded.
- The lesion is suitable for treatment under local anaesthetic.

Practice point

REC7.28: Do not treat at first visit with a LBC report of a low-grade lesion

Women who have a LBC prediction of pLSIL/LSIL should **not** be treated at the first visit.

Repeat treatment

Recurrence may occur after an ablative or excisional procedure. If, after an excisional procedure, the HSIL (CIN2/3) extends to the endocervical (deep) or stromal (lateral) margins of

the specimen, there will be a higher incidence of recurrence, but not high enough to justify routine repeat excision, in the absence of glandular or invasive disease.^{[37][38]} However, women aged 50 years and over with involved margins or women in whom adequate subsequent colposcopic examination and follow up cytology cannot be guaranteed, should be offered repeat excision and, in some cases, hysterectomy.^[39]

Practice point

REC7.29: Excision required for recurrent disease after ablation

If there is recurrence of high-grade disease after previous ablation, treatment should be by excision.

Practice point

REC7.30: Repeat excision not necessarily required for incomplete excision of high-grade lesions

Women who have incomplete excision of HSIL (CIN2/3) with positive endocervical or stromal margins do not necessarily require immediate repeat excision and could be offered test of cure (HPV and LBC) surveillance, with the exception of:

- women aged 50 years or over
- women who may not be compliant with recommended follow-up
- women in whom subsequent adequate colposcopy and follow-up cytology cannot be guaranteed.

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Colposcopy data for National Cancer Screening Register

Under the renewed NCSP, all colposcopists are required to report a minimum data set to the National Cancer Screening Register (NCSR). A colposcopy subgroup of the NCSP Quality and Safety monitoring Committee has defined the minimum data set required as part of the Quality Framework for the NCSP.

Colposcopy data can be entered into the NCSR using the Healthcare Provider Portal (this requires a Healthcare Provider Individual Identifier (HPI-I) and a Provider Digital Access (PRODA) account). The NCSR [website](#) provides information about how to access and use the Healthcare Provider Portal. Information can also be provided to the NCSR by HL7 direct links with specific clinical software systems or by using the paper form.

Healthcare professionals should ask all women whether they identify as Aboriginal and/or Torres Strait Islander, and a woman's Aboriginal and Torres Strait Islander status should be recorded on relevant clinical records, including pathology request forms, in accordance with the Australian Bureau of Statistics classification and standards.

Quality improvement in colposcopy

The NCSP Quality and Safety Monitoring Committee has developed a Quality Framework that includes quality standards and targets for individual diagnostic and therapeutic colposcopists.

Diagnostic and therapeutic colposcopists

Diagnostic and therapeutic colposcopy has been practised in the absence of any organised quality assurance program since before the commencement of the NCSP in 1991. Within the pre-renewal NCSP, colposcopy was the only screening program element not included in quality assurance monitoring. The NCSP Quality Framework includes the following statements:

1. Colposcopic assessment should be performed in a timely manner to ensure the safety of women at risk of cervical cancer precursors.
2. Women who are diagnosed with cervical cancer are appropriately referred to a certified gynaecological oncologist or gynaecological cancer treatment centre for further assessment and/or treatment.
3. Women are appropriately treated and returned from colposcopic surveillance to routine screening in accordance with the clinical management guidelines.
4. The therapeutic colposcopist adequately informs the woman and her usual cervical screening test collector of any follow-up that may be required in accordance with the clinical management guidelines.
5. The quality of the colposcopic and therapeutic assessment procedures is regularly assessed. It is mandatory for all colposcopists (diagnostic and therapeutic), who provide services to the NCSP, to participate in the cervical management quality assurance program (c-QUIP). Quality standards for diagnostic colposcopists have been developed by the NCSP to provide guidance for individual performance review.
6. Colposcopists must provide the National Cancer Screening Register with data in accordance with the minimum dataset.
7. The National Cancer Screening Register provides colposcopists with individual performance data benchmarked to national standards for quality improvement and certification purposes.

Colposcopy information for discussion with patient

Patient information

Most women attending for a colposcopy consultation have significant anxiety in advance of the appointment (see [Chapter 19. Psychosocial care](#)).^{[1][2][3]} This is often related to uncertainty about the diagnosis and possible treatment, but may reflect concern regarding the approaching gynaecological (colposcopic) examination. Colposcopists should take measures to alleviate these anxieties while protecting each woman's dignity and privacy. A Cochrane review of interventions to reduce anxiety in women undergoing colposcopy, which included six randomised controlled trials, found that music during colposcopy significantly reduced anxiety levels and pain during the procedure.^[4]

Effective information and communication is essential for all women. There is good evidence that accurate and well-presented information improves women's experience of colposcopy and reduces anxiety.^{[5][6]} Women may not remember all of the verbal information given at the time of consultation or treatment and, ideally, written information should be available where appropriate.

Ideally, women should be given relevant information at the time of cervical screening and before colposcopy. Most hospital colposcopy clinics and many colposcopists will have their own information pamphlets or leaflets. Information is also available from proprietary sources (usually free of charge) or from the Commonwealth and state- and territory-based programs of the National Cervical Screening Program (NCSP).^{[7][8]}

It is essential that women be given the opportunity to discuss their management and any concerns they may have at the time of consultation or treatment.

Questions that women may ask include the following:

- What do my test results mean?
- Do I need more tests and if so, why?
- What treatment do you advise and why?
- Are there any other options?
- Will I need time off work?
- Will I be able to drive myself home after my treatment?
- Will there be bleeding or vaginal discharge after treatment?
- How often will I need to come back to see you?
- When is my next check-up due?
- Is there anything I can do to help myself in the future?
- Can you give me some information about HPV?

Prior to the first visit for colposcopy

Written information sent to the woman should include:

- a basic description of the causes of cervical pre-cancer and cancer and the relationship to HPV infection.
- a list of the grades of abnormality that are reported in the screening test results with a brief explanation of what they mean.
- a description of the colposcopic examination and possible biopsy
- the potential outcomes of the colposcopic assessment, including commonly used treatment modalities.

- a recommendation for post-menopausal women, people experiencing vaginal dryness, or trans men to speak to their provider about a short course of topical oestrogen therapy before the colposcopic examination to reduce discomfort from the speculum and to improve the diagnostic accuracy of colposcopy and any associated LBC and/or biopsy.

At the time of the colposcopy consultation

Colposcopists should be sensitive to the psychophysiological needs of individual women undergoing colposcopy:

- Matching intra-procedural information with different coping styles reduces psychophysiological disturbance in women undergoing colposcopy.^[9]
- Check that the woman did receive the pre-visit information. If not she can read it while waiting for her consultation.
- Remind the woman about the technique of colposcopy and the possible need for a cervical biopsy.
- During the examination keep her informed as to what can be seen and what is happening and especially if and when a biopsy is taken.
- If a video-colposcopy is available and the woman wishes to watch the colposcopic image, this should be encouraged but be aware that in some women this can cause anxiety.
- Following the examination and if a biopsy has been performed, the woman should be given clear advice regarding the transient occurrence of mild pelvic discomfort and vaginal 'spotting' and should be advised to avoid sexual intercourse for a few days.
- If a biopsy has been taken she should be given clear instructions, preferably in writing, as to how she will obtain the results of the biopsy.
- Prior to leaving the consultation visit, particularly if it appears likely that she will require treatment, the woman should be given verbal and written information about any potential treatment procedures and their complications that may affect her consent to be treated.
- If treatment is not likely but she needs a follow-up visit or needs to see her GP, this information should be clearly articulated and should be confirmed in writing.

At the time of a treatment visit

The colposcopist should:

- confirm that the woman understands and consents to treatment
- if colposcopy is done under local anaesthesia, keep the woman informed about the procedure in real time
- after the procedure, ensure that the woman is given verbal and written information about potential common complications, especially bleeding and infection and what she should do if they occur. This should be reinforced by written information, including advice as to how the pathology results of any treatment will be obtained.
- provide information about necessary follow-up after treatment.

Post treatment

Information should include the following advice:

- Some women experience abdominal cramps after treatment. This can feel like a painful period. It is also normal to have a dark or watery vaginal discharge for up to 4 weeks. This may include the passing of small clots while the cervix heals.
- Avoid using tampons for 4 weeks after treatment.
- Abstain from sexual intercourse for 4 weeks after treatment.
- Avoid strenuous exercise or swimming for 10–14 days after treatment.
- Some women may have temporary alteration in menstrual pattern after an excisional treatment, including heavier and more painful flow in the subsequent period.

Note: Culturally and linguistically appropriate information should be available for Aboriginal and Torres Strait Islander women and women who speak a language other than English, preferably in their first language.^[10] However, it is often not possible for written information to be available in all languages. Women should be offered access to interpreter services when required (information on interpreter services can be accessed from [Translating and Interpreting Services](#)). Appropriately tailored information should also be available for anyone with a cervix, across the spectra of gender-diversity and sexual orientation including women who identify as lesbian or bisexual, and trans and gender diverse people with a cervix.

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Colposcopy technologies and documentation

Adjunctive technologies

A number of modern technologies based on spectroscopy and electrical impedance can be used in practice to increase the sensitivity, positive predictive value and specificity of colposcopy, including [LuViva](#), [DySIS](#) and [ZedScan](#).^[1] Of these, only ZedScan is registered with the Therapeutic Goods Administration and is undergoing evaluation in Australia. These are not commonly used in Australia.

Modalities of treatment not commonly used in Australia

Cryotherapy

This is not recommended in resource-rich countries, where alternative treatment modalities exist, as the rate of clearance of HSIL (CIN3) is poor and the persistence or recurrence of HSIL (CIN2/3) is higher than with other techniques. When used for the treatment of a symptomatic inflamed ectropion or persistent low-grade disease, a double-freeze technique is preferred, and has lower rates of residual disease compared with a single-freeze technique.^{[2][3]} It is rarely, if ever, used in Australia.

Thermal Coagulation (Semm or 'Cold' coagulation)

The thermal coagulator is a self-contained electrically powered device which works with a probe at 60–130 degrees Centigrade (it was known as 'cold' because it works at lower temperature than diathermy). The probe, which comes with half a dozen different profiles, goes through a self-sterilising cycle before being applied directly to cervix in 20-second applications that can be multiply repeated to cover the whole TZ. Studies have confirmed its efficacy in benign, low and high-grade abnormalities.^{[4][5]} There is currently a resurgence of interest in using this modality in Europe, and in future it may be promoted in Australia.

Documentation

High-quality patient management requires meticulous documentation of the woman's medical record. The results of consultations, examinations and treatments must be recorded, preferably electronically to facilitate submission of colposcopy data to the NCSR (see [Colposcopy data required for the National Cancer Screening Register](#)) and in providing written communication back to the primary care provider. Colposcopy data can be entered electronically into the National Cancer Screening Register using the Healthcare Provider Portal (this requires a Healthcare Provider Individual Identifier (HPI-I) and a Provider Digital Access ([PRODA](#)) account), or by HL7 direct links with specific clinical software systems

Description of abnormalities should be in line with the 2011 IFCPC terminology (see [2011 International Federation for Cervical Pathology and Colposcopy \(IFCPC\) nomenclature](#)). The following information should be included:

- the adequacy of the examination
- the absence (or presence) of evidence of invasive disease
- the presence of a squamous and/or glandular pre-cancerous abnormality
- the extent of the TZ, ectocervically and endocervically and hence the TZ Type; 1, 2, or 3. This should also clearly mention extension of abnormalities onto the vaginal fornices, if present.
- the number of cervical quadrants involved in any abnormality
- the overall colposcopic impression.

Colposcopic findings at the time of treatment should be recorded especially if there has been a change in appearance of the cervix.

In addition the following should be included:

- the mode and technique of treatment
- the depth of tissue destruction achieved in all ablative treatments
- the type of excision: Types 1, 2 or 3
- the size of loop/fixed profile wire used in all LEEP/LLETZ and Fisher/Utah conisation procedures and the diathermy settings
- the laser setting and length of time of application
- any complication occurring during or immediately following the treatment.

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8. Management of discordant colposcopic impression, histopathology and referral LBC prediction

Background

Various clinical scenarios may present difficulties for diagnosis and management when there is discordance between cytological and colposcopic or histopathological reports for women referred for colposcopic assessment on the basis of the results of human papillomavirus (HPV) testing and liquid-based cytology (LBC):

- A woman with a cytological prediction of a high-grade squamous intraepithelial lesion (HSIL) may have a normal colposcopy.
- Colposcopically directed biopsy may confirm a low-grade lesion after a cytological prediction of HSIL.
- A woman with a positive oncogenic HPV (any type) test result and a LBC report of negative, or prediction of a low-grade squamous intraepithelial lesion (LSIL) or HSIL, may have Type 3 transformation zone (TZ) colposcopy (previously termed 'unsatisfactory' colposcopy).
- A woman may have a positive oncogenic HPV (16/18) test result, a negative LBC report, and colposcopy that is either normal or Type 3 TZ.

The following clinical scenarios are considered in this chapter:

- Normal colposcopic findings following a LBC prediction of a low-grade or high-grade lesion (see also [Management of women with histologically confirmed low-grade squamous abnormalities](#))
- Type 3 TZ (unsatisfactory) colposcopy following LBC prediction of a low-grade or high-grade lesion (see [Summary of IFCPC colposcopic terminology of the cervix](#)).

Normal colposcopic findings following LBC prediction of a low-grade or high-grade lesion

Guidelines for the pre-renewal National Cervical Screening Program (NCSP)^[1] recommended the following management for women with normal colposcopy (Type 1 or Type 2 TZ):

- Women with normal colposcopy following a cytological prediction of LSIL should have annual cytological surveillance until two normal smears are obtained, and then resume routine screening according to the recommendation for the average population.
- Women with normal colposcopy following a cytological prediction of possible HSIL (pHSIL) should have a repeated Pap test and colposcopy 3–6 months later. If repeat colposcopy was normal, the Pap test was to be repeated in another 6–12 months.

In the context of primary HPV-based screening and reflex LBC, it is necessary to determine the following:

- the optimal follow-up protocol (HPV testing, LBC testing or co-testing, and interval) for women with a positive oncogenic HPV (any type) test result and a LBC report of pLSIL/LSIL, followed by normal colposcopy
- the safety and effectiveness of conservative treatment (follow-up testing with HPV and/or LBC) relative to diagnostic excision of the TZ in women with a positive oncogenic HPV (any type) test result and a LBC prediction of pHSIL/HSIL followed by normal colposcopy, when cytology is downgraded on cytopathology review
- the safety and effectiveness of conservative treatment relative to diagnostic excision of the TZ in women with a positive oncogenic HPV (any type) test result and a LBC prediction of pHSIL/HSIL (confirmed on review) but normal colposcopy.

Type 3 TZ (previously termed ‘unsatisfactory’) colposcopy following LBC prediction of a low-grade or high-grade lesion

Guidelines for the pre-renewal NCSP^[1] recommended that, in cases where the colposcopic assessment was unsatisfactory (TZ not fully visible; Type 3 TZ in new IFCPC terminology)^[2] in women with a cytological prediction of LSIL on a Pap test, the clinician should consider repeating the Pap test in 6–12 months. The guidelines recommended that failure to visualise the transformation zone in women with a cytological prediction of HSIL on a Pap test was an indication for diagnostic excision of the TZ.^[1]

The American Society for Colposcopy and Cervical Pathology^[3] recommends diagnostic excision of the TZ for women with cytological prediction of HSIL and unsatisfactory colposcopy, except during pregnancy. European guidelines for clinical management of abnormal cervical cytology^{[2][4]} recommend diagnostic excision of the TZ should be considered for women with HSIL cytology and unsatisfactory colposcopy. Canadian guidelines for the colposcopic management of abnormal cervical cytology and histology^[5] recommend that diagnostic excision of the TZ should be considered in this situation if endocervical curettage and/or biopsy results are negative.

In Australia endocervical curettage is not routinely practised (see [Endocervical curettage](#) in Chapter 7. Colposcopy and [Chapter 11. Management of glandular abnormalities](#)). The American Society for Colposcopy and Cervical Pathology^[3] recommends endocervical sampling (either brushing or curettage) for women with a cytology report of atypical squamous cells of undetermined significance or LSIL when the entire squamocolumnar junction and the margins of any visible lesion cannot be visualised on colposcopy. European guidelines for clinical management of abnormal cervical cytology^{[2][4]} recommend endocervical curettage after diagnostic excision of the transformation zone and excision of the lower third of the endocervical canal if the squamocolumnar junction is not visible and a high-grade cytological abnormality has been confirmed on cytopathology review.

In the context of primary HPV-based screening, it is necessary to determine the following:

- the optimal follow-up protocol (HPV testing, LBC testing or co-testing, and interval) to predict risk in the follow-up of women with a positive oncogenic HPV (any type) test result and a LBC prediction of pLSIL/LSIL, when Type 3 TZ (unsatisfactory) colposcopy is reported
- the safety and effectiveness of conservative treatment (follow-up testing with HPV and/or LBC) relative to diagnostic excision of the transformation zone in women with a positive oncogenic HPV (any type) test result and a LBC prediction of pHSIL/HSIL, when Type 3 TZ (unsatisfactory) colposcopy is reported and pHSIL/HSIL is confirmed at cytopathology review.

See:

- [Normal colposcopic findings following LBC prediction of LSIL or HSIL](#)
- [Type 3 TZ \(previously termed 'unsatisfactory'\) colposcopy following LBC prediction of LSIL or HSIL](#)
- [Discussion: Management of discordant colposcopic impression, histopathology and referral LBC prediction](#)

Author(s):

- [Dr Andrea Garrett](#) — Co-author
- [Professor Ian Hammond](#) — Co-author
- [A/Professor Marion Saville](#) — Co-author
- [Mr. C. David H. Wrede](#) — Co-author
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

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Normal colposcopic findings following LBC prediction of Negative, LSIL or HSIL

Evidence

Systematic reviews were conducted to answer the following questions:

- For women with a positive oncogenic HPV test result (not in treatment follow-up) with negative or LSIL cytology and normal colposcopy, what is the safety and effectiveness of 12-month follow-up testing with a HPV test alone, compared with co-testing?
- For women with a positive oncogenic HPV test result (not in treatment follow-up) with negative or LSIL cytology and normal colposcopy, which factors predict the presence of high-grade cervical neoplastic disease (CIN2, CIN3, cervical cancer, adenocarcinoma in situ (AIS) or cervical cancer mortality)?
- For women with a positive oncogenic HPV test result and pHSIL/HSIL referral cytology but pLSIL/LSIL or less after cytologic review, and colposcopy is normal (negative), what is the safety and effectiveness of conservative management compared with excision of the TZ?
- For women with a positive oncogenic HPV test result and pHSIL/HSIL referral cytology, confirmed pHSIL/HSIL after cytologic review, and colposcopy is normal (negative), what is the safety and effectiveness of cytological and colposcopic follow-up at 3–6 months, compared with excision of the TZ?

Outcomes for women with normal colposcopic findings following referral cytology prediction of LSIL

No randomised or pseudorandomised controlled trials were identified that compared HPV testing with co-testing (HPV and LBC) at 12-month follow-up for women with a positive oncogenic HPV (any type) test result, a cytology report of negative or LSIL and normal colposcopy, and which reported high grade-disease outcomes.

No studies were found that reported the risk of high-grade disease associated with follow-up cytology or HPV status.

Four studies reported the risks associated with referral cytology and/or HPV status for women reported as pLSIL/LSIL and normal (negative) colposcopic findings: two prospective cohort studies^{[1][2]} (level II evidence) and two retrospective cohort studies^{[3][4]} (level III-2 evidence) were identified. Follow-up ranged from 1 to 3 years. All four studies were considered at high risk of bias; none of the studies were specifically designed to answer the PICO question, so it was not clear as to whether women with different baseline cytology results or HPV status were similar in terms of important confounders such as smoking status. Furthermore, important study design aspects such as the potential blinded reading of subsequent colposcopies and histopathology (with respect to the baseline test status) were not described.

Two of the studies^{[3][4]} examined the risks of cervical intraepithelial neoplasia (CIN) grade 3 or higher (CIN3+) associated with different baseline cytology results, and one study^[2] examined the risks of CIN3+ associated with baseline HPV-positive ASC-US and LSIL (regardless of HPV status). Three studies^{[3][4][1]} examined the risks of CIN2+ disease associated with different baseline cytology results, of which one study^[1] examined the risks of CIN2+ associated with different baseline HPV status. Two studies^{[1][4]} reported the risks associated with baseline cytology results in women who were HPV positive.

One of these studies^[3] did not report HPV status. The remaining studies provided the following evidence:

- In a cohort of women with a positive oncogenic HPV (any type) test result with normal colposcopy after referral cytology reported as 'borderline dyskaryosis' or 'mild dyskaryosis', rates of later detection of CIN3+ (median follow-up 27 months) were

3.5% and 2.1%, respectively.^[4] This cohort may not be representative of women with a LBC prediction of pLSIL/LSIL identified after primary HPV testing in the renewed NCSP; the HPV test in this UK study used a higher cut-off than recommended, and the 'borderline dyskaryosis' group could have included women with pHSIL.

- In a cohort of women with a referral cytology report of LSIL and normal colposcopy, the rate of CIN3+ after 1 year follow-up was 4.0%.^[2] This cohort included women who tested HPV positive and women who tested HPV negative.
- In a cohort of women with a positive oncogenic HPV (any type) test result with normal colposcopy after referral cytology reported as 'borderline dyskaryosis' or 'mild dyskaryosis', rates of later detection of CIN2+ (median follow-up 2.6 years) were 6.2% and 12.9%, respectively.^[11]

The systematic reviews and their findings are described in detail in the [Technical report](#). As no studies were found that reported the risks of high-grade disease associated with follow-up cytology or HPV status, there was no directly relevant evidence on which to base an evidence-based recommendation. Detection of HPV, especially persistent HPV 16/18, is associated with an increased risk of high grade cervical lesions, and the HPV test is more sensitive than cytology (see [Chapter 2. The rationale for primary HPV screening](#)).

Outcomes for women with normal colposcopy following referral cytology prediction of HSIL

Systematic literature searches did not identify any studies directly addressing the management of women with HSIL cytology and a normal (negative) colposcopy. The search strategies and inclusion and exclusion criteria used are described in detail in the [Technical report](#).

In the absence of any direct evidence from the systematic review, [a general review of the literature was performed](#) on the management of women with cytological prediction of pHSIL/HSIL and normal (negative) colposcopy was undertaken to inform relevant consensus-based recommendations.

No studies were found that reported outcomes for women followed up after referral cytology prediction of pHSIL/HSIL and normal colposcopic findings, and which reported the results of cytopathology review.

One cross-sectional cohort study^[6] reported outcomes for women participating in conventional cytology (Pap test) screening with no history of a cytological abnormality, who had a cytological prediction of HSIL between 2000 and 2007. Of 340 women who underwent colposcopy, 17 had normal colposcopic findings. Biopsy was performed in nine of these women, including endocervical curettage in at least four women.^[6] Ages of the women and results of cytopathology review (if performed) were not reported.

Of the 17 women with normal colposcopy (HPV status unknown), two (11.8%) were diagnosed with cervical adenocarcinoma and another two (11.8%) with AIS.^[6] Findings for the other 13 women were not reported. No other cases of cervical adenocarcinoma or cervical adenocarcinoma in situ were identified among the 331 women with HSIL who underwent biopsy.^[6] The degree to which these findings can be generalised to women in the renewed NCSP is limited, because HPV status and the findings of cytopathology review are not available.

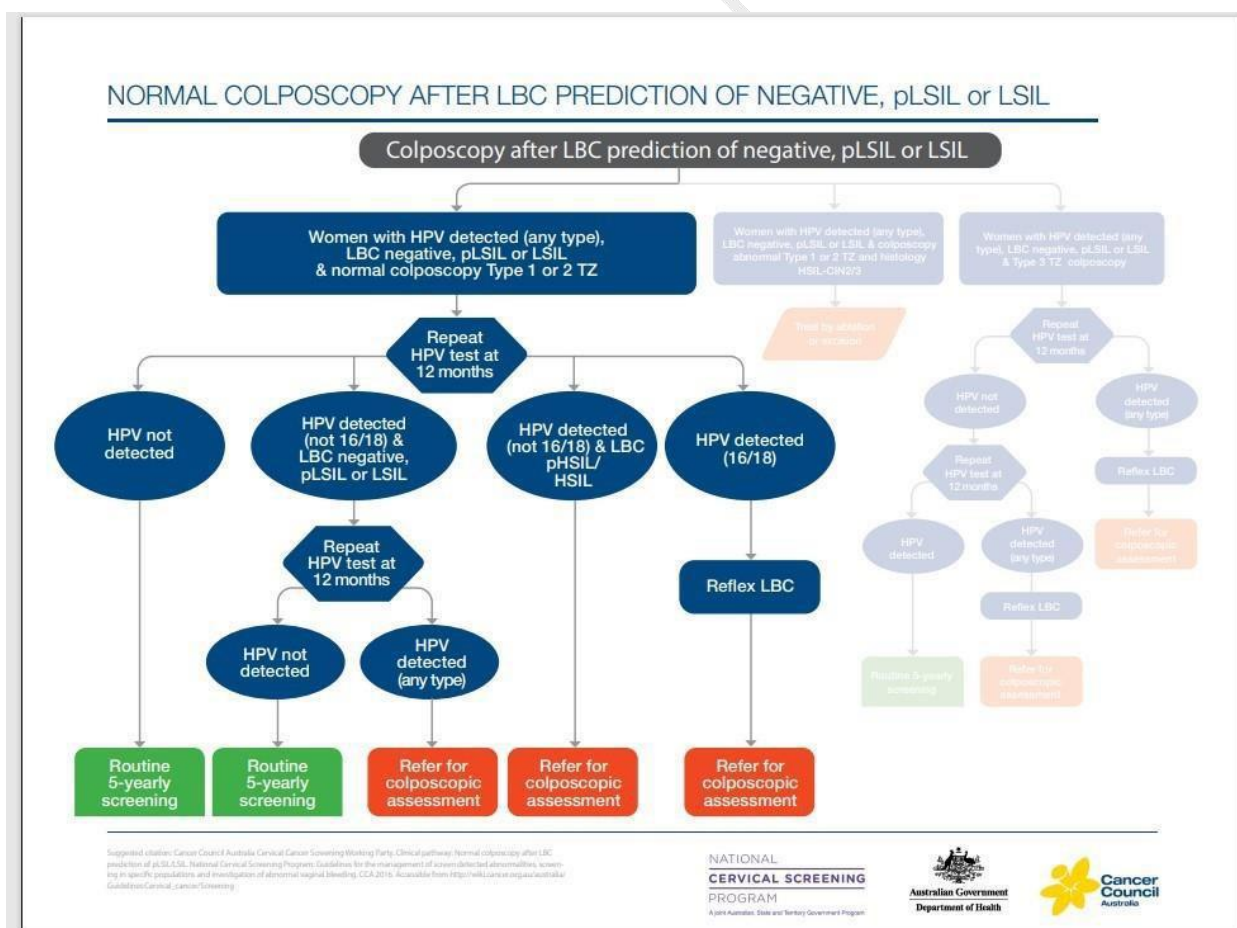
Another retrospective cohort study^[6] reported outcomes for a subgroup of 59 women (mean age 26.8 years) who underwent a loop electrosurgical excision procedure (LEEP) after a cytological prediction of HSIL and a colposcopically directed target biopsy finding of no abnormality detected (n = 34) or CIN1 (n = 25). On excisional biopsy, histologically confirmed CIN3 was diagnosed in 14 (41%) women with normal target biopsy and 16 (64%) women with CIN1 on

target biopsy. The degree to which these findings can be generalised to women in the renewed NCSP is limited, because HPV status was unknown and the study did not report whether HSIL was reported at initial referral cytology or on cytopathology review. However, this study did demonstrate the failure of colposcopically directed biopsy to detect the high-grade lesion in 41% of cases, as high grade abnormality was subsequently confirmed in an excision biopsy.^[6] A summary of the literature considered can be found in the [Technical report](#). Overall, this body of evidence is insufficient to enable accurate prediction of risk in women with normal colposcopic findings despite a LBC report of HSIL.

In Australia, it is recommended that discordant findings between referral cytology and colposcopy warrant review of the cytology prior to further management decisions. Current evidence does suggest that, in women with a normal colposcopy and HSIL on cytopathology review, the risk of CIN3 and/or invasive cervical cancer is high enough to warrant diagnostic excision of the TZ. In women with a normal colposcopy and pHSIL on cytopathology review, the risk of CIN3 and/or invasive cervical cancer is high enough to warrant diagnostic excision of the transformation zone in most cases, but in some situations a short period of observation may be appropriate (see [Chapter 9. Management of histologically confirmed low-grade squamous abnormalities](#)).

Recommendations

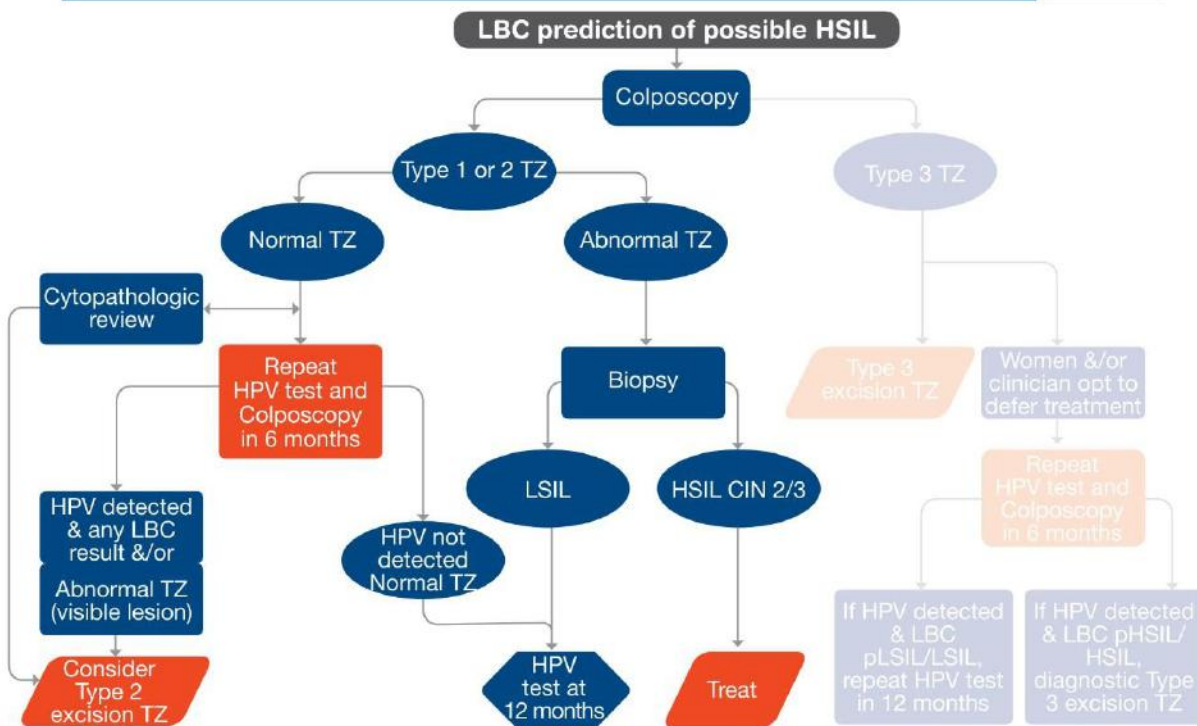
Flowchart 8.1. Normal colposcopy after LBC prediction of Negative, pLSIL or LSIL, following detection of HPV (any type)



<https://www.cancer.org.au/assets/pdf/flowchart-8-1-normal-colposcopy-after-lbc-prediction-of-negative-plsior-lsil-following-detection-of-hpv-any-type>

Flowchart 8.2. Normal colposcopy after LBC prediction of possible HSIL

NORMAL COLPOSCOPY AFTER LBC PREDICTION OF POSSIBLE HSIL



Suggested citation: Cancer Council Australia. Cervical Cancer Screening Working Party. Clinical pathways: Normal colposcopy after LBC prediction of possible HSIL. National Cervical Screening Program. Guidelines for the management of screen detected abnormalities, screening in specific populations and investigation of abnormal vaginal bleeding. G2A 5/16. Accessible from <https://www.cancer.org.au/australia/cervical-cancer/screening>.

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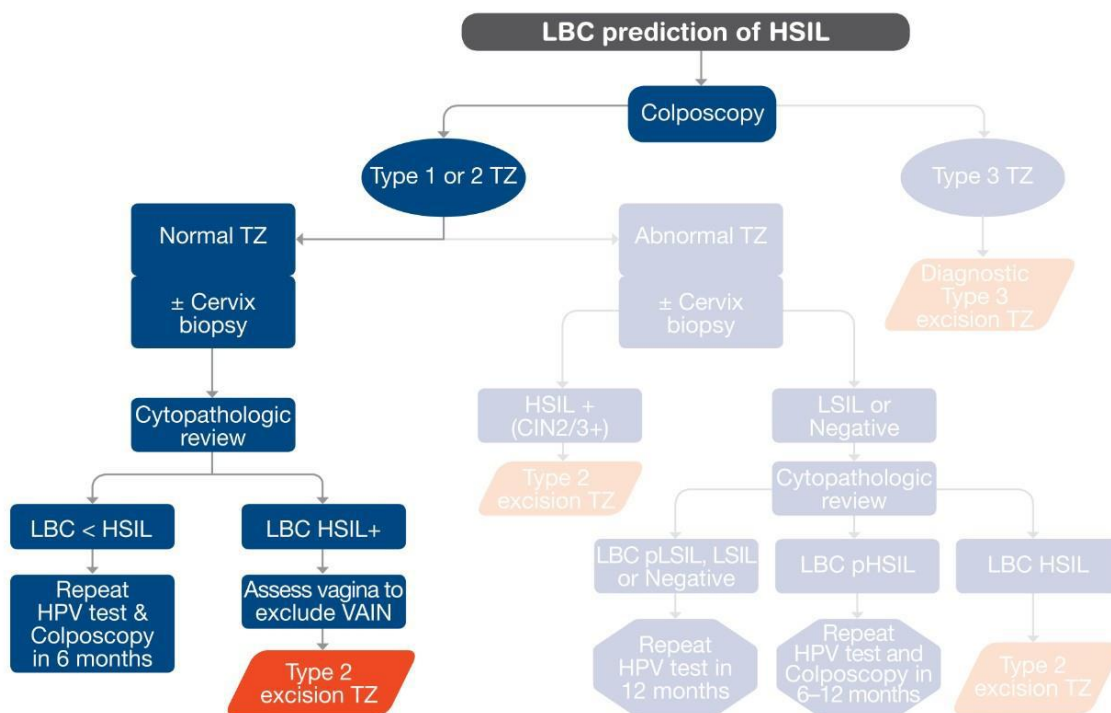
**Australian Government
Department of Health**

**Cancer Council
Australia**

https://www.cancer.org.au/assets/pdf/Normal_colp_after_LBC_prediction_of_possible_HSIL.pdf#_ga=2.1594289.1257883089.1648513003-1771580222.1646017938

Flowchart 8.3. Normal colposcopy after LBC prediction of HSIL

NORMAL COLPOSCOPY AFTER LBC PREDICTION OF HSIL



Suggested citation: Cancer Council Australia Cervical Cancer Screening Working Party. Clinical pathway: Normal colposcopy after LBC prediction of HSIL. National Cervical Screening Program. Guidelines for the management of screen detected abnormalities, screening in specific populations and investigation of abnormal vaginal bleeding. CCA 2016. Accessible from http://wiki.cancer.org.au/australia/Guidelines/Cervical_cancer/Screening

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https://www.cancer.org.au/assets/pdf/Normal_colp_after_LBC_prediction_of_HSIL.pdf#ga=2.223427099.1257883089.1648513003-1771580222.1646017938

Consensus-based recommendation

REC8.1: Normal colposcopy following LBC prediction of negative or pLSIL/LSIL

For women with a positive oncogenic HPV (any type) test result, a LBC report of negative or pLSIL/LSIL, and normal colposcopy, the HPV test should be repeated in 12 months:

- If HPV is not detected at 12 months, the woman should return to routine 5-yearly HPV screening.
- If the woman has a positive oncogenic HPV (not 16/18) test result at 12 months and a LBC report of negative or pLSIL/LSIL, the HPV test should be repeated in another 12 months.
- If the woman has a positive oncogenic HPV (any type) test at the 24 month HPV test, she should be referred directly for colposcopic assessment, which will be informed by the result of the reflex LBC.
- If the woman has a positive oncogenic HPV (not 16/18) test result at 12 months and a LBC prediction of pHSIL/HSIL or any glandular abnormality, she should be referred for colposcopic assessment at the earliest opportunity, ideally seen within 8 weeks.
- If the woman has a positive oncogenic HPV (16/18) test result at 12 months, she should be referred directly for colposcopic assessment at the earliest

opportunity, ideally seen within 8 weeks, and the reflex LBC result will inform the colposcopy.

Practice point

REC8.2: Normal colposcopy following LBC prediction of HSIL: cytopathology review

Cytopathology review is recommended to confirm HSIL before proceeding to excisional treatment for women with a normal colposcopy after a positive oncogenic HPV (any type) test result and an initial LBC prediction of pHSIL/HSIL.

Practice point

REC8.3: Normal colposcopy following LBC prediction of HSIL: exclude VAIN

When colposcopic impression is discordant with a referral LBC prediction of HSIL, colposcopic examination of the vagina is indicated to exclude a vaginal intraepithelial neoplasia **before** diagnostic excisional treatment.

Consensus-based recommendation

REC8.4: Normal colposcopy following LBC prediction of HSIL: diagnostic excision of TZ

For women who have a positive oncogenic HPV (any type) test result, normal colposcopy, and a LBC prediction of HSIL on cytopathology review, diagnostic excision of the TZ should be performed.

Consensus-based recommendation

REC8.5: Normal colposcopy following LBC prediction of pHSIL: consider diagnostic excision of TZ

For women who have a positive oncogenic HPV (any type) test result, normal colposcopy, and a LBC prediction of pHSIL on cytopathology review, diagnostic excision of the TZ should be considered, though observation is an option.

Practice point

REC8.6: Normal colposcopy following LBC prediction of pHSIL: diagnostic excision or observation

Some women with a positive oncogenic HPV test result for whom diagnostic excision of the TZ is recommended due to a confirmed LBC prediction of pHSIL on cytopathology review, despite normal colposcopic findings, may be concerned about the possibility of having unnecessary treatment. The colposcopist may have similar concerns.

Women who opt to defer treatment, particularly younger women with concerns about fertility, can be offered observation:

- A HPV test and colposcopy should be repeated at 6 months, and a diagnostic excisional procedure should be reconsidered based on the test results (HPV and reflex LBC, if performed) obtained at that time.
- If oncogenic HPV is not detected, and the colposcopic impression is unchanged, the HPV test should be repeated in 12 months and if oncogenic HPV is not detected, the woman can return to routine 5-yearly screening.

Consensus-based recommendation

REC8.7: Downgrading of discordant results

For women who have a positive oncogenic HPV (any type) test result, normal colposcopy, and a subsequent LBC report of pLSIL/LSIL or less on cytopathology review, management should be according to the reviewed cytological report (i.e. repeat HPV test in 12 months).

Practice point

REC8.8: Colposcopist should manage discordant results

Women with discordant colposcopy and LBC results should have their management supervised by the colposcopist until both the colposcopist and the woman are satisfied with the proposed management plan.

Benefits and harms

If these recommendations, including review of cytology, are followed for women who have normal colposcopy in the presence of referral LBC predicting low-grade or high-grade grade lesions, they will benefit by avoiding over-investigation or unnecessary treatment.

See [Chapter 5. Benefits, harms and cost-effectiveness of cervical screening in the renewed National Cervical Screening Program \(NCSP\)](#).

Health system implications of these recommendations

Clinical practice

It is not anticipated that there will be a significant change to clinical practice, apart from the addition of HPV testing to the recommended surveillance.

Resourcing

No material changes to the costs are anticipated.

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Appendices

[PICO questions 2a, 2b & 2c](#)

[View General evidence summary table q 2b](#)

[View Systematic review report q 2a](#)
[View General evidence summary table q 2c](#)

[View Systematic review report q 2b](#)
[View Evidence Statement q 2a](#)

[View Systematic review report q 2c](#)



Type 3 TZ (unsatisfactory) colposcopy following LBC prediction of Negative, LSIL or HSIL, following detection of HPV (any type)

Evidence

Systematic reviews were conducted to answer the following questions:

- For women with a positive oncogenic HPV (any type) test result, a LBC report of negative or LSIL, and Type 3 TZ (or unsatisfactory in previous terminology) colposcopy, what is the safety and effectiveness of 12-month follow-up testing with a HPV test alone, compared with co-testing (HPV and LBC)?
- For women with positive oncogenic HPV (any type) test result, a cytology prediction of pHSIL/HSIL, and Type 3 TZ (or unsatisfactory in previous terminology) colposcopy, what is the safety and effectiveness of conservative management, compared with diagnostic excision of the TZ?

Type 3 TZ (previously termed 'unsatisfactory') colposcopy following LBC reported negative or prediction of LSIL

No randomised or pseudorandomised controlled trials were identified that compared testing strategies and reported cancer outcomes in women with a positive HPV test result, cytology reported negative or LSIL, and Type 3 TZ (unsatisfactory) colposcopy. The search strategies and inclusion and exclusion criteria used are described in detail in the [Technical report](#). In the absence of any direct evidence from the systematic review, [a general review of the literature](#) on the management of women with negative or pLSIL/LSIL cytology and a type 3 TZ colposcopy was undertaken to inform consensus-based recommendations.

No longitudinal studies were found that followed women with an initial cytology prediction of pLSIL/LSIL and Type 3 TZ (unsatisfactory) colposcopy. Three retrospective cross-sectional cohort studies^{[1][2][3]} reported outcomes for women with pLSIL/LSIL initial cytology and an unsatisfactory colposcopy:

- In a cohort of 427 women with ASC-US or LSIL cytology who underwent colposcopy (with endocervical curettage) and the entire squamocolumnar junction was not visible, CIN2+ lesions of the endocervical canal were diagnosed in 18 women (4.2%);^[1] eight of these women either had not undergone cervical biopsy or had less than CIN2 disease on cervical biopsy. These also included two women with invasive cancer of the endocervical canal (0.5%), both of whom had a cervical biopsy report of CIN2+. CIN2+ was diagnosed in the endocervical canal in three of 256 women (1.2%) with a normal but unsatisfactory colposcopy, and 15 of 171 women (8.8%) with an abnormal and unsatisfactory colposcopy. The degree to which the findings of this study can be generalised to women in the renewed NCSP is limited, because neither HPV status nor the selection criteria for endocervical curettage was specifically reported.
- In a cohort of 118 women with ASC-US or LSIL cytology who underwent colposcopy (with endocervical curettage) and either the entire squamocolumnar junction was not visible or a visible lesion not seen in its entirety, CIN2+ was diagnosed on cervical biopsy in 18 women (15.3%).^[2] Of these women, six had endocervical as well as ectocervical disease. No additional cases were detected on endocervical curettage. The degree to which the findings of this study can be generalised to women in the renewed NCSP is limited, because neither HPV status nor the selection criteria for endocervical curettage was reported.
- In a cohort of women with normal, ASCUS or LSIL cytology who underwent cone biopsy after an unsatisfactory colposcopy (entire squamocolumnar junction not

visible or visible lesion not seen in its entirety) and CIN1 was detected on colposcopically guided biopsy, histologically confirmed CIN2+ was diagnosed in one woman (4.3%).^[4] The degree to which the findings of this study can be generalised to women in the renewed NCSP is limited, because HPV status was not reported and 25% of the women were HIV-positive.

A summary of the literature considered can be found in the [Technical report](#).

Overall, this body of evidence suggests that diagnostic excision of the TZ may detect additional clinically significant cervical lesions in women with cytology reported as LSIL and Type 3 TZ (unsatisfactory) colposcopy. In this situation, pre-renewal NCSP guidelines recommended repeating cytology in 12 months. In the renewed NCSP, it is appropriate to apply the same follow-up interval for the repeat HPV test (with reflex LBC if positive for any oncogenic HPV type).

Type 3 TZ (previously termed 'unsatisfactory') colposcopy following LBC prediction of HSIL. No randomised or pseudorandomised controlled trials were identified that compared conservative management with diagnostic excision of the transformation zone and reported cancer outcomes in women with a positive HPV test result, cytological prediction of HSIL, and Type 3 TZ (unsatisfactory) colposcopy. The search strategies and inclusion and exclusion criteria used are described in detail in the [Technical report](#).

In the absence of any direct evidence from the systematic review, [a general review of the literature](#) on the management of women with HSIL cytology and Type 3 TZ (unsatisfactory) colposcopy was undertaken to inform consensus-based recommendations.

No longitudinal studies were found that followed women with an initial cytology prediction of pHSIL/HSIL and Type 3 TZ (unsatisfactory) colposcopy, with or without cytopathology review. Two retrospective cross-sectional cohort studies^{[4][5]} reported outcomes for women with an initial prediction of pHSIL/HSIL and unsatisfactory colposcopy:

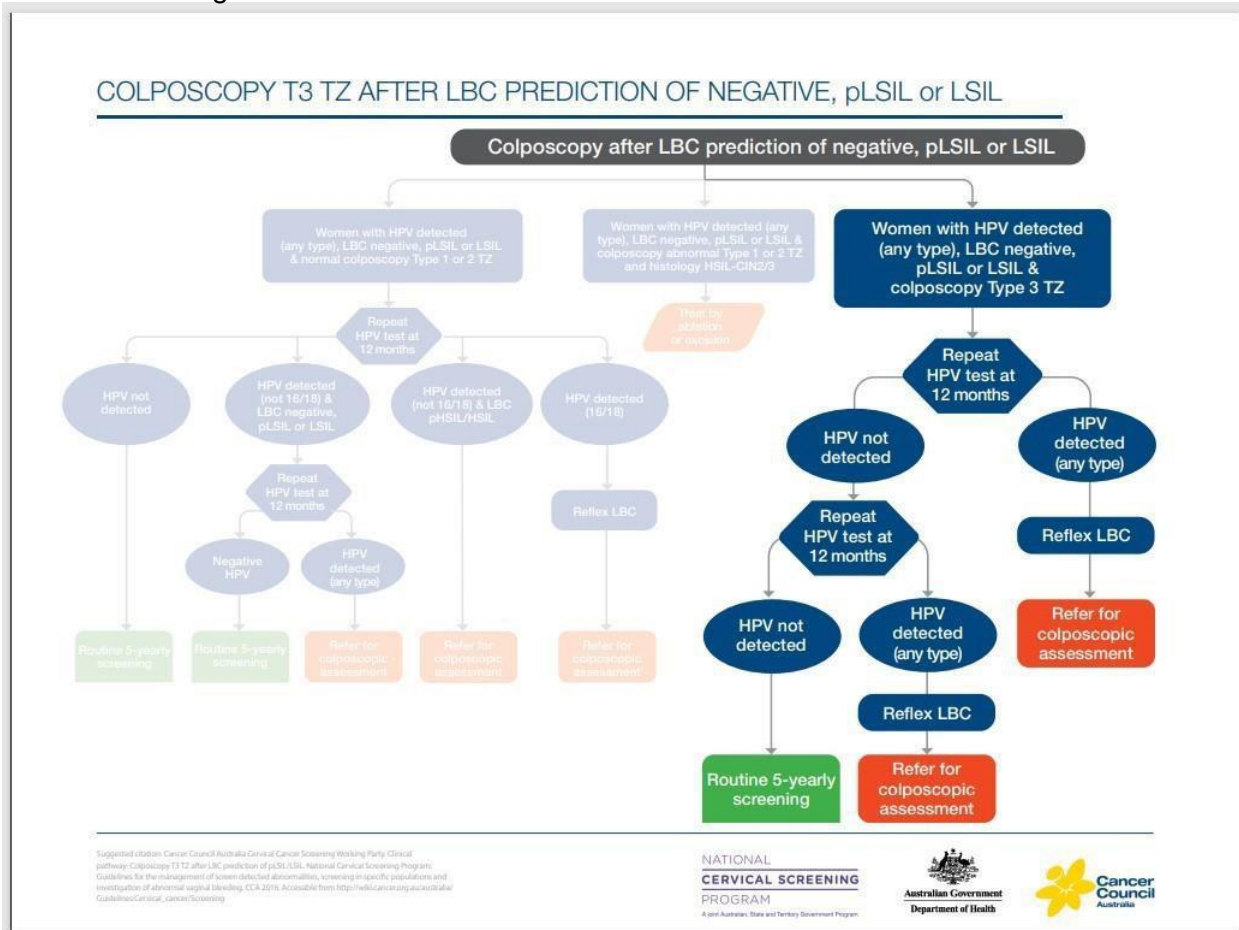
- In a cohort of 78 women with a cytology prediction of HSIL and unsatisfactory colposcopy (entire TZ including squamocolumnar junction not visible) who underwent LEEP, CIN2+ was histologically confirmed in 43 women (55.1%).^[4] Of these, one woman (1.3%) had invasive cervical cancer. CIN2+ disease (including the one case of cervical cancer) was found on LEEP in 35 (74.5%) of 47 women with HSIL cytology on review. The degree to which the findings of these studies can be generalised to women in the renewed NCSP is limited, because HPV status was not reported, and review cytology findings could not be compared with initial referral cytology findings or colposcopically directed biopsy findings for individual women. It was not possible to assess how many extra cases of CIN2+ were detected on LEEP.
- In a cohort of 65 women with a cytology report of HSIL who underwent cone biopsy after colposcopy detected no visible lesions and was unsatisfactory (entire TZ not visible), CIN2+ was diagnosed in 25 women (38.5%) and invasive cervical cancer was diagnosed in three women (4.6%).^[5] The degree to which the findings of these studies can be generalised to women in the renewed NCSP is limited, because neither HPV status nor the results of cytopathology review (if performed) was reported.

In both of these studies^{[4][5]} a significant number of women were diagnosed with CIN2+ on excisional biopsy. This finding underpins an approach involving excision of the TZ when the referral cytology is HSIL after cytopathology review and the TZ cannot be fully visualised (Type 3 TZ), irrespective of a HPV test result.

A summary of the literature considered can be found in the Technical report.

Recommendations

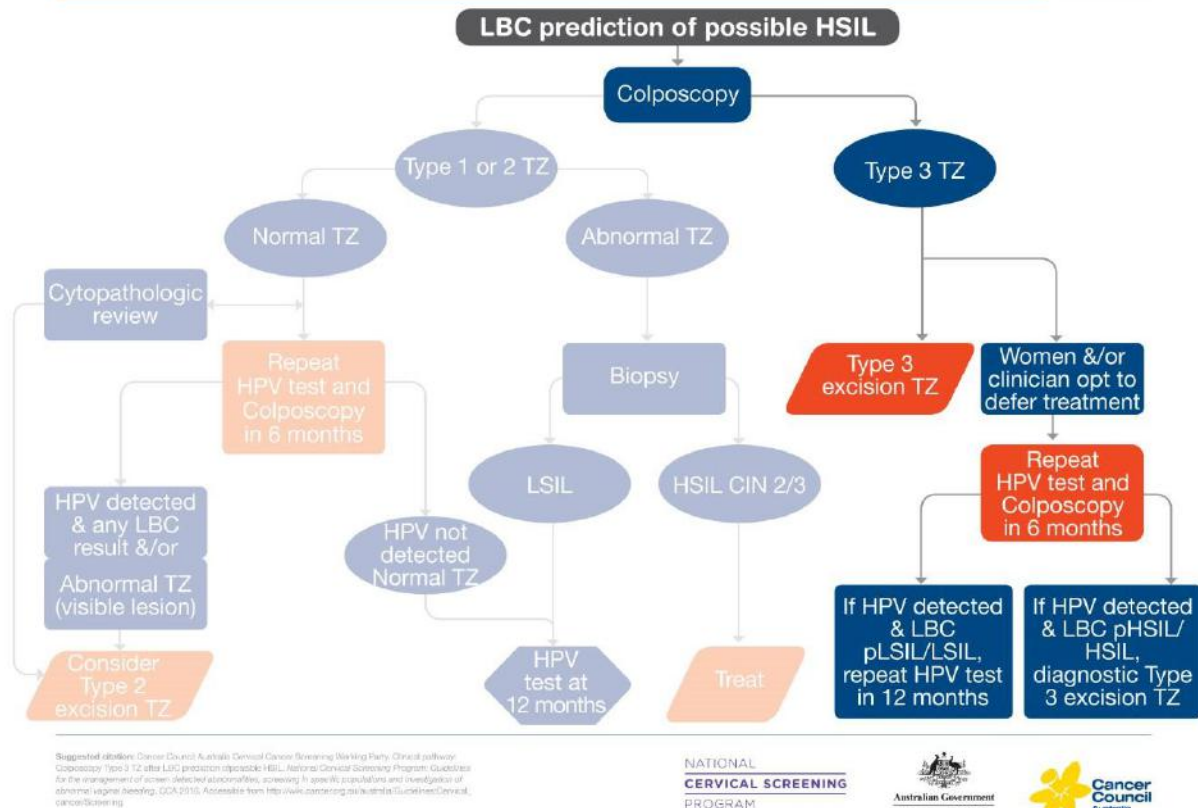
Flowchart 8.4. Colposcopy Type 3 TZ after LBC prediction of pLSIL/LSIL, or following HPV detected and negative LBC



<https://www.cancer.org.au/assets/pdf/flowchart-8-4-colposcopy-type-3-tz-after-lbc-prediction-of-plsilsil-or-following-hpv-detected-and-negative-lbc>

Flowchart 8.5. Colposcopy Type 3 TZ after LBC prediction of possible HSIL

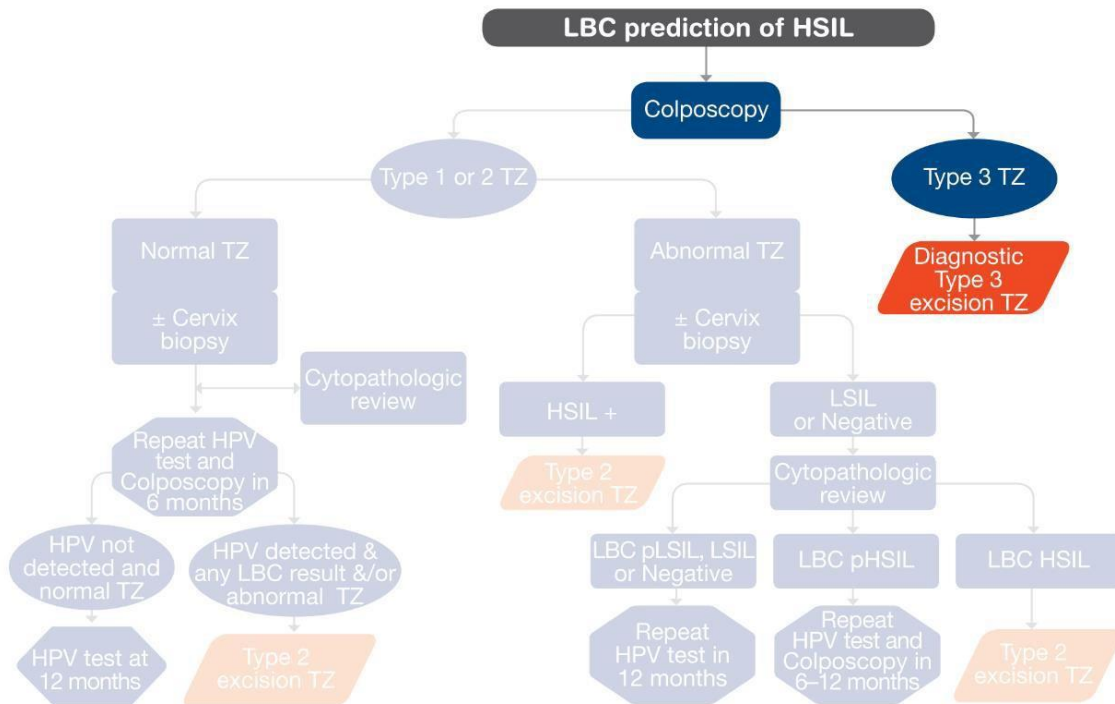
COLPOSCOPY TYPE 3 TZ AFTER LBC PREDICTION OF POSSIBLE HSIL



https://www.cancer.org.au/assets/pdf/Colp_T3_TZ_after_LBC_prediction_of_pHSIL.pdf#_ga=2.22342709.9.1257883089.1648513003-1771580222.1646017938

Flowchart 8.6. Colposcopy Type 3 TZ after LBC prediction of HSIL

COLPOSCOPY TYPE 3 TZ AFTER LBC PREDICTION OF HSIL



Suggested citation: Cancer Council Australia Cervical Cancer Screening Working Party. Clinical pathway: Colposcopy Type 3 TZ after LBC prediction of HSIL. National Cervical Screening Program: Guidelines for the management of screen detected abnormalities, screening in specific populations and investigation of abnormal vaginal bleeding OCA 2016. Accessible from http://wiki.cancer.org.au/australia/Guidelines/Cervical_cancer/Screening

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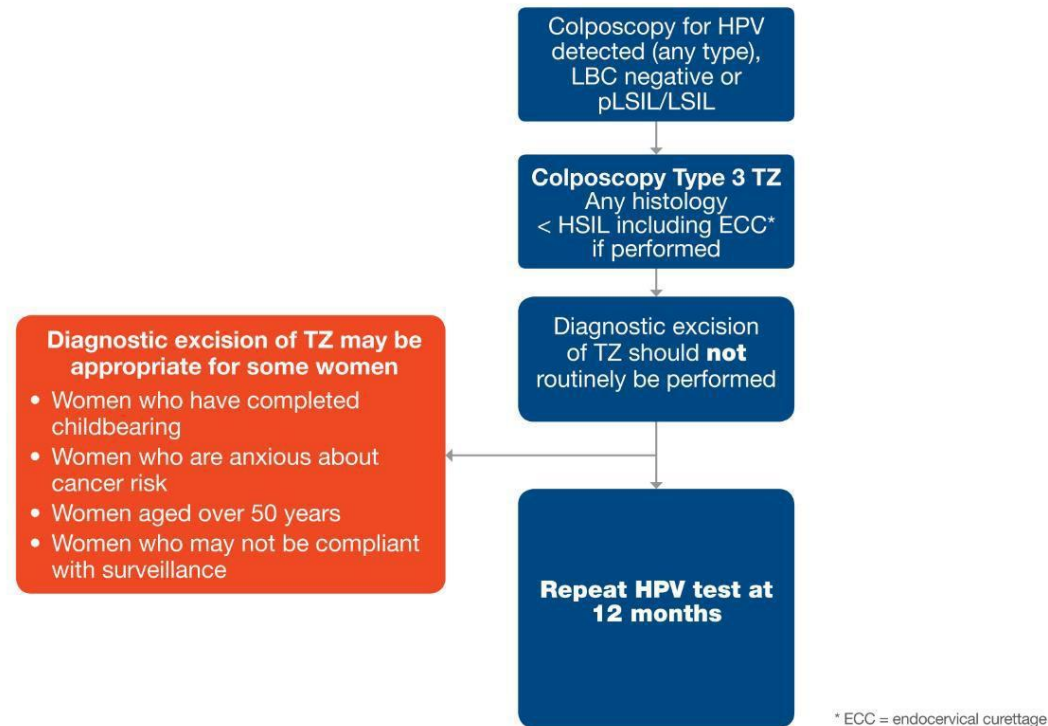
Australian Government
Department of Health

Cancer
Council
Australia

https://www.cancer.org.au/assets/pdf/Colp_T3_TZ_after_LBC_prediction_HSIL.pdf#_ga=2.268189582.1257883089.1648513003-1771580222.1646017938

Flowchart 8.7. Colposcopy Type 3 TZ and no high grade histology: follow-up or treatment for some women

COLPOSCOPY TYPE 3 TZ AND NO HIGH GRADE HISTOLOGY: FOLLOW-UP OR TREATMENT FOR SOME WOMEN



Suggested citation: Cancer Council Australia Cervical Cancer Screening Working Party. Clinical pathway: Colposcopy Type 3 TZ and no high grade histology: follow-up or treatment for some women. National Cervical Screening Program Guidelines for the management of screen detected abnormalities: screening in specific populations and investigation of abnormal vaginal bleeding. CGA 2016. Accessible from http://wiki.cancer.org.au/australia/Guidelines/Cervical_cancer/Screening

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https://www.cancer.org.au/assets/pdf/Colp_T3_TZ_no_high_grade_histology_follow-up_or_tx_for_women.pdf#_ga=2.268189582.1257883089.1648513003-1771580222.1646017938

Consensus-based recommendation

REC8.9: Repeat HPV test after Type 3 TZ colposcopy and referral LBC negative or pLSIL/LSIL

For women who have a positive oncogenic HPV (any type) test result with a LBC report of negative or pLSIL/LSIL, and colposcopy is reported as Type 3 TZ,[†] the HPV test should be repeated in 12 months:

- If oncogenic HPV is not detected at 12 months, the HPV test should be repeated 12 months later.
- If oncogenic HPV is not detected again at the second repeat HPV test, the woman should be advised to return to routine 5-yearly screening.
- If the woman has a positive oncogenic HPV (any type) test result at 12 months, she should be referred directly for colposcopic assessment, with the LBC report available to inform the assessment.

†Type 3 TZ indicates failure to visualise the upper limit of the TZ, or the entire TZ is within the endocervical canal. It corresponds to 'unsatisfactory' in previous terminology.

Practice point

REC8.10: Cytopathology review prior to observation for pLSIL/LSIL and Type 3 TZ at colposcopy

When observation is advised, cytopathology review is recommended to confirm the low-grade cytological abnormality.

- If pLSIL/LSIL is confirmed, observation is appropriate.
- If pHSIL/HSIL is indicated, then diagnostic excision of the TZ should be considered.

Practice point

REC8.11: Role of ECC in Type 3 TZ colposcopy following LBC prediction of pLSIL/LSIL

Despite a lack of evidence, endocervical curettage can be considered for women who have a positive oncogenic HPV test result (any type) with a LBC report of persistent pLSIL/LSIL and colposcopy reported as Type 3 TZ.† A negative ECC may provide additional reassurance for a conservative (observational) approach.

†Type 3 TZ indicates failure to visualise the upper limit of the TZ, or the entire TZ is within the endocervical canal. It corresponds to 'unsatisfactory' in previous terminology.

Consensus-based recommendation

REC8.12: Diagnostic excision of the TZ should not be performed if there is no cytological or histological evidence of a high-grade lesion after Type 3 TZ colposcopy

For asymptomatic women who have a positive oncogenic HPV (any type) test result, Type 3 TZ† colposcopy, and no cytological, colposcopic or histological evidence of a **high-grade lesion**, further diagnostic procedures (such as diagnostic excision of the transformation zone) should **not** routinely be performed.

†Type 3 TZ indicates failure to visualise the upper limit of the TZ, or the entire TZ is within the endocervical canal. It corresponds to 'unsatisfactory' in previous terminology.

Practice point

REC8.13: Role of diagnostic excision: exceptions to recommendation against diagnostic excision of TZ in the absence of high-grade cytology or histology

Diagnostic excision of the TZ can be offered to certain groups of women who have a positive oncogenic HPV test result, a LBC report of negative or pLSIL/LSIL, and colposcopy reported as Type 3 TZ:†

- women who have completed childbearing
- women who are anxious about cancer risk
- women aged over 50 years
- concerns exist regarding a woman's ability to comply with recommended surveillance.

†Type 3 TZ indicates failure to visualise the upper limit of the TZ, or the entire TZ is within the endocervical canal. It corresponds to 'unsatisfactory' in previous terminology.

Consensus-based recommendation

REC8.14: Diagnostic excision: Type 3 TZ colposcopy after LBC prediction of pHSIL/HSIL

For women who have a positive oncogenic HPV (any type) test result, a LBC prediction of pHSIL/HSIL after cytopathology review, and Type 3 TZ† colposcopy, diagnostic excision of the TZ should be performed.

†Type 3 TZ indicates failure to visualise the upper limit of the TZ, or the entire TZ is within the endocervical canal. It corresponds to 'unsatisfactory' in previous terminology.

Practice point

REC8.15: Cytopathology review: Type 3 TZ colposcopy following LBC prediction of pHSIL/HSIL

Cytopathology review should be considered to confirm a high-grade cytological abnormality before excision, after a positive oncogenic HPV (any type) test result and an initial LBC prediction of pHSIL/HSIL, when there is a Type 3 TZ colposcopy.

This is particularly important when the LBC prediction is pHSIL because pHSIL has a lower PPV for high-grade disease and the subsequent excision specimens show no evidence of cervical pathology in 45–55% of cases.

Practice point

REC8.16: Deferral of treatment following cytopathology review: Repeat HPV test and colposcopy in 6 months

Following cytopathology review, rarely the woman or the clinician wish to defer treatment. In this situation the woman should have a repeat HPV test and colposcopy in 6 months.

- If HPV detected (any type) and LBC pLSIL/LSIL, repeat HPV test in 12 months.
- If HPV detected (any type) and LBC pHSIL/HSIL, the woman should have diagnostic Type 3 excision of the TZ.

Benefits and harms

If these recommendations, including review of cytology, are followed for women who have a Type 3 TZ colposcopy in the presence of a LBC report of negative or prediction of pLSIL/LSIL or pHSIL/HSIL, they will benefit by avoiding over investigation or receiving unnecessary treatment. See [Chapter 5. Benefits, harms and cost-effectiveness of cervical screening in the renewed National Cervical Screening Program \(NCSP\)](#)

Health system implications of these recommendations

Clinical practice

It is not anticipated that there will be a significant change to clinical practice, apart from the addition of HPV testing to the recommended surveillance.

Resourcing

No material changes to the costs are anticipated.

References

1. ↑ ^{1.0 1.1} Goksedef BP, Akbayir O, Numanoglu C, Corbacioglu A, Guraslan H, Bakir LV, et al. [Evaluation of endocervical canal in women with minimal cervical cytological abnormalities](#). J Low Genit Tract Dis 2013 Jul;17(3):261-6 Available from: <http://www.ncbi.nlm.nih.gov/pubmed/23422642>.
2. ↑ ^{2.0 2.1} Poomtavorn Y, Suwannarurk K, Thaweeul Y, Maireang K. [Diagnostic value of endocervical curettage for detecting dysplastic lesions in women with atypical squamous cells of undetermined significance \(ASC-US\) and low grade squamous intraepithelial lesion \(LSIL\) Papanicolaou smears](#). Asian Pac J Cancer Prev 2014;15(8):3461-4 Available from: <http://www.ncbi.nlm.nih.gov/pubmed/24870740>.
3. ↑ ^{3.0 3.1} Day T, Weitzen S, Cooper AS, Boardman LA. [Should unsatisfactory colposcopy necessitate treatment of cervical intraepithelial neoplasia 1?](#) J Low Genit Tract Dis 2008 Jan;12(1):11-5 Available from: <http://www.ncbi.nlm.nih.gov/pubmed/18162806>.
4. ↑ ^{4.0 4.1 4.2} Massad LS, Tate N, Cejtin E, Collins YC. [Quantifying the risk of cervical intraepithelial neoplasia in women with unsatisfactory colposcopy results](#). J Low Genit Tract Dis 2005 Jan;9(1):23-8 Available from: <http://www.ncbi.nlm.nih.gov/pubmed/15870518>.
5. ↑ ^{5.0 5.1 5.2} Veiga FR, Russomano FB, Camargo MJ, Monteiro AC, Tristão A, Silva GV. [Prevalence of high-grade squamous intraepithelial lesions and cervical cancer among patients with unsatisfactory colposcopic examination, without visible lesion](#). Sao Paulo Med J 2009 Sep;127(5):266-9 Available from: <http://www.ncbi.nlm.nih.gov/pubmed/20169274>.

Appendices

[PICO questions 3a & 3b](#) [View Systematic review report q 3a](#) [View Systematic review report q 3b](#) [View General evidence summary table q 3a](#)

[View General evidence summary table q 3b](#)

Discussion: Management of discordant colposcopic impression, histopathology result, referral LBC prediction

Author(s):

- [Dr Andrea Garrett](#) — Co-author
- [Professor Ian Hammond](#) — Co-author
- [A/Professor Marion Saville](#) — Co-author
- [Mr. C. David H. Wrede](#) — Co-author
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

Unresolved issues

There is currently insufficient high-level evidence to guide the management of discrepancies between cytological findings and colposcopic impression in women who have positive oncogenic HPV test results, or who have pLSIL/LSIL and Type 3 TZ colposcopy. These consensus-based recommendations and practice points are considered conservative and offer a safe approach, but this may require review as future research results become available.

Future research priorities

To determine optimal management, evidence is needed from:

- prospective audits of management strategies of large cohorts of women who have positive oncogenic HPV test results with discordant cytology and colposcopic findings
- randomised controlled trials or longitudinal studies comparing management strategies for women with a positive oncogenic HPV test result, who have normal cytology or pLSIL/LSIL, and Type 3 TZ colposcopy.

9. Management of histologically confirmed low-grade squamous abnormalities

Author(s):

- [A/Prof Lyndal Anderson](#) — Co-author
- [Dr Andrea Garrett](#) — Co-author
- [Professor Ian Hammond](#) — Co-author
- [A/Professor Selvan Pather](#) — Co-author
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

Anderson, L, Garrett, A, Hammond, I, Pather, S, Cancer Council Australia Cervical Cancer Screening Guidelines Working Party. Clinical question: Management of histologically confirmed low-grade squamous abnormalities . In: National Cervical Screening Program: Guidelines for the management of screen-detected abnormalities, screening in specific populations and investigation of abnormal vaginal bleeding.

Background

According to the two-tiered nomenclature for cervical histology recommended by the Lower Anogenital Squamous Terminology (LAST) Standardization Project^[1] and adopted by the Royal College of Pathologists of Australasia, non-invasive human papillomavirus (HPV)-associated squamous lesions are classified as follows [Chapter 3. Terminology](#)

- [LSIL: low-grade squamous intraepithelial lesion](#)
- [HSIL: high-grade squamous intraepithelial lesion](#)

Current pre-renewal National Cervical Screening Program (NCSP) guidelines do not recommend treatment for histologically confirmed low-grade squamous intraepithelial lesions (LSIL); cervical intraepithelial neoplasia grade one (CIN1) or a lesser lesion detected on biopsy. These lesions are considered to be an expression of a productive HPV infection.^[2] The 2005 national guideline for the management of screen-detected cervical abnormalities^[2] recommended that women with histologically confirmed low-grade squamous abnormalities undergo repeat conventional cytology (Pap test) at 12 and 24 months, and return to routine screening if both tests are negative or continue annual cytology until two consecutive tests are negative.

Within the pre-renewal NCSP, it is common for a woman's cytology status to fluctuate between low-grade abnormality and negative,^[2] probably due to HPV infection, clearance and reinfection.^[2] Within programs based on primary HPV screening, clinical decisions can be informed by known HPV status as well as cytology.

Within the pre-renewal NCSP, the HPV status of individual women with histologically confirmed low-grade squamous abnormalities is not routinely available and recommendations are based on the assumption that it is unknown. Under the renewed NCSP, in contrast, the clinical significance of histological, colposcopic and cytological findings in women with screen-detected abnormalities is assessed in the context of known positive HPV status.

Evidence

Systematic review evidence

A systematic review was performed to identify studies evaluating efficacy and safety outcomes of management options for women with a positive oncogenic HPV-test result, a colposcopic impression of LSIL and histologically confirmed CIN1 or less on biopsy, whether concordant or discordant with referral liquid-based cytology (LBC):

- For those with a cytology finding of negative, possible low-grade squamous epithelial lesion or low-grade squamous epithelial lesion (pLSIL/LSIL), repeat HPV test at 12 months was compared with the combination of repeat LBC and HPV test (co-testing) at 12 months.
- For those with a cytology finding of possible or high-grade squamous epithelial lesion (pHSIL/HSIL), diagnostic excision was compared with co-testing at 12 months.

No randomised or pseudorandomised controlled trials were identified that compared:

- HPV testing alone with co-testing as follow-up for women with a positive HPV test result with a reflex LBC finding of negative or pLSIL/LSIL
- excisional treatment with follow-up by co-testing in women with a reflex cytology finding of pHSIL/HSIL.

The search strategies, inclusion/exclusion criteria and findings are described in detail in the [Technical report](#).

General literature review evidence

In the absence of any direct evidence from the systematic review, [a general review of the literature](#) was performed to inform consensus-based recommendations. The review focused on the management of women with:

- a positive oncogenic HPV test result
- a colposcopic impression of LSIL
- histologically confirmed CIN1 or less on biopsy
- referral cytology report of negative, or prediction of pLSIL/LSIL or pHSIL/HSIL.

Several studies examined outcomes following histologically confirmed CIN1 or less on biopsy.^{[2][3][4][5][6][7][8][9]} The most relevant findings are summarised below:

- In a prospective cohort study using data from the Kaiser Permanente Northern California health system,^[4] the crude rate of CIN3+ was 0.7% following a single negative follow-up smear, 0.2% following a single negative follow-up HPV test and 0.1% following a negative follow-up co-test in women with HPV-positive ASC-US or any LSIL and less than CIN2 on colposcopy/biopsy over a maximum of 7 years of follow-up.
- In a prospective cohort study (ASCUS-LSIL Triage Study),^[7] 45% of women with baseline ASCUS/LSIL and less than CIN2 on colposcopy/biopsy, a follow-up finding of HSIL and a positive HPV test, developed CIN3+ within 2-year follow-up. (In this cohort, ASCUS may have included ASC-H.)
- One retrospective cohort study^[8] of women who underwent loop electrosurgical excision procedure (LEEP) after referral cytological prediction of pHSIL/HSIL reported histologically confirmed CIN3+ in 41% of those with normal histology on the initial biopsy and 64% of those with CIN1 at initial biopsy. However, HPV status was not known.

Overall, available evidence suggests the following conclusions:

- For women with a positive oncogenic HPV test result, ASC-US and histologically confirmed CIN1 or a lower-grade lesion, the negative predictive value of HPV follow-up testing alone will be greater than that of cytology alone, but less than co-testing.
- For women with a positive oncogenic HPV test result and initial referral cytology of LSIL, the finding of HSIL at follow-up cytology indicates a substantial risk of future CIN3+.
- Diagnostic excision of the transformation zone (TZ) appears to be the optimal approach for women with a positive oncogenic HPV test result, a referral cytological prediction of pHSIL/HSIL, a colposcopic impression of LSIL, and histologically confirmed CIN1 or a lower-grade lesion, especially if pHSIL/HSIL is confirmed on cytopathology review.^[††] The PPV is variable and depends on the referral cytology prediction. One study reported that, where referral cytology predicted a high-grade abnormality, then the PPV for identifying HSIL on biopsy was 73%. If the referral cytology was low grade, the PPV was 48%, demonstrating a clear relationship between the PPV of colposcopic impression to the referral cytology prediction.^[†††]

A summary of the literature considered can be found in the **Technical report**.

Recommendations

When there is discordance between the LBC report and histopathology, review of both cytology and histopathology should be carried out to inform management decisions.

Consensus-based recommendation

REC9.1: HPV test 12 months after histologically confirmed LSIL (\leq CIN1)

Women who have a positive oncogenic HPV (any type) test result with a LBC report of either negative or pLSIL/LSIL, and histologically confirmed \leq CIN1 on biopsy, should have a repeat HPV test 12 months later:

- If oncogenic HPV is not detected at the repeat HPV test, the woman should return to routine 5 yearly screening.
- If the repeat test is positive for oncogenic HPV (not 16/18) and the LBC report is negative or pLSIL/LSIL, the woman should have a further repeat HPV test in 12 months.
- If the second follow-up HPV test is negative the woman should return to routine 5-yearly screening.
- If the second follow-up test is HPV positive, the woman should be referred for colposcopic assessment informed by reflex LBC.
- If the repeat test is positive for oncogenic HPV (not 16/18) and the LBC report is pHSIL/HSIL, the woman should be referred for colposcopic assessment.
- If the repeat test is positive for oncogenic HPV (16/18), the woman should be referred for colposcopic assessment informed by the reflex LBC.

Consensus-based recommendation

REC9.2: LSIL (\leq CIN1) should not be treated

Women who have a positive oncogenic HPV (any type) test result with a LBC report of negative or pLSIL/LSIL, who have undergone colposcopy and have a histologically confirmed LSIL (\leq CIN1), should **not** be treated, because these lesions are considered to be an expression of a productive HPV infection.

Consensus-based recommendation

REC9.3: Diagnostic excision when HSIL confirmed on cytopathology review

Women who have a positive oncogenic HPV test result (any type) with a LBC report of HSIL (confirmed after cytopathology review), and who have undergone colposcopy and have a histologically confirmed LSIL (\leq CIN1), should be offered diagnostic excision of the TZ.

Consensus-based recommendation

REC9.4: Option for observation following cytological prediction of pHSIL

Women who have a positive oncogenic HPV (any type) test result with a LBC prediction of pHSIL (confirmed after cytopathology review), and who have undergone colposcopy and have a histologically confirmed LSIL (\leq CIN1), could be offered diagnostic excision of the TZ.

If the colposcopist considers a period of observation is preferable to treatment, or the woman with these findings wishes to defer diagnostic excision, she can be offered observation with a HPV test and colposcopy at 6–12 months:

- If oncogenic HPV is not detected at the repeat test, the HPV test should be repeated again in 12 months.
- If the second follow-up test is negative, the woman should return to routine 5-yearly screening.
- If the woman has a positive oncogenic HPV (any type) test result at the repeat test, her reflex LBC report is negative or pLSIL/LSIL, and her colposcopic impression is normal or LSIL, the HPV test should be repeated annually.
- When oncogenic HPV is not detected at two consecutive annual tests, the woman can return to 5-yearly screening.
- If the woman has a positive oncogenic HPV (any type) test result at the repeat test, and her LBC prediction is pHSIL/HSIL or any glandular abnormality, she should have a diagnostic excision of the TZ.

Practice point

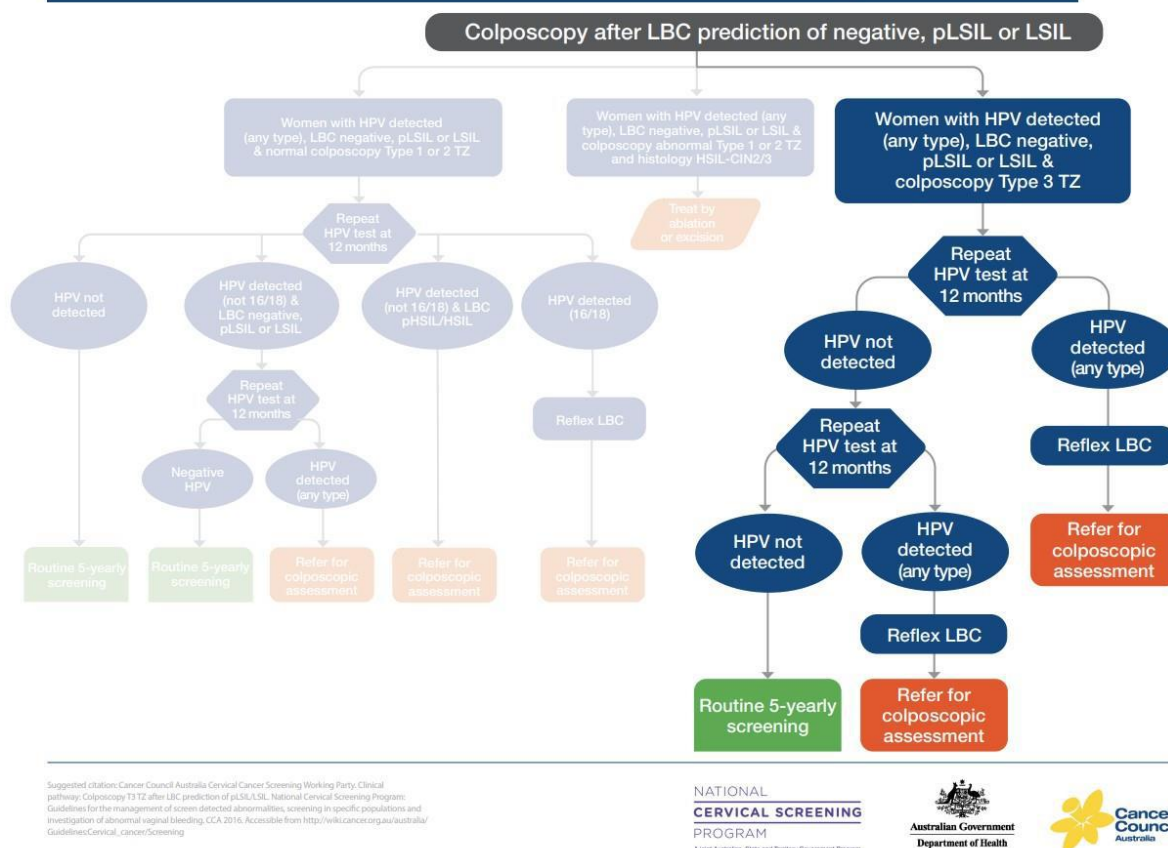
REC9.5: Criteria for observation following cytological prediction of pHSIL

Women should not be offered observation unless the colposcopic assessment meets all the following conditions:

- Colposcopy is adequate.
- TZ is completely visualised (Type 1 or 2 TZ[^]).
- LSIL (\leq CIN1) has been confirmed on histopathological review.

[^]IFCPC: International Federation of Cervical Pathology and Colposcopy 2011
Flowchart 9.1. Histological LSIL following colposcopy for LBC prediction of HSIL

COLPOSCOPY T3 TZ AFTER LBC PREDICTION OF NEGATIVE, pLSIL or LSIL



https://www.cancer.org.au/assets/pdf/colposcopy-t3-tz-after-lbc-prediction-of-negative-plsil-or-lsil#_ga=2.232357023.1257883089.1648513003-1771580222.1646017938

Practice point

REC9.6: Cytology review essential when test results are discordant

For women who have a positive oncogenic HPV (any type) test result with a histologically confirmed LSIL (\leq CIN1) after LBC prediction of pHSIL/HSIL, both the cytology and the histopathology should be reviewed by a pathologist from at least one of the reporting laboratories, who should then convey the results of the review to the colposcopist in order to inform the management plan.

Benefits and harms

Despite the recommendations contained in the pre-renewal NCSP guidelines, many women have continued to have unnecessary treatment for LSIL (\leq CIN1). These guidelines reiterate the previous advice, and colposcopists are advised not to treat these women unless there are exceptional circumstances. Compliance with these recommendations will benefit women by avoiding unnecessary treatment and consequent harms.

Cytological review for discordant results, as recommended in these guidelines, will benefit women by preventing over investigation and unnecessary treatment (see [Chapter 5. Benefits](#),

Health system implications of these recommendations

Clinical practice

These recommendations represent minimal change to those that apply to the pre-renewal NCSP.^[2]

Timely expert review of cytology and histology is recommended for women with low-grade histology results that are discordant with preceding high-grade cytology findings, before proceeding to any diagnostic treatment. Implementation of this recommendation may increase the workload of pathologists, laboratories and colposcopists. Clinicians may need to spend extra time reviewing results and providing advice to women.

The major change in clinical practice is that conventional cytology is replaced by HPV testing and reflex LBC for the follow-up of women with histologically confirmed LSIL (\leq CIN1). The high negative predictive value of HPV testing should allow a significant proportion of women to return to routine cervical screening earlier than was possible under the pre-renewed NCSP.

Resourcing

Pathology review of discordant results may increase the workload of pathology services, leading to delay in service provision and increased distress to already anxious women. Ensuring that pathology services are adequately staffed (have enough pathologists and laboratory staff) may have cost implications.

Failure of colposcopists to comply with the recommendation not to offer treatment for women with LSIL (\leq CIN1) would lead to unnecessary costs.

Barriers to implementation

These recommendations represent minimal change to those that apply to the pre-renewal NCSP.^[2] Accordingly, no significant barriers to implementation are anticipated. It is recommended that LSIL (\leq CIN1) should not be treated. Under the pre-renewed NCSP, clinical practice has not fully complied with this recommendation. It is estimated that approximately 30% of women with LSIL (\leq CIN1) undergo excisional treatment. This decision may be due to physician or patient anxiety, especially when the finding is persistent. Under the renewed NCSP, colposcopists may continue to have concerns about conservative management of low-grade abnormalities, despite evidence supporting this approach. Failure to implement this recommendation would result in unnecessary treatment and consequent harms.

Colposcopists may proceed to diagnostic excisional procedures for apparent discordant pathology results, without arranging for expert pathology review to confirm the findings. Failure to implement the recommendation for cytological and histological review may lead to unnecessary treatment.

Discussion

Unresolved issues

No unresolved issues have been identified.

The safety of this approach will be monitored by the Quality and Safety Monitoring Committee of the NCSP.

Future research priorities

Prospective studies are needed to measure compliance with recommendations, especially the recommendation against routine treatment for histologically confirmed LSIL (\leq CIN1), and the recommendation for pathology review of discordant results.

Clinical trials are needed to determine the optimal management, and duration of observation, for persistent or fluctuating LSIL (\leq CIN1).

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Appendices

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10. Management of histologically confirmed high-grade squamous abnormalities

Author(s):

- [A/Prof Lyndal Anderson](#) — Co-author
- [A/Professor Selvan Pather](#) — Co-author
- [Professor Gordon Wright](#) — Co-author
- [Professor Ian Hammond](#) — Co-author
- [A/Professor Marion Saville](#) — Co-author
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

Introduction

According to the two-tiered nomenclature for cervical histology recommended by the Lower Anogenital Squamous Terminology (LAST) standardization project^[1] and adopted by the Royal College of Pathologists of Australasia, non-invasive human papillomavirus (HPV)-associated squamous lesions are classified as:

- [LSIL: low-grade squamous intraepithelial lesion](#)
- HSIL: high-grade squamous intraepithelial lesion

HSIL can be further subcategorised, according to the grade of cervical intraepithelial neoplasia (CIN), as HSIL (CIN2) and HSIL (CIN3).

HSIL of the cervix is characterised histologically by mitotic figures in epithelial cells undergoing cell division, nuclear abnormalities including enlarged nuclei and irregular nuclear membranes, and little to no cytoplasmic differentiation in the middle third and upper third of the epithelium.

Invasive squamous cell carcinoma is categorised as:

- SISCCA: superficially invasive squamous cell carcinoma (previously termed microinvasive carcinoma)
- SCC: squamous cell carcinoma

See also [Chapter 3. Terminology](#).

See:

- [Diagnosis of HSIL](#)
- [Treatment of HSIL](#)
- [Test of Cure after treatment for HSIL \(CIN2/3\)](#)

- [Discussion: Management of histologically confirmed high-grade squamous abnormalities](#)

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Diagnosis of high-grade squamous abnormalities

Author(s):

- [A/Prof Lyndal Anderson](#) — Co-author
- [A/Professor Selvan Pather](#) — Co-author
- [Professor Gordon Wright](#) — Co-author
- [Professor Ian Hammond](#) — Co-author
- [A/Professor Marion Saville](#) — Co-author
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

Anderson, L, Pather, S, Wright, G, Hammond, I, Saville, M, Cancer Council Australia Cervical Cancer Screening Guidelines Working Party. Clinical question: Diagnosis of high-grade squamous abnormalities. In: National Cervical Screening Program: Guidelines for the management of screen-detected abnormalities, screening in specific populations and investigation of abnormal vaginal bleeding.

Background

HSIL may be suspected from the cytological examination of cells from a cervical smear or LBC preparation. However, in Australia it has been considered best practice to establish the final diagnosis on histopathological examination of tissue obtained from cervical punch biopsy or an excisional procedure.

Histological diagnosis of HSIL (CIN2/3) is necessary before proceeding to treatment, except in certain circumstances. Treatment undertaken at the time of initial colposcopic assessment is known as 'treatment at first visit' or 'see-and-treat' (see Treatment at first visit in [Chapter 7. Colposcopy](#)).

Recommendation

Consensus-based recommendation*

REC10.1: Histological diagnosis prior to treatment

For women who have a visible lesion at colposcopy, histological confirmation of HSIL is recommended before undertaking definitive treatment.

Treatment of high-grade squamous abnormalities

Author(s):

- [A/Prof Lyndal Anderson](#) — Co-author
- [A/Professor Selvan Pather](#) — Co-author
- [Professor Gordon Wright](#) — Co-author
- [Professor Ian Hammond](#) — Co-author
- [A/Professor Marion Saville](#) — Co-author
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

Anderson, L, Pather, S, Wright, G, Hammond, I, Saville, M, Cancer Council Australia Cervical Cancer Screening Guidelines Working Party. Clinical question: Treatment of high-grade squamous abnormalities. In: National Cervical Screening Program: Guidelines for the management of screen-detected abnormalities, screening in specific populations and investigation of abnormal vaginal bleeding.

HSIL (CIN2/3)

Not all CIN2 or CIN3 lesions will progress to cervical cancer. Based on studies on the natural history of cervical infections with oncogenic HPV types, it has been estimated that 30–50% of untreated CIN2 and approximately 30% of CIN3 regress spontaneously, and that approximately 5% of CIN2 and 14–31% of CIN3 progress to invasive cancer, although differing follow-up times for various studies need to be taken into account in interpreting these findings.^{[1][2][3][4][5][6]} A young age (< 25 years) and pregnancy are two factors associated with higher regression rates of untreated high-grade abnormalities.^{[7][8][9][10][11][12][13][14][15][16][17]}

For the adequate treatment of CIN2 or CIN3, the entire lesion and transformation zone (TZ) must be destroyed or excised. This can be achieved by ablative or excisional treatments (see [Chapter 7. Colposcopy](#)). Ablative methods such as CO2 laser ablation are effective but infrequently used in modern practice. Excisional methods such as a large loop excision of the TZ (LLETZ), loop electrosurgical excision procedure (LEEP) or cold-knife cone biopsy are preferred. A comparison of surgical modalities based on randomised trials reported relative equivalence in effectiveness and safety.^[18] Hysterectomy as a primary treatment of CIN2 or CIN3 may also be an option for women who are not considering a future pregnancy and have an associated benign gynaecological disease.

CIN2

Background

CIN2 was previously thought to be an intermediate state between a HPV infection and precancer.^{[19][20]} However, following LAST, CIN2 is now understood to be a morphological entity without a biological correlate.^[20] LAST emphasises that there are two biological states caused by HPV; these are LSIL (productive viral infection) and HSIL (transforming or neoplastic HPV infection). CIN2 lesions have been reported to be histologically heterogeneous, with some cases comparable to CIN3 and others similar to CIN1. The reproducibility of CIN2 diagnoses has historically been poor and low inter-observer agreement has been reported.^{[21][22][23]} This is the basis for the LAST recommendation to use p16 positivity in lesions which would be called CIN2 on H&E histopathology, in order to confirm the presence of active oncogenic HPV DNA in these lesions. Two papers published prior to the 2012 report from the LAST project, demonstrate that the risk of persistence of CIN2 lesions is influenced by the oncogenic HPV type and the persistence of the HPV infection, with lesions caused by HPV type 16 less likely to regress than lesions caused by other oncogenic HPV types or non-oncogenic types.^{[14][3]}

A number of molecular markers, of which p16^{INK4a} (p16) has been the most widely studied, have been investigated as an adjunct to cytology and histopathology to help resolve the diagnosis of ambiguous squamous intraepithelial lesions.^[20] The LAST project included a comprehensive review of biomarker data, and this underpinned the LAST recommendations.^[20]

The expression of p16, a cell cycle regulatory protein, is highly increased in tissues that overexpress the E7 HPV oncoprotein and reflects a transformed oncogenic HPV infection with associated pre-neoplastic epithelial change. Immunostaining for p16 has been investigated in cervical cytology (for example, in identifying women with minor cervical lesions who require

further investigation following a Pap smear).^[24] Its use is established in histopathology, as p16 overexpression has been reported in a high percentage of high-grade precursor squamous lesions and invasive cancers.^{[25][26][27]} The use of p16 immunohistochemistry in histopathology as recommended by LAST will help to clarify the diagnosis of CIN 2 cases and improve inter-observer variability.^[28]

Evidence

Systematic review evidence

A systematic review was performed to identify studies evaluating the safety and effectiveness of using p16 immunohistochemistry to stratify management of women with histologically confirmed CIN2 (immediate treatment or observation) compared with treating all CIN2 with excision of the TZ. No randomised or pseudorandomised studies were found that used p16 to stratify management in histologically confirmed CIN2. Details of the LAST project and recommendations are found in the Literature Review evidence section below.

Literature review evidence

In the absence of any direct evidence from the systematic review, a general review of the literature was performed to ascertain the effectiveness of p16 immunohistochemistry in clarifying a diagnosis of CIN2. A systematic review and meta-analysis of five studies^{[29][30][31][32][33]} reported a significantly higher agreement between pathologists' diagnosis of CIN2+ from cervical biopsy specimens based on haematoxylin and eosin (H&E) morphology and p16 immunohistochemistry combined ($k=0.73$; 95%CI: 0.67–0.79) when compared with H&E morphology alone ($k=0.41$; 95%CI: 0.17–0.65).^[34] A strong association between diffuse, intense staining of cervical specimens with p16 and positivity for oncogenic HPV infections, particularly HPV 16/18 has also been reported.^{[35][36]}

Until recently, CIN2 was regarded as an intermediate biological state between CIN1 and CIN3. With our greater understanding of the biology and natural history of HPV infection in anogenital sites, we now know that there are only 2 biological states caused by HPV: LSIL (productive viral infection) and HSIL (transforming HPV infection). CIN2 is a morphological entity without a biological correlate. Biologically it was a mixture of LSIL and HSIL. The Lower Anogenital Squamous Terminology (LAST) project in 2011-2012 (see also Terminology section earlier) comprehensively addressed this area of diagnostic difficulty and made evidence-based recommendations.^[20] LAST recommended that 'If the pathologist is entertaining an H&E morphologic interpretation of –IN 2 (under the old terminology, which is a biologically equivocal lesion falling between the morphologic changes of HPV infection (low-grade lesion) and precancer), p16 IHC is recommended to help clarify the situation. Strong and diffuse block positive p16 results support a categorization of precancer. Negative or non-block positive staining strongly favors an interpretation of low-grade disease or a non-HPV associated pathology.'

The Lower Anogenital Squamous Terminology (LAST) Standardization project was undertaken with the objective of developing evidence-based recommendations to unify and standardize the terminology used to classify HPV-associated lesions of the anogenital tract. The LAST recommendations were made using a rigorous process which included conducting systematic reviews and involved a consensus process which was led by a steering committee and involved five working groups which consisted of experts in the field. One working group was responsible for framing the development of historical terminology applied to HPV-associated squamous lesions of the lower anogenital tract and the impact of terminology on clinical management.

Three of the working groups performed the systematic literature reviews and developed the draft recommendations. The fifth working group will lead the ongoing implementation of the LAST recommendations.

The draft recommendations were made available for public consultation and finalized in 2012 at the LAST Consensus Conference. The project produced recommendations which help address the issues of variability and reproducibility, often found when reporting HPV-associated neoplasia. The final recommendations specify the biologically applicable histopathologic terminology for HPV-associated squamous intraepithelial lesions and superficially invasive squamous carcinomas across all lower anogenital tract sites.^[20] It also specifies the use of biomarkers in resolving histopathologic interpretations and improving diagnostic accuracy. In contrast to the use of p16 immunostaining in histological specimens, which has a strong evidence base and has been endorsed by WHO, the use of immunostaining of cervical cytology specimens remains experimental. There are no current guidelines endorsing its use in cytology preparations.

Recommendations

Consensus-based recommendation*

REC10.2: Treatment for HSIL (CIN2)

Women with a histological diagnosis of HSIL (CIN2) should be treated in order to reduce the risk of developing invasive cervical carcinoma.

Practice point

REC10.3: p16 should be used to clarify diagnosis of HSIL (CIN2)

The use of p16 immunohistochemistry is recommended to stratify the management of HSIL (CIN2) into immediate treatment or a period of observation.

Practice point

REC10.4: HSIL (CIN2) and observation

In some circumstances, it may be acceptable to offer a period of observation (generally 6–12 months) to women who have a histological diagnosis of HSIL (CIN2), and this would usually be supervised by an experienced colposcopist or at a tertiary centre. Observation may be considered for:

- women who have not completed childbearing
- women with discordant histology and LBC prediction of pLSIL/LSIL
- women with focal minor changes on colposcopy and HSIL (CIN2) on histology
- women recently treated for HSIL (CIN2).

HSIL (CIN3)

HSIL (CIN3) involves the presence of dysplastic cells in greater than two thirds of the entire thickness of the epithelium but with no signs of invasion into the stroma. Almost all HSIL (CIN3) lesions can be attributed to persistent infection by high risk HPV types.^[37] Based on the controversial 'unfortunate experiment' conducted in New Zealand, involving the long-term follow-up of a cohort of women diagnosed with CIN3 from 1955 to 1976, the cumulative risk of invasive cancer over 30 years was 31% in women who only had diagnostic biopsies and 50% in women with persistent CIN3 within 2 years after their biopsy, as opposed to 0.7% in women who were treated conventionally.[4] CIN3 is the primary endpoint in longitudinal studies of the natural history of the HPV infection pathway, therefore the only other available data on the time

period from CIN3 to invasive cancer comes from statistical modelling. Such lifetime risk estimates of cervical cancer are in line with the New Zealand study data.^{[38][39][40]} Although not all HSIL (CIN3) lesions progress to invasive cancer, based on current evidence, HSIL (CIN3) lesions need to be treated to reduce the risk of further progression to invasive cancer.

Recommendation

Consensus-based recommendation*

REC10.5: Treatment of HSIL (CIN3)

Women with a histological diagnosis of HSIL (CIN3) should be treated in order to reduce the risk of developing invasive cervical carcinoma.

Invasive carcinoma

When invasive or superficially invasive squamous cell carcinoma is confirmed by histopathology, prompt referral to a gynaecological oncologist is required. Factors that will inform further management will include stage of disease, age, medical history and general health.

Recommendation

Consensus-based recommendation*

REC10.6: Referral of women with invasive disease

A woman with a histologically confirmed diagnosis of invasive or superficially invasive (squamous cell carcinoma) should be referred to a gynaecological oncologist or a gynaecological cancer centre for multidisciplinary team review.

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Appendices

[PICO questions](#) [View Systematic review report q 6](#) [View General evidence summary table q 6](#)

Test of Cure after treatment for HSIL (CIN2 / 3)

Author(s):

- [A/Prof Lyndal Anderson](#) — Co-author
- [A/Professor Selvan Pather](#) — Co-author
- [Professor Gordon Wright](#) — Co-author
- [Professor Ian Hammond](#) — Co-author
- [A/Professor Marion Saville](#) — Co-author
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

Anderson, L, Pather, S, Wright, G, Hammond, I, Saville, M, Cancer Council Australia Cervical Cancer Screening Guidelines Working Party. Clinical question: Test of Cure after treatment for HSIL (CIN2/3). In: National Cervical Screening Program: Guidelines for the management of screen-detected abnormalities, screening in specific populations and investigation of abnormal vaginal bleeding.

Background

In women who have been treated for a high-grade squamous lesion (HSIL (CIN2/3)) the risk of recurrence and invasive cervical cancer remains elevated for 10–25 years^{[1][2][3][4][5][6]} highlighting the importance of continued post-treatment surveillance to detect residual or recurrent disease. In Australia, the combination of LBC and testing for oncogenic HPV types (co-test) is used as a Test of Cure following treatment of HSIL (CIN2/3), based on the high negative predictive value of the co-test in detecting women at risk of recurrence. However, there has been some uncertainty regarding the length of time required for a woman to be considered as cured and safe to return to the screening intervals recommended for the general population.

Data published in the Report on monitoring activities of the National Cervical Screening Program (NCSP) Safety Monitoring Committee^[7] demonstrated that, in women aged 20–69 previously treated for a high-grade CIN, the incidence of a subsequent high-grade lesion was very low, and there were no incidents of subsequent cervical cancer, following two consecutive occasions on which oncogenic HPV was not detected and LBC was reported negative (negative co-test). This holds true in more recent analyses of these data, which similarly show a low rate of subsequent high-grade lesions and no instances of cervical cancer following two consecutive negative co-tests.^[8] These data support the effectiveness of two negative consecutive co-tests as Test of Cure,^[7] as recommended in pre-renewal NCSP guidelines.

Evidence

Systematic review evidence

A systematic review was performed to identify studies evaluating the safety and effectiveness of discharging women previously treated for HSIL based on a negative co-test at 12 months versus 12 and 24 months. No randomised or pseudorandomised studies were found.

General literature review evidence

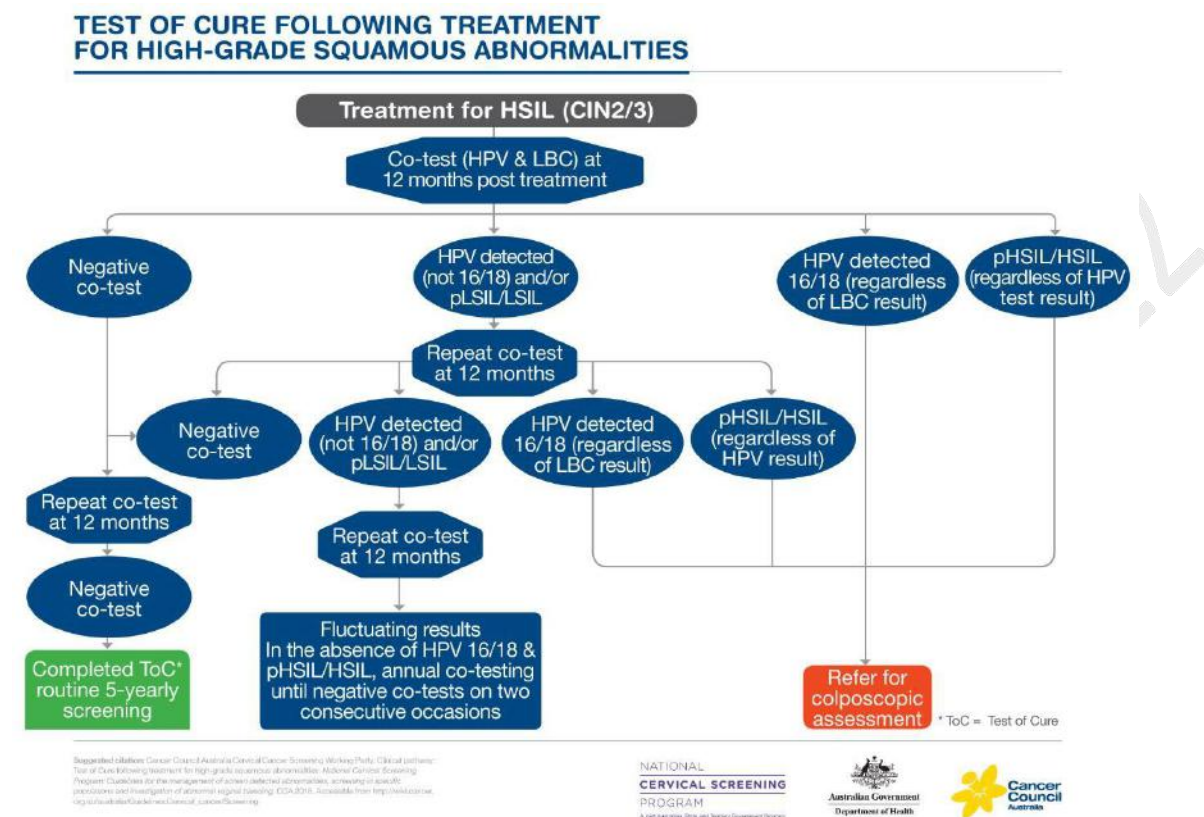
In the absence of any direct evidence from the systematic review, a general review of the literature was performed on the use of HPV testing and cytology in the follow-up of women treated for HSIL (CIN2/3).

Five recent articles were found ^{[9][10][11][2][12]} of which three were directly relevant, reporting 5-year risks of recurrent high grade CIN following one negative co-test and following two negative co-tests. Katki *et al* estimated a lower 5-year risk of recurrent CIN2+ for two negative co-tests (1.5%) when compared with one negative co-test (2.4%) ($p=0.8$). However, the authors stated that estimates were based on small numbers and therefore subject to considerable uncertainty.^[11] These findings were in agreement with reports from a Dutch study^{[10][2]} of lower 5-year cumulative risks of CIN2+ and CIN3+ disease for a negative co-test at 6 and 24 months post treatment, when compared with a negative co-test at 6 months post treatment. In this study, the 5-year cumulative risk of CIN2+ was 1.0 (0.2–4.6) and of CIN3+ was 0.0 (0.0–2.9) following a negative co-test at 6 and 24 months.

Based on the evidence from these two studies, women who have been treated for high-grade squamous lesions should have co-testing performed at 12 months after treatment and annually thereafter. When a woman undergoing annual co-testing has had a negative co-test on two consecutive occasions, she can return to routine screening.

Recommendations

Flowchart 10.1. Test of Cure following treatment for high-grade squamous abnormalities



https://www.cancer.org.au/assets/pdf/ToC_following_tx_for_HGS_abnormalities.pdf#_ga=2.227769245.1257883089.1648513003-1771580222.1646017938

Consensus-based recommendation

REC10.7: Test of Cure after treatment for HSIL (CIN2/3)

A woman who has been treated for HSIL (CIN2/3) should have a co-test[†] performed at 12 months after treatment, and annually thereafter, until she receives a negative co-test on two consecutive occasions, when she can return to routine 5 yearly screening.

[†]Co-testing can be performed by the woman's usual healthcare professional.

Consensus-based recommendation

REC10.8: Abnormal Test of Cure results: positive oncogenic HPV (16/18) test result

If, at any time post treatment, the woman has a positive oncogenic HPV (16/18) test result, she should be referred for colposcopic assessment (regardless of the reflex LBC result).

Consensus-based recommendation*

REC10.9: Abnormal Test of Cure results: LBC pHSIL/HSIL or glandular abnormality

If, at any time during Test of Cure, the woman has a LBC prediction of pHSIL/HSIL or any glandular abnormality, irrespective of HPV status, she should be referred for colposcopic assessment.

Consensus-based recommendation

REC10.10: Abnormal Test of Cure results: positive oncogenic HPV (not 16/18) test result

If, at any time post-treatment, the woman has a positive oncogenic HPV (not 16/18) test result and a LBC report of negative or prediction of pLSIL/LSIL, she should continue to have annual co-testing until she has a negative co-test on two consecutive occasions, when she can return to routine 5-yearly screening.

Practice point

REC10.11: Fluctuating Test of Cure results: positive oncogenic HPV (not 16/18) test result and/or pLSIL/LSIL

Some women may experience fluctuating results with a positive oncogenic HPV (not 16/18) test result and/or LBC prediction of pLSIL/LSIL. These women do not need colposcopic review but, if the woman is anxious, a colposcopic assessment may be appropriate to provide reassurance.

Practice point

REC10.12: Colposcopy is not necessary at the initial post-treatment visit

A post-treatment colposcopic assessment at 4–6 months has been the usual practice under pre-renewal NCSP guidelines. This practice is not evidence-based, but may provide reassurance to both the patient and clinician regarding the visual appearance of the cervix and allows for the discussion of any other relevant issues (bleeding, fertility, related symptoms etc.) following treatment.

The post-treatment review should:

- include speculum examination of the vagina and cervix (but colposcopy is not considered necessary)
- not involve HPV testing or LBC.

Subsequent post-treatment Test of Cure surveillance should be performed by the woman's GP or health professional, who should follow the recommendations for the management of any abnormal test results.

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Discussion

Author(s):

- [A/Prof Lyndal Anderson](#) — Co-author
- [A/Professor Selvan Pather](#) — Co-author
- [Professor Gordon Wright](#) — Co-author
- [Professor Ian Hammond](#) — Co-author
- [A/Professor Marion Saville](#) — Co-author
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

Anderson, L, Pather, S, Wright, G, Hammond, I, Saville, M, Cancer Council Australia Cervical Cancer Screening Guidelines Working Party. Guidelines: Cervical cancer/Screening/Discussion HSIL. In: National Cervical Screening Program: Guidelines for the management of screen-detected abnormalities, screening in specific populations and investigation of abnormal vaginal bleeding.

Benefits and harms

The practice of treating all cases of HSIL (CIN2/3) has been highly effective and has led to a reduction in the risk of subsequent cervical cancer.

A very small number of women with HSIL may be treated unnecessarily. However, it is not possible to identify these women in advance. This small risk must be weighed against the substantial evidence for the effectiveness of cervical screening and HSIL (CIN2/3) treatment to prevent the development of invasive cervical cancer. The benefits of treating HSIL (CIN2/3) outweigh the harms, and treating HSIL (CIN2/3) is the basis for the [documented success of the National Cervical Screening Program \(NCSP\)](#).

See the [Benefits, harms and cost-effectiveness of cervical screening in the renewed National Cervical Screening Program \(NCSP\)](#).

Health system implications of these recommendations

Clinical practice

Recommendations regarding the management of women with HSIL (CIN2/3) are consistent with present clinical practice.

Resourcing

No additional costs are anticipated.

Barriers to implementation

Women treated for HSIL (CIN2/3) may choose not to attend for post-treatment co-testing as recommended. An Australian study using state registry data found that 53% of women treated for high-grade cervical dysplasia attended only a single HPV follow-up test.^[1]

Some women will be very anxious if they have continuing abnormality (as may their GP) and a colposcopy may be needed for reassurance. However, treatment of LSIL (\leq CIN1), even if persistent, should be avoided wherever possible.

Discussion

Women who are undergoing Test of Cure, and who have a positive oncogenic HPV (16/18) test result with any LBC report, or LBC prediction of pHSIL/HSIL with any HPV test result, should be

referred for colposcopy to exclude recurrent or residual disease. This more cautious post-treatment management of these women is warranted.

The National HPV Vaccination Program is expected to reduce the number of oncogenic HPV 16/18 infections, high-grade abnormalities and the risk of cervical cancer directly in vaccinated women, as successive vaccinated cohorts mature and indirectly in unvaccinated women, via a reduction in the circulation of vaccine included HPV types within the population.

Unresolved issues

Although two negative co-tests are required before returning women to routine screening after treatment for HSIL (CIN2/3), there is uncertainty regarding whether one negative co-test or a single negative HPV test would be sufficient before safely returning women to routine screening intervals of 5 years. This issue will be informed by the ongoing accumulation of national data by the Australian Institute of Health and Welfare (AIHW) and will be considered by the Quality and Safety Monitoring Committee of the renewed NCSP.

For some women with a negative co-test result at 12 months but a positive HPV test and negative cytology result at 24 months, there is a possibility that the lesion is 'cured' and the positive oncogenic HPV test may indicate re-infection rather than recurrence. However, the scientific evidence to support this is currently not available.

Future research priorities

The role of p16 and ki67 in the triage of HSIL (CIN2), and its use in the renewed NCSP, should be further investigated. Long-term follow-up studies of women with HSIL (CIN2/3) cervical abnormalities that evaluate the clinical use of p16 and other molecular biomarkers, alone or in combination, are needed to guide the management of this group of women.

Outcomes of various post-treatment screening scenarios in longitudinal studies are needed to inform future recommendations for test of cure. These should compare the 5-year cumulative risk of subsequent HSIL (CIN2+). Analysis by age groups (< 30 years and ≥ 30 years) would also be informative, as the specificity of HPV testing is lower in younger women.

The role of post-treatment HPV vaccination in unvaccinated women should be considered as a potential research activity.

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- [Discussion: Management of histologically confirmed high-grade squamous abnormalities](#)

11. Management of glandular abnormalities

Author(s):

- [A/Prof Lyndal Anderson](#) — Co-author
- [Professor Ian Hammond](#) — Co-author
- [A/Professor Selvan Pather](#) — Co-author
- [Mr. C. David H. Wrede](#) — Co-author
- [Professor Gordon Wright](#) — Co-author
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

Screening

Cervical adenocarcinoma is associated with human papillomavirus (HPV) infection and can be detected by HPV testing.^[1] HPV has been identified in an estimated 99.7% of cervical carcinoma specimens.^[2] While 70% of squamous cervical cancers are related to oncogenic HPV types 16 and 18 an estimated 78% of adenocarcinomas are related to these two types^[3] and the proportion associated with HPV 18 is greater than for squamous cell carcinomas.^[4] Glandular abnormalities are also associated with a substantial risk of cervical intraepithelial neoplasia grade 3 (CIN3) and cervical cancer; in a large US cohort, 33% of HPV-positive women with a conventional cytology finding of atypical glandular cells developed CIN3 or a higher-grade lesion (CIN3+) and 9% developed cervical cancer within 5 years.^[5] Among women with the same cytology finding in whom oncogenic HPV was not detected, 0.93% developed CIN3+ and 0.37% developed cervical cancer.^[6] Glandular and squamous lesions commonly coexist,^[11] with CIN found in approximately half of women with endocervical adenocarcinoma in situ (AIS).^{[6][7]} In Australia, adenocarcinoma accounts for approximately 25% of cervical carcinomas, while adenosquamous carcinoma accounts for approximately 4%.^[8] After an initial decrease from 2.8 new cases per 100,000 women in 1991, the incidence of adenocarcinoma has remained at around 2 new cases per 100,000 women.^[9]

Cervical screening based on cytology is less effective in preventing cervical adenocarcinoma than squamous cell carcinomas.^[9] Cervical cytology is less sensitive for the detection of glandular lesions than for the detection of squamous intraepithelial lesions and squamous cell carcinoma, due to sampling and interpretation issues.^[4] Primary HPV screening has been found to be more effective than cytology for the prevention of adenocarcinoma.^[10]

Cytological glandular abnormalities are also associated with polyps, metaplasia and adenocarcinomas of the endometrium, ovary, fallopian tube and other sites, which would not be detected through HPV based cervical screening.^[4] The detection and management of these conditions is outside the scope of this guideline.

Cytology

The Australian Modified Bethesda System (AMBS 2004) for reporting glandular abnormalities recognises the following categories (see [Chapter 3. Terminology](#)):^[9]

- atypical endocervical cells of undetermined significance/atypical glandular cells of undetermined significance
- possible high-grade glandular lesion
- AIS

- adenocarcinoma.

Glandular abnormalities are uncommonly reported on cytology. In Australia, the finding of atypical endocervical/glandular cells of undetermined significance is reported in approximately 0.04% of cytology tests, possible high-grade endocervical glandular lesions in approximately 0.02–0.3%, AIS in approximately 0.01%, and adenocarcinoma in fewer than 0.01% of cytology tests.^[8]

Investigational modalities

Issues in the investigation and management of screen-detected glandular abnormalities differ from those for squamous abnormalities. These include the roles of HPV testing, colposcopy and endocervical sampling in the detection and investigation of cytological glandular abnormalities, and the optimal modality of excisional biopsy.

Colposcopy may detect minimal cervical changes in women with a cytological prediction of AIS. Colposcopy has a low sensitivity for detecting endocervical lesions, and women with endocervical glandular abnormalities on cytology have a significant cancer risk even when colposcopy is normal.^[11]

The use of endocervical sampling (by endocervical curettage or cytobrush) in the investigation of glandular abnormalities has been controversial (see [Chapter. 7. Colposcopy](#)).^[1] Endocervical brushing has higher sensitivity, is better tolerated, and produces fewer insufficient samples than endocervical curettage. However, grading may be more difficult for brush specimens.^[1] Although recommended for women with a cytology finding of atypical glandular cells in Canadian and European guidelines,^{[12][13]} endocervical curettage ECC is not frequently practised in Australia and its role has been controversial. It has little place in the management of women with a high probability of neoplasia, but might improve the chance of identifying a glandular lesion when cytology suggests a possible high-grade glandular abnormality.^[9] Guidelines for the pre-renewal National Cervical Screening Program (NCSP) advised that it could be considered as part of conservative management.^[9]

The use of excisional biopsy modalities other than cold-knife cone in the investigation of cervical glandular abnormalities remains controversial (see [Modalities of treatment](#) in Chapter 7.

Colposcopy).

See:

- [Investigation of cytological glandular abnormalities](#)
- [Follow-up after excisional treatment for AIS](#)
- [Discussion: Management of glandular abnormalities](#)

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Investigation of cytological glandular abnormalities

Author(s):

- A/Prof Lyndal Anderson — Co-author
- Dr Alison Budd — Co-author
- Professor Ian Hammond — Co-author
- A/Professor Selvan Pather — Co-author
- Mr. C. David H. Wrede — Co-author
- Professor Gordon Wright — Co-author
- Cancer Council Australia Cervical Cancer Screening Guidelines Working Party — Co-author

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Background

Atypical endocervical/glandular cells of undetermined significance

The clinical significance of atypical glandular or endocervical cells of undetermined significance cannot be clearly defined.^[1] The cytological finding of atypical endocervical/glandular cells is poorly reproducible.^[2] It predicts increased risk but cannot be considered a specific cancer precursor.^[3]

For conventional cytology within the pre-renewal NCSP, 24.2% of cases of atypical endocervical cells of undetermined significance predicted by cytology in 2012 (HPV status unknown) that were biopsied within 6 months were histologically confirmed as AIS and 6.2% of those biopsied were confirmed as adenocarcinoma.^[1] Among all cases of atypical endocervical cells of undetermined significance predicted by cytology in 2012, including cases where no histology was performed within 6 months, AIS was confirmed in 7.0% and adenocarcinoma in 1.8%.^[1]

In the Pap test-based screening era, the optimal management for women with atypical glandular or endocervical cells of undetermined significance has been uncertain.^[4] Guidelines for the pre-renewal NCSP recommended colposcopy as a mandatory component of the initial investigation for women with atypical glandular or endocervical cells of undetermined significance reported on conventional cytology following a screening Pap test.^[4]

With the transition to HPV-based cervical screening, it is necessary to define the roles of repeated HPV testing and liquid-based cytology in monitoring risk in women with a cytology finding of endocervical cells of undetermined significance or atypical glandular cells of undetermined significance.

Possible high-grade glandular lesion

Guidelines for the pre-renewal NCSP recommended that women with a Pap test result of possible high-grade glandular lesion should be referred to gynaecologist with expertise in the colposcopic evaluation of suspected malignancies or a gynaecological oncologist.^[4]

For conventional cytology within the pre-renewal NCSP, 44.7% of cases of possible high-grade endocervical glandular lesions predicted by cytology in 2012 (HPV status unknown) were histologically confirmed as AIS and 11.4% were confirmed as adenocarcinoma.^[1] Among *all* cases of possible high-grade endocervical glandular lesions predicted by cytology in 2012, including cases where no histology was performed within 6 months, AIS was confirmed in 21.5% and adenocarcinoma in 5.5%.^[1]

AIS

AIS is considered to be the precursor to invasive endocervical adenocarcinoma.^[3] When well-defined cytological criteria are used, this category correlates well with histological outcome.^[3]

For conventional cytology within the pre-renewal NCSP, 63.3% of cases of AIS predicted by cytology in 2012 (HPV status unknown) were histologically confirmed as AIS and 26.7% were confirmed as adenocarcinoma.^[1] Among *all* cases of AIS predicted by cytology in 2012, including cases where no histology was performed within 6 months, AIS was confirmed in 57.1% and adenocarcinoma in 24.1%.^[1]

Guidelines for the pre-renewal NCSP recommended that women in whom AIS was reported on conventional cytology following a screening Pap test should be referred to a gynaecologist with expertise in the colposcopic evaluation of suspected malignancies or a gynaecological oncologist, and if invasive carcinoma is not identified at colposcopic assessment, a cone biopsy should be undertaken.^[4]

The investigation and management of a cytological prediction of AIS is controversial. AIS lesions can present with only minimal changes on colposcopy and can extend into the endocervical canal. As a result the full extent of AIS lesions may not be evident on colposcopic examination which complicates the determination of excisional approaches.^[2] As AIS lesions can be multifocal, the finding of negative margins for AIS on an excision specimen does not reliably indicate that the lesion has been completely excised.^[2] Invasive adenocarcinoma cannot be excluded without a diagnostic excisional procedure.^[2]

The role of excision modalities other than cold-knife cone biopsy in the investigation of cytology-detected glandular abnormalities has been debated. Submission of single-specimen biopsies with minimal thermal damage or disruption of resection margins permits the pathologist to make an accurate assessment. The pre-renewal NCSP guideline recommended that cold-knife cone biopsy should be considered the 'gold standard' for the assessment of glandular lesions, and specifically recommended against the use of large loop excision of the transformation zone (LLETZ).^[4] Current American Society for Colposcopy and Cervical Pathology (ASCCP) consensus guidelines recommend that any modality can be used for diagnostic excision of the transformation zone (TZ) in the treatment of AIS, provided that the specimen remains intact with

interpretable margins and there is no fragmentation, including fragmentation resulting from 'top-hat' endocervical excisions (see [Modalities of treatment](#) in Chapter 7. Colposcopy).^[2]

Endocervical sampling at the time of an excisional procedure predicts residual disease in women with AIS.^[2]

In women who have undergone excisional treatment for AIS, a HPV test finding of oncogenic HPV not detected predicts low risk of persistent or recurrent disease.^[2] Conversely, a positive oncogenic HPV (any type) test result at any time during follow-up was reported as the most significant independent predictor of progressive disease in women with AIS undergoing conservative management.^[5]

Adenocarcinoma

Guidelines for the pre-renewal NCSP recommended that women with a cytological prediction of adenocarcinoma of either endocervical, extrauterine or unspecified origin, reported on conventional cytology following a screening Pap test, should be referred to a gynaecological oncologist or a gynaecological oncology unit.^[4]

Evidence

Immediate excision versus surveillance following a normal (negative) colposcopy for women with a positive oncogenic HPV test result and referral cytology predicting a glandular lesion less than AIS

Systematic review evidence

Systematic reviews were conducted to answer the following questions:

- For women who have a positive oncogenic HPV (any type) test result with referral cytological prediction of atypical endocervical cells of undetermined significance (confirmed on review) and negative colposcopy, what is the safety and effectiveness of repeating HPV and cytology testing, compared with diagnostic excisional cone biopsy)?
- For women who have a positive oncogenic HPV (any type) test result with referral cytological prediction of atypical glandular cells of undetermined significance or possible high grade glandular lesion (confirmed on review) and negative colposcopy, what is the safety and effectiveness of repeating HPV and cytology testing, compared with treatment (excisional cone biopsy)?

The systematic literature searches identified no relevant randomised or pseudorandomised controlled trials comparing surveillance with excisional cone biopsy following a normal (negative) colposcopy for HPV-positive women with cytology suggestive of a glandular lesion less than AIS. The search strategies and inclusion and exclusion criteria used are described in detail in the [Technical report](#).

General literature review evidence

In the absence of any direct evidence from the systematic review, a general review of the literature was performed on the management of HPV-positive women with a confirmed cytological finding of atypical endocervical cells of undetermined significance, atypical glandular cells of undetermined significance, or possible high-grade glandular lesion, and normal (negative) colposcopy to inform consensus-based recommendations.

For women with any glandular cytology less than AIS and a normal (negative) colposcopy:

- AIS or CIN 2+ was diagnosed in 15% of 27 women in a cohort with a cytological finding (Bethesda 2001 criteria) of atypical glandular cells (endometrial or endocervical, not otherwise specified or 'favor neoplastic') with a normal (negative) colposcopy followed by biopsy or cytological follow-up at 6 months.^[6]
- In contrast, in a cohort of 15 women with 'borderline glandular cytology' and a normal (negative) colposcopy none had CIN 2+ on biopsy or abnormal cytology on follow-up at 6, 12, 18 and 24 months.^[7]

For women with cytology predicting a possible high grade glandular lesion and a normal (negative colposcopy):

- In a series of 27 endocervical dyskaryotic smears (considered by the investigators to be equivalent to 'atypical glandular cells endocervical – favor neoplastic'), followed by a normal (negative) colposcopy, 85.2% had a cervical lesion (type not described) on either LLETZ, cervical punch biopsy or laser cone biopsy.^[8]

International (US, Canadian and European) guidelines recommend varying degrees of surveillance following a negative colposcopy for the management of 'atypical glandular cells - not otherwise specified' (or equivalent).^{[2][9][10]} US and Canadian guidelines recommend diagnostic excision of the TZ /cone biopsy following a negative colposcopy for the management of women with 'atypical glandular cells - favor neoplasia'.^{[2][9]}

A summary of the literature considered can be found in the Technical report.

For women with a positive oncogenic HPV test result with atypical glandular/endocervical cells and a normal (negative) colposcopy, the risk of CIN 2+ disease is unclear. The evidence is inconsistent and is derived from small cohorts that may have included women with possible high-grade glandular lesions and that did not consider HPV status. The difficulties associated with colposcopic prediction of glandular lesions, the high rates of CIN 2+ associated with atypical glandular/endocervical cells in Australia,^[1] and the high risk associated with atypical glandular cells in the presence of a positive oncogenic HPV test result, support a recommendation for close follow-up surveillance using a combination of oncogenic HPV testing and LBC (co-testing). A negative co-test is defined as a test in which both oncogenic HPV is not detected and LBC is reported negative.

For women with high-grade glandular abnormalities, the evidence strongly supports the use of diagnostic excision of the TZ for these women. In the pre-renewal NCSP, a cytology report predicting a possible high-grade glandular abnormality was associated with a substantial risk of underlying AIS (44.7% of cytology biopsied within 6 months; 21.5% of all cytology) and invasive cancer (11.4% of cytology biopsied within 6 months; 5.5% of all cytology).^[1]

Cold-knife cone biopsy versus other excisional modalities

Systematic literature review evidence

A systematic review was conducted to assess the safety and effectiveness of excision modalities in women with a positive oncogenic HPV test result with a cytological prediction of possible high-grade glandular or definite high-grade glandular lesion (AIS), or histologically-confirmed AIS. The systematic review compared cold-knife cone biopsy with diathermy excision procedures (loop electrosurgical excision procedure [LEEP], LLETZ), Fischer cone, laser cone, straight wire excision of the TZ (SWETZ) or needle excision of the TZ (NETZ).

The systematic literature searches identified no relevant randomised or pseudorandomised controlled trials addressing this question in women with a positive HPV test result. The search strategies and inclusion and exclusion criteria are described in detail in the [Technical report](#).

General literature review evidence

In the absence of any direct evidence from the systematic review, a general review of the literature comparing excisional modalities for women with a cytological prediction of possible high-grade glandular or definite high-grade (AIS) glandular lesion, or histologically-confirmed AIS (irrespective of HPV status) was undertaken to inform consensus-based recommendations.

Generally, positive or close margins were associated with an increased risk of disease persistence and recurrence and were more likely with LLETZ.^{[11][12][13][14][15]}

A 2014 systematic review^[15] using pooled data from cohort and case series studies found that positive margins were associated with a higher risk of residual and recurrent disease, and that higher rates of incomplete excision were associated with LLETZ (51%) than with cold-knife cone biopsy (30%) or laser cone (28%). This review reported rates of recurrence of AIS ranging from 9% to 29% after LLETZ and from 6% to 11% after cold-knife cone biopsy and concluded that the safety of LLETZ was comparable to that of cold-knife cone biopsy when negative margins were achieved.^[15]

In Australia

The findings included two Australian studies:

- A retrospective population based cohort study of 338 women (Cervical Screening Register of WA) Munro 2015^[11] reported that after adjusting for margin status, no significant differences in cancer outcomes between women with AIS who underwent LEEP or cold-knife cone biopsy after a median follow-up of 3.6 years. In this study LEEP was associated with a greater likelihood of more than one surgical specimen being excised during the procedure compared to cold-knife cone biopsy. The authors noted the need for prospective studies to confirm these findings.
- A retrospective cohort study based on review of hospital records (Royal Prince Alfred Hospital, Sydney)^[16] reported no significant differences in cancer outcomes after 9–10 years of post-treatment surveillance between women with AIS who underwent laser cone or cold-knife biopsy.

This body of evidence should be interpreted with caution: at best, it is based on small retrospective cohort studies in which the decision to perform a particular procedure was likely

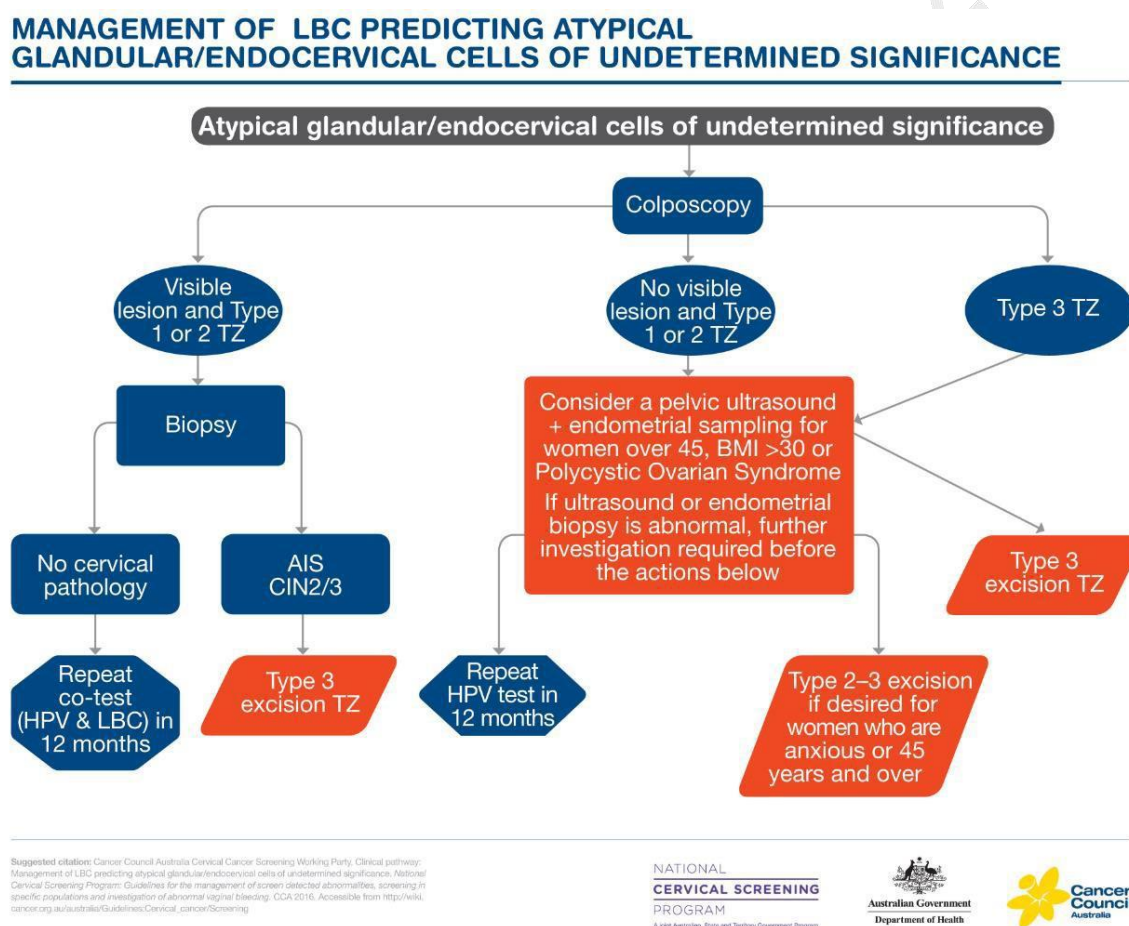
based on the clinical judgement or preference of the treating physician, and the possible inclusion of procedures undertaken for diagnostic rather than therapeutic reasons – a scenario in which positive surgical margins are not a consideration. On the basis of this evidence, it remains unclear as to whether any electrosurgical techniques are as effective and safe as cold-knife cone biopsy. Randomised controlled trials are required to provide a definitive answer.

A summary of the literature considered can be found in the Technical report.

Recommendations

Atypical glandular/endocervical cells of undetermined significance recommendations

Flowchart 11.1. Management of LBC predicting atypical glandular/endocervical cells of undetermined significance



https://www.cancer.org.au/assets/pdf/Mx_LBC_predicting_atypical_glandular_endo_of_u_significance.pdf#_ga=2.236138625.1257883089.1648513003-1771580222.1646017938

Consensus-based recommendation*

REC11.1: Colposcopy referral for atypical glandular/endocervical cells

Women who have a positive oncogenic HPV (any type) test result with a LBC report of atypical glandular/endocervical cells of undetermined significance should be referred to a gynaecologist with expertise in the colposcopic evaluation of suspected malignancies or a gynaecological oncologist.

Consensus-based recommendation***REC11.2: Follow-up after normal colposcopy and LBC prediction of atypical glandular/endocervical cells**

Women who have a positive oncogenic HPV test result (any type) with a LBC prediction of atypical glandular/endocervical cells of undetermined significance and normal colposcopy can be offered repeat co-testing (HPV and LBC) at 6–12 months:

- If the follow-up co-test is negative, co-testing should be repeated annually until the woman has two consecutive negative co-tests, after which she can return to 5-yearly screening.
- If there is either a positive oncogenic HPV (any type) test result or an abnormal LBC (any report other than negative), the woman should be referred for colposcopic assessment, and diagnostic excision of the TZ should be considered.

Practice point**REC11.3: Exclusion of upper genital tract disease before diagnostic excision**

For women who have a positive oncogenic HPV test result (any type) and who have atypical glandular/endocervical cells of undetermined significance on cytology, investigation of the upper genital tract (endometrium, fallopian tube or ovary) using endometrial sampling and/or pelvic ultrasound should be considered, before diagnostic excision of the TZ is performed or the woman is advised to return for colposcopy and further tests in 6–12 months, in these groups of women:

- women aged over 45 years
- women aged over 35 years with a BMI greater than 30
- women diagnosed with polycystic ovarian syndrome
- women with abnormal vaginal bleeding.

Practice point**REC11.4: Role of immediate diagnostic excision of TZ versus observation**

Immediate diagnostic excision of the TZ can be considered for women with atypical

glandular/endocervical cells of undetermined significance if they prefer not to take a conservative observational approach. This might apply to:

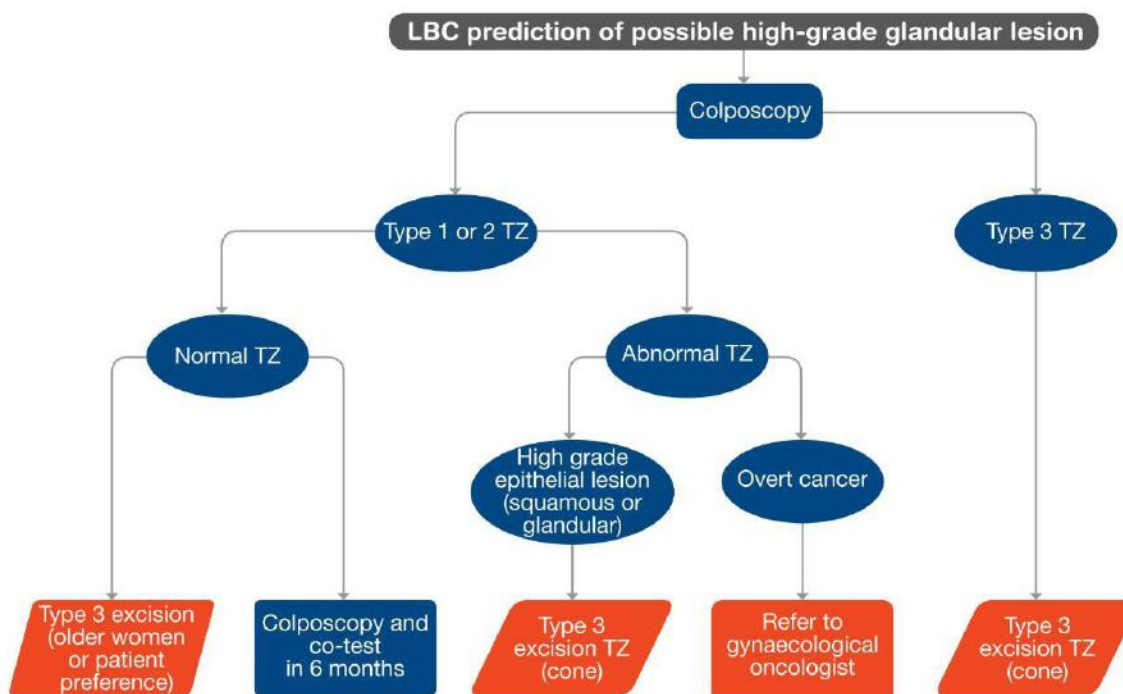
- women aged over 45 years
- women who have completed childbearing
- women who are particularly anxious about their cancer risk.

See Excision of the endocervical transformation zone.

Possible high-grade glandular lesion recommendations

Flowchart 11.2. Management of LBC prediction of a possible high grade glandular lesion

MANAGEMENT OF LBC PREDICTION OF A POSSIBLE HIGH GRADE GLANDULAR LESION



Suggested citation: Cancer Council Australia Cervical Cancer Screening Working Party. Clinical pathway: Management of LBC prediction of a possible high grade glandular lesion. Australian Cervical Screening Program. Guidelines for the management of screen detected abnormalities, screening in specific populations and investigation of abnormal vaginal bleeding. CD29.2019. Accessible from <http://ncl.cancer.org.au/australia/>

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https://www.cancer.org.au/assets/pdf/Mx_LBC_predicting_a_possible_HGG_lesion.pdf#_ga=2.193035053.1257883089.1648513003-1771580222.1646017938

Consensus-based recommendation

REC11.5: Colposcopy for possible high-grade glandular lesions

Women who have a positive oncogenic HPV (any type) test result with a LBC prediction of

possible high-grade glandular lesion should be referred to a gynaecologist with expertise in the colposcopic evaluation of suspected malignancies or a gynaecological oncologist.

Diagnostic excision of the endocervical TZ should be performed in most cases.

Practice point

REC11.6: Women who decline treatment for possible high-grade glandular lesions

Women with a LBC prediction of possible high-grade glandular lesion who decline the recommended excision should be offered surveillance with co-testing (HPV and LBC) and colposcopy in 6 months.

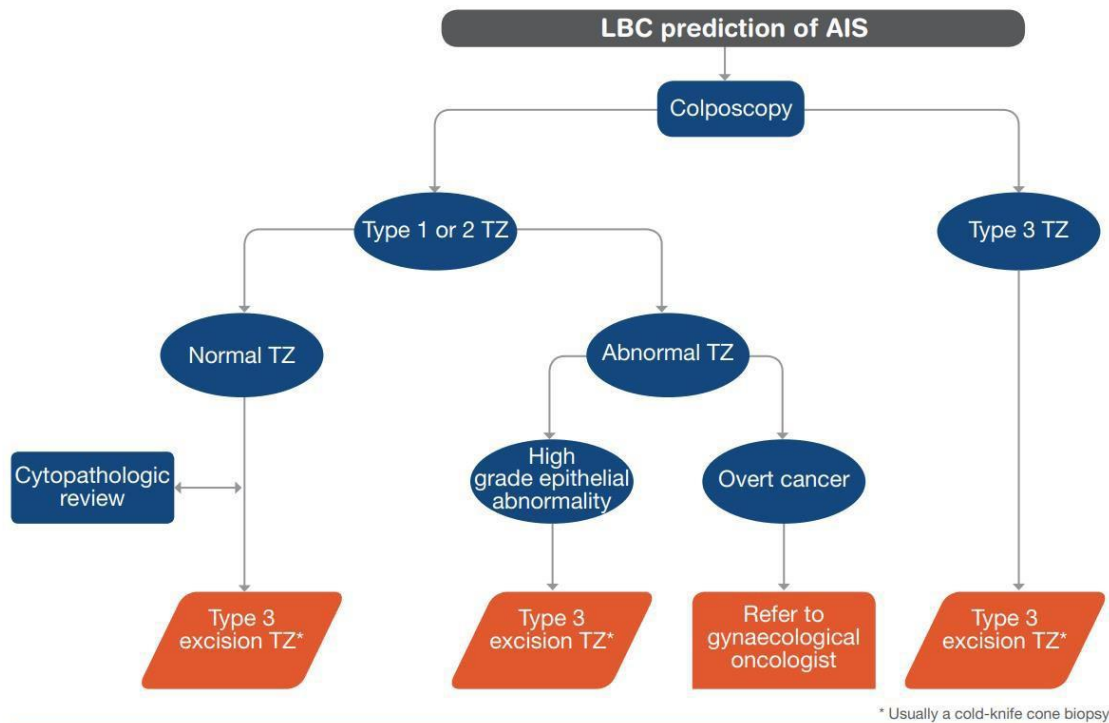
- If in 6 months the woman has a positive result, she should be encouraged to have a diagnostic excision of the TZ.
- It is important that the woman understands the potential risk of underlying disease (21.5% risk of AIS and 5.5% risk of invasive cancer).

See Excision of the endocervical transformation zone.

Endocervical adenocarcinoma in situ (AIS) recommendations

Flowchart 11.3. Management of LBC prediction of high grade glandular lesion (AIS)

MANAGEMENT OF LBC PREDICTION OF A HIGH GRADE GLANDULAR LESION (AIS)



Suggested citation: Cancer Council Australia Cervical Cancer Screening Working Party. Clinical pathway: Management of LBC prediction of a high grade glandular lesion (AIS). National Cervical Screening Program: Guidelines for the management of screen detected abnormalities, screening in specific populations and investigation of abnormal vaginal bleeding, 2016.

National Cervical Screening Program
A joint Australian, State and Territory Government initiative

Australian Government
Department of Health

Cancer Council Australia

https://www.cancer.org.au/assets/pdf/Mx_LBC_prediction_of_a_HGG_lesion_AIS.pdf#_ga=2.223098011.1257883089.1648513003-1771580222.1646017938

Consensus-based recommendation*

REC11.7: Colposcopy referral for AIS

Women with a LBC prediction of AIS should be referred to a gynaecologist with expertise in the colposcopic evaluation of suspected malignancies or to a gynaecological oncologist.

Diagnostic excision of the endocervical TZ should be performed.

See [Follow-up after excisional treatment for AIS](#)

See [Excision of the endocervical transformation zone.](#)

Adenocarcinoma recommendation

Consensus-based recommendation*

REC11.8: Referral to gynaecological oncologist for LBC prediction of invasive disease

Women who have a positive oncogenic HPV (any type) test result with a LBC prediction of invasive adenocarcinoma should be referred to a gynaecological oncologist or a gynaecological oncology centre for urgent evaluation, ideally within 2 weeks.

Table 11.1. Roles of investigational modalities in the assessment of LBC prediction of a glandular lesion

Cytolog	Colposcopy	Target biopsy	Diagnostic excision of the transformation zone	Endocervical sampling
Atypical endocervical/ glandular cells of undetermined significance	Indicated	Indicated if visible lesion at colposcopy	Not indicated in investigation of initial cytology report Indicated if persistent cytology finding Can be considered as alternative to observation if woman's preference	Can be considered
Possible high-grade glandular lesion	Indicated	Indicated if visible lesion at colposcopy	Indicated	Can be considered
AIS	Indicated	Indicated if visible lesion at colposcopy	Indicated	Can be considered
Adenocarcinoma	Indicated	Indicated for clinical	Indicated if no clinically apparent invasive lesion	Not useful

invasive
carcinoma

See [Excision of the endocervical transformation zone](#).

Excision of the endocervical transformation zone recommendations

Consensus-based recommendation*

REC11.9: Specimen for histological assessment of glandular abnormalities

When diagnostic excision of the TZ is performed in the investigation of glandular abnormalities, the method chosen should ensure that a single, intact specimen with interpretable margins is obtained for histological assessment.

Practice point

REC11.10: Cold-knife cone biopsy is the 'gold standard' for glandular abnormalities'

Cold-knife cone biopsy should be considered the 'gold standard' for the diagnostic assessment of glandular lesions. However, a diathermy excisional procedure may be appropriate in some circumstances and could provide an appropriate surgical specimen when performed by a gynaecologist with appropriate training, experience and expertise.

Practice point

REC11.11: Size of cone biopsy

The depth and extent of the cone biopsy should be tailored to the woman's age and fertility requirements. A Type 3 Excision of the TZ is usually required.

Practice point

REC11.12: Cone biopsy excision margins and multifocal AIS

Multifocal disease has been reported in 13–17% of cases of AIS, though the majority of lesions are unifocal. If the margin is close but apparently excised (less than 5 mm), close surveillance by Test of Cure, as recommended in these guidelines, is considered appropriate. In this situation further excision is not considered necessary.

See also [Modalities of treatment](#) in Chapter 7. Colposcopy.

Benefits and harms

Invasive adenocarcinoma of the cervix has not reduced in incidence since the introduction of the NCSP. These recommendations, in concert with HPV testing in primary screening, should lead to improvements in prevention of invasive adenocarcinoma. Recent Australian data showing a high positive predictive value for AIS or invasive cancer, when the referral cytology prediction is atypical endocervical cells of undetermined significance or possible AIS,^[1] supports a more aggressive approach to investigation in these women.

A potential harm is unnecessary treatment in women who do not have significant disease. However, this would be balanced by the detection of significant disease in a large proportion of these women, who are more likely to be identified by primary HPV screening in the renewed NCSP.

See [Chapter 5. Benefits, harms and cost-effectiveness of cervical screening in the renewed National Cervical Screening Program \(NCSP\)](#).

Health system implications of these recommendations

Clinical practice

The recommendations for diagnosis and treatment of screen-detected glandular abnormalities are similar to those in current practice. However surveillance of women treated for AIS now involve co-testing on an annual basis indefinitely until sufficient data has been obtained to limit the time of follow-up.

Resourcing

Because the recommendations are similar to those in the pre-renewal NCSP, no substantial resource implications are expected.

Barriers to implementation

Because the recommendations are similar to those in the pre-renewal NCSP, no substantial barriers to implementation are expected.

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Appendices

[PICO questions 5a & 5b](#)

[View Systematic review report q 5a](#)

[View Systematic review report q 5b](#)

[View General evidence summary table q 5a](#)

[View General
evidence summary
table q 5b](#)

Effective from 1 July 2022

Follow-up after excisional treatment for AIS

Author(s):

- [A/Prof Lyndal Anderson](#) — Co-author
- [Professor Ian Hammond](#) — Co-author
- [A/Professor Selvan Pather](#) — Co-author
- [Mr. C. David H. Wrede](#) — Co-author
- [Professor Gordon Wright](#) — Co-author
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

Anderson, L, Hammond, I, Pather, S, Wrede, CD, Wright, G, Cancer Council Australia Cervical Cancer Screening Guidelines Working Party. Clinical question: Follow-up after excisional treatment for AIS. In: National Cervical Screening Program: Guidelines for the management of screen-detected abnormalities, screening in specific populations and investigation of abnormal vaginal bleeding.

Background

Guidelines for the pre-renewal NCSP¹ recommended:

- that decisions about management of histologically confirmed AIS should take into account the woman's age, fertility status, and excision margins
- hysterectomy for women with histologically confirmed AIS who have completed childbearing
- that hysterectomy should not be undertaken as a treatment for AIS without first performing a cone biopsy to exclude invasive carcinoma
- that women with histologically confirmed invasive adenocarcinoma on cone or punch biopsy should be referred to a gynaecological oncologist or a gynaecological oncology unit.^[2]

For women who wish to maintain fertility and choose cytological surveillance rather than hysterectomy, the risk of recurrent AIS has been estimated at less than 10% and there is a very small risk of invasive adenocarcinoma, even when excision margins are negative.^[2]

Evidence

Systematic review evidence

A systematic review was undertaken to assess the safety and effectiveness of different follow-up options for women with AIS after an excisional procedure (cone excision or LEEP) with complete excision confirmed histologically:

- completion hysterectomy
- repeat co-testing at 12 and 24 months after excision, returning to routine screening if both tests are negative at both follow-up points
- annual cytology only.

The systematic literature search identified no relevant randomised or pseudorandomised controlled trials comparing different follow-up options for women who have undergone an excisional procedure for AIS. The search strategies and inclusion and exclusion criteria used are described in the [Technical report](#).

General literature review evidence

In the absence of any direct evidence from the systematic review, [a general review of the literature](#) was performed on the follow-up of women who have undergone excisional treatment for AIS to inform the drafting of relevant consensus-based recommendations.

Two prospective cohort studies^{[3][4]} reported cancer outcomes for women with histologically confirmed AIS managed conservatively after excisional biopsy.

For women diagnosed with AIS on cone biopsy (almost 50% with involved margins) and followed up for 3 years, the presence of involved margins and oncogenic-HPV types detection on follow-up were associated with an increased risk of progressive disease.^{[3][4]}

In a cohort of women who had follow-up including colposcopy and endocervical curettage every 6 months, residual disease was subsequently diagnosed in 55% of 20 women who had involved margins at baseline and 28.6% of the 21 women who had free margins at baseline. Twelve of the 13 women who underwent hysterectomy for persistent positive margins had residual disease including four adenocarcinomas and one squamous cell carcinoma.^[3] Follow-up using HPV testing had a higher sensitivity and better negative predictive value than cytology when using a colposcopy and histology reference standard.^[3] Sensitivity and negative predictive values were further improved when co-testing was used. These findings demonstrate that colposcopy has limited ability to detect glandular disease. In this study of 42 AIS cases, the initial colposcopy was normal in 16% of cases and the squamocolumnar junction was not visible in 55% cases.

The findings are described in more detail in the [Technical report](#).

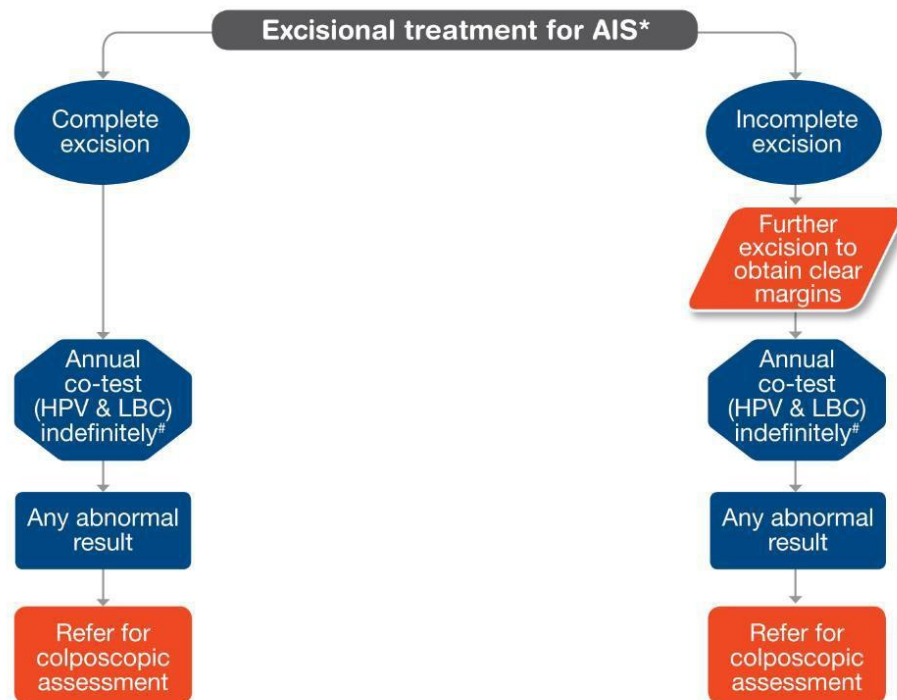
Although the evidence is limited, the findings suggest that women with AIS and clear margins can be safely followed up by annual co-testing for at least 3 years.

There was no evidence comparing completion hysterectomy with ongoing surveillance by co-testing. However, hysterectomy is not routinely required, based on expert opinion.

Recommendations

Flowchart 11.4. Follow up after excisional treatment for AIS

FOLLOW-UP AFTER EXCISIONAL TREATMENT FOR AIS



* AIS = Adenocarcinoma in situ

Until sufficient data become available that may support a policy decision that cessation of testing is appropriate

Suggested citation: Cancer Council Australia Cervical Cancer Screening Working Party. Clinical pathway: Follow-up after excisional treatment for AIS. National Cervical Screening Program Guidelines for the management of screen detected abnormalities, screening in specific populations and investigation of abnormal vaginal bleeding. CCA 2016. Accessible from http://wiki.cancer.org.au/australia/Guidelines/Cervical_cancer_screening

NATIONAL
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A joint Australian, State and Territory Government Program

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https://www.cancer.org.au/assets/pdf/Follow_up_after_excisional_treatment_for_AIS.pdf#_ga=2.223943579.1257883089.1648513003-1771580222.1646017938

Consensus-based recommendation*

REC11.13: Follow-up of completely excised AIS

Women with histologically confirmed AIS who have undergone complete excision with clear margins should have annual co-testing indefinitely.[†]

If any abnormal result is obtained on follow-up co-testing, the woman should be referred for colposcopic assessment.

[†]Until sufficient data become available to support cessation of testing.

Consensus-based recommendation*

REC11.14: Repeat excision for incompletely excised AIS

If AIS is incompletely excised (positive endocervical margin and/or deep stromal margin, not ectocervical margin) or if the margins cannot be assessed, further excision to obtain clear margins should be performed.

Consensus-based recommendation

REC11.15: Role of hysterectomy in AIS

In women who have been treated for AIS by excision, with clear margins, there is no evidence to support completion hysterectomy. In this situation, hysterectomy is not recommended.

Benefits and harms

Long-term surveillance after treatment for AIS will provide women with reassurance about detecting recurrent AIS and thus preventing invasive disease.

A positive oncogenic HPV (any type) test result has been shown to be a very good predictor of recurrent disease over the few years following treatment. Conversely, a HPV test in which oncogenic HPV is not detected has been shown to be a very good predictor of absence of recurrent disease over the few years following treatment in women with complete excision of AIS. This supports a surveillance approach using co-testing which will provide reassurance to women.

Women who persistently have a positive oncogenic HPV test result, but have no cytological abnormality suggestive of glandular disease, will be referred for colposcopic assessment to exclude occult disease. This recommendation may result in colposcopy for some women who would not have developed a clinically significant endocervical glandular lesion, with potential harms including the physical and psychological harms associated with colposcopy. However, this, should be offset against the additional reassurance provided by referral in this situation.

See [Chapter 5. Benefits, harms and cost-effectiveness of cervical screening in the renewed National Cervical Screening Program \(NCSP\)](#).

Health system implications of these recommendations

Clinical practice

The recommended Test of Cure for women treated for AIS using annual co-testing will lead to more intensive surveillance than under pre-renewal NCSP guidelines. However, this will enable the collection of valuable data on AIS recurrence and its detection, which will inform future practice.

Eventually, when more accurate risk assessment is possible, long-term surveillance may not be necessary for women who complete a specified duration of Test of Cure. Until more information is available, however, follow-up will be for an indefinite period.

Resourcing

Indefinite follow-up for AIS now involves co-testing rather than cytology alone (as in the pre-renewal program), so more HPV tests will be performed in follow-up to enable management of this relatively small group.

Whilst at this time indefinite co-testing is recommended, the ongoing monitoring of the renewed NCSP may provide data in the future to support the safety of discharging women who have had a negative co-test on multiple occasions at an earlier point.

Barriers to implementation

Women may not understand the importance of long-term surveillance for treated AIS and may fail to attend for test of cure. It will be important to educate women, and their health professionals, about the importance of long-term surveillance.

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Appendices

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[General evidence summary table q 17](#)

Discussion

Author(s):

- [A/Prof Lyndal Anderson](#) — Co-author
- [Professor Ian Hammond](#) — Co-author
- [A/Professor Selvan Pather](#) — Co-author
- [Mr. C. David H. Wrede](#) — Co-author
- [Professor Gordon Wright](#) — Co-author
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

Unresolved issues

Whilst at this time indefinite co-testing is recommended, the ongoing monitoring of the renewed NCSP may provide data in the future to support the safety of discharging women who have been negative for both HPV and cytology on multiple occasions at an earlier point.

Future research priorities

Well-designed prospective research studies are needed to compare the use of cold knife cone biopsy with diathermy loop excision (LEEP or LLETZ) in the diagnosis and treatment of AIS. If such a study were to show that loop excision was non-inferior to cold-knife cone biopsy for the outcomes of post-treatment recurrent and adenocarcinoma, loop excision could be recommended as an appropriate treatment option for AIS. This would benefit women because, unlike cold-knife cone procedures, loop excision does not require hospital admission and general anaesthesia.

Studies evaluating endocervical curettage would provide useful evidence to determine its role in clinical practice.

Long-term data from the National Cancer Screening Register should be analysed to determine the minimal effective surveillance period for women undergoing annual Test of Cure for post-treatment AIS before returning to routine 5-yearly screening.

12. HPV screening strategies for Aboriginal and Torres Strait Islander women

Author(s):

- [A/Professor Alison Brand](#) — Co-author
- [Professor Ian Hammond](#) — Contributor
- [Dr Joanne Mountford](#) — Contributor
- [Dr Vivienne Milch](#) — Co-author
- [A/Prof Megan Smith](#) — Co-author
- [A/Prof Lisa Whop](#) — Co-author
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

Background

Cervical cancer incidence and mortality rates are higher among Aboriginal and Torres Strait Islander women than non-Aboriginal and Torres Strait Islander women.¹

The current National Cervical Screening Program (NCSP) does not make separate policy recommendations for Aboriginal and Torres Strait Islander women. Limited available evidence on participation in cervical screening by Aboriginal and Torres Strait Islander women suggests that they are under-screened.^{2,3} The Australian Government Department of Health recognises that there are cultural, linguistic and access barriers to cervical screening for these women.¹

Evidence

Systematic review evidence

The systematic literature search identified no randomised or pseudorandomised controlled trials that examined modified screening strategies for Aboriginal and Torres Strait Islander women, compared with the strategy recommended for the general population: primary human papillomavirus (HPV) test-based screening with partial genotyping every 5 years for women aged 25–69 years, immediate referral to colposcopy for women with a positive oncogenic HPV (16/18) test result, and cytology triage for women with a positive oncogenic HPV (not 16/18) test result.

The search strategy and inclusion and exclusion criteria are described in detail in the [Technical report](#).

General literature review evidence

In the absence of any direct evidence from the systematic review, [a general review of the literature](#) was performed to identify current evidence-based clinical practice guidelines for cervical screening, and studies evaluating screening strategies, for Aboriginal and Torres Strait Islander women.

No relevant evidence-based clinical practice guidelines based on systematic reviews of evidence were identified. No studies were found that directly compared alternative screening strategies for Aboriginal and Torres Strait Islander women.

A general literature search was also conducted to quantify the relative risk of and burden of cervical cancer among Aboriginal and Torres Strait Islander women, compared with the general Australian female population. The search strategies and findings are described in detail in the [Technical report](#).

The literature review made the following findings:

A national retrospective study found that, between 1998 and 2005, the age-standardised incidence rate for cervical cancer was 2.7 times higher (95% confidence interval 2.2–3.2) for Aboriginal and Torres Strait Islander women (20 per 100,000) than for non-Aboriginal and Torres Strait Islander women (7 per 100,000).⁴ In 2011–2015, the age-standardised incidence rate of cervical cancer improved somewhat, but was still 2.2 times higher for Aboriginal and Torres Strait Islander women (13.9 per 100,000) than for other Australian women (6.4 per 100,000).⁵ [Chapter 1. Cervical cancer in Australia](#) shows incidences of cervical cancer and cervical cancer outcomes by Indigenous status. See also the tables in the [literature review report](#).

There are no current or previous national data on screening participation by Aboriginal and Torres Strait Islander women. This is primarily because Aboriginal and Torres Strait Islander status was not recorded routinely on pathology forms (the primary source of data for previous state-based Pap test registers) and recording of Indigenous status on the National Cancer Screening Register (NCSR) is incomplete.^{1,6} The renewal of the NCSP provided an opportunity to correct this situation. However, this continues to be a challenge and requires a coordinated strategy involving primary health care, pathology practices, Indigenous communities, other stakeholders and the NCSR.

National data from primary healthcare organisations funded by the Department of Health to provide services to Aboriginal and Torres Strait Islander people show that, in December 2013, 32% of the Aboriginal and Torres Strait Islander women who were regular clients of these services had undergone a cervical screening test in the previous 2 years, 40% had been tested in the previous 3 years, and 46% had been tested in the previous 5 years.¹ However, these records may not capture screening visits if clients had undergone screening outside their usual primary healthcare organisation.¹

A cross-sectional study reported that the age-adjusted prevalence of oncogenic HPV genotypes was similar for Aboriginal or Torres Strait Islander women and non-Aboriginal and Torres Strait Islander women, both overall and in each age group (31.3% versus 30.0% respectively, overall).⁷ The prevalence of HPV 16/18 was also similar in each age group for Aboriginal or Torres Strait Islander women and non-Aboriginal and Torres Strait Islander women, however oncogenic HPV (not 16/18) types were more common in Aboriginal or Torres Strait Islander women aged 31–40 (35.0%) than in non-Aboriginal and Torres Strait Islander women the same age (22.5%).⁷ The prevalence of HPV DNA (including oncogenic and non-oncogenic types) was higher for Aboriginal and Torres Strait Islander women than for non-Indigenous women when standardised to the general Australian population (47.5% versus 41.5%). However this finding was driven by differences in the prevalence of low-risk (non-oncogenic) HPV genotypes (28.7% versus 24.8%), and confidence intervals overlapped in both cases.⁷

National data on HPV vaccine coverage in Aboriginal and Torres Strait Islander girls first became available in 2021.^{8,9} Nationally, the proportion of females who initiated the HPV vaccine course by age 15 was 86.7% among Aboriginal and Torres Strait Islander females and 85.6% among non-Indigenous females, for the cohort turning 15 in 2019. Initiation by age 15 exceeded 80% for Aboriginal and Torres Strait Islander girls in every state and territory except South

Australia (72.3%), and exceeded 90% in New South Wales, the Northern Territory, and Victoria. Coverage with a complete vaccine course by age 15 was lower among Aboriginal and Torres Strait Islander females (71.6%) than among non-Indigenous females (80.0%) for the cohort turning 15 in 2019.⁹ Among the Aboriginal and Torres Strait Islander girls who started the vaccine course, the proportion who eventually completed it by age 15 was around 80% or less in South Australia, Western Australia and Tasmania, and 90% or higher in the remaining states and territories.⁸ These data suggest that any barriers to commencement and completion of HPV vaccination courses may vary for Indigenous people living in different parts of Australia. Australia formally transitioned to adopt a 2-dose HPV vaccine schedule in 2018, and the cohort turning 15 in 2019 includes a mix of those on a 2-dose schedule and those on a 3-dose schedule, so it is too early to tell the extent to which a reduced dose schedule might improve coverage with a complete course. For both schedules, the final dose is due 6 months after the first, and so would still be affected by factors such as higher absenteeism in the second half of the school year. For those who received only two doses under the previous 3-dose schedule, the dose offered in the second half of the school year was the one most commonly missed.¹⁰ Note that unvaccinated females in Australia also have some indirect protection due to herd effects from vaccinated people, including females and males.

A national ecological study reported that the reduction in hospital admissions involving a diagnosis of genital warts in the first 4 years after the inception of the National HPV Vaccination Program was similar in young Aboriginal or Torres Strait Islander women and non-Aboriginal and Torres Strait Islander women (86.7% versus 76.1%; 95% confidence intervals overlapped).¹¹ A study of 39 sentinel sexual health clinics also reported that the reduction in genital warts in the 7-year period after the introduction of HPV vaccination was similar for Aboriginal and Torres Strait Islander people and non-Indigenous people, both for females (directly offered vaccination) and for heterosexual males (who at that point were only protected via herd effects from female vaccination).¹² A repeat cross-sectional study among young Aboriginal and Torres Strait Islander females aged 18-26 years attending for cervical screening in four clinics located in Central Australia, North Queensland and rural New South Wales reported that the prevalence of vaccine-preventable HPV types fell by 94%, from 24% in the pre-vaccine survey to 1.4% in the repeat survey in 2014-2015.^{13, 14, 15}

2021 evidence review: self-collection

A general review of the literature was undertaken to identify studies assessing the acceptability to Aboriginal and Torres Strait Islander women of screening on a self-collected sample (including uptake of this option) and adherence to follow-up among Aboriginal and Torres Strait Islander women in whom HPV is detected in a self-collected sample. Three studies assessing acceptability (including uptake) were identified,^{16,17,18} two of which were in women who were under- or never-screened and who had used or been offered self-collection as part of pilot studies of clinic-based self-collection.^{16,17} One other study was conducted among Aboriginal and Torres Strait Islander women with a mix of screening histories (30% up to date; 40% previous screeners who were overdue; 30% never screened) who were asked for opinions on self-collection (and cervical screening more broadly) but had not used it.¹⁸ In the two studies where previously under-screened women were offered the option of self-collection, approximately 80% or more agreed to screening, mostly using a self-collected sample.^{16,17} More than 90% of those who used self-collection reported that it was simple, afforded them privacy, that they were satisfied with the collection method and process, and that they would use it again.¹⁶ The study among Aboriginal and Torres Strait Islander women with a mix of screening histories and who had not used self-collection reported that relatively few would elect to use self-collection themselves, but those who were interested in self-collection tended to be those who had never screened or were significantly overdue for screening.¹⁸ Regardless of their personal preference,

however, most women in this study were supportive of self-collection being offered as an alternative option, and could see advantages such as increased autonomy, control over the process and privacy. They also expressed that the option to use self-collection could help engage people in screening who would not otherwise. Those women who indicated they would not prefer to use self-collection expressed concerns about administering the test correctly or had difficulties doing so, or preferred a doctor to collect the sample.^{16,18} Only one study provided information about adherence to recommended follow-up, and the number of Aboriginal and Torres Strait Islander women requiring follow-up was small (39 women).¹⁶ The proportion of women who attended for recommended follow-up was 56% (22/39) overall. Almost all of the women who had HPV (16/18) detected attended for colposcopy (8/9), but attendance for follow-up was lower among the women with HPV (not 16/18) detected (14/30). The second pilot study did not report adherence to follow-up specifically in Aboriginal women.¹⁷ Both pilot studies were undertaken with under-screened women and so may have limited applicability to a broader population. They also included additional support for women to complete the follow-up pathway, such as individual support from a primary healthcare nurse and offering accompaniment, transport or financial support to attend recommended follow-up.

Synthesis

Current evidence does not support the use of a more intensive screening strategy for Aboriginal and Torres Strait Islander women. To date, the NCSP has not been successful in reducing the incidence and mortality of cervical cancer among Aboriginal and Torres Strait Islander women. More effective strategies are needed to increase their participation in the NCSP. Strategies for improving equity, accessibility, effectiveness and cultural sensitivity of cervical screening services for Aboriginal and Torres Strait Islander women should be explored. Data collection systems should be improved to ensure that accurate data for Aboriginal and Torres Strait Islander women are available for inclusion in the NCSR.

Recommendations

Consensus-based recommendation

REC12.1: Cervical Screening for Aboriginal and Torres Strait Islander women

Aboriginal and Torres Strait Islander women should be invited and encouraged to participate in the NCSP and have a 5-yearly HPV test, as recommended for all Australian women.

Practice point

REC12.2: Invitations to screen for Aboriginal and Torres Strait Islander women

Specific efforts should be made to maximise delivery of culturally appropriate invitations to Aboriginal and Torres Strait Islander women.

Practice point

REC12.3: Cervical screening services for Aboriginal and Torres Strait Islander women

Specific efforts should be made to provide accessible and culturally safe screening, diagnostic and treatment services to Aboriginal and Torres Strait Islander women.

Practice point

REC12.4: Eligibility for screening on self-collected sample: Aboriginal and Torres Strait Islander people

All eligible people, including Aboriginal and Torres Strait Islander people, should be offered the choice of HPV testing on a self-collected vaginal sample or on a clinician-collected sample.

Practice point

REC12.5: Data collection and recording Aboriginal and Torres Strait Islander status

Healthcare professionals should ask all women whether they identify as Aboriginal or Torres Strait Islander, and a woman's Aboriginal and Torres Strait Islander status should be recorded on relevant clinical records, including pathology request forms, in accordance with the Australian Bureau of Statistics classification and standards. Aboriginal and Torres Strait Islander status influences clinical management of tests in some cases.

Benefits and harms

In the absence of evidence to support specifically tailored screening protocols for Aboriginal and Torres Strait Islander women, participation in the NCSP is expected to reduce rates of cervical cancer among Aboriginal and Torres Strait Islander peoples.

Invitations to participate in screening may cause unnecessary anxiety for some Aboriginal and Torres Strait Islander women if they have not received adequate education and explanation about cervical cancer and its link with HPV infection. Culturally sensitive education should be implemented to minimise this potential harm.

The option for all people eligible for cervical screening, including Aboriginal and Torres Strait Islander people, to choose self-collection if they prefer is expected to make cervical screening more culturally appropriate, by providing women with more choice and agency in screening, and more autonomy and control over their health and their body.

See [Chapter 5. Benefits, harms and cost-effectiveness of cervical screening in the renewed National Cervical Screening Program \(NCSP\)](#).

Health system implications of these recommendations

Clinical practice

Healthcare professionals who provide screening services for Aboriginal and Torres Strait Islander women need to be able to allocate enough time to provide education about screening, the option of self-collection, and encouragement to participate in the program.

Improved resources for cervical screening for Aboriginal and Torres Strait Islander women should be made available.

For all women who present for cervical screening the healthcare professional should ascertain the woman's Aboriginal and Torres Strait Islander status and record this on the pathology request form. This information is collected by the National Cancer Screening Register.

Resourcing

There may be too few nurses or Aboriginal health workers adequately trained as cervical screening test providers. Training more personnel will have cost implications. Self-collection may enable more healthcare professionals to provide cervical screening (for example males or those known personally to the woman), as cultural barriers and embarrassment are reduced when the woman collects her own sample. There is evidence from Queensland that the introduction of LBC in place of conventional cytology for cervical screening in a remote high-risk population (mainly Aboriginal and Torres Strait Islander people) led to a reduction in the rate of unsatisfactory smears.²³ In the Renewed program it is anticipated that this benefit will be continued as unsatisfactory rates are extremely low for HPV tests. Well-designed and conducted research is needed to explore opportunities to implement point-of-care testing in

remote communities, enabling counselling and, if needed, further assessment and treatment on the same day.

Barriers to implementation

Some Aboriginal and Torres Strait Islander women are unable to access a culturally safe healthcare professional and they may not receive an invitation to participate in the NCSP if their name or mailing address has changed, if mail is not delivered to their residence (for example, those that live in remote areas), or if mail is not delivered to a single consistent residence.

Aboriginal and Torres Strait Islander women may refuse the invitation for cultural reasons or a lack of understanding about cervical cancer and its prevention. Education about HPV testing and prevention of cervical cancer is very important, and should be delivered in culturally sensitive and appropriate ways, by people in whom these women have confidence.

Aboriginal and Torres Strait Islander women, especially those in rural and remote areas, often use the services of nurses and Aboriginal Health workers who are trained cervical screening test providers. The aim is to provide the most appropriate service for individual women.

Aboriginal Health workers and women may face multiple barriers to providing cervical screening including other health and social issues that may be a priority during an appointment. Most importantly, it can take time for workers to build trust and educate women about the need for screening.²⁴

Discussion

Unresolved issues

Indigenous status is not always collected on pathology request forms and was not always routinely collected by the state and territory Cervical Screening Registers. This lack of data collection prevents the accurate assessment of cervical screening issues in Aboriginal and Torres Strait Islander women. Whilst the NCSR does collect data regarding Indigenous status, these data are incomplete and it remains the role of the clinician or healthcare provider to make note of Aboriginal status on relevant clinical records, including pathology request forms.

Future research priorities

Strategies to improve recruitment of Aboriginal and Torres Strait Islander women should be developed, implemented and evaluated. Consideration could be given to the development and evaluation of culturally appropriate information to support the invitation to screen. More research is required to determine why cervical screening participation in some specific communities in the Northern Territory and Queensland is higher than in others, and to translate the approaches of the more highly screened communities to the wider Aboriginal and Torres Strait Islander population. Aboriginal and Torres Strait Islander researchers need to be involved in the development of research strategies to provide culturally appropriate evidence base to translate into practice.

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Appendices

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13. Screening after total hysterectomy

Author(s):

- [A/Professor Deborah Bateson](#) — Co-author
- [A/Professor Alison Brand](#) — Co-author
- [Professor Ian Hammond](#) — Co-author
- [Dr Joanne Mountford](#) — Co-author
- [A/Professor Marion Saville](#) — Co-author
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

Background

Total hysterectomy involves the removal of the cervix and the uterus and closure of the top of the vaginal canal, creating a vaginal vault. Removal of the cervix eliminates the risk of developing a cervical cancer and the need for cervical cytology. However, cytology of the vaginal vault can enable screening for pre-invasive disease of the vagina such as vaginal intraepithelial neoplasia (VAIN) or recurrence of previously treated cervical or vaginal cancer.

High-grade cervical intraepithelial neoplasia (CIN), prior to or at the time of total hysterectomy, is a known risk factor for the development of secondary VAIN, with reported recurrence rates of 0.9–7.4%.^[1] However, VAIN is far less common than CIN and the incidence of vaginal cancer is less than a third of the incidence of cervical cancer, accounting for less than 0.5% of all cancers in Australian women.^[2]

Based on an analysis of data from long-term follow-up studies conducted in women treated for high-grade CIN, Soutter *et al* found that, in the context of cytology follow-up after hysterectomy, the rate of invasive disease remained elevated in comparison with the rate in the general population, until at least 20 years after treatment.^[3] Long-term vaginal cytology follow-up of hysterectomised women with a history of high-grade CIN has been recommended, but it should be noted that this recommendation was prior to the introduction of HPV testing.^[3] Pre-renewal National Cervical Screening Program (NCSP) guidelines^[4] recommended that women undergoing hysterectomy for high-grade CIN should be advised to continue annual cytologic surveillance, and noted the need for further investigation of the role of human papillomavirus (HPV) testing for this group.

Since 2006 under the pre-renewal NCSP, co-testing with HPV testing and cervical cytology has been used in Australia in the follow-up of women treated for high-grade CIN by ablation or excision of the transformation zone (TZ). A negative co-test is defined as a test occasion at which oncogenic HPV is not detected and the cytology report is negative. Women with two consecutive negative co-testing results during annual co-testing were returned to routine 2-yearly screening. This 'Test of Cure' approach, is based on the high negative predictive value of co-testing in identifying women at risk of recurrence. Comparison of screening outcomes for this strategy with those under pre-2006 guidelines, has shown this strategy to be safe.^[5]

At this time it is uncertain whether a shorter period of surveillance could be recommended in the future. The safety of discharging women back to routine screening after only one occasion on which oncogenic HPV is not detected, or only one negative co-test, has not yet been conclusively established in Australia.

General literature review evidence

Structured literature searches were conducted to ascertain the effectiveness of further screening with vaginal vault cytology or HPV tests in hysterectomised women in each of the following groups:

1. women who have never had abnormal cytology or a positive oncogenic HPV test result
2. women with a history of a positive oncogenic HPV test result and cytological prediction of a high-grade lesion (squamous or glandular), or women who have recently completed treatment for a high-grade lesion who are under surveillance or have returned to routine screening after treatment, with no evidence of abnormality on the hysterectomy specimen
3. women who have had a high-grade abnormality treated by total hysterectomy, with complete excision of the lesion in the hysterectomy specimen
4. women who had completed Test of Cure after treatment for CIN2+ before hysterectomy, with no abnormality in the hysterectomy specimen.

Three relevant recent articles were identified that reported data from women who had undergone total hysterectomies for benign conditions. In a prospective study, 4% of women (4 cases out of 102) who had undergone hysterectomy for uterine fibromatosis developed VAIN after a mean latency period of 10 years. All cases tested HPV16 positive at the time of VAIN diagnosis and had a positive cytology test. Two years after treatment for VAIN, two women previously diagnosed with VAIN 3 recurred and tested HPV16 positive at the time of relapse.^[6] The presence or absence of any abnormal cytology or HPV history could not be ascertained from the articles.^{[7][8]} Based on aggregated data from studies identified by a systematic review of the literature, Stokes-Lampard *et al* reported that 1.8% of women who had had a hysterectomy for a benign indication had an abnormal smear and no cancers were detected.^[7] No relevant recent articles were identified that reported outcomes for women with a history of high-grade abnormalities who:

- had been treated and were undergoing surveillance
- had completed a Test of Cure and had returned to routine screening prior to having a total hysterectomy with no evidence of any abnormality in the hysterectomy specimen.

A small number of retrospective studies in women with abnormal vaginal cytology after hysterectomy were identified. Although based on small samples (15–125 women), the results of these studies suggested that women who have had a total hysterectomy for CIN should continue post-treatment surveillance.^{[9][1][10]}

One small prospective study which aimed to identify prognostic factors for the development of VAIN found that oncogenic HPV DNA was identified in seven out of eight women who developed VAIN post-hysterectomy.^[11]

Soutter *et al*^[3] performed a meta-analysis of 26 cohorts who had received treatment for CIN, including four cohorts who received hysterectomy treatment. They found that there was no significant difference in the incidence of invasive recurrence between those series in which women were treated with a total hysterectomy and those in which one of the conservative methods of treatment (ablation or excision) was used. The authors concluded that follow-up for women after hysterectomy for CIN should be the same as for women treated conservatively.^[3] Taken together, these findings provide evidence to support ongoing surveillance for hysterectomised women with a history of high grade CIN, but apply to screening and surveillance using cervical cytology alone. These findings are less relevant to the renewed

NCSP, which is based on primary HPV testing, and within which post-treatment surveillance is based on co-testing (HPV and LBC).

Recommendations

Women who have had a total hysterectomy do not need further surveillance if both the following conditions apply:

- The woman has been treated for histologically confirmed HSIL and has completed Test of Cure according to pre-renewal NCSP guidelines^[4] implemented since 2006.
- No evidence of cervical pathology was detected on the hysterectomy specimen.

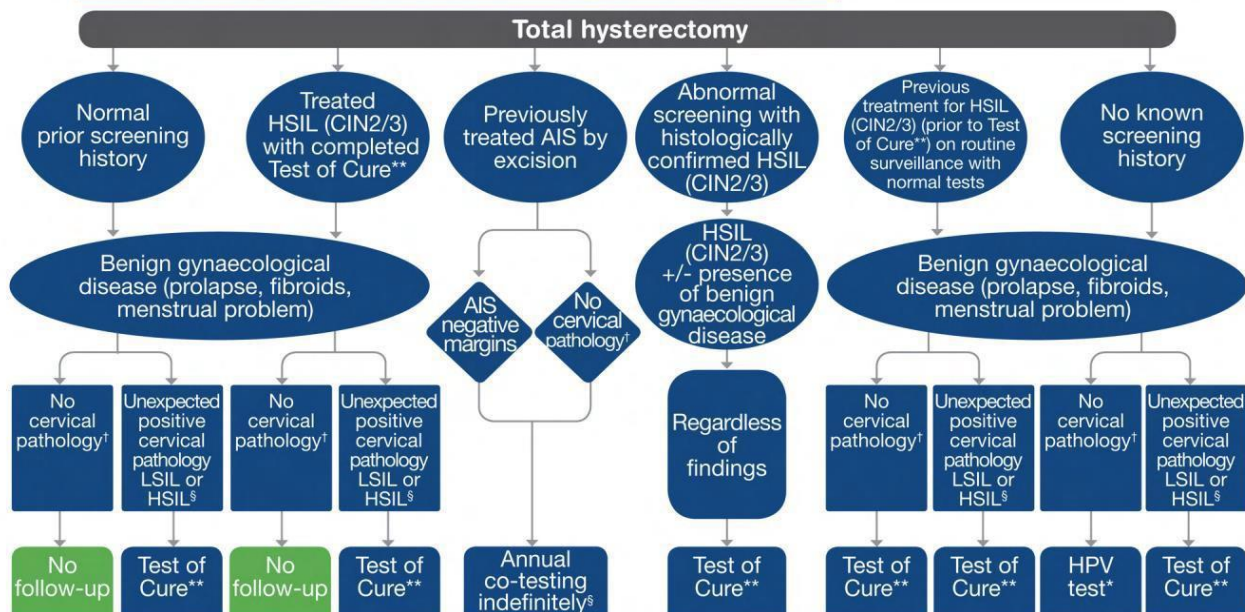
Women who have had a total hysterectomy should be advised to complete Test of Cure if they have been treated for histologically confirmed HSIL, but have not completed Test of Cure.

Women who have had a total hysterectomy (for any of the reasons listed in Flowchart 13.1) and who have completed Test of Cure do not need any further surveillance or testing.

Women who have had **subtotal hysterectomy** (cervix remains in situ) should be screened every 5 years with a HPV test. Any abnormalities should be managed according to the relevant recommendations in these guidelines.

Flowchart 13.1. Vaginal screening after total hysterectomy

VAGINAL SCREENING AFTER TOTAL HYSTERECTOMY



* HPV test to be taken from the vaginal vault 12 months after treatment & annually thereafter until the woman has tested negative on 2 consecutive occasions, after which she does not need further testing

§ Annual co-testing indefinitely is recommended for AIS until sufficient data become available that may support a policy decision that cessation of testing is appropriate

† No cervical pathology (LSIL, HSIL or AIS) found on examination of the cervix

** No further testing/follow-up after completion of Test of Cure

Suggested citation: Cancer Council Australia Cervical Cancer Screening Working Party. Clinical pathway: Vaginal screening after total hysterectomy. National Cervical Screening Program: Guidelines for the management of screen detected abnormalities, screening in specific populations and investigation of abnormal vaginal bleeding. CCA 2016. Accessible from http://wiki.cancer.org.au/australia/Guidelines/Cervical_cancer/Screening

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https://www.cancer.org.au/assets/pdf/Vag_screening_after_total_hysterectomy.pdf#_ga=2.231808159.1257883089.1648513003-1771580222.1646017938

Table 13.1. Total hysterectomy

VAGINAL SCREENING AFTER TOTAL HYSTERECTOMY

Total hysterectomy [†]									
Prior screening history	Normal			Treated HSIL (CIN2/3) with completed Test of Cure		Abnormal screening with histologically confirmed HSIL (CIN2/3)	Previous treatment for HSIL (CIN2/3) (prior to Test of Cure) on routine surveillance with normal tests		No known screening history
Indication for hysterectomy	Benign gynaecological disease				HSIL (CIN2/3) ± associated benign gynaecological disease	Benign gynaecological disease			
Cervical pathology in histology specimen	No cervical pathology	Positive for cervical pathology LSIL or HSIL	No cervical pathology	Positive for cervical pathology LSIL or HSIL	Regardless of findings	No cervical pathology	Positive for cervical pathology LSIL or HSIL	No cervical pathology	Positive for cervical pathology LSIL or HSIL
Recommended follow-up	No follow up	Test of cure	No follow up	Test of Cure	Test of Cure	Test of Cure	Test of Cure	HPV 12/24 months	Test of Cure

[†] not including total hysterectomy performed for AIS

Recommended citation: Cancer Council Australia Cervical Cancer Screening Advisory Panel. Cervical pathology: Total hysterectomy. National Cervical Screening Program: Guidelines for the management of lower genital tract abnormalities, including in women with hysterectomy and management of abnormal Pap smear findings. 2020. Available from: <http://www.nccps.org.au/cervical-screening-program/>

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Note: If invasive cervical cancer reported in cervical pathology, patient to be referred to gynaecological oncologist for further management.

Total hysterectomy

Consensus-based recommendation*

REC13.1: Total hysterectomy for benign disease

Women with a normal cervical screening history, who have undergone hysterectomy for benign disease (e.g. menorrhagia, uterine fibroids or utero-vaginal prolapse), and have no cervical pathology at the time of hysterectomy, do not require further screening or follow up.

Consensus-based recommendation*

REC13.2: Total hysterectomy after completed Test of Cure

Women who have had a total hysterectomy with no evidence of cervical pathology, have previously been successfully treated for histologically confirmed HSIL and have completed Test of Cure, do not require further follow-up. These women should be considered as having the same risk for vaginal neoplasia as the general population who have never had histologically confirmed HSIL and have a total hysterectomy.

If unexpected LSIL or HSIL is identified in the cervix at the time of hysterectomy, then these women require follow-up with an annual co-test on a specimen from the vaginal vault until they have a negative co-test on two consecutive occasions.

Consensus-based recommendation

REC13.3: Total hysterectomy after adenocarcinoma in situ (AIS)

Women who have had a total hysterectomy, have been treated for AIS, and are under surveillance, should have a co-test on a specimen from the vaginal vault at 12 months and annually thereafter, indefinitely.[†]

Women who have a total hysterectomy, as completion therapy or following incomplete excision of AIS at cold-knife cone biopsy or diathermy excision, should have a co-test on a specimen from the vaginal vault at 12 months and annually thereafter, indefinitely.

[†] Until sufficient data become available to support cessation of testing

Consensus-based recommendation*

REC13.4: Total hysterectomy for treatment of high-grade CIN in the presence of benign gynaecological disease

Women who have had a total hysterectomy as definitive treatment for histologically confirmed HSIL in the presence of benign gynaecological disease, irrespective of cervical margins, should have a co-test on a specimen from the vaginal vault at 12 months after treatment and annually thereafter until the woman has tested negative by both tests on two consecutive occasions.

After two annual consecutive negative co-tests, the woman can be advised that no further testing is required.

Consensus-based recommendation*

REC13.5: Total hysterectomy after histologically confirmed HSIL without Test of Cure

Women who have been treated for histologically confirmed HSIL, are under surveillance or have returned to routine screening without Test of Cure, and have had a total hysterectomy with no evidence of cervical pathology, should have a co-test on a specimen from the vaginal vault at 12 months and annually until the woman has tested negative on two consecutive occasions.

After two annual consecutive negative co-tests, the woman can be advised that no further testing is required.

Consensus-based recommendation*

REC13.6: Total hysterectomy and no screening history

Women who have had a total hysterectomy with no evidence of cervical pathology, and whose cervical screening history is not available, should have a HPV test on a specimen from the vaginal vault at 12 months and annually thereafter until they have a negative HPV test on two consecutive occasions.

After two annual consecutive negative HPV tests, women can be advised that no further testing is required.

Note: It is expected that amendments to relevant Medicare Benefits Schedule items to support testing on a self-collected sample for this specific use will be effective from 1 November 2022 pending any external impacts such as upcoming elections and caretaker period.

Practice point

REC13.7: Colposcopy referral for any positive co-test result following total hysterectomy

Women who have had a total hysterectomy and are under surveillance with co-testing, and have a positive oncogenic HPV (any type) test result and/or any cytological abnormality, should be referred for colposcopic assessment.

Practice point

REC13.8: Vaginal bleeding following total hysterectomy

Women who have vaginal bleeding[†] following total hysterectomy should be assessed by their GP or gynaecologist, regardless of the results of any surveillance tests.

[†]Vaginal bleeding is quite common in the early weeks following hysterectomy and, where appropriate, should be investigated by the treating gynaecologist.

Practice point

REC13.9: Total hysterectomy after genital tract cancer

Women who have been treated for cervical or endometrial cancer are at risk of recurrent cancer in the vaginal vault. These women should be under ongoing surveillance from a gynaecological oncologist. Therefore, they will be guided by their specialist regarding appropriate surveillance and this is outside the scope of these guidelines.

Subtotal hysterectomy

Practice point

REC13.10: Subtotal hysterectomy

Women who have undergone subtotal hysterectomy (the cervix is not removed) should be invited to have 5-yearly HPV testing in accordance with the recommendation for the general population. Any detected abnormality should be managed according to these guidelines.

Benefits and harms

For women who have had a total hysterectomy, who have a prior history of histologically confirmed HSIL, there is evidence to support continued surveillance for a limited period of time. For women who have had a hysterectomy with a prior history of AIS there is currently no evidence to inform the decision to discontinue surveillance. The potential harms of surveillance are minimal, especially in relation to the enhanced safety conferred by continuing surveillance. See [Chapter 5. Benefits, harms and cost-effectiveness of cervical screening in the renewed NCSP.](#)

Health system implications of these recommendations

Clinical practice

These recommendations are generally consistent with current clinical practice, apart from the addition of HPV testing, to enhance recommended surveillance.

Resourcing

No material changes to the costs are anticipated.

Barriers to implementation

Women may not understand the importance of follow-up after total hysterectomy, believing that they are now 'cured'. The treating gynaecologist should be encouraged to provide appropriate information regarding the risk of recurrent disease in the vagina, the need for surveillance and

should provide the general practitioner with a management plan outlining the recommended surveillance.

Discussion

Unresolved issues

In the future, it is possible that women who have had a total hysterectomy may be discharged after test of cure following only one negative co-test, or a single HPV-only test, but sufficient data to support such management will need to be accrued via the safety monitoring process for the NCSP.

Future research priorities

Currently there is insufficient evidence to determine the most appropriate follow-up for patients who have had AIS and had a total hysterectomy. Research to inform the method and duration of follow up of these women should be given priority.

A prospective audit of a large cohort of women undergoing hysterectomy for benign reasons with a history of high grade CIN (potentially via the safety monitoring of the NCSP) is needed to provide the evidence required to ascertain the appropriate frequency, duration and test modality for follow-up testing from the vaginal vault.

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Appendices

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14. Screening in pregnancy

Author(s):

- [A/Professor Deborah Bateson – Co-author](#)
- [Dr Marsali Newman – Co-author](#)
- [Dr Lyndal Anderson – Co-author](#)
- [Dr Vivienne Milch – Co-author](#)
- [A/Professor Alison Brand – Contributor](#)
- [Professor Ian Hammond – Contributor](#)
- [Dr Joanne Mountford – Contributor](#)
- [Dr Lara Roeske – Contributor](#)
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party – Co-author](#)

Contents

Background

Cervical screening during pregnancy is a special circumstance, as additional consideration needs to be given for the wellbeing of the fetus. The incidence of cervical cancer in pregnancy is low, with estimates in the literature ranging from 3.3 to 26 cases per 100,000 births.^{[1][2]} However, early-stage cervical cancer may be more frequently encountered by clinicians caring for women during their pregnancy due to higher age-specific incidence rates in the 30–39 year age group, compared with younger ages,^[3] and more women delaying pregnancy.^[4] Although most cases of cervical abnormalities are likely to be asymptomatic and identified through screening, it is important to consider non-obstetric causes when a pregnant woman reports vaginal bleeding (see [Chapter 18. Investigation of abnormal vaginal bleeding](#)).^[5]

Approximately five per cent of pregnant women will have abnormal cervical cytology.^[6] It is strongly recommended that, routine antenatal care should include cervical screening when this is due or overdue. For some women, pregnancy may be the first, or only, opportunity for cervical screening and cervical cancer is more likely to be diagnosed in never screened or under-screened women.^[9] For pregnant women who accept their cervical screening specimen being collected by a practitioner the tool of choice should be a [broom type brush](#), as the endocervical(cytobrush) brush is not recommended. The use self-collection of a vaginal sample for HPV testing is not contraindicated during pregnancy, and pregnant women should be offered the choice of either a practitioner or self-collected sample.

Conservative management of high-grade squamous intraepithelial lesions (HSIL) is recommended during pregnancy.^[10] Colposcopy is performed to exclude the presence of invasive cervical cancer, to confirm the presence of pre-invasive disease and reassure the pregnant woman that it is safe to continue with her pregnancy. When HSIL is diagnosed during pregnancy, treatment can be delayed until after delivery^[8] because progression of cervical intraepithelial neoplasia (CIN) to invasive disease during pregnancy is rare, with a range of 0–3% of cases.^{[10][11][12]} Almost all cases are microinvasive and amenable to curative treatment.

Postpartum regression of CIN lesions is common.^{[13][14]} A meta-analysis of studies found that women treated for CIN during pregnancy were at an increased risk of preterm birth (< 37 weeks) and premature rupture of membranes, compared with women with untreated CIN who gave birth before treatment.^[15] However, when invasive disease is suspected or confirmed in pregnancy, expert management by a gynaecologic oncologist is required due to the increased risk of poor pregnancy outcomes.

Evidence

General literature review evidence

A general literature search was conducted to identify recent studies reporting on the natural history of cervical dysplasia during pregnancy and its management.

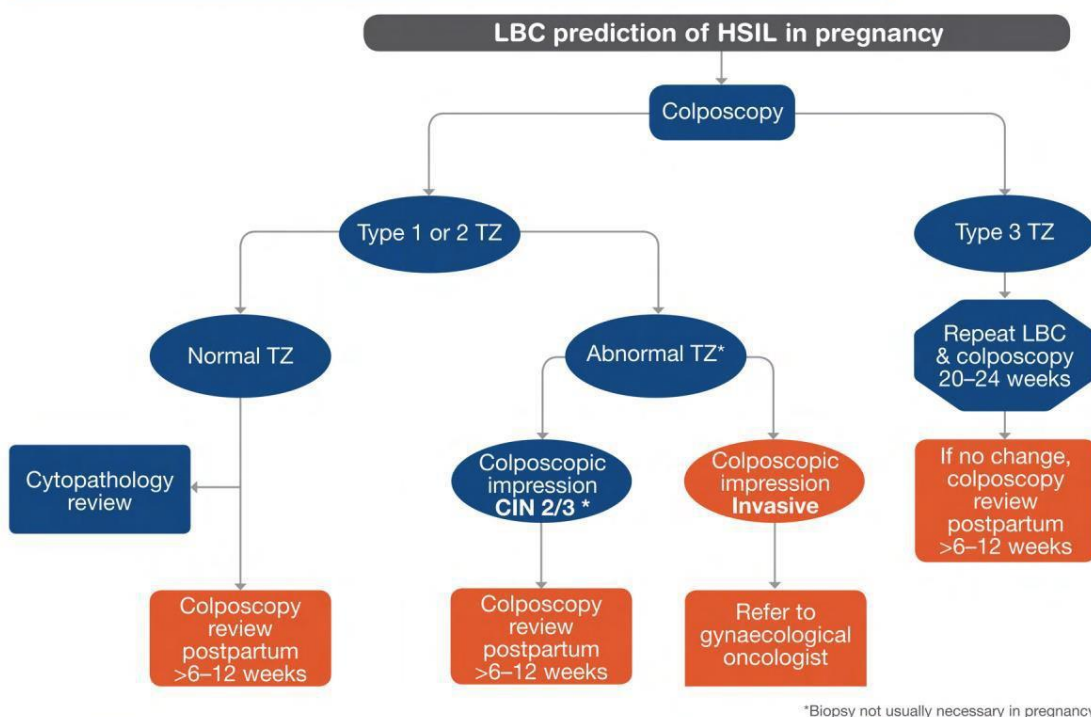
The available evidence consists of only small studies, with somewhat diverse findings for the natural history of progression and regression of HSIL or histologically confirmed HSIL identified during pregnancy.^{[16][17][18][19][20]} Microinvasive or invasive disease was identified in a small number of cases, most of which were diagnosed post partum.^{[16][17][18][19]}

There is evidence to support the safety of colposcopy^{[10][8][3][14]} and biopsy^[14] during pregnancy. Biopsy of the cervix in pregnancy is associated with a small risk of excessive bleeding from the cervical biopsy site, but is considered otherwise safe.^{[14][8][2][10]}
The findings are summarised in the [Technical report](#).

Recommendations

Flowchart 14.1. Management of a LBC prediction of HSIL in pregnancy

MANAGEMENT OF A LBC PREDICTION OF HSIL IN PREGNANCY



*Biopsy not usually necessary in pregnancy

Suggested citations: Cancer Council Australia Cervical Cancer Screening Working Party. Clinical pathway: Management of a LBC prediction of HSIL in pregnancy. National Cervical Screening Program: Guidelines for the management of screen detected abnormalities, screening in specific populations and investigation of abnormal vaginal bleeding. CCA 2016. Accessible from <http://nku.cancer.org.au/australia/> Guidelines Cervical_cancer/Screening

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https://www.cancer.org.au/assets/pdf/Mx_of_LBC_prediction_of_HSIL_in_pregnancy.pdf#_ga=2.190386731.1257883089.1648513003-1771580222.1646017938

Consensus-based recommendation

REC14.1: Positive oncogenic HPV (not 16/18) test result with LBC negative or pLSIL/LSIL in pregnancy

Pregnant women who have a positive oncogenic HPV (not 16/18) test result with a LBC report of negative or prediction of pLSIL/LSIL should have a repeat HPV test in 12 months.

Consensus-based recommendation

REC14.2: Positive oncogenic HPV (not 16/18) test result with LBC pHSIL/HSIL or any glandular abnormality in pregnancy

Pregnant women who have a positive oncogenic HPV (not 16/18) test result with a LBC prediction of pHSIL/HSIL or any glandular abnormality should be referred for early colposcopic assessment.

† When practical and not deferred until the postpartum period.

Consensus-based recommendation

REC14.3: Positive HPV (16/18) test result in pregnancy

Pregnant women who have a positive oncogenic HPV (16/18) test result should be referred for early colposcopic assessment regardless of their LBC test result. If the screening sample was collected by a healthcare professional then the laboratory will undertake reflex LBC. If the screening sample was self-collected then a sample for LBC should be collected at the time of colposcopy.

When practical and not deferred until the postpartum period.

Consensus-based recommendation*

REC14.4: Referral of pregnant women with invasive disease

Pregnant women should be referred and seen within 2 weeks by a gynaecological oncologist/gynaecological cancer centre for multidisciplinary team review and management in the following situations:

- LBC prediction of invasive disease
- colposcopic impression of invasive or superficially invasive squamous cell carcinoma of the cervix
- histologically confirmed diagnosis of invasive or superficially invasive squamous cell carcinoma of the cervix.

Consensus-based recommendation*

REC14.5: Colposcopy during pregnancy

The aim of colposcopy in pregnant women is to exclude the presence of invasive cancer and to reassure them that their pregnancy will not be affected by the presence of an abnormal cervical screening test result.

Practice point

REC14.6: Colposcopy during pregnancy

Colposcopy during pregnancy should be undertaken by a colposcopist experienced in assessing women during pregnancy.

Consensus-based recommendation*

REC14.7: Cervical biopsy in pregnancy is usually unnecessary

Biopsy of the cervix is usually unnecessary in pregnancy, unless invasive disease is suspected on colposcopy or reflex LBC predicts invasive disease.

Consensus-based recommendation*

REC14.8: Defer treatment until after pregnancy

Definitive treatment of a suspected high-grade lesion, except invasive cancer, may be safely deferred until after the pregnancy.

Practice point

REC14.9: Follow-up assessment after pregnancy

If postpartum follow-up assessment (colposcopy and/or HPV test and reflex LBC if necessary) is required, it should be done no less than 6 weeks after delivery and preferably at 3 months. This interval is optimal to reduce the risk of reflex LBC interpretation difficulties or unsatisfactory reflex LBC.

The cervical sample (for HPV test and reflex LBC if necessary) could be collected at the time of postpartum check or at the time of the colposcopic assessment.

Practice point

REC14.10: Vaginal oestrogen prior to postpartum colposcopy

For women who are breastfeeding, the use of intra-vaginal oestrogen cream or pessary prior to colposcopy may improve visualisation of the cervix and the quality of any cervical sample for LBC.

Daily for two weeks and cease approximately 3 days before colposcopy.

Practice point**REC14.11: Cervical screening in pregnancy**

Routine antenatal and postpartum care should include a review of the woman's cervical screening history. Women who are due or overdue for screening should be screened.

Practice point**REC14.12: Cervical screening in pregnancy**

A woman can be safely screened at any time during pregnancy, provided that the correct sampling equipment is used. An endocervical brush should not be inserted into the cervical canal because of the risk of associated bleeding, which may distress women.

Practice point**REC14.13: Self-collection in pregnancy**

All women who are due for cervical screening during pregnancy may be offered the option of collection of a vaginal swab for HPV testing, after counselling by a health care professional about the small risk of bleeding. Women testing positive for HPV (not 16/18) on a self-collected sample should be advised to return so that a cervical sample for LBC can be collected by the healthcare provider.

Benefits and harms

Biopsy is not recommended in pregnancy but may be required, especially when there is suspicion of invasive disease. There is evidence that it is safe to biopsy the cervix during pregnancy, although there may be a risk of excess bleeding.^{[16][12][10]} However, the risk of an undiagnosed cervical cancer in pregnancy outweighs the risk of bleeding from a biopsy.

Deferring treatment of pre-invasive high grade lesions during pregnancy will prevent possible complications of pregnancy loss and excessive bleeding. There is a small risk of progression to invasive cervical cancer during pregnancy, although an Australian case series showed no cases of progression.^[20] Most commonly, this will be microinvasive disease, rather than a clinically apparent cancer.

See [Chapter 5. Benefits, harms and cost-effectiveness of screening in the renewed NCSP](#).

Health system implications of these recommendations

Clinical practice

The recommendations are consistent with current clinical practice. However changes to the cervix in pregnancy make colposcopic assessment more challenging. Although the squamocolumnar junction and the transformation zone (TZ) are more exposed during pregnancy, complete visualisation of all four quadrants of the cervix is often hindered by oedema, cyanosis, vaginal wall protrusion and thick mucus production.^[9] Although colposcopy is safe to perform during pregnancy, an experienced colposcopist should perform the examination owing to the difficulty in differentiating between changes occurring as a result of pregnancy and those due to cervical pathology. A lack of experience could potentially lead to an overestimation of the severity of dysplasia, a mistaken diagnosis of invasive disease and unnecessary investigation during pregnancy.^[21]

Resourcing

No additional costs are anticipated.

Barriers to implementation

None.

Figure 12.1. Collection tools for cervical screening in pregnant women

Figure 12.1.1. Cyto-broom: recommended for use in pregnant women to collect a cervical screening specimen



Image source: Victorian Cytology Services Limited.

Figure 12.1.2. Endocervical brush (cytobrush): not recommended for use

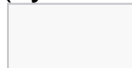


Image source: Victorian Cytology Services Limited.

Figure 12.1.3. Self-collection swab

Image source: Victorian Cytology Services Limited.

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Appendices

PICO question 13

[View Literature summary and evidence report question 13](#)

15. Women experienced early sexual activity or victims of abuse

Author(s):

- [A/Professor Deborah Bateson](#) — Co-author
- Dr Marsali Newman – Co-author
- Dr Vivienne Milch – Co-author
- [Dr Andrea Garrett](#) — Co-author
- [Professor Ian Hammond](#) — Contributor
- [Dr Lara Roeske](#) — Contributor
- [A/Professor Lisa Whop](#) — Contributor
- [Mr. C. David H. Wrede](#) — Contributor
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

Background

Human papillomavirus (HPV) infection often occurs shortly after first sexual activity.^[1] HPV infections are more likely to occur in adolescent women than in older women, as the process of squamous metaplasia of the transformation zone of the cervix is more active during adolescence and represents a vulnerability to the establishment of HPV infections.^[2] There is also evidence that individuals who have been victims of sexual abuse as children have higher rates of anogenital HPV detection than individuals with no such history.^[3]

Women who experience first sexual activity at an early age and are subsequently infected with oncogenic HPV may have a higher risk of carcinogenesis over time if these infections are persistent, since persistent infections are associated with an increased risk of cervical cancer.^[4] Most HPV infections are transient and are cleared in adolescents and young women without the detection of cervical intraepithelial neoplasia (CIN) within 36 months.^[5]

The incidence of cervical cancer in women younger than 25 years of age is very low. Since the introduction of the National Cervical Screening Program (NCSP), age-specific incidence rates in this group of women have remained relatively stable over the past two decades.^[6] The introduction of the National HPV Vaccination Program, which offers the HPV vaccine to girls at age 12–13 years, provides an additional level of protection for young women. Furthermore, there is some evidence that vaccination of women after first sexual intercourse may prevent reinfection or reactivation of the disease with vaccine included HPV types.^[7]

The prevalence of vaccine-included HPV types 16/18/6/11 is now very low in young women, and has reduced by 35% since 2005–2007 in unvaccinated women, as well as in vaccinated women.^[8] HPV 16 is the dominant contributor to cervical cancer and precancer in young women; prior to HPV vaccination, HPV 16 was detected in 70% of CIN grade 3 (CIN3) in women aged 16–25 years.^[9]

Since the introduction of the National HPV Vaccination Program, there has been a steady decline in the detection of high-grade abnormalities in women under 20 years of age^[6] and a reduction in the risk of high-grade cervical abnormalities in women who completed the vaccine series at the ages of 12–26 and who had not started screening before the implementation of the vaccination program.^[10]

Anogenital HPV infections are transmitted mainly by skin-to-skin or mucosa-to-mucosa contact. Penetrative sexual intercourse is not strictly necessary for transmission and HPV can be

transferred to the cervix from original infection at the introitus. Therefore, genital skin-to-skin contact, vaginal sex, oral sex, and anal sex represent types of sexual activity that may facilitate the person-to-person transmission of anogenital types of HPV.

Evidence

Systematic review evidence

No randomised or pseudorandomised controlled trials were found that evaluated the safety and effectiveness of alternative screening strategies in women with a history of early sexual intercourse or sexual abuse in comparison to other women.

General literature review evidence

In the absence of any direct evidence from the systematic review, [a general review of the literature was performed](#) to ascertain the effectiveness of cervical screening in:

- women who have had first sexual intercourse at the age of 14 years or younger
- women who have experienced childhood sexual abuse

Sixteen studies were identified. No studies directly addressed the clinical question. However, one study provided indirect evidence based on the re-analysis of individual data from studies on cervical cancer risk conducted worldwide.^[11] In this study, the relative risk for invasive cervical carcinoma in women who first had intercourse at the age of 14 years or younger was similar to the risk in women who first had intercourse at 16–18 years of age. In Australia, the median age at first sexual intercourse has been estimated to be 16–17 years of age.^{[12][13]}

Although a number of studies were identified by the search, no other recent studies reported relevant outcome data by age of sexual debut. Studies found that regression of cervical abnormalities was common in young women^{[5][14][15][16]} and that CIN3+ was rare.^{[17][18][19][20][16]}

There is a lack of evidence that women who have experienced early sexual intercourse will benefit from commencing cervical screening before age 25 years.

Recommendations

MSAC evidence-based recommendation

REC15.1: Routine cervical screening is not recommended in young women

Routine cervical screening is not recommended in women under the age of 25 years.

Consensus-based recommendation

REC15.2: Early sexual activity and cervical screening in young women

Evidence does not support screening for women aged less than 25, even when they have experienced early sexual activity. However, for those who experience their first sexual activity at a young age (<14 years) and who had not received the HPV vaccine before sexual debut, a single HPV test between 20 and 24 years of age could be considered on an individual basis, but is not required.

Note: It is expected that amendments to relevant Medicare Benefits Schedule items to support testing on a self-collected sample for this specific use will be effective from 1 November 2022 pending any external impacts such as upcoming elections and caretaker period.

Consensus-based recommendation

REC15.3: Women with postcoital or intermenstrual bleeding

Women at any age who have signs or symptoms suggestive of cervical cancer or its

precursors, where other common causes of abnormal vaginal bleeding such as a sexually transmitted infection have been excluded, should have a co-test[†] and be referred for appropriate investigation to exclude genital tract malignancy.

[†] Co-testing (HPV and LBC) is recommended as the presence of blood has the potential to adversely affect the sensitivity of the HPV and/or LBC tests.

Benefits and harms

The minimal benefits of cervical screening in young women should be weighed against the increased risk of harm that unnecessary excisional procedures could have for future obstetric outcomes (see [Chapter 14. Screening in Pregnancy](#)) and psychosocial well-being (see [Chapter 19. Psychosocial care](#)).

Positive oncogenic HPV test results and mild cytological abnormalities are frequently encountered in women younger than 25 years. However, high rates of regression of low and high-grade CIN lesions have been reported in the literature and the positive predictive value of cytology screening tests appears to be lower in this age group.^{[16][17]}

Investigation and potential treatment of these lesions, that will most likely regress, may lead to unnecessary harms (psychosocial, obstetric and financial). It is considered that the harms outweigh the benefits for young women.

See [Chapter 5. Benefits, harms and cost-effectiveness of cervical screening in the renewed NCSP](#).

Health system implications of these recommendations

Clinical practice

A single cervical screening test may be performed before 25 years of age in women for whom there is concern about early sexual activity or sexual abuse prior to age 14 years. These are considered to be special circumstances and are not applicable to the general population of women under 25 years of age. A significant proportion of women experience their first sexual intercourse at age 14–16 years.^[21] It is far less common for women to have first intercourse at age 13 years and below, and this may be more often related to child sexual abuse.^[21] These data support confining recommendations to women who have experienced early sexual activity or been victims of child sexual abuse prior to the age of 14 years. Recommendations regarding symptomatic women are consistent with current clinical practice.

Resourcing

This recommendation is considered unlikely to require significant resources provided that cervical screening test providers restrict the screening of women under 25 years of age to those in whom the sexual history confirms either early sexual activity or child sexual abuse (prior to 14 years of age) and on a case-by-case basis.

Barriers to implementation

Young women may choose not to disclose their age of first sexual activity or that they have a history of sexual abuse during childhood. However, as there is a lack of evidence that women with early sexual activity will benefit from commencing cervical screening earlier than 25 years of age, this is unlikely to affect safety in regard to the development of cervical cancer in these young women.

Discussion

Unresolved issues

Uncertainty remains as to whether early sexual activity increases the risk of cervical cancer in young women as there is no currently available evidence to support an increased risk. The

National HPV Vaccination Program is expected to reduce the number of at-risk women although the overall impact of vaccination will depend on how many young women were HPV-naïve before being vaccinated. Substantial indications of the effect of the National HPV Vaccination Program have already been observed in women including a reduction in the risk of high-grade cervical abnormalities in women who completed the vaccine series at the ages of 12–26 and who had not started screening before the implementation of the vaccination program,^[10] a decline in the detection of high-grade abnormalities in women under 25 years of age^[6] and a substantial decline in the prevalence of vaccine-included HPV types in women aged 18–24 years.^[8] HPV vaccination is also expected to reduce the risk of high-grade abnormalities in unvaccinated women indirectly, via a reduction in the circulation of vaccine included HPV types within the population. A recent observational study reported a reduction in the prevalence of HPV 16/18/6/11 in unvaccinated young women in Australia since the implementation of HPV vaccination, suggesting herd immunity.^[8]

Nevertheless, vaccination should not be withheld from young women post sexual debut as there is some evidence of protection even in women who were exposed to HPV prior to being vaccinated,^[2] in addition to protection against any vaccine included HPV types to which they have not been previously exposed .

Future research priorities

Prospective cohort studies following women from the age at first sexual activity until the age of CIN3 diagnosis, with regular interval follow-up, are required to ascertain the importance of early first sexual activity in the development of cervical pre-cancer.

Effectiveness of post-exposure HPV vaccination of young women and correlation with type of HPV in those found to have a positive oncogenic HPV test result.

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Appendices

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10](#)

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evidence summary
table question 10](#)

16. Screening in immune-deficient women

Author(s):

- Dr Vivienne Milch – Co-author
- A/Professor Lyndal Anderson – Co-author
- Dr Marsali Newman – Co-author
- [A/Professor Alison Brand](#) — Contributor
- [Professor Ian Hammond](#) — Contributor
- [A/Professor Selvan Pather](#) — Contributor
- [Dr Lara Roeske](#) — Contributor
- [Mr. C. David H. Wrede](#) — Contributor
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

Brand, A, Hammond, I, Pather, S, Dr Lara Roeske, Wrede, CD, Cancer Council Australia Cervical Cancer Screening Guidelines Working Party. Clinical question: Screening in immune-deficient women. In: National Cervical Screening Program: Guidelines for the management of screen-detected abnormalities, screening in specific populations and investigation of abnormal vaginal bleeding.

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Background

This section refers to women with acquired immune deficiency because of viral infection (e.g. human immunodeficiency virus (HIV)) or treatment with immunosuppressant drugs to prevent transplant rejection or to control an autoimmune disease (e.g. rheumatoid arthritis), as well as inherited primary immunodeficiency disorders (e.g. common variable immunodeficiency).

Research on immune deficiency and cervical cancer has mostly focused on women with HIV and renal transplant recipients.

Cervical prevalence of oncogenic human papillomavirus (HPV) in HIV-positive women without cytological abnormalities is higher than their counterparts from the general population.^{[1][2]}

Shared behavioural risk factors for HIV and HPV potentially play some role in these observed differences. While HPV16 remains the most common type, in infected women with cytological abnormalities there appears to be a shift in the prevalence of HPV oncogenic types from HPV16 to other high risk types and a higher risk of multiple HPV infections with increasing severity of cervical disease; in a meta-analysis of 20 studies, HIV-positive women with a cytological prediction of high-grade squamous intraepithelial lesion (HSIL) were significantly more likely to have a positive oncogenic HPV (not 16/18) test result and to have multiple HPV infections, compared with HIV-negative women with HSIL.^[4] In renal transplant recipients, prevalence estimates of oncogenic HPV types vary, with some studies finding estimates similar to the general population^{[3][4][5]} and others reporting higher estimates.^[6] Shared behavioural risk factors for HIV and HPV potentially play some role in these observed differences.

HIV infection has been consistently associated with HPV infection and pre-cancerous cervical lesions,^{[7][8][9]} and a significantly higher rate of cervical cancer in women with HIV/acquired immune deficiency syndrome (AIDS) was reported in a meta-analysis of six population-based studies (incidence ratio: 5.8).^[10] High incidence rates of cervical cancer have been reported by some subsequent studies,^{[11][12]} although others have found incidence to be the same as in the general population.^[13] Antiretroviral therapy (ART) and highly active antiretroviral therapy (HAART) do not appear to have reduced cervical cancer incidence in women with HIV/AIDS^{[14][15][16]} and a systematic review by Cobucci (2015)^[17] found that the risk of invasive cervical cancer has increased since the introduction of HAART (RR=1.46, 95%CI: 1.09–1.94). In the past, ART/HAART was only prescribed to people with a low CD4 count, and this is likely to have influenced results of previous studies. Since 2015, however, HAART has been recommended for anyone living with HIV, irrespective of CD4 count.

In solid organ transplant recipients, the majority of population-based studies have reported a higher incidence of cervical cancer than in their immunocompetent counterparts (standardised incidence ratios between 2–3).^{[18][19]} In contrast, a large US cohort study, using linked data from national and local registries, found the same incidence in transplant recipients as in the general population.^[20] There is also some evidence of a higher incidence of cervical intraepithelial neoplasia (CIN) in organ transplant recipients, although more research in this area is needed.^[21]

Screening appears to play an important role in whether or not risk is increased compared to the general population, with studies in screened populations suggesting no difference in risk^{[20][22][23]} in contrast to other studies that have identified higher risks of cervical cancer.^[10]

Evidence

The literature searches were performed to identify data for HIV-positive women and transplant recipients, because these groups were identified as being immune-deficient in the pre-renewal National Cervical Screening Program (NCSP) guidelines^[24] and are the predominant focus of research activities.

Systematic review evidence

Two systematic reviews were performed to identify studies that evaluated the safety and effectiveness of screening HIV-positive women and organ transplant recipient women using a modified recommended screening strategy (starting at an age less than 25 years and/or screening at intervals less than 5 years and/or referring all women with a positive oncogenic HPV test result to colposcopy irrespective of reflex liquid based cytology (LBC) result), compared with the recommended screening strategy for the general population. The search strategies and inclusion and exclusion criteria used are described in detail in the [Technical report](#).

No randomised or pseudo-randomised controlled trials were found that evaluated the safety and effectiveness of screening immune-deficient women using strategies other than those recommended for the general population, compared with screening strategies used for the general population.

General literature review evidence

In the absence of any direct evidence from the systematic review, [a general review of the literature was performed](#) investigating cervical screening and the risk of progression among HIV-positive women and transplant recipients.

In the Women's Interagency HIV Study, the risks of CIN2+ and CIN3+ were assessed among women with normal cervical cytology, according to HIV status and oncogenic HPV status at baseline. HPV status was ascertained from cervicovaginal lavage samples: [25][26]

- In women in whom oncogenic HPV was not detected, the 5-year cumulative risk of CIN2+ and CIN3+ was the same, regardless of HIV status and CD4 count, and was less than 1% in both HIV-negative women and HIV-positive women, including in each CD4 count stratum (< 350, 350–500, and >500). [26][25]
- In women with a positive oncogenic HPV test result, the 5-year cumulative risk for CIN2+ was 16% (95% CI:9–23%) in HIV-positive women versus 10% (95% CI:0–21%) in HIV-negative women. [25]
- In multivariate analyses, there was no clear gradient in increasing risk for CIN2+ or CIN3+ with decreasing CD4 counts. [25]
- Among HIV-positive women who were positive for HPV16, the 5-year cumulative risks for CIN2+ and CIN3+ were 29% (95%CI:6-46) and 10% (95%CI:0-23) respectively. [25][26]

Other studies have reported that clearance of oncogenic HPV types other than 16/18 appeared to differ in immune-deficient women, compared with other women, however clearance of HPV16 infections did not. [27][28][29] In HIV-positive women, progression from low-grade cytological abnormalities to a higher-grade abnormality (either cytological or histological) appears to increase and regression to negative cytology appears to decrease with lower CD4 counts. [30]

In regard to the performance of HPV testing (Hybrid Capture 2) for detecting high-grade CIN in women with HIV, sensitivity was reported to be somewhat greater in HIV-positive women (96.4% for CIN3; 99.2% for CIN2+) than in HIV-negative women (90.9% for CIN3; 85.5% for CIN2+), and the negative predictive value was high in both HIV-positive and HIV-negative women (99.8% and 99.5% respectively for less than CIN2). Specificity was lower in HIV-positive women. However, the positive predictive value of HPV testing in detecting CIN2 or CIN3 was equally as high in HIV-positive as in HIV-negative women. [31]

It has been hypothesised that the difference in incidence of cervical cancer in immune-deficient women observed between studies may be due to the extent to which the women included in the different studies have been screened. [29][32] Low participation in cervical screening by HIV-positive women and transplant recipients has been reported in some studies. [33][34][35] The influence of screening on risk is also indirectly supported by findings from studies reporting that risk in immune-deficient women is much more elevated for non-cervical HPV-related cancers (e.g. anal, vaginal, vulval, for which effective screening is not available) than for cervical cancer, even though the HPV attributable fraction for these cancers is lower than for cervical cancer. [36][20]

[A review of international guidelines was also performed.](#) The review focused on guidelines for HPV-based screening for immune-deficient women, as these guidelines are the most relevant for the renewed NCSP. Two recent guidelines now include recommendations for HPV-based screening, and both guidelines recommend a three-year interval for HIV-positive women:

- The World Health Organization (WHO 2013) recommends that sexually active HIV-positive women should be screened as soon as the woman has tested HIV positive and those who are HPV-negative to be rescreened within 3 years. [37]
- Recent US guidelines recommend 3-yearly co-testing with HPV and cytology for HIV-positive women aged 30 years or older. [38]

The evidence regarding screening and treatment to prevent cervical cancer in immune-deficient women is of lower quality than that in the general population, due to the absence of long-term randomised controlled trials comparing screening strategies in these women. Given that the

evidence is unclear about the safety of lengthening the screening interval to 5 years for immune-deficient women, and that two international guidelines recommend a 3-year interval in the context of HPV testing in this population, it is considered safer to retain a 3-yearly interval in the renewed NCSP until further evidence about the negative predictive value of HPV testing in this population is better understood.

The US guidelines recommend 3-yearly co-testing^[38] but the review of the evidence carried out in Australia for the Medical Services Advisory Committee (MSAC) suggests that co-testing offers little additional benefit, compared with HPV testing alone. This is in line with other international recommendations and, therefore, co-testing is not recommended in this population or the wider program, as oncogenic HPV testing alone offers very similar benefits to co-testing.^[37] Therefore, the 3-year interval recommendation in this guideline is in accordance with WHO guidelines and supported by US guidelines for screening and treatment of precancerous lesions for cervical cancer prevention in HIV-positive women.

Recommendations

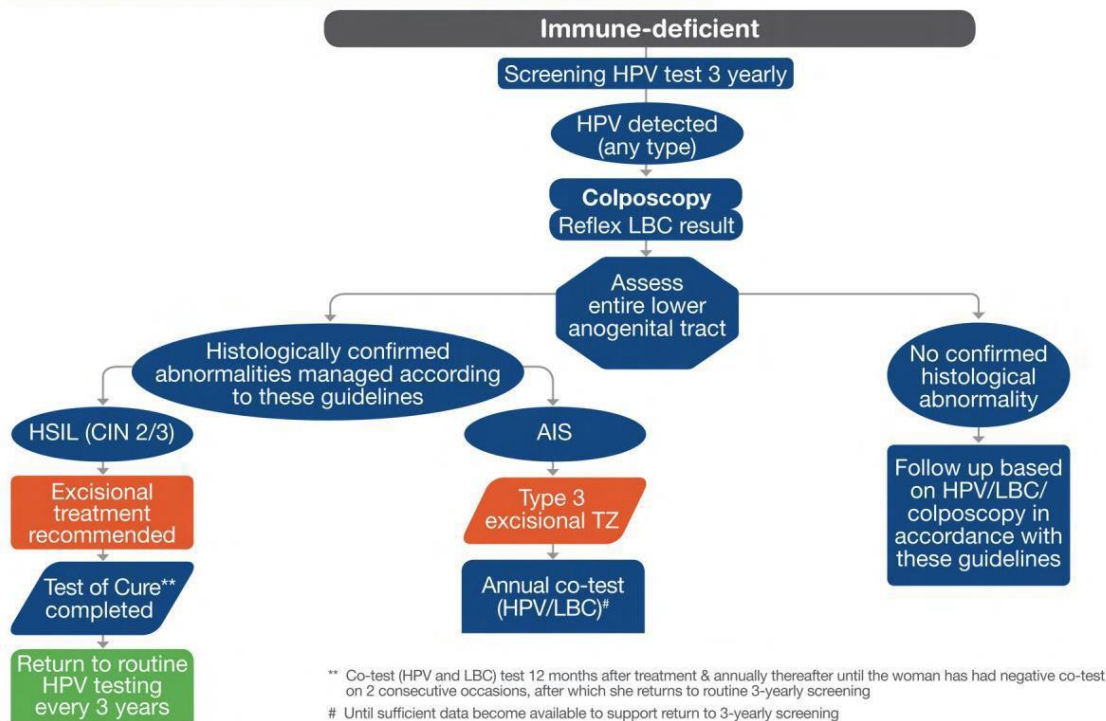
The following recommendations apply to the following groups:

- women with HIV
- solid organ transplant recipients.

These groups have been defined as sufficiently immune-deficient to warrant more frequent screening and a lower threshold for colposcopy referral than the general female population, based on current literature and pre-renewal NCSP guidelines.^[24] Note that this list is not exhaustive and does not include all patients with auto-immune conditions.

Flowchart 16.1. Management of screen detected abnormalities in immune-deficient women

MANAGEMENT OF SCREEN DETECTED ABNORMALITIES IN IMMUNE-DEFICIENT WOMEN



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https://www.cancer.org.au/assets/pdf/Mx_SD_abnormalities_in_immune_deficient_women.pdf#_ga=2.196850476.1257883089.1648513003-1771580222.1646017938

Screening interval recommendations

Consensus-based recommendation

REC16.1: Immune-deficient women in whom oncogenic HPV is not detected

Immune-deficient women who have a HPV test in which oncogenic HPV types are **not** detected should be screened every 3 years with a HPV test.

Management of abnormalities

Consensus-based recommendation

REC16.2: Colposcopy referral: positive oncogenic HPV test result (any type) in immune-deficient women

Women who are immune-deficient and have HPV (any type) detected should be referred for colposcopic assessment. If the screening sample was collected by a healthcare provider, then reflex LBC will be performed by the laboratory. If the screening sample was self-collected, then LBC should be undertaken at colposcopy.

Consensus-based recommendation*

REC16.3: Colposcopy assessment and treatment in immune-deficient women

Assessment and treatment of immune-deficient women with screen-detected abnormalities should be by an experienced colposcopist or in a tertiary centre.

Consensus-based recommendation***REC16.4: Colposcopy of whole lower genital tract in immune-deficient women**

The entire lower anogenital tract should be assessed, as the same risk factors apply for cervical, vaginal, vulval, perianal and anal lesions.

Consensus-based recommendation***REC16.5: Treatment in immune-deficient women**

When treatment of the cervix is considered necessary in immune-deficient women, it should be by excisional methods.

Practice point**REC16.6: Histological abnormalities of the cervix in immune-deficient women**

Women with histologically confirmed abnormalities should be managed according to the same guidelines as women who are not immune-deficient.

Practice point**REC16.7: Test of Cure for treated immune-deficient women**

Women who are immune-deficient and treated for HSIL (CIN2/3) should have follow-up with Test of Cure as recommended in [these guidelines](#). Women who complete Test of Cure should return to routine 3-yearly screening with a HPV test.

Special recommendations**Practice point****REC16.8: Screening before solid organ transplantation**

Women aged between 25 and 74 years should have a review of cervical screening history when they are added to the organ transplant waiting list and while they remain on the waiting list, to confirm they are up to date with recommended screening for the general population. Women who are overdue for screening, or become due while on the waiting list, should be screened with a HPV test so that any abnormalities can be investigated or treated as necessary prior to transplantation and commencement of immunosuppressive therapy.

Practice point**REC16.9: Screening women with a new diagnosis of HIV**

Women aged between 25 and 74 years who have a new diagnosis of HIV should have a review of their cervical screening history to ensure they are up to date with screening in line with the recommended 3-yearly interval for this group.

Practice point**REC16.10: Other groups that may require special consideration**

The groups listed below could be considered for screening every 3 years with a HPV test in

accordance with the recommendation for HIV-positive women and solid organ transplant recipients:

- women with congenital (primary) immune deficiency
- women who are being treated with immunosuppressant therapy for autoimmune disease (e.g. inflammatory bowel disease, systemic lupus erythematosus, rheumatoid arthritis, neuromyelitis optica, sarcoidosis)
- allogenic bone marrow transplant recipients treated for graft versus host disease.

Practice point

REC16.11: Regular screening for immune-deficient women

Women who are immune deficient should be educated regarding the increased risk from HPV infection and encouraged to attend for regular screening every 3 years.

Practice point

REC16.12: Young women with long term immune deficiency

For young women who are sexually active and who have been immune deficient for more than 5 years, a single HPV test between 20 and 24 years of age could be considered on an individual basis (regardless of HPV vaccination status).

** Note that screening on a self-collected sample is not currently reimbursed by Medicare for people aged less than 24 years 9 months.*

Practice point

REC16.13: Guidance for immune-deficient women and their healthcare professionals

It is important that immune-deficient women and their healthcare professionals are guided by a clinical immunology specialist when using these guidelines.

See also:

- [Management of low-grade squamous abnormalities](#)
- [Management of high-grade squamous abnormalities](#)
- [Management of glandular abnormalities](#)

Benefits and harms

There is evidence of an increased risk of CIN in immune-deficient women, but evidence is also suggestive that screening plays an important role in reducing or removing excess risk of cervical cancer. The current recommendations will ensure the prompt treatment of any precancerous lesions before progression to cervical cancer. Diagnostic assessments and potential treatment required in these women, currently under increased surveillance for their underlying disease, may cause additional anxiety and distress.

However, it is generally considered that the benefits outweigh the harms for immune-deficient women.

See the [Chapter 5. Benefits, harms and cost-effectiveness of cervical screening in the renewed National Cervical Screening Program \(NCSP\)](#).

Health system implications of these recommendations

Clinical practice

Recommendations regarding the management of immune-deficient women are consistent with present clinical practice.

Resourcing

No additional costs are anticipated.

Barriers to implementation

Some immune-deficient women may choose not to attend for cervical screening as frequently as recommended. Less frequent screening has been reported in both women with HIV and organ transplant recipients.^{[33][34][35]}

Discussion

There is some evidence to support increased progression of cervical abnormalities in HIV-positive women compared with HIV-negative women.^[30] Although HAART has been in use for two decades, there is only limited evidence of an increased likelihood of lesion regression and a higher clearance rate of oncogenic HPV positive SIL in adherent users.^{[30][39][40]} Overall, there is insufficient direct evidence to support a change from the screening recommendations in pre-renewal NCSP guidelines,^[24] which recommended colposcopy referral for any screen-detected abnormality.

When CIN is diagnosed in HIV-positive women, excisional therapy is recommended. However, failure rates are high, necessitating frequent post-treatment surveillance. Massad *et al*^[41] reported that most lesions detected after therapy in HIV-positive women were low grade which may be indicative of new HPV infections that are less likely to progress.

The burden of HPV-related cancers can be expected to increase in HIV-positive women given successful prolongation of life with ART and potentially longer duration of HPV persistence.^[38]

Unresolved issues

There is insufficient evidence available to determine the optimal cervical screening strategy in immune-deficient women. Current recommendations reflect a cautious approach until further data become available. The effect of ART on progression of cervical disease is still unclear.

These guidelines have not investigated the need for special consideration in other groups of women who may be immune deficient either due to a disease, immunosuppressive drugs or both. This group is heterogeneous due to by varying degrees of disease severity, duration, types and length of treatments.

Future research priorities

Long-term randomised controlled trials, comparing screening strategies in immune-deficient women, are needed to inform future guidelines. It is anticipated that the renewed NCSP and the National Cancer Screening Register will facilitate the collection of data on immune-deficient women to support future recommendations. Modelled analysis may help in determining whether routine 5-yearly screening could be suitable for this group of women.

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17. DES-exposed women

Author(s):

- [Professor Bruce Armstrong](#) — Co-author
- [A/Professor Alison Brand](#) — Co-author
- [Professor Ian Hammond](#) — Co-author
- [Professor Gordon Wright](#) — Co-author
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

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Background

Diethylstilbestrol (DES) is a synthetic oestrogen, transplacental carcinogen and an endocrine disrupting compound.^[1] It was prescribed from the 1940s until the early 1970s, predominantly to pregnant women in the first trimester, to prevent miscarriages by stimulating the synthesis of oestrogen and progesterone in the placenta.^[1] It has been estimated that 15,000 Australian women used the drug during pregnancy.^[2] DES is no longer registered for human use in Australia.

The first study to provide conclusive evidence of an association between in utero exposure to DES and clear cell adenocarcinoma (CCA) was reported in 1970 by Herbst and Scully, who found vaginal CCA in seven women aged 15–22 years.^[3] Subsequent studies have consistently confirmed this finding, and the most recent review of human carcinogens by the International Agency for Research on Cancer (2012) states that there is substantial evidence indicating that women exposed in utero to DES have a markedly increased risk of clear cell carcinoma of the vagina and cervix.^[1]

Vaginal adenosis is a known precursor of CCA that affects between 34–88% of DES-exposed women and less than 4% of unexposed women.^[1]

Evidence

Systematic review evidence

A systematic review was conducted to identify studies that evaluated the safety and effectiveness of screening women who were exposed to DES in utero and their daughters, using screening strategies other than those recommended for the general population, compared with those recommended for the general population. The search strategy and inclusion and

exclusion criteria used are described in detail in the [Technical report](#). No relevant randomised controlled trials or paired diagnostic performance studies were found.

General literature review evidence

In the absence of any direct evidence from the systematic review, [three separate general reviews of the literature were performed](#) to ascertain:

1. whether clear cell carcinomas are HPV positive
2. the risks of cervical and vaginal squamous cell carcinomas overall or high-grade cervical intraepithelial neoplasia (CIN) or high-grade vaginal intraepithelial neoplasia (VAIN) in women exposed to DES in utero, compared with women who were not exposed to DES
3. the risks of cervical and vaginal carcinomas or dysplasia in daughters of women who were exposed to DES in utero, compared with daughters of women who were not exposed.

Clear cell carcinomas

Nineteen studies were identified that tested for the presence of HPV DNA in samples of clear cell carcinoma of the cervix or vagina. Overall, about a third of 158 samples of clear cell carcinoma of the cervix were found to be HPV positive. The findings are summarised in the [Technical report](#).

Squamous cell carcinomas in women exposed in utero

A Dutch study reported no excess risk for combined cervical and vaginal squamous cell carcinoma in a cohort of over 12,000 women exposed to DES in utero (standard incidence ratio 0.64; 95%CI 0.31–1.17).^[4] In this study, women were recruited in 1992 and were followed prospectively until 2008.

In another analysis, data was combined from three studies initiated in the 1970s with long-term follow-up on 4653 women exposed to DES and 1927 unexposed controls. The cumulative risk of CIN2/CIN2+ in women exposed to DES in utero was 6.9% versus 3.4% in women who were not exposed to DES (hazard ratio 2.28; 95%CI 1.59–3.27).^[5]

Squamous cell carcinomas in daughters of women exposed in utero

A recent study reported data, confirmed from medical notes, from 463 daughters of women exposed to DES in utero and 330 unexposed women. No significant increased risk of cervical dysplasia was found in the daughters:^[6]

- relative risk (RR) of any cervical lesion 1.45 (95%CI: 0.69–3.05)
- RR of moderate/severe cervical lesions 0.93 (95%CI: 0.29–2.94)].

Recommendations

Consensus-based recommendation

REC17.1: Screening in DES-exposed women

Women exposed to DES in utero should be offered an annual co-test and colposcopic examination of both the cervix and vagina indefinitely.

Consensus-based recommendation*

REC17.2: Colposcopy referral for abnormalities in DES-exposed women

Women exposed to DES in utero who have a screen-detected abnormality should be managed by an experienced colposcopist.

Practice point

REC17.3: Daughters of women exposed to DES

These women should be screened in accordance with the NCSP policy (5-yearly HPV testing). Evidence of an adverse effect on the daughters of women exposed to DES in utero has not been found.

However, if these women have concerns, testing similar to that recommended for their DES-exposed mothers could be considered on an individual basis. Self-collection for HPV testing is not recommended.

Benefits and harms

On the basis of the evidence summarised above, we have proposed that HPV testing be added to the previous recommendations for annual cytological testing as part of screening offered to women exposed to DES in utero. The addition of HPV testing is expected to increase the detection of CCA in DES-exposed women. It is important, however, that clinicians are aware that not all CCA are HPV positive and that co-testing with cytology is necessary for early detection.

There is very little evidence available on the risk of cervical cancer or CIN in the daughters of women exposed in utero to DES. Due to the lack of evidence, the possibility that the risk of cancer in the daughters of women exposed in utero to DES is different to the risk in the general female population cannot be excluded, but is considered unlikely. If requested, annual co testing (HPV and LBC) can be offered by clinicians to these women to provide reassurance.

See [Chapter 5. Benefits, harms and cost-effectiveness of cervical screening in the renewed National Cervical Screening Program \(NCSP\)](#).

Health system implications of these recommendations

Clinical practice

These recommendations are consistent with present clinical practice.

Frequent follow-up of this cohort of women will enable the timely observation and early treatment of any DES-associated changes.

Resourcing

No material changes to costs are anticipated.

Barriers to implementation

There are no barriers to implementation.

Discussion

Unresolved issues

There remains uncertainty as to whether daughters of women who were exposed to DES in utero experience a higher risk of clear cell carcinoma of the vagina or of other cervical or vaginal neoplasms than women without this maternal history.

Future research priorities

Where it is possible to do so, efforts should be made to follow-up additional cohorts of daughters of women who were exposed to DES in utero to ascertain whether or not they have a greater risk of cervical or vaginal neoplasms than women in the same populations without this maternal history.

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18. Signs and symptoms of cervical cancer

Identification and Investigation of abnormal vaginal bleeding

Author(s):

- [A/Professor Deborah Bateson](#) — Co-author
- [A/Professor Alison Brand](#) — Contributor
- [Professor Ian Hammond](#) — Contributor
- [Dr Joanne Mountford](#) — Contributor
- [A/Professor Lisa Whop](#) — Contributor
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

Bateson, D, Brand, A, Hammond, I, Mountford, J, Whop, L, Cancer Council Australia Cervical Cancer Screening Guidelines Working Party. Clinical question: Investigation of abnormal vaginal bleeding. In: National Cervical Screening Program: Guidelines for the management of screen-detected abnormalities, screening in specific populations and investigation of abnormal vaginal bleeding.

Background

Abnormal vaginal bleeding includes intermenstrual bleeding, postcoital bleeding, and postmenopausal bleeding.

Intermenstrual bleeding is defined as vaginal bleeding at any time other than during normal menstruation or following sexual intercourse. Postcoital bleeding is vaginal bleeding after sexual intercourse. Intermenstrual bleeding and postcoital bleeding are not diagnoses; they are symptoms that warrant further assessment.^[1] Intermenstrual and postcoital bleeding can be associated with genital tract malignancy and premalignant conditions, as well as other conditions such as polyps, leiomyomas, ovulatory disorders, endometrial disorders, sexually transmitted infections, hormonal contraception and trauma.^{[2][3]} It is understood that most vaginal bleeding actually originates in the uterine body or cervix.

Current Australian clinical practice guidelines developed by the Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG)^[4] and by Cancer Australia^{[4][5]} recommend that cervical cancer should be excluded in all women with persistent abnormal vaginal bleeding. The aim of these guidelines is to assist healthcare professionals in the management of intermenstrual bleeding or postcoital bleeding, including testing and, if warranted, referral to a gynaecologist. Heavy menstrual bleeding (HMB) originates in the uterus and is not a symptom of cervical cancer.

While cancer is an uncommon cause of abnormal vaginal bleeding in women of any age, and is rare in young women, postcoital bleeding particularly warrants investigation because it may be a symptom of cervical cancer.^[1] A systematic review estimated the overall point prevalence of postcoital bleeding in the community at 0.7–9%, based on data from eight studies conducted mainly in Europe.^[6]

The RANZCOG advises that women reporting postcoital bleeding should have a co-test (HPV and LBC) and a test for chlamydia. A single episode of postcoital bleeding in a woman with a normal co-test and normal cervical appearance does not warrant immediate referral for colposcopy but recurrence or persistence of postcoital bleeding mandates referral to a gynaecologist.^[1]

Intermenstrual and other irregular bleeding patterns are common, particularly in women using hormonal contraception (combined hormonal contraceptive pill or vaginal ring, progestogen-only pill, progestogen-only injection, implant or intrauterine device), or hormonal treatment.^[7]

The RANZCOG advises that women at risk of sexually transmitted infections should have appropriate tests performed, and that those with persistent unexplained intermenstrual bleeding should have a co-test (HPV and LBC), transvaginal ultrasound, and referral to a gynaecologist.

Postmenopausal bleeding always requires investigation and specialist referral to exclude genital tract disease including cervical and endometrial malignancy. The presence of blood has the potential to adversely affect the sensitivity of any of the available tests for human papillomavirus (HPV) and liquid-based cytology (LBC). For this reason co-testing (HPV and LBC on the same sample) is recommended for women with abnormal vaginal bleeding suggestive of cervical cancer, and follow-up should be based on presenting symptoms, clinical evaluation and the test results.

A co-test cannot be performed on a self-collected vaginal sample.

See: [Cervical screening and women with symptoms that may be associated with cervical cancer](#).

Evidence

Systematic review evidence

A systematic review was performed to identify studies evaluating the safety and effectiveness of direct referral to colposcopy, compared with HPV testing and cytology, in women with postcoital bleeding, intermenstrual bleeding or heavy menstrual bleeding. No randomised or pseudorandomised controlled trials were found.

The search strategy and inclusion/exclusion criteria are described in detail in the [Technical report](#).

General literature review evidence

In the absence of any direct evidence from the systematic review, [a general review of the literature](#) was performed to inform consensus-based recommendations for investigating abnormal vaginal bleeding, in particular postcoital bleeding and intermenstrual bleeding.

No relevant evidence-based clinical practice guidelines based on systematic reviews of evidence were identified. No studies were found that assessed the safety and effectiveness of direct referral to colposcopy, compared with HPV testing and cytology in women with abnormal uterine bleeding.

One systematic review,^[6] two prospective cohort studies^{[8][9]} and seven retrospective cohort studies^{[10][11][12][13][14][15][16]} reported outcomes in women with postcoital bleeding, including cytology findings, rates of cervical intraepithelial neoplasia grades 2 and 3 (CIN2, CIN3), invasive cervical carcinoma, and other diagnoses. Outcomes were reported according to known pre-referral cytology status and age group, where available. No studies reported cervical abnormalities according to HPV status in women with postcoital bleeding.

The systematic review^[6] included two studies based on data from the Finnish national screening registry and national cancer registry.^{[17][18]} The first study^[17] reported outcomes for women tested in 1963–1971 after the introduction of a mass cervical screening program and followed up at the end of 1972. Women with postcoital bleeding and normal referral cytology showed a 15-fold higher risk of developing invasive cervical carcinoma than women without postcoital bleeding.

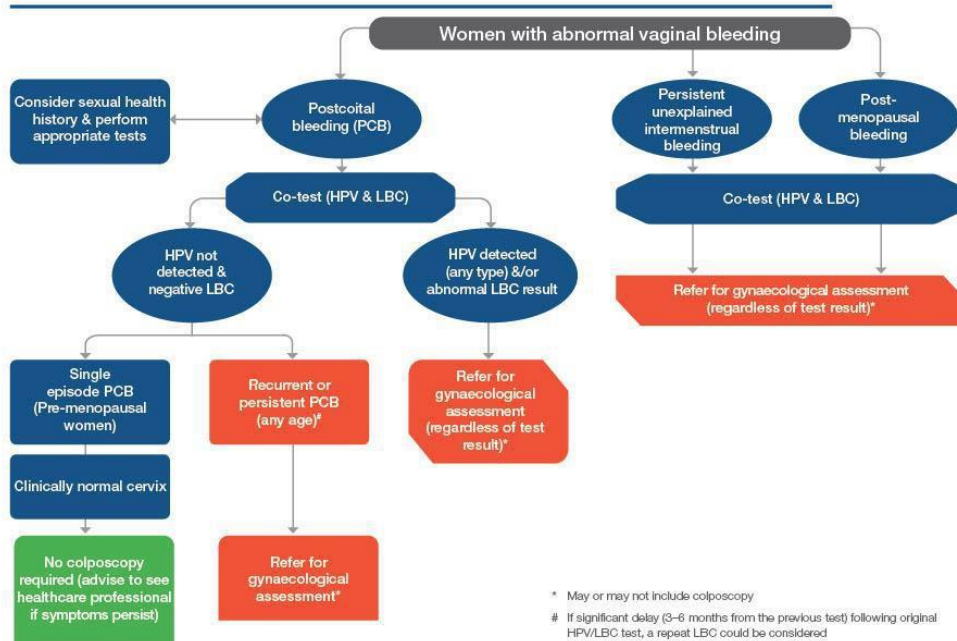
However, the later study,^[18] which reported outcomes in women screened from 1985–1990 and followed up to 1994, found that postcoital bleeding carried a 3-fold risk of invasive cervical carcinoma in women with normal referral cytology. The reduction in risk associated with postcoital bleeding was presumed to be due to changes in prevalence and incidence of cancer since screening had been introduced.^[6] The same systematic review estimated rates of invasive cervical cancer among women with postcoital bleeding (with community populations) to be approximately one in 44,000 for those aged 20–24 years, one in 5600 for those aged 25–34 years, one in 2800 for those aged 35–44 years and one in 2400 for those aged 45–54 years.^[6] In retrospective cohort studies, reported rates of invasive cervical carcinoma diagnosed in women with postcoital bleeding and normal or no referral cytology ranged from nil to 3.6%.^{[12][13][10]} One study reported rates of CIN3 of 2.3% among women with postcoital bleeding and normal cytology who attended colposcopy.^[13] Among women with postcoital bleeding and abnormal referral cytology, rates of invasive cervical cancer ranged from nil to 5%.^{[10][11][14]} We did not identify published studies, and we are unaware of any ongoing studies, directly evaluating the use of HPV testing or co-testing (the combination of HPV testing and LBC) in the investigation of postcoital bleeding in women.

A summary of the literature considered can be found in the [Technical report](#).

Recommendations

Flowchart 18.1. Investigation of women with abnormal vaginal bleeding

INVESTIGATION OF WOMEN WITH ABNORMAL VAGINAL BLEEDING



Suggested citation: Cancer Council Australia Cervical Cancer Screening Working Party Clinical pathway: Investigation of women with abnormal vaginal bleeding. National Cervical Screening Program Guidelines for the management of tissue detected abnormalities, screening in specific populations and investigation of abnormal vaginal bleeding. CCA 2021. Accessible from <https://helix.cancer.org.au/australian-guidelines/cervical-cancer/screening>

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Department of Health

Cancer
Council

<https://www.cancer.org.au/assets/pdf/flowchart-18-1-investigation-of-women-with-abnormal-vaginal-bleeding>

Consensus-based recommendation

REC18.1: Postcoital and intermenstrual bleeding and testing for HPV and LBC

When women present with postcoital or intermenstrual bleeding, appropriate investigations including a clinician-collected cervical sample for a co-test,[†] should be performed and not delayed due to the presence of blood.

[†]The woman's recent cervical screening history should be considered.

Consensus-based recommendation

REC18.2: Postcoital bleeding in pre-menopausal women

Pre-menopausal women who have a **single** episode of postcoital bleeding and a clinically normal cervix do not need to be referred for colposcopy if oncogenic HPV is not detected and LBC is negative.

REC18.3: Persistent or recurrent post coital bleeding in pre-menopausal women

Pre-menopausal women with recurrent or persistent postcoital bleeding, even in the presence of a negative co-test, should be referred to a gynaecologist for appropriate assessment, including colposcopy, to exclude genital tract malignancy.

Practice point

REC18.4: Postcoital bleeding and sexually transmitted infections

Sexually transmitted infections, including chlamydia infection, should be considered in all women presenting with postcoital bleeding. It is necessary to obtain a sexual health history and perform appropriate tests and investigations.

Consensus-based recommendation*

REC18.5: Symptomatic women with LBC prediction of cervical cancer

Women with symptoms and a LBC prediction of invasive cervical cancer should be referred to a gynaecological oncologist or gynaecological cancer centre for assessment, ideally within 2 weeks.

Consensus-based recommendation

REC18.6: Women with intermenstrual bleeding

Women with persistent unexplained intermenstrual bleeding require appropriate investigation and should be referred for gynaecological assessment which may or may not include colposcopy. Common benign causes including a sexually transmitted infection or hormonal contraception-related bleeding should be excluded.

Consensus-based recommendation

REC18.7: Postmenopausal women with vaginal bleeding require specialist referral

Postmenopausal women with any vaginal bleeding, including postcoital bleeding, should be referred for a specialist gynaecological assessment (which may or may not include colposcopy) regardless of test results, to exclude genital tract malignancy.

Practice point

REC18.8: Circumstances that do not require co-testing or referral for colposcopy

The following circumstances do not require co-testing or referral for colposcopy:

- a) Breakthrough or irregular bleeding due to hormonal contraception
- b) Contact bleeding at time of obtaining a routine cervical screening test sample
- c) Heavy regular periods (heavy menstrual bleeding)
- d) Irregular bleeding due to a sexually transmitted infection (STI), eg. chlamydia.

Benefits and harms

While cancer is an uncommon cause of abnormal vaginal bleeding in women of any age, postcoital bleeding in particular warrants investigation because it may be a symptom of cervical cancer. For premenopausal women, with a single episode of postcoital bleeding, these recommendations will limit over-investigation, especially referral for colposcopy. Investigation and management of sexually transmitted infections in women with postcoital and intermenstrual bleeding will also avoid over-referral for colposcopy. Overall, these recommendations are conservative, since the majority of women who are investigated will not be found to have serious disease. The reassurance provided by confirmation of disease-free status should be considered a benefit. Given the small but serious risk of underlying invasive cancer, these recommendations are considered to represent the best balance of benefits and harms.

See [Chapter 5. Benefits, harms and cost-effectiveness of cervical screening in the renewed National Cervical Screening Program \(NCSP\)](#).

Health system implications of these recommendations

Clinical practice

Some healthcare professionals are reluctant to perform a cervical examination during bleeding. Therefore, implementation of the recommendation for a clinician-collected sample for a co-test (HPV and LBC) despite the presence of blood requires education for healthcare professionals.

Resourcing

The use of co-testing is recommended as part of the initial investigation of women presenting with postcoital bleeding and unexplained intermenstrual bleeding. This may affect costs and laboratory workloads. Updates to the guidelines in 2019 provided greater clarity on colposcopy referral in order to reduce over-referral for common benign causes including sexually transmitted infections and hormonal contraception-related causes.

Barriers to implementation

Healthcare professionals may remain concerned by the presence of postcoital bleeding, despite the reassurance of negative findings on co-testing, and may continue to refer women with only one episode of postcoital bleeding and a clinically normal cervix. Over use of the co-test and referral for colposcopy for women whose abnormal bleeding is due to a common benign cause appears to have occurred at the start of the renewed program. Therefore, the ongoing education of healthcare professionals is of paramount importance to successful implementation of this recommendation.

Discussion

Unresolved issues

No unresolved issues have been identified.

Future research priorities

Future research could be carried out using routinely collected data to determine the most appropriate approach to managing younger women with symptoms.

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Appendices

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Effective from 1 July 2022

Investigations of other symptoms: Vaginal discharge and deep dyspareunia

Author(s):

- [Professor Ian Hammond](#) — Contributor
- [Professor Marion Saville](#) — Author
- A/Professor Deborah Bateson – Author
- Dr Vivienne Milch – Co-author
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

Hammond, I, Saville, M, Cancer Council Australia Cervical Cancer Screening Guidelines Working Party. Guidelines: Cervical cancer/Screening/Signs and symptoms. In: National Cervical Screening Program: Guidelines for the management of screen-detected abnormalities, screening in specific populations and investigation of abnormal vaginal bleeding.

Cervical screening and women with symptoms that may be associated with cervical cancer

The Cervical Screening Test (CST) is for asymptomatic women, aged 25–74, who are participating in the National Cervical Screening Program. Women with symptoms suggestive of cervical cancer require *diagnostic* testing at any age and not 'cervical screening'.

The vast majority of symptomatic women, especially younger women, will NOT have cervical cancer and benign gynaecological causes are far more common.

Young women with postcoital or intermenstrual bleeding are far more likely to have a benign cause eg: chlamydia infection or bleeding related to hormonal contraception.

Abnormal vaginal bleeding is the most common symptom of cervical cancer and is covered in detail in [Investigation of abnormal vaginal bleeding](#).

- Vaginal discharge and/or deep dyspareunia are commonly due to benign gynaecological conditions and should be investigated appropriately and if necessary referred for gynaecological assessment. In the absence of bleeding, **vaginal discharge and/or deep dyspareunia**, may very rarely be the initial presentation of cervical cancer.

If due for cervical screening, then a routine CST would be most appropriate rather than a co-test (HPV and LBC) for these women. **Co-testing is not indicated in the vast majority of women** presenting with vaginal discharge and/or dyspareunia.

- Unexplained persistent unusual vaginal discharge, especially if malodorous and blood-stained, may be associated with a cervical cancer and should be investigated by clinical examination of the cervix, a co-test and tests for a genital infection: (HPV and LBC):
 - if the co-test is abnormal the patient should be referred for colposcopy;
 - even if the co-test is negative (no HPV detected and LBC normal), referral for gynaecological assessment should be considered;
 - if a CST was recently performed with a low-risk result, consider referral for gynaecological assessment without a co-test.

- The investigation of unexplained persistent deep dyspareunia (in the absence of bleeding or discharge) should include a CST if due for routine screening and referral for gynaecological assessment should be considered.

Women who present for a routine Cervical Screening Test (CST) and who have vaginal discharge or deep dyspareunia, should in the first instance have a CST.

Consensus-based recommendation

REC18.8: Women with abnormal vaginal discharge and/or deep dyspareunia

Almost all women with vaginal discharge and/or deep dyspareunia have benign gynaecological disease. They should be investigated appropriately, and if due for cervical screening a routine CST should be performed (rather than a co-test).

Consensus-based recommendation

REC18.9: Women with unexplained persistent unusual vaginal discharge

In women of any age, unexplained persistent unusual vaginal discharge, especially if malodorous or blood stained, should be investigated with a co-test (HPV and LBC) and the woman should be referred for gynaecological assessment.

Consensus-based recommendation

REC18.10: Women with unexplained persistent deep dyspareunia

Women with unexplained persistent deep dyspareunia in the absence of bleeding or vaginal discharge should have a CST if due and referral for gynaecological assessment should be considered.

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Persistence of any unexplained gynaecological symptoms always warrants further investigation and referral as appropriate.

HPV test and LBC both requested and performed on a clinician-collected cervical sample (not a self-collected sample).

Liquid based cytology(LBC) is a way of preparing cervical samples for examination in the laboratory.

Women with a positive HPV test result of any oncogenic HPV types detected using HPV testing platforms in a pathology laboratory.

HPV test and LBC both requested and performed on a cervical sample.

Effective from 1 July 2022

19. Psychosocial Care

Author(s):

- [Kim Hobbs](#) — Author
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

Kim Hobbs, Cancer Council Australia Cervical Cancer Screening Guidelines Working Party. Guidelines: Cervical cancer/Screening/Psychosocial care . In: National Cervical Screening Program: Guidelines for the management of screen-detected abnormalities, screening in specific populations and investigation of abnormal vaginal bleeding.

Anxiety and distress

It is well documented that the finding of an abnormality on cervical screening has the potential to cause anxiety and distress.^{[1][2][3][4][5][6][7][8][9][10]} The degree and duration of psychological distress experienced by women with abnormal cervical screening depends on their understanding of the meaning of the results.^{[4][10]} As women are usually asymptomatic when a cervical abnormality is detected on routine screening, they may feel particularly vulnerable and distressed. Younger women and those who have never had children are at increased risk of high levels of anxiety.^[3] Women's concerns may be centred around several themes:

- perceived threat to life, frequently with an assumption that there will be inevitable progression to invasive cancer
- worry about future fertility
- concern about risk of transmission to an intimate partner
- concerns about disclosing human papillomavirus (HPV) status to an intimate partner
- guilt, shame and self-blame associated with past sexual behaviour
- anger and mistrust of intimate partners; suspicion about infidelity.

As the trend in cervical screening shifts towards HPV testing, there is an emerging literature on the specific psychosocial and psychosexual issues associated with the psychological impact of positive HPV results and women's understanding of the implications of this result.

Confirmation of a positive HPV result may carry with it an additional burden of psychological distress due to the direct association with exposure to a sexually transmitted infection.^{[10][11][12][13][14][15][16][17][18][19][20][21][22][23][24]} Anxiety, fears and confusion surrounding the uncertainty of the meaning of cervical pathology are compounded by issues of stigma and poor understanding about exposure to HPV. Psychosocial and psychosexual consequences may be significant and persistent, with the potential to result in clinical depression or an anxiety disorder requiring psychological interventions and treatment.

With increasing knowledge and understanding across the community that exposure to HPV infection is a pre-requisite for the development of cervical cancer, the general public understands the causal link between sexual behaviour and cancer more clearly than the implication of a cytological prediction of an intraepithelial lesion after a screening test.

Women who have not received vaccination, even though it was available to them, may feel distressed that they have failed to adequately protect themselves from infection. Those who have received the full course of HPV immunisation may feel distressed that the vaccine has 'failed'.

Anger about exposure to HPV may lead to suspicion about the fidelity of the intimate partner and have a negative effect on intimate relationships. Additionally, women may have fears about transmitting the virus to current or future sexual partners. Psychosexual function may be impaired with decreased libido and lower frequency of intercourse.^[25]

Management of distress

Information needs to be delivered in a sensitive manner and should be tailored to individual patient characteristics: age, education level, health literacy, parity, cultural/religious beliefs, mental health concerns and language proficiency.

- Information should be delivered compassionately, non-judgmentally and in plain language (not medical jargon).
- Provision of printed information resources should supplement verbal communication. If possible, pamphlets, fact sheets or booklets should be available in community language translations for culturally and linguistically diverse populations.

Information provided to women could:

- explain the natural history of HPV infection
- normalise the incidence of HPV infection as a commonly acquired community infection
- reinforce that HPV infections are usually transient and do not progress to invasive cancer
- reinforce the benefits of having identified the infection through screening, enabling monitoring and intervention as appropriate to prevent cancer by treating pre-cursor lesions
- convey the message that, although HPV infection is relatively common, cervical cancer is uncommon in screened populations
- address concerns about transmitting the virus to intimate partners and discuss safe sex practices
- provide reassurance to reduce the stigma associated with HPV infection, then directing the conversation towards addressing the necessary next steps in evaluation and investigation
- explain the colposcopic procedure and possible outcomes.

Healthcare providers should be mindful that the emotional distress associated with receiving information about a positive HPV result may temporarily impair a woman's capacity to process and understand the result. Prior to the end of the consultation, health-care providers should reiterate the information and the next steps to be taken, checking that the woman has clearly understood the information.

Providing adequate information in a supportive environment, offering opportunities to ask questions and seek clarification, and ensuring a plan for communicating the next steps or investigations will usually be sufficient to allay the distress of most women. For those who demonstrate persistent elevated anxiety and distress, referral to other services for counselling may be helpful. Available services vary according to location, but may include women's health

services, GPs (who can initiate a mental health care plan), or counselling services within the local health facility.

Effective counselling strategies may be beneficial in alleviating distress for most women.^{[26][27][28][29][30]}

Counselling techniques and interventions with evidence of effectiveness may include:^[31]

- psycho-education
- brief emotional support
- supportive-expressive therapy
- cognitive behavioural therapy (CBT)
- problem-solving approaches
- relaxation, meditation or mindfulness skills.

Ideally, counselling should be offered as a face-to-face (where possible) discussion, rather than by phone or letter. Formal referral to a suitably qualified counsellor (such as a clinical psychologist, social worker, sexual health counsellor or women's health counsellor) should be considered for women who experience persistent emotional distress. Australian guidelines for screening, assessment and management of anxiety and depression in adult cancer patients provide a useful resource.^[31]

Women with special needs

Some women with pre-existing psychosocial comorbidities may require referral to specialist services for expert assessment and intervention. Such women may be under-screened and therefore at higher risk of HPV infection.^{[32][33]} Factors to consider as special circumstances include:

- a history of trauma (including torture) – women may experience 'triggering' of trauma responses when informed about a positive HPV test. They should be offered immediate mental health assessment and counselling.^{[32][34]}
- known prior sexual abuse (childhood or adult)^{[35][36]}
- current or past history of intimate partner violence^{[37][38]}
- disabilities (physical and intellectual)^[39]
- history of substance misuse
- significant mental health history
- a history of female genital mutilation and/or surgical revision procedures.

Women from culturally and linguistically diverse backgrounds need to be given information in their first language, via health care interpreters or printed information resources. This is especially important for women from countries where there is no population-based cervical screening.

Women without stable accommodation and those who are socially marginalised may be non-compliant with necessary investigations following a positive oncogenic HPV test result. They may be difficult to locate or lost to follow up, frequently only re-emerging when symptomatic.^[40] For some women the first disclosure of sexual abuse may occur at the time of first speculum examination or in the context of receiving a positive HPV test result. Clinicians need to be aware of, and consider referral to, specialist state-based sexual assault counselling services for women with an identified background of sexual abuse.

For all women with additional psychosocial risk factors health professionals have a duty of care to be aware of the range of specialist treatment services within their jurisdictions, and to refer appropriately following consultation and consent from the woman.

Education and information

It is important to educate women about the need for cervical screening and to differentiate HPV testing from other sexually transmitted infection testing. For vulnerable women who may not be well connected to mainstream health services, attendance for cervical screening affords health professionals an additional opportunity to provide education about screening for other sexually transmitted infections and safe sex practices such as condom use, pregnancy counselling and emergency contraception.^{[41][42][43][44][45][46][47][48][49][50][51][52][53][10]}

Association of cervical screening with HPV testing may deter some women from participating in screening programs.^[10] Attitudes and behaviours may include:

- perceptions by women that they are not at risk of HPV infection due to their personal behaviours.
- deeming HPV screening as unnecessary if they have received HPV vaccination.^[54]
- avoidance due to fear of a positive result and what that may mean for intimate relationships.

Women with psychosocial risk factors may be difficult to engage in screening programs.^{[55][56][57]} For those who do undertake screening, elevated psychological distress following a positive HPV result may impede their ability to continue with recommended investigations and to adhere to cervical screening guideline recommendations.^[58]

Education is required to counter the potential for distress that may be experienced by some women as the changes to cervical screening policy are implemented. The change to primary HPV testing, the later recommended age to commence screening and the longer screening interval may be perceived by some women as a cost-driven reduction in surveillance, thus exposing them to an increased risk of developing invasive cancer.

Effective education and information may assist women in decision-making, at the same time assisting their psychological adjustment, treatment compliance and satisfaction with care.

Psychosocial resources

Although the overwhelming majority of women who have a positive HPV test will not go on to develop cervical cancer, psychosocial guidelines that have been developed for addressing issues of anxiety and psychological distress in the context of cancer are useful for all health professionals.

The most comprehensive evidence-based guideline on psychosocial care is the 2003 [Clinical practice guidelines for the psychosocial care of adults with cancer](#) published by the National Breast Cancer Centre (now Cancer Australia).

This resource has been supplemented by:

[Psychosocial Care Referral Checklist \(2008\)](#)

[Clinical Guidance for Responding to Suffering in Adults with Cancer \(2014\)](#)

All of these resources can be accessed from [Cancer Australia](#)

For information and resources about sexual health see [Health Direct Australia](#) or refer to specialist sexual health services in your local jurisdiction.

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20. Transitioning to the renewed National Cervical Screening Program

Author(s):

- A/Professor Deborah Bateseon – Co-author
- Dr Vivienne Milch – Co-author
- Dr Marsali Newman – Co-author
- Ms Kirsteen Fleming – Co-author
- [Professor Karen Canfell](#) — Co-author
- [Dr Lara Roeske](#) — Contributor
- [A/Professor Marion Saville](#) — Co-author
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

Background

This chapter describes the management for women who participated in cervical screening before the introduction of the renewed National Cervical Screening Program (NCSP) on 1 December 2017, when the Pap test was replaced by primary screening using human papillomavirus (HPV) testing, with reflex liquid-based cytology (LBC) for women with a positive oncogenic HPV (any type) test result.

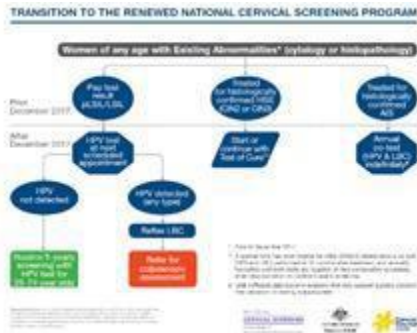
Among women attending for their first test since the renewal of the NCSP there will be women who have had a previous screen detected abnormality and who are currently undergoing investigation, treatment or follow-up for:

- abnormal Pap test result
- histologically confirmed high-grade squamous intraepithelial lesion (HSIL) (cervical intraepithelial neoplasia grades 2 to 3 (CIN2/3))
- histologically confirmed adenocarcinoma in situ (AIS).

Women who have participated in the pre-renewal NCSP and have not had any previous abnormality, or who have returned to routine screening after a Test of Cure, are recommended to attend for their first HPV test 2 years after their most recent Pap test or at age 25, whichever is later.

Recommendations

Flowchart 20.1. Transition to the renewed National Cervical Screening Program



Practice point

REC20.1: HPV test has replaced the Pap test

All Pap tests have been replaced by HPV testing.

Conventional Pap tests are no longer used.

Reflex LBC is performed on any clinician-collected sample with a positive oncogenic HPV (any type) test result.

Co-testing (HPV and LBC) should be performed only as recommended in these guidelines, in the follow-up of screen-detected abnormalities or the investigation of abnormal vaginal bleeding.

Practice point

REC20.2: HPV testing for women in follow-up after pLSIL/LSIL

Women who are in follow-up for pLSIL/LSIL cytology in the previous program (pre-renewal NCSP) should have a HPV test at their next scheduled follow-up appointment.

- Women with a positive oncogenic HPV (any type) test result should be referred for colposcopic assessment. If the test sample was collected by a healthcare professional then the laboratory will undertake, reflex LBC. If the test sample was self-collected then a sample for LBC should be collected at the time of colposcopy.
- If oncogenic HPV is not detected, the woman can return to 5-yearly screening.

Practice point

REC20.3: Colposcopic management of a prior screen-detected abnormality should continue

Women who have been referred for colposcopic assessment following any cytological abnormality in the pre-renewal NCSP should continue their colposcopic management according to these guidelines.

Practice point**REC20.4: Prior treatment and Test of Cure**

Women who have been treated for HSIL (CIN2/3) in the pre-renewal NCSP and are undergoing, or have not yet commenced Test of Cure, should start or continue Test of Cure in accordance with these guidelines.

Women should have an annual co-test (HPV and LBC) performed at 12 months after treatment, and annually thereafter, until both tests are negative on two consecutive occasions, when they can return to routine 5-yearly screening. A co-test cannot be performed on a self-collected sample.

Practice point**REC20.5: Prior treatment for AIS**

Women who have been treated for AIS in the pre-renewal NCSP, and are undergoing or have not yet commenced surveillance, should have annual co-testing (HPV and LBC) indefinitely.[†] A co-test cannot be performed on a self-collected sample.

[†]Until sufficient data become available that may support a policy decision that cessation of testing is appropriate.

See also:

[Chapter 10. Management of histologically confirmed high-grade squamous abnormalities](#)

[Chapter 11. Management of glandular abnormalities](#)

Appendices

APPENDIX A: Modelled evaluation of predicted benefits, harms and cost-effectiveness in renewed NCSP

Guidelines: Cervical cancer/Screening/Modelled evaluation of predicted benefits, harms and cost-effectiveness in renewed NCSP

Author(s):

- Professor Karen Canfell — Co-author
- Ms Michaela Hall — Co-author
- Jie Bin Lew — Co-author
- A/Professor Marion Saville — Co-author
- Dr Kate Simms — Co-author
- Dr Megan Smith — Co-author
- Cancer Council Australia Cervical Cancer Screening Guidelines Working Party — Co-author

Introduction

A modelling approach was used to predict the impact of the renewed National Cervical Screening Program (NCSP), when implemented in conjunction of these guidelines, on benefits, harms, cost-effectiveness and resource utilisation. The estimates presented here are an update of predictions that underpinned the Medical Services Advisory committee (MSAC) recommendations.^[1]

The findings are summarised in Chapter 5. Benefits, harms and cost-effectiveness of cervical screening in the renewed NCSP. This appendix briefly describes the modelling methods and details the updates included since the model platform was used for the MSAC evaluation. Updates affecting the overall effectiveness and costs associated with the renewed NCSP include changes in:

- guidelines for the management of women post colposcopy
- assumptions about compliance with colposcopy
- end age for screening.

Methods

Model platform

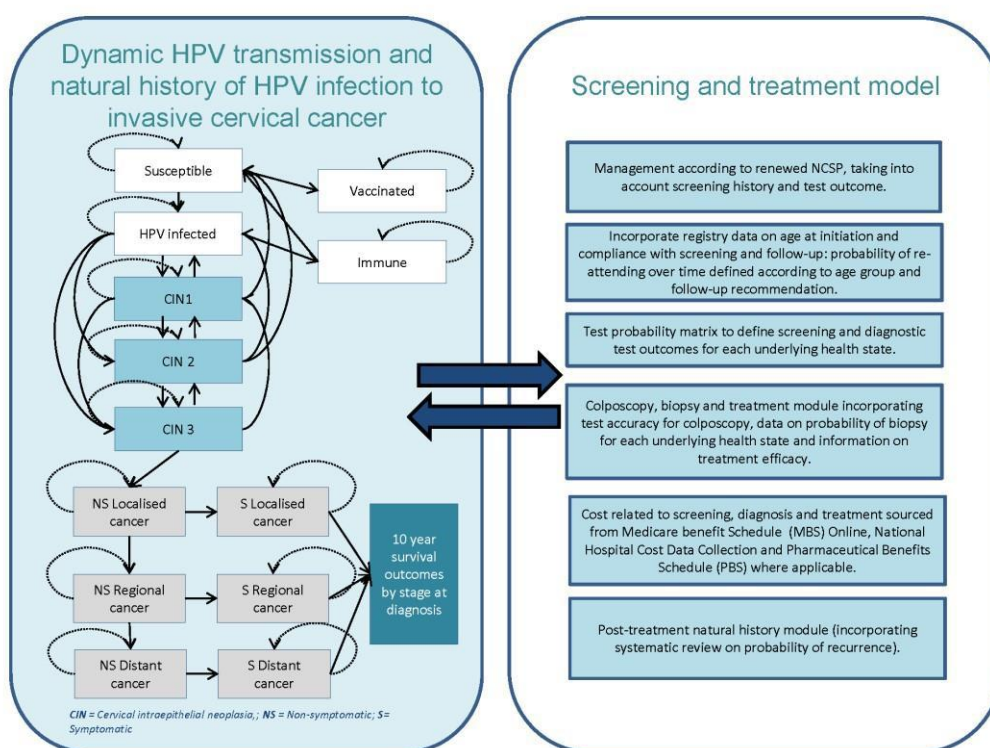
We used the same model platform that was used for the MSAC evaluation. This platform has been used for a number of human papillomavirus (HPV) vaccination evaluations as well as

screening technology, screening interval and screening management evaluations performed on behalf of national cervical screening programs in Australia, New Zealand and England. A schematic of the model is shown in Figure A.1. The model consists of several elements:

1. a dynamic model of sexual behaviour, HPV transmission and vaccination in females and males based on vaccination uptake rates reported by the National HPV Vaccination Program Register
2. a multi-HPV-type model of the natural history of HPV infection, progression, regression, the development of cervical intraepithelial neoplasia (CIN) and invasive cervical cancer
3. a model of cervical screening, diagnosis and treatment of CIN
4. a multiple-cohort implementation which separately models HPV exposure, CIN development, screening, and all downstream processes, for each age cohort of females
5. a population component that applies demographic data to the outputs to estimate cross-sectional results.

A more detailed description of the model, including data sources, model validation and calibration targets and previous applications of the model, can be found in MSAC's NSCP renewal executive summary report.^[1]

Figure A.1. Schematic diagram of model structure

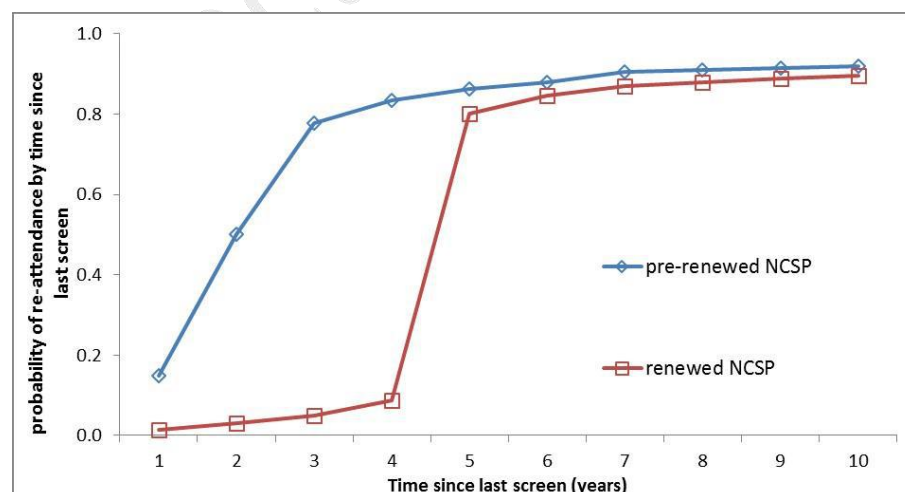


This flow diagram represents the natural history assumptions specific to a single HPV type. If multiple HPV infections exist, each will have the same flow dynamics, but the rates of progression and regression occur independently for each HPV type.

Screening compliance assumptions

When modelling the pre-renewed NCSP, we incorporated data on age-specific screening initiation and compliance with screening and management recommendations in Australian women, informed by an analysis of data obtained from Victoria Cervical Cytology Registry (VCCR). When modelling the renewed NCSP, assumptions were based on the introduction of a call-and-recall system, with women sent invitations at age 25 years. We assumed that the number of women who attend their first screening test at age 25 years (the new initiation age) will be at least equivalent to the number who, under the pre-renewed NCSP, had their first screening test before, or at, the age of 25. For the purposes of this modelled evaluation, we assumed that no screening occurs before the age of 25 years under the renewed NCSP. Compliance with re-attendance for women in routine screening under the renewed NCSP was evaluated assuming implementation of the call-and-recall screening organisation system. The behaviour of women under a call-and-recall system was informed by data from England, where such a system has been implemented. While the proportion of women who attend before or at the recommended screening interval (5 years under the renewed NCSP) is informed by the screening pattern observed in England, we assume that the coverage at 7 years is equivalent to that currently observed under the pre-renewed NCSP (i.e. that changing the recommended screening interval, by itself, will not change behaviour in very under-screened women). The modelled probability of re-attending, according to the time since last screening test, is shown in Figure A.2. We assumed that, for a given recall timeframe, the probability of attending a follow-up test in the renewed NCSP is equivalent to that currently observed under the pre-renewed NCSP. As part of the MSAC evaluation, we previously explored a range of screening attendance assumptions, including slower screening uptake rates and a less 'efficient' call-recall system (in which there was a higher rate of early re-attendance and a lower rate of on-time attendance). Details of the impact of these screening assumptions can be found in MSAC's NCSP renewal executive summary report.^[1]

Figure A.2. Probability of re-attendance for women in routine screening



Changes from the model used for the MSAC Evaluation (to reflect these draft guidelines)

Updates to the management of women post-colposcopy

We have incorporated into the model the new recommendations in these guidelines for post-colposcopy management. These include recommendations for women who were referred with a positive oncogenic HPV (16/18) test result, or women under follow-up with a positive oncogenic HPV (any type) test result, with each of the following colposcopy results (see [Colposcopy terminology](#) in Chapter 7. Colposcopy):

- i) normal transformation zone (TZ) (negative colposcopy)
- ii) abnormal TZ and histologically confirmed CIN2 or lesser-grade lesion
- iii) type 3 TZ.

We have also incorporated new recommendations, according to these guidelines, for women referred to colposcopy who subsequently received pre-cancer treatment.

Table A.1 summarises updated post-colposcopy management for women referred with a positive oncogenic HPV (any type) test result and a liquid-based cytology (LBC) report of negative, possible low-grade squamous intraepithelial lesion (pLSIL) or low-grade squamous intraepithelial lesion (LSIL). Table A.2 shows updated post-colposcopy management for women who have an LBC prediction of possible high-grade squamous intraepithelial lesion (pHSIL) or high-grade squamous intraepithelial lesion (HSIL). These updates have been incorporated into the model.

Table A.1. Changes in post-colposcopy management for women with an LBC report of negative, pLSIL or LSIL, based on the renewed NCSP recommendations

	Normal TZ	Type 3 TZ	Colposcopy abnormal and biopsy < CIN2	Treated for CIN2+ and under test-of-cure
MSAC model assumptions*	Co-testing at 12 and 24 months	Co-testing at 12 and 24 months	Co-testing at 12 and 24 months	Co-testing at 12 and 24 months
	Referral to colposcopy if any positive‡ at 12 months or 24 months	Referral to colposcopy if any +ve test‡ at 12 or 24 months	Referral to colposcopy if pHSIL+ or if both oncogenic HPV +ve (any type) and pLSIL+	Colposcopy if LBC pHSIL+ Otherwise, continue annual co-testing until 2 consecutive

			No referral to colposcopy if oncogenic HPV (any type) +ve and LBC negative, or oncogenic HPV not detected and cytology pLSIL/LSIL	double negatives
Updated model assumptions[†]	HPV testing at 12 months	HPV testing at 12 and 24 months	HPV testing at 12 months	Co-testing at 12 and 24 months
	Referral to colposcopy if oncogenic HPV (16/18) +ve, or oncogenic HPV (non 16/18) +ve with reflex LBC pHSIL+	Referral to colposcopy if oncogenic HPV +ve (any type) at either visit§	Referral to colposcopy if oncogenic HPV (16/18) +ve, or oncogenic HPV (non 16/18) +ve with reflex LBC pHSIL+	Colposcopy if cytology pHSIL+ or oncogenic HPV (16/18) +ve (irrespective of LBC)
	Discharge to routine screening if oncogenic HPV not detected	Return to routine screening if oncogenic HPV not detected at 12 months and 24 months	Discharge to routine screening if oncogenic HPV not detected	Otherwise, continue annual co-testing until 2 consecutive double negatives

TZ: transformation zone

Co-testing: HPV test and LBC

pHSIL+: possible HSIL or higher-grade lesion

pLSIL+: possible LSIL or higher-grade lesion

+ve: positive test result

* Model assumptions used for the MSAC evaluation (for the base case MSAC evaluation)

[†] Model assumptions reflecting the updated recommendations in these guidelines

‡ Oncogenic HPV (any type) detected or any abnormality on LBC

§ In the model, we assumed that women attending their visit at 24 months would be referred to colposcopy if they have a positive oncogenic HPV (16/18) test result, but not for a positive oncogenic HPV (not 16/18) test result.

Table A.2. Changes in post-colposcopy management for women with an LBC report of pHSIL or HSIL, based on the renewed NCSP

	Normal TZ	Type 3 TZ	Colposcopy abnormal and biopsy < CIN2	Treated for CIN2+ and under test-of-cure
MSAC model assumptions*	Return for a LBC and colposcopic assessment at 6 and 12 months	Cold-knife cone biopsy is recommended. However, women who are concerned about fertility† can have a repeat colposcopy in 4 months. If the TZ is still not visible, diagnostic excision is recommended	Co-testing at 12 and 24 months Referral to colposcopy if pHSIL+ or if both oncogenic HPV (any type) +ve and pLSIL+ No referral to colposcopy if oncogenic HPV (any type) +ve and cytology negative, or oncogenic HPV not detected and LBC pLSIL/LSIL	Co-testing at 12 and 24 months Colposcopy if LBC pHSIL+ Otherwise, continue annual co-testing until 2 consecutive double negatives
Updated model assumptions**	Diagnostic excision of the TZ is recommended§ Women who had confirmed pHSIL and are concerned about fertility† can have a repeat assessment at 6 and 18 months with an	Diagnostic excision of the TZ is recommended regardless of whether the referring LBC is pHSIL or HSIL§	Diagnostic excision of the TZ is recommended Women who had confirmed pHSIL and are concerned about fertility† can have a repeat assessment at 12 and 24 months with	Co-testing at 12 and 24 months Colposcopy if LBC pHSIL+ or oncogenic HPV (16/18) +ve (irrespective of LBC) Otherwise, continue annual co-testing until

HPV and LBC
co-test[‡]

an HPV and
LBC co-test[‡]

2
consecutive
double
negatives

TZ: Transformation zone

pHSIL+: possible HSIL or higher-grade lesion

pLSIL+: possible LSIL or higher-grade lesion

*Model assumptions used for the MSAC evaluation (for the base case MSAC evaluation)

** Model assumptions reflecting the updated recommendations in these guidelines

[†]Based on Australian fertility rates for 2011, we have estimated the probability that a woman would have no further births from the age of 35 on as 64%. By age 40, this has increased to 92% and by age 45 it is over 99%. We therefore assume the following for the purposes of this modelled evaluation:

- (i) All women aged < 35 years will choose to defer excisional biopsy
- (ii) 35% of women aged 35–39 will choose to defer excisional biopsy
- (iii) 8% of women aged 40–44 years will choose to defer excisional biopsy
- (iv) No women aged 45+ will choose to defer excisional biopsy.

§ We assume all women will undergo diagnostic excision of the transformation zone at this point.

[‡] It is assumed that:

- (i) women have a co-test (HPV and LBC), along with a colposcopy, at both visits
- (ii) a woman undergoes diagnostic excision of the transformation zone if oncogenic HPV (any type) is detected, or oncogenic HPV is not detected and LBC prediction is pHSIL/HSIL.
- (iii) if oncogenic HPV is not detected and cytology is negative at both visits, women are referred to routine screening.

Updates to colposcopy compliance assumptions

Modelling undertaken for the MSAC evaluation assumed that compliance with colposcopy referral was dependent on the accompanying cytology result, and was generally higher in women referred with a pHSIL/HSIL. This was based on observed data from the Victorian Cervical Cytology Register, and is likely due to the fact that, under the pre-renewal NCSP, women referred with a high-grade cytology prediction receive reminder letters and phone calls if they have not attended colposcopy within a certain interval (shorter than the interval for reminders sent for women without a high-grade cytology prediction). We sought advice on whether these assumptions should be revised by considering management protocols for following up women within the primary HPV screening arm of the Compass trial, given that the Compass protocol closely resembles the proposed clinical pathway recommended in this guideline. Based on Compass management, we assumed that:

- women who are referred for colposcopy (regardless of the reflex LBC result) are followed up in the same way as for women with a pHSIL/HSIL cytology under the pre-renewal NCSP
- women will attend colposcopy at a rate similar to what is observed in women who test pHSIL/HSIL on cytology under the pre-renewal NCSP program.

Updates to HPV exit testing assumptions used in modelling

For the MSAC evaluation, when we provided predictions for women having primary HPV screening, we assumed that exit testing would be offered to women aged 60–64 years, which we described as screening ending at 64 years. As an exploratory analysis, we considered a scenario in which exit HPV testing would be offered to women aged 65–69 years, which we described as screening ending at 69 years. MSAC has since recommended that women have an exit HPV test between 70 and 74 years of age.

Furthermore, these new guidelines recommend women aged 70–74 years who have an are oncogenic HPV (any type) positive test result at their final screening test be referred directly to colposcopy, regardless of the HPV type or the reflex LBC result. This management process differs from the MSAC model, which assumed there was no referral to colposcopy for women who had an oncogenic HPV (not 16/18) positive test result but who had a negative LBC report. Therefore, we updated the model to account for this change in management of women at their final screening visit.

Results

Note: The model incorporated assumptions about compliance with screening in the renewed NCSP after taking into account the introduction of a call-and-recall system for screening. The specific assumptions for adherence were described in detail in the MSAC evaluation^[2] and are summarised here (see [screening compliance assumptions](#)). The predicted impact of the renewed NCSP, and associated cervical cancer incidence and mortality reductions, are predicated on achieving the level of compliance assumed.

Incremental impact of the changes from the model used for MSAC

Table A.3 summarises the incremental impact of each change that was made from the model used for the MSAC evaluation. This was done to determine the relative impact of each change on overall model predictions. Incorporation of the new recommendations in these guidelines for women who were referred to colposcopy with a cytology report of negative or pLSIL/LSIL and had a (i) negative colposcopy, (ii) type 3 TZ (iii) a histologically confirmed < CIN2 lesion, or (iv) received treatment for CIN2/3, results in a further 3% reduction in cervical cancer incidence and mortality in unvaccinated cohorts and a 1–3% reduction in cohorts offered vaccination, compared with the prior predictions for the renewed NCSP. The change results in 2% more colposcopies in unvaccinated cohorts and 9% fewer colposcopies in cohorts offered vaccination.

Incorporation of the updated guidelines for women who were referred to colposcopy with a cytology report of pHSIL/HSIL and had a (i) negative colposcopy, (ii) type 3 TZ, or (iii) a biopsy-confirmed <CIN2 lesion results in a further 5–6% reduction in cervical cancer incidence and mortality in unvaccinated cohorts and a 4% reduction in cohorts offered vaccination, compared with the prior predictions for the renewed NCSP. This change has no effect on colposcopies in unvaccinated cohorts but increases colposcopies by a further 2% in cohorts offered vaccination.

Incorporating the changes to the compliance assumptions for women referred to colposcopy results in a further reduction of 2% in cervical cancer incidence and mortality in unvaccinated cohorts and a 1–2% reduction in cohorts offered vaccination, compared with the prior predictions for the renewed NCSP. The change results in an increase in colposcopy referrals of 7% in unvaccinated cohorts and 5% in cohorts offered vaccination. Incorporating the changes to the screening end-age, we predict a 2–3% reduction in cervical cancer incidence and mortality in both unvaccinated cohorts and cohorts offered vaccination, compared with the prior predictions for the renewed NCSP. This change results in a 1% increase in colposcopies for both unvaccinated cohorts and cohorts offered vaccination.

As an exploratory analysis, we also evaluated a scenario in which women were not managed differently at their final screening test at ages 70–74, and were instead managed the same way as women who tested HPV positive at younger ages (i.e. we assume that there is no special exit test offered to women at their final screen). In this case, we predict < 0.5% increase in cervical cancer incidence, compared with the scenario in which women who have a positive oncogenic HPV (any type) test result are referred to colposcopy at their final test when aged 70–74 years. These findings suggest that extending the screening end-age has a substantial impact on effectiveness of the program, but providing different management for women who have an oncogenic HPV (any type) positive test result does not have as great an impact on effectiveness.

A.3. Changes in cervical cancer incidence, mortality and number of colposcopies predicted under the new model assumptions compared with pre-renewal NCSP

	Unvaccinated cohorts			Cohorts offered vaccination		
	Cancer cases	Cancer deaths	Colposcopies	Cancer cases	Cancer deaths	Colposcopies
MSAC model*	–19%	–21%	+26%	–15%	–18%	–5%
Updated model†	–31%	–36%	+36%	–24%	–29%	–7%
Incremental impact after incorporating each change						
Referral LBC negative or pLSIL/LSIL and any of: a) colposcopy result Type 3 TZ b) histologically confirmed < CIN2	–3%	–3%	2%	–1%	–3%	–9%

c)
colposcopy
negative
d) treated
for CIN2/3

Referral	-5%	-6%	0%	-4%	-4%	2%
LBC						
pHSIL/HSIL						
and any of:						
a)						
colposcopy						
result Type						
3 TZ						
b)						
histologically						
confirmed <						
CIN2						

c)
colposcopy
negative

Updated	-2%	-3%	7%	-2%	-1%	5%
compliance						
assumptions						
Exit HPV	-2%	-3%	1%	-2%	-3%	1%
test offered						
at age 70–						
74 years						
(extend end-						
age by 5						
years)						

Note: Figures are based on the female Australian population as predicted for 2017. Due to rounding, direct adding of the incremental numbers may not result in the presented final impact number.

* Model assumptions used for the MSAC evaluation (for the base case MSAC evaluation)

† Model assumptions reflecting the updated recommendations in these guidelines.

Overall benefits of the renewed NCSP incorporating these guideline recommendations

The impact of the Renewed NCSP on predicted cervical cancer cases, deaths, colposcopies and treatments for CIN2/3, is shown in Table A.4. Under the renewed NCSP when these

guidelines are incorporated, we predict a 31–36% reduction in cervical cancer cases and death in unvaccinated cohorts, and a 24–29% reduction in cohorts offered vaccination, compared with the pre-renewal NCSP. This is equivalent to 265 fewer cancer cases and 82 fewer deaths annually in unvaccinated cohorts, and 85 fewer cancer cases and 28 fewer deaths annually in cohorts offered vaccination.

Table A.4. Predicted annual numbers of cervical cancer cases and deaths for the pre-renewal NCSP and the renewed NCSP (showing differences in case numbers and relative percentage differences)

	Pre-renewal NCSP		Renewed NCSP	
	If HPV vaccination had not been introduced	For cohorts offered vaccination as 12 year olds	If HPV vaccination had not been introduced	For cohorts offered vaccination as 12 year olds
Cervical cancer cases	850	353	584 (–265; –31%)	267 (–85; –24%)
Cervical cancer deaths	227	94	145 (–82; –36%)	66 (–28; –29%)

Note: Figures are based on female Australian population as predicted for 2017.

We also predict an increase in colposcopies for unvaccinated cohorts, but this increase will not be seen in cohorts offered vaccination. Although there would have been a substantial increase in colposcopies if HPV vaccination had not been introduced, it should be noted that 70% of these additional colposcopies would have occurred in women less than 35 years of age. However, all of these women will have been offered vaccination by 2017, when these new clinical guidelines will be implemented. After taking into account the effect of HPV vaccination, the overall impact of the renewed NCSP on colposcopy and treatment-related harms is expected to be as good or better, when compared to the pre-renewal NCSP.

Costs and cost-effectiveness

Table A.5 shows the estimated cost of the NCSP before and after renewal. If HPV vaccination had not been introduced, a 19% reduction in program costs is predicted under the renewed NCSP. For cohorts offered vaccination, a 26% reduction is predicted under the renewed NCSP. This is equivalent to a cost saving of \$41 million per annum for unvaccinated cohorts and \$50 million per annum for vaccinated cohorts. It should be noted that these cost savings may not be fully realised, since they are predicated on the assumption that there will be an overall reduction in GP visits due to a reduced number of screening visits. In practice, however, these screening

visits may be replaced by routine visits for other conditions with no obvious reduction in costs to the health system.

Since the renewed NCSP is predicted to be both cost saving and life–year saving, it is not possible to calculate an incremental cost-effectiveness ratio compared with the pre-renewal NCSP. Table A.5 shows the disaggregated discounted costs and life–years predicted for the pre-renewal NCSP and the renewed NCSP.

Table A.5. Predicted annual cost of the program and the predicted discounted costs and effects for the pre-renewal NCSP and the renewed NCSP (showing differences in costs and relative percentage differences)

	Pre-renewal NCSP		Renewed NCSP	
	If HPV vaccination had not been introduced	For cohorts offered vaccination as 12 year olds	If HPV vaccination had not been introduced	For cohorts offered vaccination as 12 year olds
Annual cost* of the screening program	\$223 million	\$192 million	\$182 million (–\$41 million; – 19%)	\$142 million (–\$50 million; – 26%)
Discounted costs†	\$383	\$325	\$304	\$227
Discounted life-years†	21.6219	21.6239	21.6229	21.6242

Note: Calculations of the annual cost of the screening program are based on female Australian population as predicted for 2017. †Discounting at 5% per annum starting from 12 years of age.

Conclusion

After incorporating the management recommendations in these guidelines, the renewed NCSP is expected to be even more effective than previously estimated for the MSAC evaluation. After taking into account the impact of vaccination, the effect on colposcopies and treatment rates is expected to be consistent with current levels. The renewed NCSP is also predicted to be both cost saving and life–years saving.

References

1. ↑ ^{1.0 1.1 1.2} Medical Services Advisory Committee. *National Cervical Screening Program renewal: executive summary. Report November 2013. MSAC application no. 1276. Assessment report.* Canberra: Australian Government Department of Health; 2014 Available from: [http://www.cancerscreening.gov.au/internet/screening/publishing.nsf/Content/E6A211A6FFC29E2CCA257CED007FB678/\\$File/Executive%20Summary%20notated%2013.6.14.pdf](http://www.cancerscreening.gov.au/internet/screening/publishing.nsf/Content/E6A211A6FFC29E2CCA257CED007FB678/$File/Executive%20Summary%20notated%2013.6.14.pdf).
2. ↑ Medical Services Advisory Committee. *National Cervical Screening Program renewal: executive summary. Report November 2013. MSAC application no. 1276. Assessment report.* Canberra: Australian Government Department of Health; 2014 Available from: [http://www.cancerscreening.gov.au/internet/screening/publishing.nsf/Content/E6A211A6FFC29E2CCA257CED007FB678/\\$File/Executive%20Summary%20notated%2013.6.14.pdf](http://www.cancerscreening.gov.au/internet/screening/publishing.nsf/Content/E6A211A6FFC29E2CCA257CED007FB678/$File/Executive%20Summary%20notated%2013.6.14.pdf).

APPENDIX B: Guidelines development process

Guidelines: Cervical cancer/Screening/Guidelines development process

Author(s):

- Professor Karen Canfell — Co-author
- Suzanne Hughes — Co-author
- Dr Kate Simms — Co-author
- Associate Professor Megan Smith — Co-author
- Jutta von Dincklage — Co-author
- Cancer Council Australia Cervical Cancer Screening Guidelines Working Party — Co-author

Introduction

The Australian Government Department of Health strategy for reviewing the policy and operation of the National Cervical Screening Program (NCSP) began in November 2011. In April 2014, the Medical Service Advisory Committee (MSAC)^{[1][2]} recommended that a 5-yearly primary human papillomavirus (HPV) test for women aged 25–69 years, including partial genotyping for HPV 16/18 and an exit test between 70 and 74 years of age, should replace the current 2-yearly Pap test for women aged 18–69 years. Some aspects of the management pathway were specified by MSAC, including that:

- women with a positive oncogenic for HPV (16/18) test result should be referred for colposcopy
- reflex liquid-based cytology (LBC) would be performed on all women with a positive oncogenic HPV (any type) test result:
- to inform colposcopy, in the case of a positive oncogenic HPV (16/18) test result
- for triage, in the case of a positive oncogenic HPV (not 16/18) test result.
- women with a positive oncogenic HPV (not 16/18) test result and triage LBC prediction of possible high-grade squamous intraepithelial lesion (pHSIL) or a high-grade squamous intraepithelial lesion (HSIL) would be referred for colposcopy.

Subsequent to the MSAC recommendations, new clinical management guidelines were needed in Australia to:

- support the proposed renewed clinical pathway
- provide guidance for clinicians regarding the follow up of women with a positive screening result
- inform national cervical screening policies and operations
- inform the development of a National Cancer Screening Register
- develop health professional and consumer communications and resources.

The Department of Health commissioned Cancer Council Australia to develop the clinical management guidelines for the prevention of cervical cancer. The project formally commenced in June 2015, funded by the Department of Health.

Guideline development group and guideline scope

Professor Ian Hammond and Associate Professor Marion Saville, who were members of the National Cervical Screening Program Renewal Steering Committee, were appointed as chairs of this guideline project. A multi-disciplinary working party (Cancer Council Australia Cervical Cancer Screening Guidelines Working Party) was established, involving representatives from all relevant specialities and disciplines involved in the diagnosis and management of cervical cancer, including consumer representatives.

Declarations of interests were collated from all nominated individuals and evaluated prior to the first working party meeting. Management of competing interests describes the process and provides the complete Conflict of interest register, including evaluation outcomes. All working party members were advised to forward any further updates to their declarations of interest, in line with the Code of practice for dealing with conflict of interests.^[3] Any updates were forwarded for evaluation and the register updated accordingly.

A project team based at Cancer Council Australia was responsible for project governance and management. A technical project team based at Cancer Council NSW conducted the systematic reviews, literature reviews and modelling required for this project. The technical team was also responsible for liaising with the working party members in regards to content development, content drafting and compiling the Appendix D. Technical report.

The clinical practice guidelines were developed according to the procedures and requirements for meeting the 2011 NHMRC standard for clinical practice guidelines.^[4] The development program was designed to meet the scientific rigour required by the standard for developing high-quality, evidence-based clinical practice guidelines. A series of NHMRC resources and handbooks^{[5][6][7][8][9][10][11][12][13]} guided the process and outlined the major steps and expectations involved in developing guidelines. These documents provided the definitions and protocols for developing research questions and search strategies, conducting systematic literature reviews, summarising and assessing the relevant literature and finally, formulating and grading the recommendations. They also included checklists and templates created to satisfy designated standards of quality and process.

At an initial teleconference meeting, the working party confirmed the scope of the guidelines and the clinical questions to be included. The aim was to revise the *2005 NSCP guideline Screening to prevent cervical cancer: guidelines for the management of asymptomatic women with screen detected abnormalities*.^[14] The clinical questions addressed areas of uncertainty and clinical scenarios that required reconsideration as a result of the renewed NCSP. For completeness, MSAC recommendations and relevant NHMRC-approved 2005 recommendations^[14] considered to be unaffected by the renewed National Cervical Screening Program were included. The method by which each recommendation was developed is identified in the guidelines (see Assessing the body of evidence and formulating recommendations).

The included clinical questions, as well as additional topics such as cervical cancer epidemiology and terminology, were allocated to specific working party members to act as lead author teams according to their areas of expertise.

Steps in preparing clinical practice guidelines to NHMRC criteria

The evidence underpinning the recommendations has been synthesised from systematic reviews of the literature and generated from modelling analyses for those aspects of clinical management involved in the pathway to colposcopy that constitute major changes to the NCSP. During the first working Party meeting it was agreed that certain 2005 NHMRC-approved guidelines sections remained valid, whereas others required review. For those requiring review, systematic reviews were undertaken to identify relevant evidence where new recommendations were anticipated, and general literature reviews were conducted when no significant changes were considered likely and it was anticipated that only additional practice points might be required. Based on the available evidence, the 2005 NHMRC-approved guidelines^[14] have been combined with current revisions in this document to provide comprehensive recommendations for management.

For every clinical question the below steps were followed:

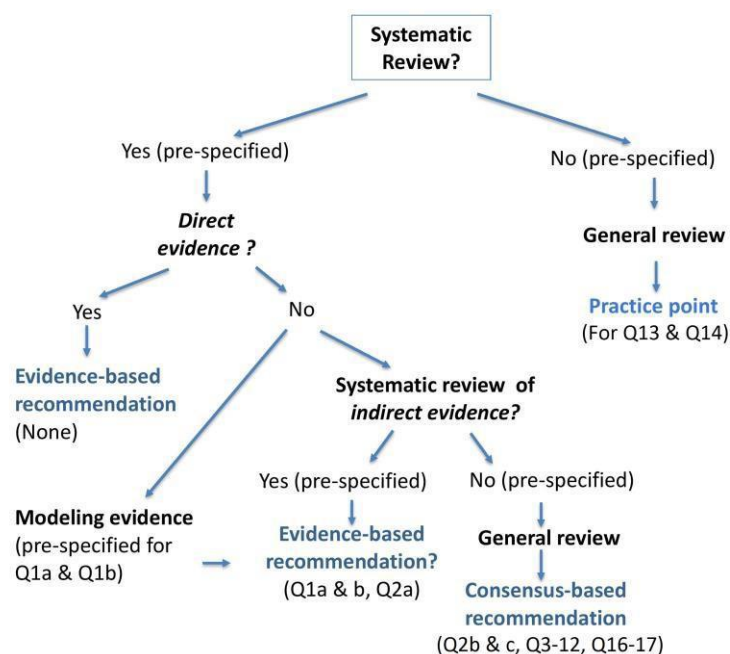
1. A structured clinical question in PICO format (population, intervention, comparator, outcomes) was developed by the working party.
2. For each question, a systematic or general literature review was undertaken as outlined in Figure B.1.

Systematic reviews were undertaken for most questions, as the aim was to develop evidence-based recommendations if the evidence permitted. As the systematic reviews were addressing questions concerned with the management flow-on effects of new screening tests, it was anticipated that there may be limited, if any evidence, available directly addressing many of the questions.

The working party determined, *a priori*, that in the event that a systematic review found no evidence directly addressing a PICO question, a general literature review was to be undertaken to inform the drafting of consensus-based recommendations, with the exception of three questions. For these three questions it was planned that the systematic reviews would be extended to include evidence that indirectly addressed the question and that modelling analyses would also be used to provide evidence for two of these questions.

For two questions clinical questions the working party did not anticipate that the NHMRC approved 2005 recommendations would be significantly impacted by the renewed National Cervical Screening Program and as a result determined a priori that only general reviews were to be undertaken to inform the drafting of additional practice points.

Figure B.1. Review process



3. All systematic reviews and modelling analyses were documented in a Technical report and the results of each general review were summarised in a review summary.

4. Where available, the body of evidence for each systematic review and/or modelling analysis were assessed and recommendations and practice points formulated following the NHMRC process and recommendation categories.

Where no evidence was found directly addressing a clinical question, a general review of the literature was considered when drafting consensus-based recommendations or practice points.

Where a systematic review was not undertaken a general review of the literature was considered when drafting practice points.

Adapted MSAC recommendations and consensus-based recommendations based on the 2005 NCSP guidelines are clearly identified.

5. Content narrative was developed based on the findings of the reviews.

Developing a structured clinical question

All proposed questions were reviewed on the basis of their purpose, scope and clinical importance to the target audience and those requiring systematic reviews were structured according to the PICO (populations, interventions, comparisons, outcomes) framework (see [Appendix C. Clinical question list](#)).

Systematic reviews and modelling analyses

Each question that was addressed by a systematic review and/or modelling analyses is accompanied by a detailed Technical report.

Search for existing relevant guidelines and systematic reviews

Relevant recent (2005 onwards) guidelines were identified by scanning the citations identified by the literature search, searching the National Guideline Clearinghouse and the Guidelines Resource Centre and, in the case of guidelines for screening immune-deficient women, consulting experts in that field.

To be considered for adoption, guidelines had to be directly relevant, based on systematic reviews of the evidence and meet the pre-specified criteria of scores of greater or equal to 70% for the domains rigour of development, clarity of presentation and editorial independence of the AGREE II instrument.

No existing clinical practice guidelines suitable for adoption were identified.

Developing a search strategy for systematic reviews

For each PICO question, literature search strategies were developed and conducted by the technical team. Most searches included terms for HPV and were limited or widened as necessary according to the PICO question. Search strategies were designed to maximise sensitivity and used both text terms and subject headings for each included electronic database. The following electronic databases were searched for articles published from 2004 until 31st August 2015:

- *Medline* – bibliographic references and abstracts to articles in a range of languages on topics such as clinical medical information and biomedicine, and including the allied health fields, biological and physical sciences
- *EMBASE* – major pharmacological and biomedical database indexing drug information from 4550 journals published in 70 countries
- *Cochrane Central Register of Controlled Trials (CENTRAL)* – contains references to controlled trials in health care
- *Database of Abstracts of Reviews of Effects* – contains details of systematic reviews that evaluate the effects of healthcare interventions and the delivery and organisation of health services
- *Health Technology Assessment* – details on ongoing and completed health technology assessments (studies of the medical, social, ethical, and economic implications of healthcare interventions).
- *The Cochrane Database of Systematic Reviews* – contains systematic reviews of primary research in human health care and health policy, and are internationally recognised as the highest standard in evidence-based health care.

A search filter to retrieve relevant literature considering Aboriginal and Torres Strait Islander peoples was added to each question.

The reference lists of all identified articles were checked for additional potentially relevant articles. The systematic literature search strategies for each PICO question are documented in the Technical report for of each question (see [Appendix D. Technical report](#)).

Screening of literature results for systematic reviews

All retrieved literature results were screened against pre-specified inclusion and exclusion criteria specific for each question (see [Appendix D. Technical report](#)) in two stages:

- a) First screen: the titles and abstracts of all retrieved literature were screened and only potentially relevant citations were retained.
- b) Second screen: the full text of each remaining citation was assessed against the pre-specified inclusion and exclusion criteria for that question. Articles that met the inclusion criteria were included in the systematic review. The retrieved articles that were not included and the reason for their exclusion were documented and are included in the technical reports (see [Appendix D. Technical report](#)).

Critical appraisal and data extraction of each included article in systematic reviews

For each included study, two assessors independently assessed the risk of bias using a study design specific assessment tool and where necessary pre-specified criteria. Any disagreements were adjudicated by a third reviewer.

The characteristics of the study and the relevant data was extracted and summarised in study characteristics and results tables. Each data extraction was checked by a second assessor.

These tables are included in [Appendix D. Technical report](#)).

Summary of the relevant evidence in systematic reviews

For each outcome examined, the results, level of the evidence according to NHMRC levels (Table B.1), the risk of bias due to study design, and the relevance of the evidence for each included study were documented in a body of evidence table in the Technical report for that question.

Table B.1. Designations of levels of evidence according to type of research question (NHMRC, 2009)

Level	Intervention	Diagnosis	Prognosis	Aetiology	Screening
I	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies	A systematic review of	A systematic review of level II studies

				level II studies	
II	A randomised controlled trial	A study of test accuracy with: an independent, blinded comparison with a valid reference standard, among consecutive patients with a defined clinical presentation	A prospective cohort study	A prospective cohort study	A randomised controlled trial
III-1	A pseudo-randomised controlled trial (i.e. alternate allocation or some other method)	A study of test accuracy with: an independent, blinded comparison with a valid reference standard, among non-consecutive patients with a defined clinical presentation	All or none	All or none	A pseudo-randomised controlled trial (i.e. alternate allocation or some other method)
III-2	<p>A comparative study with concurrent controls:</p> <p>Non-randomised, experimental trial</p> <p>Cohort study</p> <p>Case-control study</p> <p>Interrupted time series with a control group</p>	A comparison with reference standard that does not meet the criteria required for Level II and III-1 evidence	Analysis of prognostic factors amongst untreated control patients in a randomised controlled trial	A retrospective cohort study	<p>A comparative study with concurrent controls:</p> <p>Non-randomised, experimental trial</p> <p>Cohort study</p> <p>Case-control study</p>

III-3	<p>A comparative study without concurrent controls:</p> <p>Historical control study</p> <p>Two or more single arm study</p> <p>Interrupted time series without a parallel control group</p>	Diagnostic case-control study	A retrospective cohort study	A case-control study	<p>A comparative study without concurrent controls:</p> <p>Historical control study</p> <p>Two or more single arm study</p>
IV	Case series with either post-test or pre-test/post-test outcomes	Study of diagnostic yield (no reference standard)	Case series, or cohort study of patients at different stages of disease	A cross-sectional study	Case series

Source: National Health and Medical Research Council. NHMRC additional levels of evidence and grades for recommendations for developers of guidelines. Canberra: NHMRC; 2009. (https://www.nhmrc.gov.au/files/nhmrc/file/guidelines/developers/nhmrc_levels_grades_evidence_120423.pdf)

Modelling analyses

Modelling analyses were planned a priori to address two of the clinical questions which related to the management of women in whom HPV types 16 and/or 18 are not detected, but with a positive oncogenic HPV (not 16/18) test result. Clinical tests that allow partial genotyping for HPV 16/18 are comparatively new, and the overwhelming majority of trials of HPV-based screening used earlier clinical tests which did not specifically identify whether or not HPV types 16 and/or 18 were identified.

One clinical trial (ATHENA)^[15] compared cytology-based screening with a clinical HPV test which that provided partial genotyping, but however it did not randomise women with a positive oncogenic for non-16/18 HPV types (not 16/18) test result to different kinds of management. A second clinical trial (Compass) was underway in Australia at the time this guideline was commissioned^[16]; while directly relevant, longitudinal data were not yet available from this trial to address these clinical questions. Therefore, it was thought very likely that the systematic review

would not identify any studies that could directly answer the question of how to manage women with a positive oncogenic HPV (not 16/18) test result.

It was also considered a priori that management of these women could not be informed by trials that reported outcomes in women with a positive oncogenic HPV (any type) test result, because their underlying risk would certainly be higher than, and not comparable to, the risk in women in whom HPV 16/18 was not detected but with a positive oncogenic HPV (not 16/18) test result. This consideration was made because the risk associated with HPV 16/18 is known to be far greater than that for other HPV types, and HPV 16/18 also generally make up a high proportion of infections among women with a positive oncogenic HPV (any type) test result, and thus would strongly influence the overall risk in that group.

Modelled analyses were undertaken using a simulation model that had previously been used in the effectiveness and economic evaluation of the proposed changes to the NCSP performed for MSAC.^[17] As part of the evaluation for MSAC, this model had been customised to include detailed modelling of both the pre-renewal NCSP in Australia, and of the proposed changes. It included detailed local data on screening behaviour, screening test performance calibrated to fit observed Australian pathology data, and detailed clinical management pathways informed by an expert advisory group, the Renewal Steering Committee (RSC). Model predictions for age-specific endpoints, such as cervical cancer incidence and mortality, and rates of screen-detected abnormalities, were consistent with observed Australian data. The detailed model of cervical cancer screening, diagnosis and cancer treatment and survival in Australia was overlaid on a natural history model which had been developed over the course of a decade. The natural history model had been validated to observed data in many settings when an appropriate setting-specific screening models were overlaid. The model also has a dynamic HPV transmission component, which allowed the impact of the National HPV Vaccination Program (NHVP) to be taken into account, including both direct and indirect effects (herd protection). The HPV transmission model has also been validated against observed reductions in HPV infections since the inception of the NHVP.^[18] All model assumptions had been previously reviewed by the RSC, the Economic Subcommittee of MSAC and MSAC itself.

There are no NHMRC levels of evidence for modelling studies.

Assessing the body of evidence and formulating recommendations

The working party participated in a face-to-face meeting at which the technical team presented the preliminary findings of the systematic reviews, general literature searches, and modelling analyses.

For clinical questions for which there was evidence from systematic reviews, the author teams, in collaboration with the technical team, assessed the volume of the evidence, its consistency, clinical impact, generalisability and applicability, and developed evidence statements (see [Appendix D. Technical report](#)) as documented in the NHMRC Evidence Statement. This process is described in NHMRC's *Additional levels of evidence and grades for recommendations for developers of guidelines* (2009).^[19]

Following grading of the evidence and development of evidence statements, expert authors formulated evidence-based recommendations and determined a grade (Table B.2, Table B.3).

Where a systematic review yielded insufficient evidence on which to base an evidence-based recommendation, the expert authors drafted consensus-based recommendations (Table B.4). Practice points, on topics outside the scope of the clinical questions, were developed to support recommendations, as necessary.

This guideline also includes recommendations developed outside the wording group process (Table B.5):

- evidence-based recommendations by MSAC, based on systematic reviews undertaken during the NCSP renewal process,^{[1][2]} labelled as MSAC evidence-based recommendations
- recommendations determined by NCSP policy^[20]
- consensus-based recommendations modified from pre-renewal NCSP guidelines (2005).^[14]

Table B.2. Grading of recommendations

Component of Recommendation	Recommendation Grade			
	A	B	C	D
	Excellent	Good	Satisfactory	Poor
Volume of evidence ^{1**}	One or more level I studies with a low risk of bias or several level II studies with a low risk of bias	One or two level II studies with a low risk of bias or a systematic review/several level III studies with a low risk of bias	One or two level III studies with a low risk of bias, or level I or II studies with a moderate risk of bias	Level IV studies, or level I to III studies/systematic reviews with a high risk of bias
Consistency ^{2**}	All studies consistent	Most studies consistent and inconsistency may be explained	Some inconsistency reflecting genuine uncertainty around clinical question	Evidence is inconsistent
Clinical impact	Very large	Substantial	Moderate	Slight or restricted
Generalisability	Population/s studied in body of evidence are the same as the target	Population/s studied in the body of evidence are similar to the target	Population/s studied in body of evidence differ to target population for guideline but it	Population/s studied in body of evidence different to target population and hard to judge whether it is sensible to

	population for the guideline	population for the guideline	is clinically sensible to apply this evidence to target population ³	generalise to target population
Applicability	Directly applicable to Australian healthcare context	Applicable to Australian healthcare context with few caveats	Probably applicable to Australian healthcare context with some caveats	Not applicable to Australian healthcare context

¹ Level of evidence determined from level of evidence criteria

² If there is only one study, rank this component as 'not applicable'

³ For example results in adults that are clinically sensible to apply children OR psychosocial outcomes for one cancer that may be applicable to patients with another cancer.

**For a recommendation to be graded A or B, the volume and consistency of evidence must also be graded either A or B!

Source: National Health and Medical Research Council. *NHMRC additional levels of evidence and grades for recommendations for developers of guidelines*. Canberra: NHMRC; 2009. (https://www.nhmrc.gov.au/files/nhmrc/file/guidelines/developers/nhmrc_levels_grades_evidence_120423.pdf)

Table B.3. Overall recommendation grades

Grade of recommendation	Description
A	Body of evidence can be trusted to guide practice
B	Body of evidence can be trusted to guide practice in most situations
C	Body of evidence provides some support for recommendation(s) but care should be taken in its application
D	Body of evidence is weak and recommendation must be applied with caution

Source: National Health and Medical Research Council. *NHMRC levels of evidence and grades for recommendations for developers of guidelines*. Canberra: NHMRC; 2009. (https://www.nhmrc.gov.au/files/nhmrc/file/guidelines/developers/nhmrc_levels_grades_evidence_120423.pdf)

Table B.4. NHMRC approved recommendation types and definitions

Type of recommendation	Definition
Evidence-based recommendation	A recommendation formulated after a systematic review of the evidence, indicating supporting references
Consensus-based recommendation	A recommendation formulated in the absence of quality evidence, after a systematic review of the evidence was conducted and failed to identify admissible evidence on the clinical question
Practice point	A recommendation on a subject that is outside the scope of the search strategy for the systematic review, based on expert opinion and formulated by a consensus process

Source: National Health and Medical Research Council. Procedures and requirements for meeting the NHMRC standard for clinical practice guidelines. Melbourne: National Health and Medical Research Council, 2011

Table B.5. Key to types of recommendations in these guidelines

Type	Source	Description [#]
Evidence-based recommendation	Developed for this guideline	Recommendations formulated by the guideline development group based on a systematic review of quality evidence and graded according to an NHMRC-approved method
MSAC evidence-based recommendation	Developed by MSAC from MSAC-commissioned evaluation	Evidence-based recommendation from MSAC review
Policy recommendation	Determined by NCSP policy	Recommendations based on NCSP policy
Consensus-based recommendation	Developed for this guideline	Recommendations formulated by the guideline development group, using a using a consensus-reaching process, when a systematic review was undertaken and insufficient quality evidence was found on which to base a recommendation

Consensus-based recommendation	Adopted/modified from pre-renewal NCSP guidelines	Recommendations based on 2005 NHMRC-approved guidelines formulated by the guideline development group, using a consensus-reaching process
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#When viewed online, the description for each recommendation appears when the reader places the cursor over the question mark symbol in the recommendation heading.

General literature reviews

General reviews were undertaken to support the drafting of:

- consensus-based recommendations in the absence of evidence directly addressing the PICO question
- practice points.

The general reviews are documented in review summaries. The review summary for each question contains a summary of:

- potentially relevant guidelines, including the relevant 2005 NHMRC-approved guidelines.
- literature searches– undertaken using the Medline and Embase databases and designed to maximise specificity
- key characteristics and results of the most relevant studies identified.

The technical team presented their preliminary findings at a face-to-face meeting of the working party. Consensus-based recommendations and practice points were drafted by the lead authors, based on a consideration of any relevant evidence and expert opinion. These were then presented to the working party for consideration.

Writing the content

Guideline chapters were drafted using the following format:

- general introduction to the clinical question
- background to the clinical question, including its clinical importance and historical evidence, where relevant
- review of the evidence including, for systematic review evidence, the number, quality and findings of studies identified by the systematic review
- evidence statements for systematic reviews and modelling analyses in tabular form including levels of evidence and references for studies included in the systematic review,
- evidence-based recommendation(s) and corresponding grade(s), consensus-based recommendations and practice points
- implications for implementation of the recommendations where applicable, including possible effects on usual care, organisation of care, and any resource implications
- discussion, including unresolved issues, relevant studies currently underway, and future research priorities
- references.

The content draft was then reviewed by all working party members. The draft documents underwent several iterations until agreement on these drafts was reached.

Review of the draft chapters

All draft chapters were circulated to the working party. The whole group was asked to review the content and submit feedback. Members were asked to submit further suggestions on consensus-based recommendations and practice points.

A face-to-face meeting with all working party members was held to review and finalise the draft guidelines for public consultation. Prior to this meeting, the latest iteration draft guidelines were circulated via the wiki. All working party members were asked to review the content, individual recommendations and practice points in detail, and to identify and note any controversies and points to be discussed at the group meeting.

During the meeting, each recommendation and practice point was tabled as an agenda item. Each was reviewed and approved by consensus, which was reached by voting. The working party Chairperson nominated a particular recommendation/practice point to be reviewed and the panellists had the opportunity to discuss any issues and suggest revisions to recommendations and practice points. Each recommendation and practice point was approved once consensus was reached by the eligible panellists (excluding representatives of the funding bodies and any panellists who could not participate due to conflict of interest).

Public consultation

A complete draft of the guideline was sent out for public consultation from 15 February to 15 March 2016. Submissions were invited from the general public, professional societies and groups, and other relevant stakeholders. Relevant professional societies and groups, consumer groups and other relevant stakeholders were contacted.

All feedback on the draft received during the consultation period in Australia was compiled and sent to the relevant author team to review their draft content, assessing and considering the submitted comments. Each additional paper submitted during public consultation was assessed by the methodologist team against the review protocol.

All public consultation comments and suggested amendments were considered at a face-to-face meeting of the working party on 1 April 2016. Subsequent changes to the draft were agreed by consensus, based on consideration of the evidence and, in the absence of evidence, expert opinion. The consensus process was similar to that followed during earlier face-to-face working party meetings.

Organisations endorsing the guidelines

The following medical colleges and professional bodies endorse these guideline:

- The Royal Australian College of General Practitioners (RACGP)
- The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG)
- The Royal College of Pathologists of Australasia (RCPA)
- Australian Society for Colposcopy and Cervical Pathology (ASCCP)

- Australian Society of Gynaecologic Oncologists (ASGO).

Dissemination and implementation

A multi-strategy approach will be followed for the dissemination and implementation of the guideline, as this has shown to positively influence guideline uptake.^{[21] [22]}

This will include a campaign to raise awareness of the new guidelines that incorporates organised media coverage through multiple outlets. The guidelines will be distributed directly to relevant professional and other interested groups and through meetings, national and international conferences, and other professional development and continuing medical education (CME) events. Local expert leaders will be identified and approached to facilitate dissemination and act as champions for the guidelines.

A significant effort will be made to have the guidelines introduced to senior undergraduate medical students and to encourage the relevant learned colleges to support the guidelines and to foster their integration into hospital and community practice through resident and registrar education activities.

The guidelines will be made available as an online guideline via the Cancer Council Australia Cancer Guidelines Wiki. The online guideline version increases availability as well as accessibility, and usage will be tracked and analysed with a web analytics solution. Interlinking and listing the guidelines on national and international guideline portal is an important part of the digital dissemination strategy. Important Australian health websites, such as EviQ and healthdirect Australia will be approached to link to the online guideline. The guideline will also to be listed on national and international guideline portals such as Australia's Clinical Practice Guidelines Portal, Guidelines International Network guidelines library and National Guidelines Clearinghouse. The Cancer Guidelines Wiki is a responsive website that is optimised for mobile and desktop access.

As part of the online guideline, an online learning module will be developed to reinforce the guidelines content knowledge for participants, thus support guideline implementation and uptake.

The Cancer Guidelines Wiki is based on semantic web technology, so the guidelines are available in a machine-readable format, which offers the possibility to easily integrate the guideline content with systems and web applications used in the Australian healthcare context. Use of the guidelines as part of core curriculum in specialty exams will be encouraged.

As the guidelines form part of the renewed National Cervical Screening Program, additional promotion and awareness of the guidelines will be incorporated into the overarching program communication activities for health professionals, pathologists and consumers in the lead up to 1 December 2017 and post implementation.

It is recognised that a planned approach is necessary to overcome specific barriers to implementation in particular settings and to identify appropriate incentives to encourage uptake of guideline recommendations. Implementation of the guidelines will require a combination of effective strategies and may include further CME initiatives and interactive learning, the development and promotion of computer-assisted decision aids and electronic decision-support systems, and the creation of audit and other clinical tools.

Future updates

The incoming literature updates will continue to be monitored for each review question. If there is strong evidence emerging in a specific area, even if not considered previously, the Cancer Council Australia Cervical Cancer Screening Guidelines Working Party will be reconvened to assess if this evidence warrants further systematic review(s) and updating of recommendations.

It is recommended that these guidelines should be updated within 5 years.

Review of National Cervical Screening Program data – 2020 partial update

In March 2020, the NCSP Clinical Expert Panel (CEP) proposed a recommendation change to the Quality Safety Monitoring Committee (QSMC) for the clinical management of women following an Intermediate Risk result (HPV non 16/18 positive with reflex LBC prediction negative, pLSIL or LSIL).

Under the 2016 guideline recommendation, these women are recommended to be re-tested at 12 months and managed as higher risk and referred to colposcopy if any HPV is detected in their follow-up test. This recommendation has resulted in large numbers of women being referred for colposcopy as the proportion of women with persistent infection is higher than predicted.

QSMC members reviewed national data provided by the National Cancer Screening Register from the first two years of the renewal, this review was used to draft an update of the guidance within section 6. Management of oncogenic HPV test results.

To follow the same processes as the 2016 guideline revision, the working party was convened to review the updated content and NCSP data (see: 2020 Working party members and contributors). Professor Ian Hammond having since retired from clinical practice stepped down as guideline Chair, Professor Marion Saville, former deputy Chair was nominated by Professor Hammond and members of the NCSP and invited by CCA to Chair this partial update of the guideline. Members of the working party were also asked to review their declarations of competing interests and update their details.

The updated content was reviewed by the guideline working party early July 2020 and prepared for a 10-day period of public consultation at the end of August 2020.

Public consultation – 2020

Two updated, draft sections of the guideline, HPV oncogenic types not 16/18 and Self-collected vaginal samples, were released for a 10-day public consultation between 20–30 August 2020. The updated sections were made available for download from 18 Dec 2020 with clear guidance that the change in management and new recommendations were from 1 Feb 2021, this was to allow time for any preparatory activities.

Further information about public consultation can be found here: [Public consultation information](#).

The two sections noted above were revised in response to public consultation comments and all agreed amendments are documented in the Register of public consultation submissions.

Update to support policy change to expand access to self-collection – 2022 partial update

In April 2021, the Medical Services Advisory Committee supported an application to expand access to self-collection to include everyone eligible for cervical screening, giving all eligible people a choice in how their screening sample is collected [23]. The change in policy was announced in late 2021 and scheduled to come into effect on 1 July 2022[24].

In 2021, a review of guidelines content was undertaken by Professor Marion Saville (guidelines Working Party Chair), the NCSP Clinical Expert Panel (CEP), and the Department of Health to identify sections which needed to be updated to support the self-collection policy change. Minor additional changes were also recommended by the CEP: updates for clarification in some sections related to colposcopy, and updates to the chapter on signs and symptoms, to reflect updated RANZCOG advice [25].

The Department of Health commissioned Cancer Council Australia to update the clinical management guidelines, based on the review by the guidelines Working Party Chair and CEP. The project formally commenced in November 2021, funded by the Department of Health. A project team based at Cancer Council Australia was responsible for project governance and a technical project team based at the Daffodil Centre (University of Sydney, a joint venture with Cancer Council NSW) conducted literature reviews and drafted content updates in collaboration with the Working Party (see: 2022 Working party members and contributors). Professor Marion Saville, Working Party Chair for the 2020 partial update to the guidelines, acted as Chair for this partial update of the guideline. Some members of the original 2016 Working Party were not available to participate and new members were included in the Working Party. Members of the Working Party were asked to review or provide their declarations of competing interests and their details.

Guidelines updates were discussed with the Working Party on 4 November 2021. Updated content was reviewed by the guideline working party in mid November 2021, and prepared for a 14-day period of public consultation starting from 22 November 2021.

Public consultation – 2021

Five updated, draft guideline chapters (Chapter 3 – Terminology, Chapter 6 – Management of Oncogenic HPV test result, Chapter 7 – Colposcopy, Chapter 12 – Screening in Aboriginal and Torres Strait Islander women)) were released for a 15-day public consultation between 22 November – 7 December 2021. Relevant professional societies and groups, consumer groups and other relevant stakeholders were contacted shortly prior to 22 November, then again once the draft updates were open for public consultation.

All feedback on the draft updates received during the consultation period in Australia was compiled and sent to the Working Party and Technical Team. Public consultation comments and suggested amendments were considered at a Working Party meeting on 9 December 2021. Subsequent changes to the public consultation draft were agreed by consensus, based on consideration of the evidence and, in the absence of evidence, expert opinion. Based on the decisions in this meeting, an updated draft of the guidelines affected by the partial update were re-circulated to the Working Party for feedback between 23 December 2021 and 17 January 2022.

Updates to the section Signs and symptoms of cervical cancer were reviewed by the CEP.

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The development of this guideline was funded by the Department of Health. The views of the funding body have not influenced the content of the guideline.

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APPENDIX C: CLINICAL QUESTIONS LIST

Clinical question list

Questions 1

Relevant guidelines content page: [Oncogenic HPV types not 16/18](#)

Question 1a

Primary PICO

For women who are positive for hr-HPV types other than 16 or 18 and have pLSIL/dLSIL reflex liquid based cytology (intermediate risk), what is the safety and effectiveness of immediate colposcopy compared to colposcopy delayed by 12 months based on later HPV test results (assuming referral to colposcopy if any HPV positive at 12 months)?

Population	Study design	Intervention	Control	Outcomes
Women who are positive for hr-HPV types other than 16 or 18 and have pLSIL/dLSIL (ASC-US/LSIL) liquid based cytology (intermediate risk)	Randomised or pseudo randomized controlled trial	Immediate Colposcopy	Repeat HPV test in 12 months; Colposcopy if positive	Cervical cancer Cervical dysplasia Prevalence of lesions

Secondary PICO (In the event that no randomised or pseudo-randomised controlled trials were identified that directly addressed the primary PICO)

For women undergoing routine cervical screening what is the risk of CIN3+ for women who are positive for HPV oncogenic types other than 16 and 18 and have p/dLSIL cytology compared with women who have p/d LSIL cytology regardless of HPV status, p/dHSIL cytology regardless of HPV status, or are HPV 16/18+ regardless of cytology?

Population	Study design	Exposure	Control
Women undergoing routine cervical screening	Longitudinal or cross-sectional prognostic	Positive for HPV oncogenic types other than 16 and 18 and have p/dLSIL cytology	p/ p/ H 16

Question 1b

Primary PICO

For women who are positive for hr-HPV types other than 16 or 18 and have negative or pLSIL/dLSIL reflex liquid based cytology (intermediate risk), what is the safety and effectiveness of repeating HPV testing in 12 and 24 months compared to repeating HPV test at 12 months only before returning to 5 yearly screening?

Population	Study design	Intervention	Control
Women who are positive for hr-HPV types other than 16 or 18 and have negative or pLSIL/dLSIL (ASC-US/LSIL) liquid based cytology (intermediate risk)	Randomized or pseudo randomized controlled trial	Repeat HPV test in 12 and 24 months; Colposcopy and reflex LBC if positive or if both negative discharge back to screening	Repeat HPV test in 12 months; Colposcopy if positive and if negative discharge to screening

Secondary PICO (In the event that no randomised or pseudo-randomised controlled trials were identified that directly addressed the primary PICO)

For women undergoing routine cervical screening what is the risk of subsequent CIN3+ for women who are positive for HPV oncogenic types other than 16 and 18 and have negative cytology compared with women who have p/d LSIL regardless of HPV status or who have p/d LSIL and are positive for HPV oncogenic types other than 16 and 18?

Population	Study design	Exposure	Comparator
Women undergoing routine cervical screening	Longitudinal prognostic	Positive for HPV oncogenic types other than 16 and 18 and have NILM cytology	p/dLSIL or positive for HPV oncogenic types other than 16 and 18 and have p/dLSIL cytology

Questions 2

Relevant guidelines content page: [Normal colposcopic findings following LBC prediction of LSIL or HSIL](#)

Question 2a

Primacy PICO

For HPV positive women who are not in treatment follow-up and who have negative or LSIL cytology and who have undergone colposcopy and the colposcopy was negative, what is the safety and effectiveness of testing with repeat HPV test at 12 months when compared with repeat cytology and HPV testing in 12 months?

Population	Study design	Intervention	Control
HPV positive women who have undergone colposcopy and the colposcopy was negative and cytology was: i. negative,	Randomized or pseudo randomized controlled trial	Repeat HPV test at 12 months; Colposcopy (and reflex LBC test) if positive	Repeat cytology and HPV testing at 12 months: Colposcopy if HPV positive test or if cytology pHSIL or worse, and another 12 months follow-up if HPV negative p/dLSIL; repeat HPV and cytology test in 12 months if HPV negative and cytology p/dLSIL or negative

ii. p/d LSIL		If negative HPV test in 12 months	
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Secondary PICO (In the event that no randomised or pseudo-randomised controlled trials were identified that directly addressed the primary PICO)

For HPV positive women who are not in treatment follow-up and who have negative or p/dLSIL cytology on referral and who had colposcopy and the colposcopy was negative what are the predictors of subsequent detection of high-grade disease?

Population	Study design	Exposure	Comparator	Outcomes
Women who have p/dLSIL or negative cytology who have undergone colposcopy and no abnormalities were seen on colposcopy	Cohort	Referral cytology Referral HPV status Age	Other Referral cytology Referral HPV status Age	Cervical Cervical Precancer lesion de

Question 2b

For women who are HPV positive with p/dHSIL referral cytology and p/dLSIL or less after cytologic review and colposcopy is negative, what is the safety and effectiveness of conservative management compared with excision of the transformation zone?

Population	Study design	Intervention	Control	Outcomes
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HPV positive women who have undergone colposcopy and the colposcopy was negative and referral cytology was p/d HSIL and review cytology was p/d LSIL or less	Randomized or pseudo randomized controlled trial	Conservative management	Excision of the transformation zone	C m C di Pr gr
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dHSIL = definite HSIL; dLSIL = definite LSIL; HSIL = high-grade squamous intraepithelial lesion; LSIL = low-grade squamous intraepithelial lesion pHSIL = possible HSIL; pLSIL = possible LSIL

Question 2c

For women who are HPV positive with p/dHSIL referral cytology and p/dHSIL after cytologic review and colposcopy is negative, what is the safety and effectiveness of cytologic and colposcopic follow-up at 3-6 months compared with excision of the transformation zone?

Population	Study design	Intervention	Control	O
HPV positive women who have undergone colposcopy and the colposcopy was negative and referral and review cytology was p/d HSIL	Randomized or pseudo randomized controlled trial	Conservative management; cytologic and colposcopic follow-up at 3-6 months	Excision of the transformation zone	C m C d P g

dHSIL = definite HSIL; HSIL = high-grade squamous intraepithelial lesion; pHSIL = possible HSIL

Questions 3

Relevant guidelines content page: [Type 3 TZ \(previously termed 'unsatisfactory'\) colposcopy following LBC prediction of LSIL or HSIL](#)

Question 3a

For HPV positive women currently not in treatment follow-up and have negative or LSIL cytology who have undergone colposcopy and the colposcopy was unsatisfactory what is the safety and effectiveness of repeat HPV test at 12 months compared with repeat cytology and HPV testing in 12 months?

Population	Study design	Intervention	Control
HPV positive women who have undergone colposcopy and the colposcopy was unsatisfactory and cytology was: i. negative, ii. p/d LSIL	Randomized or pseudo randomized controlled trial	Repeat HPV test at 12 months; Colposcopy (and reflex LBC test) if positive and if negative HPV test in 12 months	Repeat cytology and HPV testing at 12 month; Colposcopy if HPV positive test or if cytology pHSIL or worse, and another 12 months follow-up if HPV negative p/dLSIL; repeat HPV and cytology test in 12 months if HPV negative and cytology p/dLSIL or negative

Question 3b

For HPV-positive women with a referral cytology finding of p/dHSIL and who have an unsatisfactory colposcopy, what is the safety and effectiveness of conservative management compared with diagnostic excision of the transformation zone?

Population	Study design	Intervention	Control	Outcomes
HPV positive women who have undergone colposcopy and the colposcopy was unsatisfactory and cytology was:	Randomized or pseudo-randomized controlled trial	Conservative management: Co-testing at 3-6 months or repeat HPV test at 12 months	Diagnostic excision of the transformation zone	Cervical intraepithelial neoplasia Cervical dysplasia Cervical cancer

p/d HSIL				Pre gra
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dHSIL = definite HSIL; HSIL = high-grade squamous intraepithelial lesion; pHSIL = possible HSIL

Question 4

Relevant guidelines content page [Chapter 9. Management of histologically confirmed low-grade squamous abnormalities](#)

For HPV positive women currently not in treatment follow-up who have undergone colposcopy (without treatment) with colposcopy LSIL and CIN 1 or less on biopsy what is the safety and effectiveness of excisional treatment or testing with repeat HPV test at 12 months when compared with repeat cytology and HPV testing in 12 months?

Population	Study design	Intervention	Control	Outcomes
HPV positive women, who have undergone colposcopy and colposcopy LSIL, confirmed by biopsy CIN1 or less, and referral cytology was: i. negative or p/d LSIL or ii. p/dHSIL	Randomized or pseudo randomized controlled trial	Excisional treatment or Repeat HPV test at 12 months	i. Negative cytology or p/dLSIL: Repeat cytology and HPV testing at 12 months: Colposcopy if HPV positive test or if cytology pHSIL or worse, and another 12 months follow-up if HPV negative p/dLSIL; repeat HPV and cytology test in 12 months if HPV negative and cytology p/dLSIL or negative ii. p/dHSIL: repeat cytology and colposcopy in 6 months	Cervical cancer mortality Cervical cancer diagnosis Precancerous high grade lesi

Questions 5

Relevant guidelines content page: [Investigation of cytological glandular abnormalities](#)

Question 5a

For women who are HPV positive with atypical endocervical cells of undetermined significance (confirmed on review) and negative colposcopy what is the safety and effectiveness of repeating HPV and cytology testing when compared with treatment with excisional cone biopsy?

Population	Study design	Intervention	Control	Outcomes
Women who are HPV positive with atypical endocervical cells of undetermined significance (confirmed on review) and colposcopy negative	Randomized or pseudo randomized controlled trial	Repeat HPV and liquid based cytology testing at 6 months	Excisional cone biopsy cervix	Cervical cancer mortality Other gynaecologic cancer (endometrial, ovarian) Cervical cancer diagnosis Precancerous high grade (including AIS) detection

Question 5b

For women who are HPV positive with atypical glandular cells of undetermined significance (AGUS) or possible high grade glandular lesion (confirmed on review) and negative colposcopy what is the safety and effectiveness of repeating HPV and cytology testing when compared with treatment with excisional cone biopsy?

Population	Study design	Intervention	Control	Outcomes
Women who are HPV positive with AGUS or possible HGGA (confirmed on review) and colposcopy negative	Randomized or pseudo randomized controlled trial	Repeat HPV and liquid based cytology testing at 6 months	Excisional cone biopsy cervix	Cervical cancer mortality Cervical cancer diagnosis Endometrial cancer Ovarian cancer

				Precancerous lesion (if detected)
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Question 6

Relevant guidelines content page: [Treatment of HSIL CIN2](#)

For women with biopsy confirmed CIN2 what is the safety and effectiveness of p16 immunohistochemistry and treating only p16 positive CIN2 while conservatively managing p16 negative CIN2 when compared with treating all CIN2 cases?

Population	Study design	Intervention	Control	Outcomes
Women with biopsy confirmed CIN2	Randomized or pseudo randomized controlled trial	Using p16 immunohistochemistry to stratify management: p16 positive cases treated with excision and p16 negative cases conservatively managed	Treat all CIN2 with excision of transformation zone.	Cervical cancer Cervical intraepithelial neoplasia Precancerous lesion

Question 7

Relevant guidelines content page: [Follow-up after excisional treatment for AIS](#)

For women who are HPV positive with adenocarcinoma in situ (AIS) or possible high-grade glandular lesion cytology or biopsy confirmed AIS, what is the safety and effectiveness of large loop excision of the transformation zone (LLETZ), Fischer cone, laser cone or straight wire/needle excision of the transformation zone (SWETZ/NETZ) compared with cold knife cone biopsy?

Population	Study design	Intervention	Control	Outcomes
Women who are HPV positive with AIS or possible high-grade glandular lesion cytology or biopsy confirmed AIS	Randomized or pseudo randomized controlled trial	LLETZ or Fischer cone or	Cold knife cone biopsy	Cervical cancer Cervical intraepithelial neoplasia

		laser cone or SWETZ or NETZ or Any electro-surgery of the transformation zone		Precancerous (including recurrent) Completeness Depth of excision
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Question 8

Relevant guidelines content page: [Investigation of abnormal vaginal bleeding](#)

For women with postcoital, intermenstrual bleeding or heavier periods (menorrhagia), what is the safety and effectiveness of direct colposcopy compared with HPV test and cytology?

Population	Study design	Intervention	Control	Outcomes
Women with postcoital (PCB) or intermenstrual bleeding (IMB) or menorrhagia	Randomized or pseudo randomized controlled trial	Direct referral to colposcopy	Cytology and HPV	Cervical cancer Cervical intraepithelial neoplasia Precancerous lesion detection

Question 9

Relevant guidelines content page: [Screening in immune-deficient women](#)

For women who are at higher risk of cervical cancer due to immunosuppression what is the safety and effectiveness of screening using strategies other than those recommended for the general population compared to those recommended for the general population?

Population	Study design	Intervention	Control
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Chronically immuno-suppressed or immuno-compromised asymptomatic women or Potentially immune suppressed or immune compromised women	Screening randomized controlled or pseudo-randomized trial	Modified recommended screening strategy: starting at an age <25 years and/or screening intervals less than 5 years and/or referring all HPV positive women to colposcopy irrespective of reflex cytology result	Recommended screening strategy Primary HPV screening every 5 years from ages 25 – 69 years using partial genotyping with women positive for HPV16/18 referred to colposcopy and women positive for other oncogenic types undergoing cytology triage
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Question 10

Relevant guidelines content page: [Women who have experienced early sexual activity or have been victims of sexual abuse](#)

For women with a history of sexual abuse or early sexual debut what is the safety and effectiveness of screening using strategies other than those recommended for the general population compared to those recommended for the general population?

Population	Study design	Intervention	Control
History of sexual abuse or early sexual debut	Screening randomized or pseudo-randomized controlled trial	Modified recommended screening strategy: Starting at an age <25 years	Recommended screening strategy Primary HPV screening every 5 years from ages 25 – 69 years using partial genotyping with women positive for HPV16/18 referred to colposcopy and women positive for other oncogenic types undergoing cytology triage

Question 11

Relevant guidelines content page: [Screening in DES-exposed women](#)

For women who were exposed to diethylstilboestrol (DES) in utero and their daughters what is the safety and effectiveness of screening using strategies other than those recommended for the general population compared to those recommended for the general population?

Population	Study design	Intervention	Control
Asymptomatic women exposed in utero to DES and their daughters	Screening randomized or pseudo- randomized controlled trial	Current practice: Annual vaginal examination, cervical and vaginal cytology test, HPV test and colposcopy of the lower genital tract	Recommended screening strategy for general population: Primary HPV screening every 5 years from ages 25 – 69 years using partial genotyping with women positive for HPV16/18 referred to colposcopy and women positive for other oncogenic types undergoing cytology triage

Question 12

Relevant guidelines content page: [Screening in Aboriginal and Torres Strait Islander women](#)

For women who are of Aboriginal or Torres Strait Islander descent what is the safety and effectiveness of screening using strategies other than those recommended for the general population compared to those recommended for the general population?

Population	Study design	Intervention	Control
Women of Aboriginal or Torres Strait Islander descent	Screening randomized or pseudo-randomized controlled trial	Modified recommended screening strategy: - starting at an age <25 years - other	Recommended screening strategy for general population: Primary HPV screening every 5 years from ages 25 – 69 years using partial genotyping with women positive for HPV16/18 referred to colposcopy and women positive for other oncogenic types undergoing cytology triage

Question 13

Relevant guidelines content page: [Screening in pregnancy](#)

For women who are pregnant update the literature of management of abnormal cytology in pregnancy p.74 from the old guidelines. Describe guidance for excluding presence of invasive cancer. How can we support the exclusion of the presence of the invasive cervical cancer? Are there any circumstances that you would manage or treat pregnant women differently to the general population?

Questions 14

Relevant guidelines content page: [After total hysterectomy](#)

For groups of women (literature review or PICO) who have had a hysterectomy. What should the recommendation be in regard to further 'screening'?

Women with total hysterectomy for benign conditions who have never had an abnormal HPV or cytology. Do they need any further screening?

Women who have had in the past been HPV positive with high grade abnormality (squamous or glandular) who have been treated satisfactorily and are on surveillance or have returned to normal screening, who then have a total hysterectomy with no evidence of abnormality on the hysterectomy specimen.

Women who have had a high grade abnormality treated by total hysterectomy, with complete excision of the lesion in the hysterectomy specimen. What follow up would be reasonable.

Women who have had a high grade lesion (CIN2+) who have been treated and have completed test of cure and returned to routine screening, subsequently have hysterectomy with no abnormality in the hysterectomy specimen. Is there any need for further screening?

Question 16

Relevant guidelines content page: [Test of Cure after treatment for HSIL \(CIN2/3\)](#)

For women have been treated for a high grade precancerous squamous lesion what is the safety and effectiveness of testing with HPV test and cytology at 12 months after treatment and discharging if double-negative compared with testing at 12 and 24 months and discharging if double-negative at both 12 and 24 months?

Population	Study design	Intervention	Control	Outcome
Women who have been treated for high grade precancerous squamous lesions	Randomized or pseudo randomized controlled trial	Cytology and HPV testing 12 months after treatment with discharge if double negative	Cytology and HPV testing 12 and 24 months after treatment with discharge if double negative on both occasions	Cervical cancer Cervical intraepithelial neoplasia Precancerous lesion (including detection)

Question 17

Relevant guidelines content page: [Follow-up after excisional treatment for AIS](#)

For women have been treated for adenocarcinoma in situ (AIS) with cone excision or LEEP and with clear histologic margins what is the safety and effectiveness of cytology and HPV testing at 12 and 24 months and discharging if double-negative at both 12 and 24 months or completion hysterectomy compared to cytology?

Population	Study design	Intervention	Control	Outcome
Women treated for AIS with cone excision or LEEP with complete excision and clear histological margins	Randomized or pseudo randomized controlled trial	Cytology and HPV testing 12 and 24 months after treatment with discharge if double negative on both occasions Or Completion hysterectomy	Annual cytology	Cervical cancer Cervical intraepithelial neoplasia Precancerous lesion (including detection)

APPENDIX D: Technical Report

Guidelines: Cervical cancer/Screening/Technical report

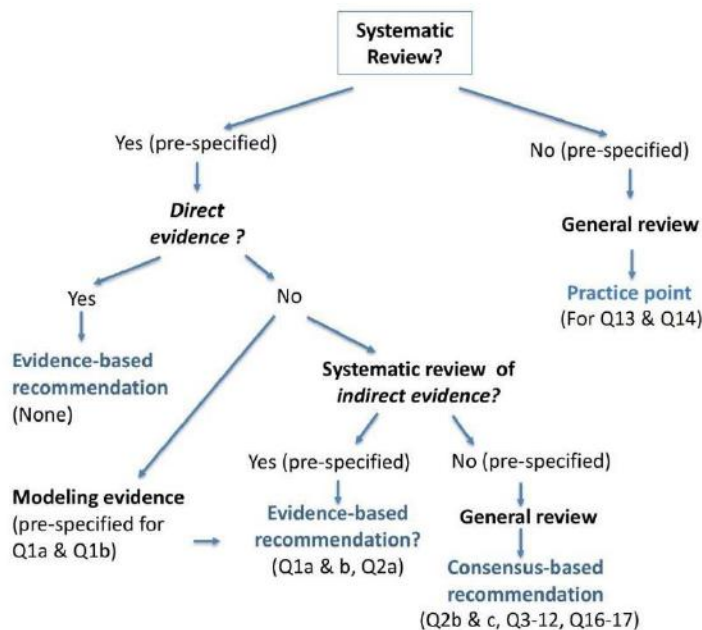
This Technical Report accompanies the Clinical management guidelines for the prevention of cervical cancer, developed by Cancer Council Australia.

It outlines the guideline development process and methodology, lists the clinical questions, provides all accompanying NHMRC Statement Forms, the detailed technical documentation for each question and the risk of bias assessment tools used to assess the included literature as a result of a systematic review.

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- [Evidence Statement question 1b](#)
- [Evidence Statement question 2a](#)

Systematic review, modelling and literature review reports

[Management of oncogenic HPV test results - Oncogenic HPV types not 16/18](#)

- [Systematic review report question 1a](#)
- [Systematic review report question 1b](#)

- [Modelling report question 1a & 1b](#)

[Colposcopy - Normal colposcopic findings following LBC prediction of LSIL or HSIL](#)

- [Systematic review report question 2a](#)
- [Systematic review report question 2b](#)
- [Systematic review report question 2c](#)
- [General evidence summary table question 2b](#)
- [General evidence summary table question 2c](#)

[Colposcopy - Type 3 TZ \(previously termed 'unsatisfactory'\) colposcopy following LBC prediction of LSIL or HSIL](#)

- [Systematic review report question 3a](#)
- [Systematic review report question 3b](#)
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[Management of histologically confirmed high-grade squamous abnormalities](#)

[Treatment of HSIL](#)

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Cohort studies (risk factors) risk of bias assessment tool

- [Cohort studies risk of bias assessment form](#)
- [Cohort studies risk of bias assessment help sheet](#)

Appendix E: Working Party Members

2022 partial update to support policy change to expand access to self-collection

Name	Association
Professor Marion Saville	Chair, Working Party; Executive Director, Australian Centre for Prevention of Cervical Cancer
Dr Lyndal Anderson	Senior Clinical Lecturer, The University of Sydney and University of Western Sydney; New South Wales Health Pathology; Associate Professor University of Sydney; Associate Professor Western Sydney University
A/Professor Deborah Bateson	Medical Director, Family Planning NSW; Clinical Associate Professor, Obstetrics, Gynaecology and Neonatology, The University of Sydney, NSW
A/Professor Alison Brand	Chair, Australia New Zealand Gynaecological Oncology Group (ANZGOG); Associate Professor, Obstetrics, Gynaecology and Neonatology, The University of Sydney; Staff Specialist, Westmead Hospital
Professor Karen Canfell	Director, Daffodil Centre, University of Sydney and Cancer Council NSW
Ms Kirsteen Fleming	State Nurse Coordinator, Family Planning NSW
Dr Andrea Garrett	Gynaecological oncologist, The Wesley Hospital and Royal Brisbane and Women's Hospital
Dr Vivienne Milch	General Practitioner and Medical Director Cancer Australia
Ms Roslyn Moore	Consumer Representative
Dr Marsali Newman	Anatomical Pathologist, Anatomical Pathology Austin Health, Heidelberg, Victoria
A/Professor Selvan Pather	Staff Specialist, Chris O'Brien Lifehouse; Clinical Associate Professor, Obstetrics, Gynaecology and Neonatology, The University of Sydney
A/Professor Megan Smith	Co-lead, Cervical Cancer and HPV Stream (high-income countries), The Daffodil Centre
A/Professor Lisa Whop	Research Fellow, Australian National University
Dr C. David H. Wrede	Consultant Gynaecological Surgeon, Obstetrics and Gynaecology Consulting Group; Chair of Senior Medical Staff, The Royal Women's Hospital
The Daffodil Centre Technical Team	
A/Professor Megan Smith	Principal Research Fellow, The Daffodil Centre
Laura Sergeant	Project Coordinator, The Daffodil Centre
Chloe Jennett	Program Coordinator and PhD Student, The Daffodil Centre
Amy Pagotto	Senior Research Assistant, The Daffodil Centre
Caitlin McLachlan	Research Assistant, The Daffodil Centre
Cancer Council Australia	
Megan Varlow	Director of Cancer Control Policy

Department of Health representatives	
Karla Lister	Director, Cervical Screening Section
Dr Dejan Krstik	Acting Director, Cervical Screening Section

2020/2021 review and partial update (intermediate risk updates) Cervical Cancer Screening Guidelines Working Party members and contributors

Name	Association
Professor Marion Saville	Chair, Working Party; Executive Director, Victorian Cytology Service Incorporated
Dr Lyndal Anderson	Senior Clinical Lecturer, The University of Sydney and University of Western Sydney; New South Wales Health Pathology; Associate Professor University of Sydney; Associate Professor Western Sydney University
A/Professor Deborah Bateson	Medical Director, Family Planning NSW; Clinical Associate Professor, Obstetrics, Gynaecology and Neonatology, The University of Sydney, NSW
A/Professor Alison Brand	Chair, Australia New Zealand Gynaecological Oncology Group (ANZGOG); Associate Professor, Obstetrics, Gynaecology and Neonatology, The University of Sydney; Staff Specialist, Westmead Hospital
A/Professor Karen Canfell	Director, Cancer Research Division, Cancer Council NSW
Kirsteen Fleming	State Nurse Coordinator, Family Planning NSW
Dr Andrea Garrett	Gynaecological oncologist, The Wesley Hospital and Royal Brisbane and Women's Hospital
Kim Hobbs	Clinical Specialist Social Worker, Department of Social Work/ Department of Gynaecological Cancer, Westmead Hospital
A/Professor Selvan Pather	Staff Specialist, Chris O'Brien Lifehouse; Clinical Associate Professor, Obstetrics, Gynaecology and Neonatology, The University of Sydney
A/Professor Lisa Whop	Research Fellow, Australian National University
Dr C. David H. Wrede	Consultant Gynaecological Surgeon, Obstetrics and Gynaecology Consulting Group; Chair of Senior Medical Staff, The Royal Women's Hospital
Professor Gordon Wright	Professor, Pathology, Faculty of Health Sciences and Medicine, Bond University; Queensland Medical Laboratory, Pathology Department, Gold Coast Hospital, QLD
CCA Project Team	
Tamsin Curtis	Project Manager

Megan Varlow Director of Cancer Control Policy

CCNSW Systematic review and modelling team

Dr Megan Smith (co-author) Program Manager, Cervical Cancer Guidelines Cancer Screening Group, Cancer Council NSW

Maddison Sherrah Data Analyst, Cancer Council NSW

Department of Health representatives

Sonya Glasson National Cervical Cancer Screening Program

Daniela Gagliardi National Cervical Cancer Screening Program

2016 Cervical Cancer Screening Guidelines Working Party members and contributors

Name	Association
Professor Ian Hammond	Chair, Working Party; Chair Steering Committee for the Renewal Implementation Project, National Cervical Screening Program, Department of Health, Australia Adjunct Professor, School of Anatomy, Physiology and Human Biology, University of Western Australia Clinical Professor, School of Women's and Infants Health, University of Western Australia
A/Professor Marion Saville	Deputy Chair, Working Party; Executive Director, Victorian Cytology Service Incorporated, VIC
A/Prof Lyndal Anderson	Senior Staff Specialist, Tissue Pathology and Diagnostic Oncology, Royal Prince Alfred Hospital, NSW
Emeritus Professor Bruce Armstrong	Emeritus Professor, School of Public Health, The University of Sydney, NSW and Adjunct Professor, School of Population Health, The University of Western Australia
A/Professor Deborah Bateson	Medical Director, Family Planning NSW; Clinical Associate Professor, Obstetrics, Gynaecology and Neonatology, The University of Sydney, NSW
A/Professor Alison Brand	Chair, Australia New Zealand Gynaecological Oncology Group (ANZGOG); Associate Professor, Obstetrics, Gynaecology and Neonatology, The University of Sydney; Staff Specialist, Westmead Hospital, NSW
Kirsteen Fleming	State Nurse Coordinator, Family Planning NSW
Dr Andrea Garrett	Gynaecologic Oncologist, VMO at The Wesley Hospital and Royal Brisbane and Women's Hospital, Brisbane
Kim Hobbs	Clinical Specialist Social Worker, Departments of Gynaecological Cancer and Social Work, Westmead Hospital NSW

Roslyn Moore	Consumer representative
Dr Joanne Mountford	General Practitioner and Liaison Physician, Victorian Cytology Service Incorporated, VIC
A/Professor Selvan Pather	Staff Specialist, Chris O'Brien Lifehouse; Clinical Associate Professor, Obstetrics, Gynaecology and Neonatology, The University of Sydney, NSW
Dr Larissa (Lara) Roeske	General Practitioner and Liaison Physician, Victorian Cytology Service Incorporated, VIC
Lisa Whop	PhD Candidate & Research Fellow, Menzies School of Health Research, QLD
Chenyi Wong	Consumer representative
Mr C David H Wrede	Consultant Gynaecologist, Lead Clinician for Dysplasia, The Royal Women's Hospital, Melbourne and the Parkville Gynae-Oncology Group, VIC

Professor Gordon Wright	Professor, Pathology, Faculty of Health Sciences and Medicine, Bond University; Queensland Medical Laboratory, Pathology Department, Gold Coast Hospital, QLD
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2016 Observers/non voting members (Cervical Cancer Screening Programs)

Name	Association
Alison Lang	Assistant Director, Population Health Division, Department of Health, ACT
Dr Alison Budd	Senior data analyst, Cancer & Screening Unit, Australian Institute of Health and Welfare, ACT
Nerida Steel	Program Manager, WA Cervical cancer Prevention Program, WA
Dr Gary Fentiman	National Cervical Screening Programme, National Screening Unit, Ministry of Health, New Zealand

2016 Cancer Council Australia Guideline Project Team and Cancer Council NSW Systematic Review and Modelling Team

Name	Association
Jutta von Dincklage	Head, Clinical Guidelines Network, Cancer Council Australia
Laura Wuellner	Project Manager, Clinical Guidelines Network, Cancer Council Australia
Professor Karen Canfell	Director, Cancer Research Division, Cancer Council NSW
Jessica Darlington-Brown	Project Manager, Cervical Cancer Guidelines Cancer Screening Group, Cancer Council NSW
Michaela Hall	Research Assistant- Modelling technical support, Cervical Cancer Guidelines Cancer Screening Group, Cancer Council NSW

Suzanne Hughes	Project Officer, Cervical Cancer Guidelines Cancer Screening Group, Cancer Council NSW
Harriet Hui	Research Assistant, Cervical Cancer Guidelines Cancer Screening Group, Cancer Council NSW
Chloe Jennett	Research Assistant, Cancer Research Division, Cancer Council NSW
Jie Bin Lew	Senior Research Programmer, Cervical Cancer Guidelines Cancer Screening Group, Cancer Council NSW
Megan Smith	Program Manager, Cervical Cancer Guidelines Cancer Screening Group, Cancer Council NSW
Dr Kate Simms	Modelling team member, Cervical Cancer Guidelines Cancer Screening Group, Cancer Council NSW
Dr Louiza Velentzis	Post-doctoral Research Fellow, Cancer Research Division, Cancer Council NSW
Dr Susan Yuill	Research Assistant, Cervical Cancer Guidelines Cancer Screening Group, Cancer Council NSW

See also:

Appendix F. Project team contributions

Medical writer/editor

Name	Association
Jennifer Harman	Medical Editor, Meducation, NSW

Appendix F: Project team contributions

2022 partial update to support policy change to expand access to self-collection

Cancer Council Australia Guideline Project Team and Daffodil Centre Technical Team

Name	Association	Contribution
Ms Megan Varlow	Director of Cancer Control Policy, Cancer Council Australia	Provided project governance and led technical development of online guidelines.
A/Prof Megan Smith	Daffodil Centre	Drafted updates and new text for guidelines chapters 3,6,7,12, and 15; oversaw literature reviews and revised literature review summaries; reviewed updated guidelines content and flowcharts.
Ms Laura Sergeant	Project Coordinator, Cervical Cancer Guidelines, The Daffodil Centre	Project management for the guidelines update, and assisting with drafting and reviewing updates to the guidelines and flowcharts.
Prof Karen Canfell	Director, The Daffodil Centre	Oversight of the guidelines and updates
Ms Chloe Jennett	Project Manager, The Daffodil Centre	Drafted updates for chapter 14; project management
Ms Amy Pagotto	Senior Research Assistant, The Daffodil Centre	Drafted the literature review summaries for chapters 6 and 12.
Ms Caitlin McLachlan	Research Assistant, The Daffodil Centre	Assisted with referencing
Ms Jane Green	Graphic Designer, Everlasting Magic Design	Updated flowcharts

2020/2021 partial update: intermediate risk

Cancer Council Australia Guideline Project Team and

Cancer Council NSW Technical Team

Name	Association	Contribution
Ms Megan Varlow	Director of Cancer Control Policy, Cancer Council Australia	Provided project governance.
Prof Karen Canfell	Director, Cancer Research Division, Cancer Council NSW	Co-drafted updates and new text for guidelines chapter 6; oversaw data analysis; reviewed updated guidelines content and flowcharts
Dr Megan Smith	Senior Research Fellow, Cancer Research Division, Cancer Council NSW	Co-drafted updates and new text for guidelines chapter 6; oversaw data analysis; reviewed updated guidelines content and flowcharts.
Ms Maddison Sherrah	Data Analyst, Cancer Council NSW	Data analysis to support updates to Chapter 6
Ms Tamsin Curtis	Project Manager, Cancer Council Australia	Project management and led technical development of online guidelines

2016 original guidelines development

Cancer Council Australia Guideline Project Team and

Cancer Council NSW Systematic Review and Modelling Team

Name	Association	Contribution
Ms Jutta von Dincklage	Head, Clinical Guidelines Network, Cancer Council Australia	Provided project governance, guideline development management and lead technical development of online guidelines.

Ms Laura Wuellner	Project Manager, Clinical Guidelines Network, Cancer Council Australia	Provided project management for content revision, including wiki and referencing
Prof Karen Canfell	Director, Cancer Research Division, Cancer Council NSW	Led the CCNSW technical team and provided oversight of the systematic reviews and all modelled evaluations
Ms Jessica Darlington-Brown	Project Manager, Cervical Cancer Guidelines, Cancer Research Division, Cancer Council NSW	Project management of the CCNSW technical team and assisting with development and reviewing of the content of the cervical cancer guidelines wiki
Ms Michaela Hall	Research Assistant- Modelling technical support, Cervical Cancer Guidelines, Cancer Research Division, Cancer Council NSW	Performed the modelled evaluation of the risk assessment for Chapter 6 and assisted in the modelled effectiveness and cost effectiveness evaluation for Chapter 6.
Ms Suzanne Hughes	Project Officer, Cervical Cancer Guidelines, Cancer Research Division, Cancer Council NSW	<p>Acted as the lead systematic reviewer, specific contributions include the following:</p> <p>Undertook systematic reviews for chapters 6, 8, 10 – 11, 15 and 17</p> <p>Undertook general literature reviews for parts of chapters 8 and 11</p> <p>Drafted summary points or sections of evidence summary tables for parts of chapters 6, 8, 9 and 11</p> <p>Reviewed and updated literature summaries for chapters 9 - 11</p> <p>Reviewed and updated parts of chapters 6, 8 - 11</p> <p>Contributed to draft of Appendix 2</p>
Ms Harriet Hui	Research Assistant, Cervical Cancer Guidelines, Cancer Research Division, Cancer Council NSW	Assisted with systematic reviews, referencing, collating public consultation comments for various stakeholders, developing and finalising the consultation submission register and developing the glossary. Reviewing content on the cervical cancer guidelines wiki and development of the flowcharts.
Ms Chloe Jennett	Research Assistant, Cervical Cancer Guidelines, Cancer Research Division, Cancer Council NSW	Assisted with various systematic reviews, upload of evidence and content onto the cervical cancer guidelines wiki and assisting the Cancer Council NSW project manager throughout the duration of the project
Ms Jie Bin Lew	Senior Research Programmer, Cervical Cancer Guidelines, Cancer Research Division, Cancer Council NSW	Assisted in the modelled effectiveness and cost effectiveness evaluation and in developing systematic review questions
Ms Megan Smith	Program Manager, Cervical Cancer Guidelines, Cancer Research Division, Cancer Council NSW	<p>Performed systematic reviews, assisted in the modelled effectiveness and cost effectiveness evaluation and in developing systematic review questions and led the writing of several chapters, specific contributions include:</p> <p>Co-drafted Chapter 16 and Appendix B.</p> <p>Reviewed and updated chapters 1, 6, 12, 13, 14, 15, 16, 17, 18 and 20.</p> <p>Reviewed and updated literature summaries for chapters 6, 10, 11, 12, 13, 14, 15, 16, 17, and 18.</p> <p>Extracted data and contributed to literature review for Chapter 16.</p> <p>Drafted summary points for chapters 6, 10, 11, 12, 13, 14, 15, 16, 17, and 18.</p> <p>Contributed to design of modelling for Chapter 6</p>
Dr Kate Simms	Postdoctoral Research Fellow, Cervical Cancer Guidelines, Cancer Research Division, Cancer Council NSW	<p>Performed the modelled analysis for Chapter 5, and led the modelled analysis for the effectiveness and cost-effectiveness evaluation for Chapter 6.</p> <p>Assisted in developing systematic review questions.</p>

Dr Louiza S Velentzis	Post-doctoral Research Fellow, Cervical Cancer Guidelines, Cancer Research Division, Cancer Council NSW	<p>Performed general evidence reviews and had a lead role in writing several chapters. Specific contributions include: Led the writing and updated chapters 10, 13-15 and 17 Co-drafted chapters 5 and 16.</p> <p>Conducted literature reviews for chapter 5 (sections on fertility/early pregnancy outcomes and obstetric complications); chapter 10, chapter 11 (section on follow-up after excisional treatment for AIS), and chapters 13, 14, 15, 17.</p> <p>Extracted data and drafted general evidence summary tables for chapters 10, 11 (questions 7 and 17), and chapters 13, 14, 15, 17.</p>
Dr Susan Yuill	Research Assistant, Cervical Cancer Guidelines, Cancer Research Division, Cancer Council NSW	<p>Acted as the secondary systematic reviewer, specific contributions include the following: Undertook systematic reviews for chapters 6, 8 – 12, 16 and 18 Undertook general literature reviews for parts of chapters 9, 12 and 18 Reviewed and updated literature summaries for chapters 8, 10 – 11 and 16 Reviewed and updated parts of chapters 9 – 11, 16 and 18</p>

Medical writer/editor[\[edit source\]](#)

Name	Association	Contribution
Ms Jennifer Harman	Medical Editor, Meducation, NSW	Provided medical writing and editing services across various chapters

APPENDIX G: Conflict of interest register

Guidelines: Cervical cancer/Screening/Conflict of interest register

A Code of Practice for Declaring and Dealing with Competing Interests

[Declarations of interest register \(partial update 2020\)](#) (see: [Guideline development process – 2020 partial update](#))

[Declarations of interest register \(2016\)](#)

APPENDIX H: Safety monitoring of the Renewed cervical screening program

Background

The National Cervical Screening Program (NCSP) Safety Monitoring Committee (SMC) was established in 2005 in response to the National Health and Medical Research Council's (NHMRC) 2005 Guidelines "Screening to prevent cervical cancer: guidelines for the management of asymptomatic women with screen detected abnormalities."^[1] It was established due to concerns some stakeholders raised regarding the change in management of women with low grade abnormalities and treated high grade abnormalities, from the 1994 guidelines.

The safety monitoring methodology estimated the change in rate of cervical cancer incidence following low grade cytology or a treated high-grade intraepithelial abnormality under the 2005 Guidelines relative to the 1994 Guidelines. A cohort study design was used to select individuals who entered the study at a given time, either following a low-grade Pap test or a histologically confirmed high grade intraepithelial abnormality, and were followed up for five years. The number of women diagnosed with cervical cancer was counted during the follow up time and rate ratios (hazard rates) of cervical cancer were calculated using proportional hazards regression modelling.

Safety monitoring analyses to date have not raised any safety concerns and the outcomes have reassured stakeholders regarding the safety of the 2005 Guidelines.^[2] Furthermore, the safety monitoring process has demonstrated the importance of monitoring the outcomes of the National Cervical Screening Program more broadly in a changing environment.

Quality and Safety Monitoring Committee

The Quality and Safety Monitoring Committee (QSMC) was established in 2014 in response to the Medical Services Advisory Committee recommendations to replace the two yearly Pap test with a five yearly HPV test for the NCSP. The QSMC replaced the SMC as it was recognised that this significant change to the screening program would require a broader remit than that of the SMC.

The QSMC has a role in monitoring the quality and safety of the NCSP and reports to the Standing Committee on Screening of the Australian Health Ministers' Advisory Council. The QSMC is developing a quality and safety monitoring programme as part of a Quality Framework for the NCSP. The Framework will be available from the cancerscreening.gov.au website following its approval by the Standing Committee on Screening.

The Quality Framework includes a set of Quality Standards, Measures and Benchmarks across the cervical screening pathway including colposcopy and these will be monitored by the QSMC on an annual basis. A process for the NCSP to address quality issues is also presented in the Framework.

Safety Monitoring

The Quality Framework will also include safety monitoring parameters across the cervical screening pathway to ensure the NCSP remains safe at this time of significant change. The methodology for safety monitoring will be developed following the finalisation of these Clinical Management Guidelines however will be informed by the safety monitoring approach being undertaken as part of the COMPASS clinical trial in Victoria.^[3]

The QSMC will review the safety monitoring parameters on an annual basis and provide advice to the Standing Committee on Screening should any safety concerns arise. Further information on this process is described in the Quality Framework.

Author(s):

- [Ms Alison Lang](#) — Author
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

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3. Canfell K, Castle P, Caruana M, Gebiski V, Darlington-Brown J, Heley S, Brotherton J, Gertig D, Saville M. *Protocol for Compass: a randomised controlled trial of primary HPV vs. cytology screening for cervical cancer in HPV-unvaccinated and vaccinated women in Australia*. Victorian Cytology Service Inc and The University of Sydney 2014.

APPENDIX I: Glossary (terms and abbreviations)

Guidelines:Cervical cancer/Screening/Glossary Glossary - List of common terms Download

Term	Definition
Adenomyosis	A condition of the uterus where the endometrium (cells that line the inside of the uterine body) also grow into the myometrium (wall of the uterus).
Adequate colposcopy	The cervix is clearly seen and not obscured by blood, inflammation or scarring.
ASC-H	Atypical squamous cells, possible high-grade lesion In the standard US Bethesda System, a category of atypical squamous cells, possible high-grade lesion. Equivalent to possible high-grade squamous intraepithelial lesion (pHSIL) in the Australian Modified Bethesda System.
ASC-US	Atypical squamous cells, undetermined significance In the standard US Bethesda System, a category of atypical squamous cells of undetermined significance: The nature of the abnormality is uncertain or unequivocal. Equivalent to possible low-grade squamous intraepithelial lesion (pLSIL) in the Australian Modified Bethesda System.
ASCUS	Atypical squamous cells, undetermined significance In the previous versions of the US Bethesda System, a category of atypical squamous cells of undetermined significance: The nature of the abnormality is uncertain or unequivocal. Included lesions equivalent to both possible low-grade squamous intraepithelial lesion (pLSIL) and possible high-grade squamous intraepithelial lesion (pHSIL) in the Australian Modified Bethesda System. Later versions (including the current version) of the Bethesda System split this category into ASC-H and ASC-US.
Biopsy	Removal of tissue for medical examination.
BNA	Borderline nuclear abnormalities (British Society for Clinical Cytology) Post 2008: considered equivalent to atypical squamous cell, undetermined significance (ASC-US) in the Bethesda 2001 reporting system considered equivalent to possible LSIL (pLSIL) in the Australian modified Bethesda reporting system Pre 2009: included atypical squamous cells cannot exclude HSIL (ASC-H) and border line changes in endocervical cells. (Denton KJ et al., (2008) The revised BSCC terminology for abnormal cervical cytology. Cytopathology 19: 137-157)
BMD	Borderline or mild dyskaryosis considered equivalent to atypical squamous cell, undetermined significance (ASCUS) and low-grade squamous intraepithelial lesion (LSIL) in the Bethesda reporting system and possible LSIL (pLSIL) in the Australian modified Bethesda reporting system
CD4 count	The number of CD4 T lymphocytes (CD4 cells) per cubic millimetre of blood, a measure of immune system function.
CIN	Cervical Intraepithelial Neoplasia Refers to abnormal changes in the cells on the surface of the

	<p>cervix that are seen using a microscope (i.e. histologically-confirmed).</p> <p>CIN1 – mild dysplasia</p> <p>CIN2 – moderate dysplasia</p> <p>CIN 3 – severe dysplasia to carcinoma in situ</p> <p>(The term CIN2+ refers to CIN2,3, or invasive cervical cancer; CIN3+ refers to CIN3 or invasive cervical cancer) CIN2/3 refers to CIN2 or CIN3.</p>
Cumulative incidence rate	The cumulative incidence rate is a cumulative hazard for a specific disease and should be distinguished from crude (or absolute) risk.
CKC	Cold-knife conisation (cold-knife cone biopsy) is the removal of cone shaped piece of tissue from the cervix using a scalpel.
Coagulopathy	Coagulopathy is a condition in which the blood's ability to coagulate (clot) is impaired.
Cohorts offered vaccination	<p>Women who were part of a cohort who were offered vaccination as pre-adolescents (12-13 years), in the context of the National HPV Vaccination Program as implemented in Australia.</p> <p>Specifically, we modelled a cohort of women born in 1997 who were offered vaccination as 12 year olds in 2009. This is the same cohort that was analysed in the Economic Evaluation of the Renewal report.</p>
Colposcopy	The examination of the cervix and vagina with a magnifying instrument called a colposcope, to check for abnormalities.
Colposcopists	Health professionals, usually gynaecologists, trained to perform colposcopy.
Columnar epithelium	Epithelium which has cells of much greater height than width i.e. endocervical epithelium.
Congenital anomaly	Congenital anomaly is a structural or functional abnormality (anomaly) that occur during intrauterine life and can be identified prenatally, at birth or later in life.
Congenital TZ	<p>Congenital transformation zone</p> <p>During early embryonic life, the cuboidal epithelium of the vaginal tube is replaced by the squamous epithelium, which begins at the caudal end of the dorsal urogenital sinus. This process is completed well before birth and the entire length of vagina and the ectocervix is meant to be covered by squamous epithelium. This process proceeds very rapidly along the lateral walls, and later in the anterior and posterior vaginal walls. If the epithelialization proceeds normally, the original squamocolumnar junction will be located at the external os at birth. On the other hand, if this process is arrested for some reason or incomplete, the original squamocolumnar junction will be located distal to the external os or may rarely be located on the vaginal walls, particularly involving the anterior and posterior fornices. The cuboidal epithelium remaining here will undergo squamous metaplasia. This late conversion to squamous epithelium in the anterior and posterior vaginal walls, as well as the ectocervix, results in the formation of the congenital transformation zone.</p>

	Thus, it is a variant of intrauterine squamous metaplasia, in which differentiation of the squamous epithelium is not fully completed due to an interference with normal maturation. Excessive maturation is seen on the surface (as evidenced by keratinization) with delayed, incomplete maturation in deeper layers. Clinically, it may be seen as an extensive whitish-grey, hyperkeratotic area extending from the anterior and posterior lips of the cervix to the vaginal fornices. Gradual maturation of the epithelium may occur over several years. This type of transformation zone is seen in less than 5 % of women and is a variant of the normal transformation zone.
Condyloma	A 'knob like' or warty growth on the genitals caused by an infection with the human papillomavirus.
Cost-effectiveness	A cost-effectiveness evaluation is a form of economic analysis that compares the relative gain in effectiveness and relative gain in costs of two or more possible scenarios
CO2 Laser	Carbon Dioxide Laser A gas laser (based on a gas medium containing carbon dioxide, helium, nitrogen, some hydrogen, water vapour and/or xenon) that is used in cervical ablation, cervical conisation and ablation of genital condyloma (warts).
Co-test	HPV test and LBC both requested and performed on a cervical sample.
Co-testing	HPV test and LBC both requested and performed on a cervical sample.
Cryotherapy	The use of extreme cold in surgery. Used in treatment of cervix with specially designed cryoprobe, but its use is limited to low resource countries.
CST	Cervical Screening Test; can be performed on either a self-collected or clinician collected sample
Cyanosis	A bluish discolouration of the skin due to poor circulation or inadequate oxygenation of the blood.
Cytobroom	A plastic broom-shaped device used to sample cells from the cervix.
Deciduosis	A visual change on the cervix that is seen commonly in pregnancy, characterised by multiple small, yellow/red elevations of cervical mucosa.
Diathermy point	Straight wire excision of the transformation zone (SWETZ) or needle excision of the transformation zone (NETZ).
Discounted costs	Discounted costs represent the total predicted cost associated with cervical cancer screening for the lifetime of a woman, which is discounted by 5% per year after the age of 12 years (the age at which the earlier intervention, vaccination, occurs).
Discounted life–years	Discounted life–years represent the predicted probability of remaining alive each year after birth, which is discounted by 5% per year after the age of 12 years (the age at which the earlier intervention, vaccination, occurs).
Dysplasia	Dysplasia is an abnormality of epithelial growth and differentiation. Categorised as mild, moderate and severe and correlates with CIN1, CIN2 and CIN3.

Dynamic model	A dynamic model captures time-dependent changes in the state of the system, which is in contrast to a static model, which is time-independent. For instance, the change in the number of infected women over time due to vaccination may influence the rate of new infections due to herd immunity, and cannot be captured through a static model.
Ectopy	Cervical ectopy or ectropion is a condition in which the endocervical columnar epithelium protrudes through the external cervical os and onto the vaginal portion of the cervix.
ECC	Endocervical curettage: The removal of tissue from the endocervical canal of the cervix.
Endometriosis	A condition when the endometrium is found in abnormal sites around the body, most commonly in extrauterine sites in the pelvis.
Exophytic lesion	A lesion that grows outwards from an epithelial surface.
Experienced colposcopist	An experienced colposcopist is usually considered to be one who is, or has been, associated with a tertiary referral centre and has experience in the management of patients with complex problems.
Fischer cone	The Fischer cone is a conisation specimen obtained by using a Fischer cone biopsy excisor, and uses similar electrosurgical technology as used in loop excision procedures.
Gynaecological oncologist	A gynaecological oncologist is a gynaecologist who has received special training in the management of genital tract cancer in women and has been certified by the RANZCOG: Certified Gynaecological Oncologist (CGO).
HPV 16/18	HPV types 16 and or 18 detected using routine HPV screening tests in laboratory
HPV not 16/18	Only Oncogenic HPV types other than 16 and/or 18 detected using routine HPV screening tests in laboratory.
HPV any type	Any oncogenic HPV types detected using routine HPV screening tests in a laboratory.
HPV positive	Women with a positive HPV test result of any oncogenic HPV types detected using HPV testing platforms in a pathology laboratory.
HPV detected	Women with a positive HPV test result of any oncogenic HPV types detected using HPV testing platforms in a pathology laboratory.
HPV negative	Women in whom oncogenic HPV types are not detected by the HPV testing platform.
HPV not detected	Oncogenic HPV types not detected by the HPV testing platform.
HPV Test	A test for oncogenic HPV types (on either a clinician-collected sample or a self-collected sample)
Hr-HPV type	HPV types associated with high risk of cervical high grade precancerous lesions and cancer.
HSIL	High-grade squamous intraepithelial lesion. In the Australian context, HSIL is used to refer to a cytology predictive of a high grade precancerous lesion (AMBS 2004), or histologically

	confirmed high grade precancerous lesion (HSIL-CIN2 or HSIL-CIN3 as per LAST terminology).
Hysterectomy (total)	Complete surgical removal of the uterus including the cervix.
LBC	Liquid based cytology (LBC) is a way of preparing cervical samples for examination in the laboratory.
Intermenstrual bleeding	Vaginal bleeding at any time other than during normal menstruation or following sexual intercourse.
Leiomyoma	Leiomyoma is a benign tumour arising from the smooth muscle of the uterus, commonly known as a fibroid.
Loop diathermy	Loop electrosurgical excision procedure (LEEP) or large loop excision of the transformation zone (LLETZ).
LSIL	Low-grade squamous intraepithelial lesion. In the Australian context, LSIL is used to refer to a cytology predictive of a low grade precancerous lesion (AMBS 2004), or histologically confirmed low grade precancerous lesion (LSIL –HPV, LSIL – condyloma and LSIL –CIN1 as per LAST terminology).
Lympho-vascular space invasion	The spread of malignant cells from a cancer, to the blood vessels or lymphatics. In the cervix it is described most commonly in early invasive disease and is important in determining the need for further treatment in superficially invasive squamous cell carcinoma.
Metaplastic squamous epithelium	Metaplasia is a non-neoplastic transformation of one mature cell type to another type that is not normally present at that location. In the cervix this refers to the transformation of endocervical columnar epithelium to squamous epithelium, described as metaplastic squamous epithelium.
Mild dyskaryosis	Mild dyskaryosis (British Society for Clinical Cytology) considered equivalent to low-grade squamous intraepithelial lesion (LSIL) in the Bethesda 2001 reporting system considered equivalent to definite LSIL in the Australian modified Bethesda reporting system; renamed Low-grade dyskaryosis in 2008. (Denton KJ et al., (2008) The revised BSCC terminology for abnormal cervical cytology. Cytopathology 19: 137-157)
Multi-HPV-type model	A model which takes into account different rates of progression and regression of infection/CIN caused by different HPV types (for instance, CIN caused by HPV 16 is less likely to regress, and more likely to progress, than CIN caused by other HPV types)
Multiple-cohort model	A multiple-cohort model can simulate outcomes for cohorts born at different ages
Nabothian cysts	A mucus filled cyst on the surface of the cervix (this is a normal finding)
NCSP	National Cervical Screening Program A joint program of the Australian, state and territory governments. It aims to reduce morbidity and mortality from cervical cancer, in a cost-effective manner through an organised approach to cervical screening. The program encourages women in the target population to have regular cervical screening.

Needle excision	Straight wire excision of the transformation zone (SWETZ) or needle excision of the transformation zone (NETZ).
Necrosis	The death of living cells and tissues.
Negative colposcopy	A colposcopy in which no abnormalities are seen: it does not include the subsequent reports on any biopsy taken. Also called a 'normal' colposcopy and implies that the entire transformation zone of the cervix is visible.
Negative co-test	Oncogenic HPV types not detected and LBC negative.
Normal cervical screening history	Women who have participated in the NCSP with no detected abnormalities.
NPV	Negative predictive value: the probability that a negative test result is a true negative.
Oedema	A condition characterised by an excess of watery fluid collecting in the tissues or cavities of the body.
Oncogenic HPV	Potentially cancer-causing HPV DNA types, pathogenically linked to intraepithelial neoplasia – e.g. of the uterine cervix (termed CIN)
Oncogenic HPV types	Oncogenic HPV are HPV types considered capable of causing cancer. Types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 and 68 are included in tests suitable for cervical screening. Some tests also detect type 66.
Partial HPV genotyping	Testing for subgroups of high risk HPV types e.g. types 16 or 18
PCB	Postcoital bleeding Vaginal bleeding after intercourse.
pHSIL	Possible HSIL in the Australian Modified Bethesda System is broadly equivalent to ASC-H in US Bethesda system.
pLSIL	Possible LSIL in the Australian Modified Bethesda System is broadly equivalent to ASCUS in US Bethesda system.
Polyp (ectocervical/endocervical) inflammation	A polyp is a small protrusion of tissue that looks like a ball on the end of a slim stalk, and can be visible on the cervix, usually arising from the endocervical or endometrial tissue of uterus. Polyps are usually not neoplastic but can unusually be neoplastic or cancerous.
Positive oncogenic HPV (16/18)	Women with a positive HPV test result of HPV types 16 and/or 18 detected using routine HPV testing in a pathology laboratory.
Positive oncogenic HPV (not 16/18)	Women with a positive HPV test result of other oncogenic HPV types (not including type 16 or 18) detected using routine HPV testing in a pathology laboratory.
Positive oncogenic HPV (any type)	Women with a positive HPV test result of any oncogenic HPV types detected using routine HPV testing in a pathology laboratory.
Profiled electrosurgical excision	This type of excision uses a specific type of 'loop' that can be inserted into the cervical canal and allows for a rotational excision of a 'cone' shaped piece of tissue.
Reflex cytology	Reflex cytology refers to the automatic performance of a cytological examination of a liquid based cervical sample that has tested positive for oncogenic HPV types, determined by the pathologist.

Reflex LBC	Reflex liquid-based cytology LBC (cytology) A test performed on a liquid-based cytology sample when there is a positive oncogenic HPV test result. Reflex LBC may allow for the triage of women along different pathways, negative, LSIL and HSIL, glandular. For women who have HPV16 and/or 18, and who are being referred directly to colposcopy, the reflex LBC result would inform the colposcopic assessment.
Registry	A database of identifiable persons containing defined demographic and health information, established for a specific purpose. In the case of cervical screening or other cancer screening registers, the purpose includes inviting eligible persons for screening, sending reminders when they are overdue for screening, follow up of abnormalities, statistical reporting and research.
Register	A database of identifiable persons containing defined demographic and health information, established for a specific purpose. In the case of cervical screening or other cancer screening registers, the purpose includes inviting eligible persons for screening, sending reminders when they are overdue for screening, follow up of abnormalities, statistical reporting and research.
Self-collection/ self-collected sample	A lower vaginal sample that can be used to perform an HPV test. The lower vaginal sample could be collected by the patient, or the healthcare professional (if the patient has difficulty collecting the sample by themselves or prefers the provider to collect the sample using a self-collection swab without using a speculum). LBC cannot be performed on a self-collected sample.
Sexual activity	Sexual intercourse, oral sexual contact or genital skin-to-skin contact.
SIL	A squamous intraepithelial lesion (SIL) is an abnormal growth of epithelial cells on the surface of the cervix, commonly called squamous cells.
SISCCA	Superficially invasive squamous cell carcinoma (previously termed micro-invasive carcinoma).
Squamous epithelium	In the cervix and the vagina this is a stratified squamous epithelium that consists of layers of cells arranged in layers on a basement membrane.
Squamocolumnar junction	The junction where the ectocervical squamous epithelium and the endocervical columnar epithelium meet, and may be located on the visible ectocervix or may be within the endocervical canal.
Squamous metaplasia	In the cervix this refers to the transformation of endocervical columnar epithelium to squamous epithelium, described as metaplastic squamous epithelium.
Stenosis	A narrowing of a cylindrical canal.
Subclinical	Not clinically apparent.
Thermal coagulation	Also known as 'Semm' or 'Cold' coagulation.
Triage cytology	The results of liquid based cytology are used to determine the optimum management.

TZ	<p>Transformation zone</p> <p>This region of the cervix where the columnar epithelium has been replaced and/or is being replaced by the new metaplastic squamous epithelium is referred to as the transformation zone. It corresponds to the area of cervix bound by the original squamocolumnar junction at the distal end and proximally by the furthest extent that squamous metaplasia has occurred as defined by the new squamocolumnar junction. In premenopausal women, the transformation zone is fully located on the ectocervix. After menopause through old age, the cervix shrinks with the decreasing levels of estrogen. Consequently, the transformation zone may move partially, and later fully, into the cervical canal.</p> <p>The transformation zone may be described as normal when it is composed of immature and/or mature squamous metaplasia along with intervening areas or islands of columnar epithelium, with no signs of cervical carcinogenesis. It is termed an abnormal or atypical transformation zone (ATZ) when evidence of cervical carcinogenesis such as dysplastic change is observed in the transformation zone. Identifying the transformation zone is of great importance in colposcopy, as almost all manifestations of cervical carcinogenesis occur in this zone.</p> <p>Type 1 TZ: the whole TZ including all the upper limit is ectocervical</p> <p>Type 2 TZ: the upper limit of the TZ is partly or wholly visible in the canal and is completely visible around 360 degrees</p> <p>Type 3 TZ: part or the entire upper limit of the TZ cannot be seen in the canal.</p> <p>Type 1 excision (for Type 1 TZ): usually to 8mm and not more than 10mm length of cervical tissue excised</p> <p>Type 2 excision (for Type 2 TZ): not more than 15mm length of tissue excised</p> <p>Type 3 excision (for Type 3 TZ): equivalent to 'cone biopsy' and >15mm length.</p>
Type 1 TZ	The whole TZ including all the upper limit is ectocervical.
Type 1 excision	Type 1 excision (for Type 1 TZ): usually to 8mm and not more than 10mm length of cervical tissue excised.
Type 2 TZ	The upper limit of the TZ is partly or wholly visible in the canal and is completely visible around 360 degrees.
Type 2 excision	Type 2 excision (for Type 2 TZ): Not more than 15mm length of tissue excised.
Type 3 excision	Type 3 excision (for Type 3 TZ): Equivalent to 'cone biopsy' and > 15mm length.
Ulceration	The loss of a small or large portion of a surface epithelium, leading to a 'raw' area. Can be caused by local trauma, inflammation and cancer.
Under-screened	Women who are over 30 years of age and are 2 or more years overdue for their routine 5-yearly cervical screening test.

Unvaccinated cohorts	Women who were not offered HPV vaccination, and who experience no herd immunity effects from the National HPV Vaccination Program.
Vaginal stenosis	Narrowing of the vagina.
≤	Less than or equal to
≥	Greater than or equal to

List of common abbreviations and acronyms

[Glossary - List of common abbreviations and acronyms](#) **Download**

Term/Abbreviation Association

AGC	Atypical glandular cells
AGUS	Atypical glandular cells of undetermined significance
AIHW	Australian Institute of Health and Welfare
AIN	Anal intra-epithelial neoplasia
AIS	Adenocarcinoma in situ
AMBS	Australian Modified Bethesda System
ASCCP	Australian Society for Colposcopy and Cervical Pathology
ASC-H	Atypical squamous cells, possible high-grade lesion
ASCUS	Atypical squamous cells, undetermined significance
ASR	Age-standardised to the Australian population
ASRW	Age-standardised to the world standard population
BNA	Borderline nuclear abnormalities (British Society for Clinical Cytology)
BMD	Borderline or mild dyskaryosis
CCC	Clear cell carcinoma
CGIN	Cervical glandular intraepithelial neoplasia
CIN	Cervical intraepithelial neoplasia
CIN1	Cervical intraepithelial neoplasia 1
CIN2	Cervical intraepithelial neoplasia 2
CIN3	Cervical intraepithelial neoplasia 3
CIN2/3	Cervical intraepithelial neoplasia 2 or 3
CIR	Cumulative incidence rates
CKC	Cold-knife conisation
DCV	Direct colposcopic vision
DES	Diethylstilboestrol
ECC	Endocervical curettage
FIGO	The International Federation of Gynaecology and Obstetrics
FU	Follow-up
HGGA	High-grade glandular atypia
HGGL	High-grade glandular lesion
HPV	Human papillomavirus
HPV 16/18	HPV types 16 and/or 18
HPV +ve (any type)	HPV positive (any oncogenic type)
HPV –ve	HPV negative
Hr-HPV	High-risk (oncogenic) human papillomavirus
HSIL	High-grade squamous intraepithelial lesion
IARC	International Agency for Research on Cancer
IFCPC	The International Federation of Cervical Pathology and Colposcopy
IMB	Intermenstrual bleeding
LAST	Lower anogenital squamous terminology
LBC	Liquid-based cytology

LEEP	Loop electrosurgical excision procedure
LC	Carbon dioxide laser cone biopsy
LLETZ	Large loop excision of the transformation zone
LSIL	Low-grade squamous intraepithelial lesion
MSAC	The Australian Medical Services Advisory Committee
MST	Multi-disciplinary team
NCI	National Cancer Institute
NCSP	National Cervical Screening Program
NCSR	National Cancer Screening Register
NETZ	Needle excision of the transformation zone
NHMRC	National Health and Medical Research Council
Not HPV 16/18	All/ any other oncogenic HPV types other than 16 and 18
NPV	Negative predictive value
PBAC	Pharmaceuticals Benefits Advisory Committee
PCB	Post-coital bleeding
PCR	Polymerase chain reaction
PPV	Positive predictive value
PTL	Preterm labour
RANZCOG	The Royal Australian and New Zealand College of Obstetricians and Gynaecologists
RCPA	Royal College of Pathologists of Australasia
SCC	Squamous cell carcinoma
SIL	Squamous intraepithelial lesion
SIR	Standardised incidence rate
SISCCA	Superficially invasive squamous cell carcinoma (previously termed micro-invasive carcinoma)
SWETZ	Straight wire excision of the transformation zone
TBS	The Bethesda System
TZ	Transformation zone
VAIN	Vaginal intra-epithelial neoplasia
≤	Less than or equal to
≥	Greater than or equal to

APPENDIX J: Safety monitoring of renewed cervical screening program

Guidelines: Cervical cancer/Screening/Safety monitoring of renewed cervical screening program

Author(s):

- [Ms Alison Lang](#) — Author
- [Cancer Council Australia Cervical Cancer Screening Guidelines Working Party](#) — Co-author

Background

The National Cervical Screening Program (NCSP) Safety Monitoring Committee (SMC) was established in 2005 in response to the National Health and Medical Research Council's (NHMRC) 2005 Guidelines "Screening to prevent cervical cancer: guidelines for the management of asymptomatic women with screen detected abnormalities."¹ It was established due to concerns some stakeholders raised regarding the change in management of women with low grade abnormalities and treated high grade abnormalities, from the 1994 guidelines. The safety monitoring methodology estimated the change in rate of cervical cancer incidence following low grade cytology or a treated high-grade intraepithelial abnormality under the 2005 Guidelines relative to the 1994 Guidelines. A cohort study design was used to select individuals who entered the study at a given time, either following a low-grade Pap test or a histologically confirmed high grade intraepithelial abnormality, and were followed up for five years. The number of women diagnosed with cervical cancer was counted during the follow up time and rate ratios (hazard rates) of cervical cancer were calculated using proportional hazards regression modelling.

Safety monitoring analyses to date have not raised any safety concerns and the outcomes have reassured stakeholders regarding the safety of the 2005 Guidelines.² Furthermore, the safety monitoring process has demonstrated the importance of monitoring the outcomes of the National Cervical Screening Program more broadly in a changing environment.

Quality and Safety Monitoring Committee

The Quality and Safety Monitoring Committee (QSMC) was established in 2014 in response to the Medical Services Advisory Committee recommendations to replace the two yearly Pap test with a five yearly HPV test for the NCSP. The QSMC replaced the SMC as it was recognised that this significant change to the screening program would require a broader remit than that of the SMC.

The QSMC has a role in monitoring the quality and safety of the NCSP and reports to the Standing Committee on Screening of the Australian Health Ministers' Advisory Council. The QSMC is developing a quality and safety monitoring programme as part of a Quality Framework for the NCSP. The Framework will be available from the cancerscreening.gov.au website following its approval by the Standing Committee on Screening.

The Quality Framework includes a set of Quality Standards, Measures and Benchmarks across the cervical screening pathway including colposcopy and these will be monitored by the QSMC on an annual basis. A process for the NCSP to address quality issues is also presented in the Framework.

Safety Monitoring

The Quality Framework will also include safety monitoring parameters across the cervical screening pathway to ensure the NCSP remains safe at this time of significant change. The methodology for safety monitoring will be developed following the finalisation of these Clinical Management Guidelines however will be informed by the safety monitoring approach being undertaken as part of the COMPASS clinical trial in Victoria.^[3]

The QSMC will review the safety monitoring parameters on an annual basis and provide advice to the Standing Committee on Screening should any safety concerns arise. Further information on this process is described in the Quality Framework.

References

1. ↑ National Health and Medical Research Council. [*Screening to prevent cervical cancer: guidelines for the management of asymptomatic women with screen detected abnormalities*](#). Canberra: NHMRC; 2005.
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