MINISTRY OF HEALTH
MANATŪ HAUORA

New Zealand Government

National Cervical Screening Programme: HPV Primary Screening Clinical Pathway to Introduce Self-Testing

Public Consultation

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Purpose

In November 2019, the National Cervical Screening Programme (NCSP) introduced a policy change as part of the planning for implementing human papillomavirus (HPV) primary screening. This policy change includes the choice of self-testing as a universal option.

The option of self-testing as part of the HPV primary screening clinical pathway has not been previously consulted on by professional bodies and advocacy groups. This explains the proposed changes and the reasons for them, and seeks feedback from NCSP stakeholders.

This consultation paper proposes a number of changes to the clinical pathway for HPV primary screening that was set out in an NCSP public consultation paper in 2015, to reflect the new policy changes and emerging international data. The initial proposed HPV screening clinical pathway from the 2015 consultation is in Appendix 1.

Changes to the pathway are based on emerging international data, including experience with HPV primary screening in Australia since December 2017. In this proposal, everyone in the screening programme will be offered a choice of a clinician-collected sample or a self-collected sample (self-testing).

This consultation ensures that all NCSP stakeholders:

- are fully informed of changes being proposed for the current cervical screening programme
- have the opportunity to consider and provide feedback on the proposed changes
- are informed of the outcomes of the consultation and the decisions for change.

The outcomes of this consultation will inform the next phases of planning for HPV programme implementation.

Background

In May 2014 the Associate Minister of Health approved policy work to consider a major change to the NCSP. This was from liquid-based cytology testing to HPV testing as the primary screening test, in line with similar changes in other countries.

Nearly all cervical cancers are caused by HPV, a vaccine-preventable disease. In New Zealand, free HPV immunisation is offered to everyone aged 9 to 26, including non-residents. The vaccine does not provide complete protection, and not all people in this age group are vaccinated. This means regular cervical screening is still needed for those who have been vaccinated against HPV.

In 2015, the World Health Organization (WHO) endorsed the HPV screening test as the most effective cervical cancer screening method, as human papillomavirus causes 99 percent of cervical cancers. International evidence convincingly shows that HPV primary screening is the most effective screening method to identify the risk of developing cervical cancer and will further reduce both its incidence and mortality.

As HPV immunisation rates increase, it is internationally recognised that, as the prevalence of cervical abnormalities in the population falls, the performance of cytology as a primary screening test will progressively reduce.[1]

The body of evidence from a number of large-scale trials has demonstrated that primary screening through HPV testing is more sensitive in detecting pre-cancerous abnormalities (CIN2+/AIS) and therefore enabling better cancer prevention than cytology-based screening.[2] The greater sensitivity of HPV primary screening allows the screening interval to be extended from three to five years. HPV screening also allows self-testing to be safely introduced. Research shows that self-testing with more comprehensive pathway support increases participation and equitable outcomes by reducing barriers to screening. Improving the sensitivity of the primary screening test is likely to result in an initial increase in colposcopy referrals, although this has been modelled to fall after the first round of HPV screening and as an increasing proportion of the population is immunised.

International research shows that HPV primary screening provides 60 to 70 percent more protection against invasive cervical cancer when compared with cytology screening.[3] Many countries have changed to primary HPV testing, including Australia, England, Scotland and the Netherlands.

The 2015 and 2018 Parliamentary Review Committee and Te Rōpū Whakakaupapa Urutā (2020) recommended that HPV primary screening, including self-testing, be

1 Palmer TJ, McFadden M, Pollock KGJ, et al. 2016. HPV immunisation and cervical screening – confirmation of changed performance of cytology as a screening test in immunised women: a retrospective population-based cohort study. *British Journal of Cancer* 114: 582–9.

2 Ronco G, Dillner J, Elfstrom KM, et al. 2014. Efficacy of HPV-based screening for prevention of invasive cervical cancer: follow-up of four randomised controlled trials. *Lancet* 383: 524–32.

3 Ronco G, Dillner J, Elfstrom KM, et al. 2014. Efficacy of HPV-based screening for prevention of invasive cervical cancer: follow-up of four randomised controlled trials. *Lancet* 383: 524–32.

funded and implemented as a matter of urgency. Professional groups (including the Royal NZ College of General Practice) and Māori advocacy groups are strongly advocating for implementing HPV primary screening in order to support equitable health outcomes.

The New Zealand HPV immunisation programme, combined with HPV primary screening with the option of self-testing, will provide the most effective protection against HPV and cervical cancer. This will enable the programme to work towards elimination of cervical cancer in New Zealand within 10 years, and specifically supporting equitable outcomes for Māori and Pacific people (based on the World Health Organization elimination threshold of ≤4/100,000 population).

Adding a universal option of self-testing

The transition to HPV primary screening[4] will give everyone the option of either a self-test or a clinician-taken sample. New Zealand studies suggest that offering HPV self-testing, alongside more comprehensive pathway support, will increase participation and equitable outcomes by reducing barriers to screening.[5]

An HPV test using a swab can be done by the participant or by a clinician, if preferred. During the introductory stages of the programme change, self-testing would be done in a clinical or community health care setting. The clinician who orders the test will remain responsible for all follow-up. It is important that the clinician provides education and support about cervical screening at the time of the test to ensure the participant is fully informed and understands the importance of ongoing participation in the NCSP.

[4] HPV screening is done by a vaginal swab that can be taken by the patient or by a clinician, and which is then tested for HPV. The cytology screening approach involves the use of a speculum by a clinician to take a cervical sample, from which both an HPV test and cytology triage can be taken. HPV self-testing is a significantly less invasive experience.

[5] Adcock A, Cram F, Lawton B, et al. 2019. Acceptability of self-taken vaginal HPV sample for cervical screening among an under-screened indigenous population. *Australian and New Zealand Journal of Obstetrics and Gynaecology* 59: 301–7.

International analysis has concluded that tests performed on a self-test sample are similarly sensitive to those performed on clinician-taken samples, as long as a polymerase chain reaction (PCR) assay for detecting HPV DNA is used.[6] [7] [8] [9]

Modelling undertaken in Australia to assess the impact of self-testing[10] concluded that offering even a single HPV self-test has considerable potential to improve outcomes for screened and under-screened participants. HPV primary screening provides the opportunity for the option of self-testing for everyone and the ability to safely adopt a five-year screening interval. This supports increased participation by removing one of the key barriers to screening: the need for a speculum examination. However, anyone who is HPV positive will need a subsequent speculum examination for cytology or colposcopy examination.

6 Arbyn M, Smith S, Temin S, et al. 2018. Detecting cervical pre-cancer and reaching underscreened women by using HPV testing on self-samples: updated meta-analyses. *BMJ* 363: k4823.

7 Polman N, Ebisch R, Heideman D, et al. 2019. Performance of human papilloma virus testing on self-collected versus clinician–collected samples for the detection of cervical intraepithelial neoplasia of grade 2 or worse: a randomised, paired screen positive, non-inferiority trial. *Lancet Oncology* 20(2): 229–238.

8 Arbyn M, Verdoodt F, Snijiders P, et al. 2014. Accuracy of the human papilloma virus testing on self-collected versus clinic-collected samples: a meta analysis. *Lancet Oncology* 15: 172–83.

9 UK National Screening Committee (Costello Medical Consulting Ltd). 2017. *Cervical l cancer screening – HPV self-sampling*. Version date 14 March 2017.

10 Smith M, Lew JB, Simms K, et al. 2016. Impact of HPV sample self-collection for under-screened women in the renewed cervical screening programme. *MJA* 204(5): epub 21 March.

Consultation goals and objectives

The main objective of this consultation is to refine the HPV primary screening clinical pathway to include the option of self-testing, as part of planning for implementing HPV primary screening. This will:

- inform the policy, standards and management guidelines for HPV testing within the NCSP
- establish the processes and systems required to implement HPV as the primary screening test
- inform workforce capacity requirements
- ensure HPV testing is accessible and equitable for all those eligible.

This consultation paper ensures all NCSP stakeholders and professional groups are informed to facilitate understanding of the changes being proposed and why they are being considered by the NCSP. The incorporation of views and feedback on the proposed changes will inform the design and implementation of the revised cervical screening pathway.

Outcomes

The outcome of this consultation will be the development of a final HPV primary screening clinical algorithm with the option of self-testing, to inform development of guidelines, policy and procedures. This will also inform the next steps of planning, including designing a detailed information technology system for implementing the programme.

Guiding principles

Guiding principles for the change to primary HPV screening are that the final approach should:

- deliver a best-practice national cervical screening programme by international comparison
- make screening coverage more equitable across all population groups
- improve equity of outcomes (cervical cancer incidence and mortality) across all population groups
- maintain and improve the safety and quality of screening for all those enrolled
- maintain a skilled and competent workforce to deliver the national programme
- be managed to ensure a smooth transition to the new primary screening pathway
- maintain and improve the NCSP Register's capability to support the programme
- allow all participants to choose whether their sample is a self-test or is taken by a clinician.

Key considerations for health professionals

This is a clinical pathway with a population health approach and serves as a guideline for health professionals. Clinical decision making and monitoring individual patient risk remain the prerogative of the treating clinician.

Revised proposed screening pathway

The revised proposed screening pathway will allow all participants to choose between a self-test or a clinician-taken sample. The revised pathway will also change the management of participants who are under 50 years of age with HPV Other (not 16/18) and low-grade/normal cytology. Anyone who chooses the self-test option for screening tests and has a positive HPV result (any type) will require a speculum examination to collect a cytology sample.

Cytology and clinical examination provide additional information which will ensure those with the highest risk are prioritised for colposcopy. Sample takers may discuss direct referral of HPV 16/18 positive cases to colposcopy (for example, without cytology) with local colposcopy services for those who face barriers in having a cytology sample taken. Please see the 'Guidance for direct referral to colposcopy for those who are hrHPV 16/18 positive' section of this document for more details.

Rationale for the change

Follow-up of those identified with HPV Other and normal or low-grade cytology

In the 2015 consultation pathway, those with a positive result for HPV Other (not 16/18) at primary screening and normal or low-grade cytology at triage are recommended to have a repeat HPV test in 12 months. If HPV is detected (any type), they would be referred to colposcopy, with a cytology test taken or reported on the sample before referral.

There is sufficient data from the Australian programme to indicate that for those under 50 years of age, a subsequent test in 12 months is safe and will reduce the number of referrals to colposcopy because some cases will resolve and become HPV negative. The Australian programme has proposed a similar change to their pathway, and this will be formally adopted in Australia on 1 February 2021.

The updated proposed changes introduce a new pathway **for participants under 50 years of age who remain HPV positive with normal or low-grade cytology at**

the 12-month recall test. For this group, the pathway depends on the result of the recall test.

- If the HPV result is negative, return to five-yearly screening.
- If the HPV result is positive (any type), report the cytology. A clinician-taken sample will need to be collected if the HPV result is based on a self-test.
  - If the cytology result is possible or definite high-grade, refer to colposcopy.
  - If the cytology result is normal or low-grade, **repeat the HPV test in a further 12 months**.
    - If this third HPV test is negative, return to five-yearly screening.
    - If this third HPV test is positive (any type), report the cytology and refer for colposcopy irrespective of the cytology result. If the HPV test was a self-test, a clinician-taken cytology sample is recommended before colposcopy to assist with prioritisation and assessment.

Anyone over 50 years with an HPV positive result at the 12 month recall test will continue to be referred to colposcopy.

Management of those who are HPV 16/18 positive at primary screening, with negative cytology

Currently, this group will be referred for colposcopy. Data from the United Kingdom, United States and Australia has indicated that the proportion with high-grade in situ lesions is relatively low. However, Australia has identified a significant number of cases of previously undetected invasive cervical cancers, particularly adenocarcinomas in this group in the first round of HPV primary screening. The current pathway will therefore not be altered and this group will continue to be referred to colposcopy. It is likely that the management of this group will be reviewed after the first five years of HPV primary screening, or as more evidence becomes available.

Guidance for direct referral to colposcopy for those who are hrHPV 16/18 positive

Direct screening provider referral to colposcopy, at which time a cytology sample could be collected, will be at the clinician's discretion, based on individual patient risk, particularly for anyone in an under-screened group or who may face barriers. This should be discussed with colposcopy services.

Colposcopy is not the optimal next test for those with a positive HPV result. It is equally sensitive to cytology screening but is a more invasive procedure and more expensive for the health system. Having a cytology result available is useful to colposcopists for the following reasons.

- It supports prioritisation of referred cases to determine who should be seen first. For example, if the cytology result is possible or definite high-grade, the referral would be prioritised.
- An abnormal cytology result can assist the colposcopist in the interpretation of colposcopic appearances and further management. For example, if atypical glandular cells were reported but there is no visible lesion, this would require more intensive follow-up, such as a multi-disciplinary meeting review[11] of the cytology.

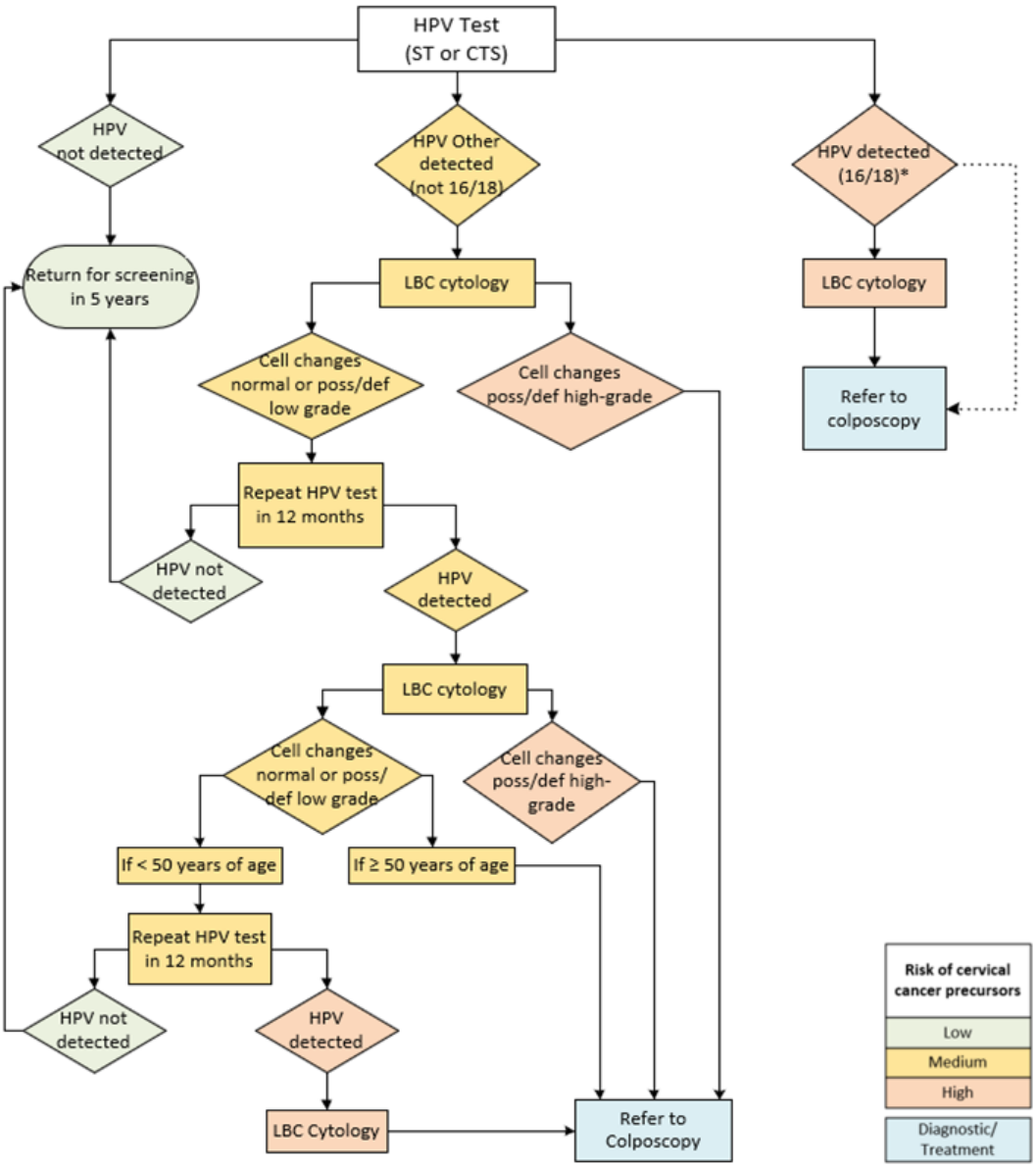
Performing colposcopy without cytology means the colposcopist is less informed. This raises the likelihood of more cervical biopsies or treatment than the patient may require, and therefore poses a risk of harm from overtreatment. Additionally, integration of the HPV primary screening clinical pathway with primary care provides an opportunity to discuss questions and concerns, and is essential to the success of the HPV screening programme. An appointment with the patient's primary care provider is an opportunity for education and discussion of concerns.

For these reasons, direct referral by a screening provider to colposcopy needs to be regarded as an exception, to support those with an identified higher risk of cervical cancer rather than an option for all.

Unscreened or under-screened groups, and others who may face barriers, may also be referred to screening support services for additional support.

[11] A multi-disciplinary meeting constitutes a review of patient information and treatment by a panel of gynaecologists, colposcopists, and pathologists.

Proposed new HPV screening clinical pathway for asymptomatic participants



ST = self-test
CTS = clinician-taken sample
LBC Cytology: reflex cytology or clinically taken cytology sample
*Sample takers may discuss direct referral of HPV 16/18 positive patients to colposcopy (i.e. without cytology) with local colposcopy services. Direct referral should be at the clinician's discretion, based on individual patient risk, particularly for anyone in an under-screened group or who may face barriers. Please refer to "Guidance for Direct Referral to Colposcopy for those who are hrHPV 16/18 positive" for more details.

Considerations for implementation

As HPV primary screening introduces a more sensitive screening test, it is expected there will be an initial increase in disease detection in the first few years of implementation, with an impact on colposcopy services. The screening clinical pathway will be revisited for review after the first round of screening to ensure that best clinical practice is maintained.

Consideration of the international experience has informed the proposed approach over the first five years of the programme change to ensure the sustainability of colposcopy services. International programmes which transferred from cytology-based cervical screening to HPV-based screening have experienced an increase in the demand for colposcopy, regardless of clinical algorithms used. Pilots in NHS England experienced a 60 percent increase in colposcopy volumes. The Swedish programme published an 80 percent increase in colposcopy volumes. The Australian programme originally modelled a 10 to 15 percent increase over the whole country, but the increased demand was closer to 60 percent.

Modelling undertaken for New Zealand estimates that that in a moderate uptake environment, 40 percent of those overdue for a test would take up the self-testing option. This increase in screening coverage among unscreened and under-screened groups is estimated to increase colposcopy referrals by 4 to 7 percent in the first two years.

The proposed model supports sustainability based on emerging evidence as the programme transitions through the first five-year screening cycle. It will enable safe and effective service delivery to support prioritisation of high-risk patients, reduce the risk of overtreatment and ensure that those most in need are seen in appropriate timeframes. The revised clinical pathway also supports the management of the expected initial increase in colposcopy referrals during the transition period to ensure programme sustainability in New Zealand.

Glossary

- **HPV any type**: high-risk HPV detected of any type, including HPV type 16/18
- **HPV Other**: high-risk HPV detected that is not type 16/18
- **HPV 16/18**: HPV detected type 16/18

Next steps

The NCSP will inform stakeholders once this paper is released for public consultation with information on how to provide feedback. Feedback from the public consultation will be collated and carefully considered, and published on the National Screening Unit website.

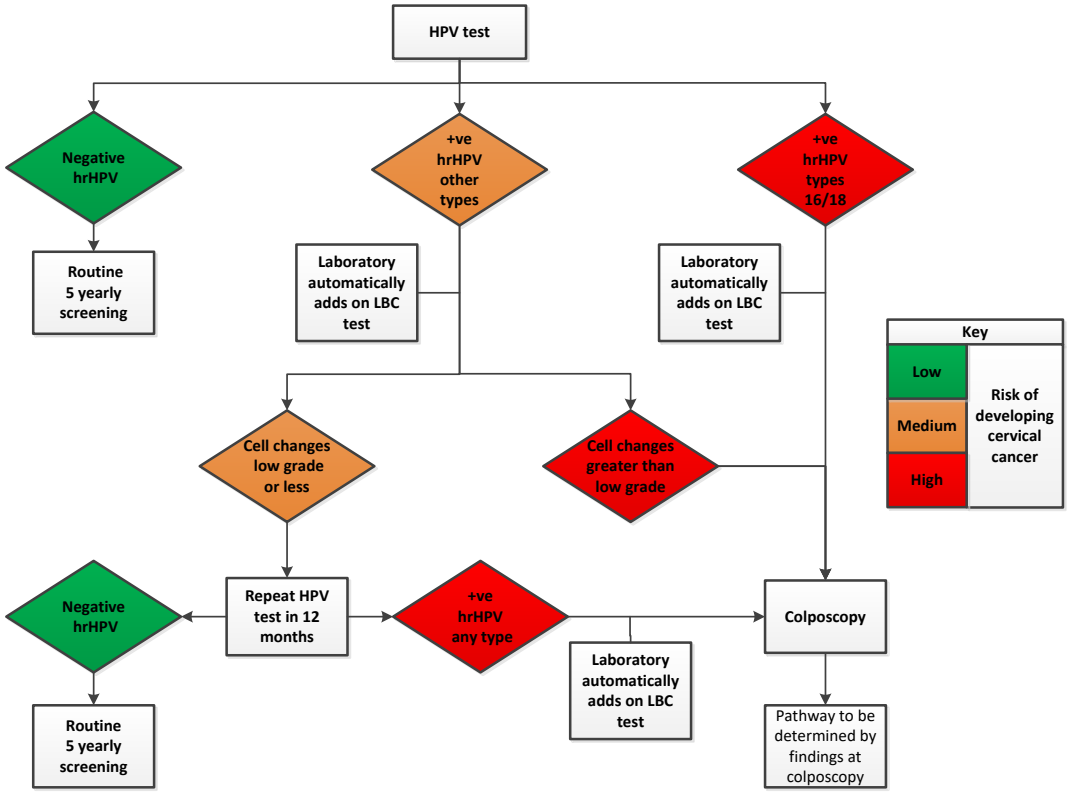
Further changes to the pathway will then be updated and presented to the NCSP advisory groups for further advice, before finalisation.

Appendix 1: Initial Proposed HPV Primary Screening Clinical Pathway (2015)

In 2015, the NCSP released a public consultation document to seek feedback on the change to HPV primary screening and the proposed clinical pathways. The process outlined new clinical pathways for use with the change from liquid-based cytology screening to human papillomavirus primary screening.[12]

Figure 1 outlines the initial proposed HPV primary screening pathway developed as a result of the public consultation of 2015 and further advice from the HPV Technical Reference Group.

Figure 1: 2015 HPV screening clinical pathway for asymptomatic patients



[12] For more information on the change in clinical pathway and consultation process in 2015, please visit **https://www.nsu.govt.nz/health-professionals/national-cervical-screening-programme/hpv-primary-screening**

The primary test

- The first test on a sample will be an HPV test with partial genotyping. Partial genotyping means that the HPV test used will be able to tell whether the high-risk type of HPV present is type 16 or 18 or another high-risk HPV (hrHPV). These results determine the next steps in the pathway.

Negative for hrHPV

- Those who test negative for hrHPV types will be advised to continue with routine five-yearly screening.

Positive for hrHPV types 16 or 18

- Positive test results for hrHPV 16 or 18 will be referred directly for colposcopy assessment.
- The laboratory will automatically add on a cytology test (adjunct test), and the results of this will help the colposcopist with assessment and treatment decisions.

Positive for other types of hrHPV (not 16 or 18)

- For a positive test result for other types of hrHPV (not 16 or 18) a cytology test will automatically be added by the laboratory (reflex test). The results of this test will determine what happens next.
- If the cytology test shows that high grade changes, the patient will be referred directly to colposcopy.
- If there are no changes detected or changes are low grade, the patient will be asked to have another HPV test in 12 months' time.
  - If, 12 months later, the test is positive for any type of hrHPV, the patient will be referred to colposcopy, and a cytology test will be done to help the colposcopist with assessment and treatment decisions.
  - If, 12 months later, the test is negative, the patient will be advised to return to routine five-yearly screening.