Section 4: Management of participants after HPV testing

HPV testing refers to testing for high-risk HPV types (HPV). High-risk HPV types are those types of HPV that are associated with the development of high-grade abnormalities and invasive cervical cancer. These HPV types are also commonly referred to as oncogenic HPV types. Primary HPV testing includes partial HPV genotyping to distinguish HPV types 16 and 18 from another 12 HPV types, collectively known as HPV detected Other and include HPV 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68.

All screening tests have false positive and false negative results. The HPV test is a more sensitive test for CIN2+ and has a better negative predictive value than cytology. The improved negative predictive value of an HPV not detected result means regular interval screening can be extended. There are fewer false negative tests with HPV primary screening.[1-4] Participant with HPV 16 or 18 should be referred to colposcopy. Cytology is used as a second test to triage participants with HPV detected Other test results to assist in ongoing management.

The terms used to describe HPV test results in the NCSP are:

- HPV not detected
- HPV detected
- HPV detected 16
- HPV detected 18
- HPV detected Other
- HPV detected (any type)
- HPV test invalid
- HPV test unsuitable for analysis

RECOMMENDATIONS	
R4.01 Ensure participants and whānau are provided with information about HPV and cervical screening	**Practice point** Participants and whānau must be provided with advice and reassurance regarding HPV and HPV test results. Participants and whānau are provided with information about HPV and their follow-up care. Provide NCSP resources to participants and whānau where appropriate, at time of screening and when notified of results.

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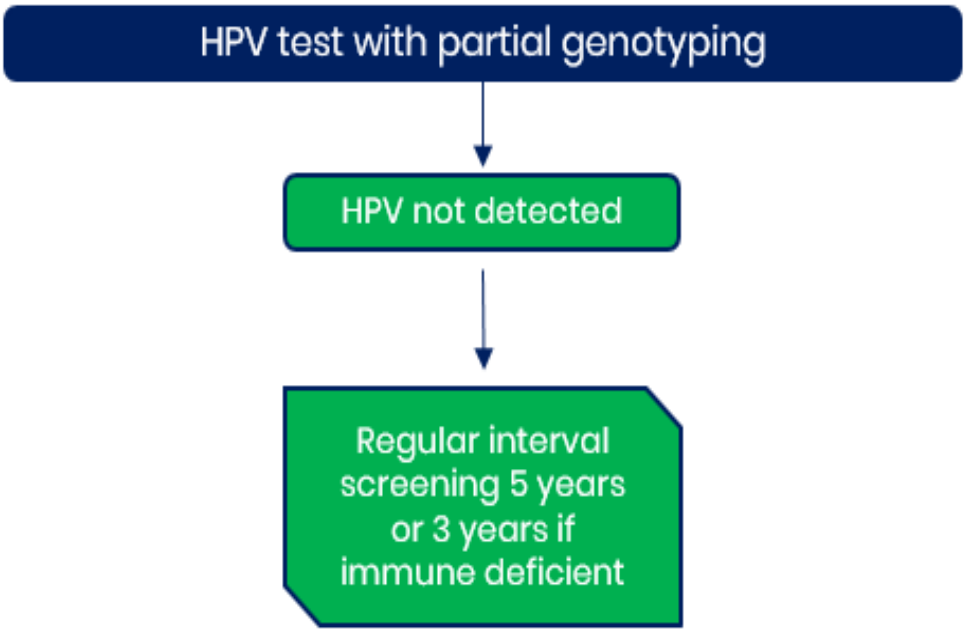
HPV not detected

Where HPV is not detected, participants are at very low risk of cervical intraepithelial neoplasia grade 3 (CIN3) and cervical cancer for at least five years.[1, 2]

People who are immune deficient are known to be at greater risk of developing cervical lesions after HPV infection than those who are immune competent and so should be screened every three years.

RECOMMENDATION – HPV NOT DETECTED	
R4.02 HPV not detected	**Evidence-based recommendation** Participants with a screening test result of HPV not detected' should be re-screened in five years. If a participant is immune deficient, they should be rescreened in three years.

Figure 1: HPV not detected - Cervical screening pathway (clinician-collected or self-collected)



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2. Gilham, C, Sargent, A, Crosbie E.J., & Peto, J. (2023) Long-term risks of invasive cervical cancer following HPV infection: follow-up of two screening cohorts in Manchester. British Journal of Cancer (2023) 128:1933–1940; https://doi.org/10.1038/s41416-023-02227-9

HPV detected 16 or 18

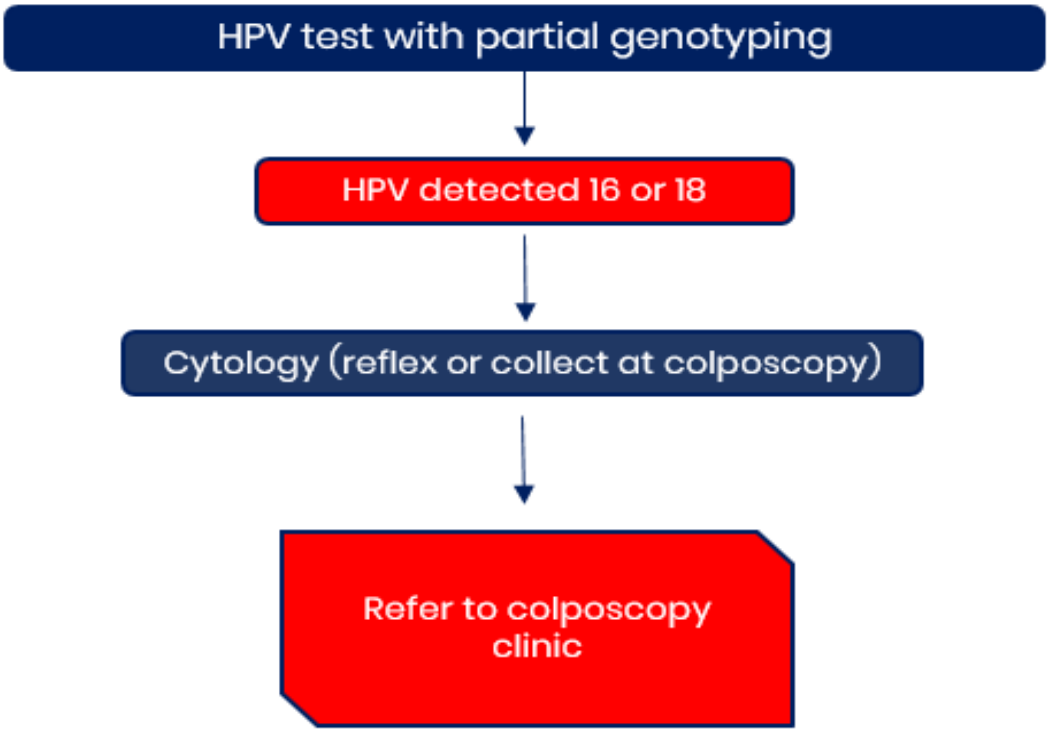
Persistence of infection with HPV types 16 or 18 is associated with a higher risk of CIN2+ disease compared with HPV Other high-risk HPV types.[1] [2] Worldwide, HPV 16 or 18 infections account for about 70% of cervical cancers.[3] Research in Aotearoa New Zealand has shown that approximately 65% of participants with cervical cancer have HPV 16 or 18 detected. The prevalence is not significantly different between Māori and non-Māori. [4] [5]

The prevalence of the different high-risk HPV types in Aotearoa New Zealand associated with cervical cancer is very similar to other countries such as Australia and the United Kingdom, despite differences in the proportion of the screening population that is vaccinated. This means that the research findings from other countries into types of HPV associated with cervical cancer is also applicable to Aotearoa New Zealand. [6]

All participants with HPV 16 or 18 should be referred to colposcopy when the HPV result is received, whether or not cytology has been performed. Where a cytology result is not available prior to colposcopy, a sample for cytology will be taken at the colposcopy visit.

RECOMMENDATIONS – HPV DETECTED 16 or 18	
R4.03 HPV detected 16 or 18 and a reflex cytology result	**Practice point** Participants with HPV detected 16 or 18 with a reflex cytology which is negative or abnormal should be referred to colposcopy irrespective of the result. This includes an unsatisfactory cytology report.
R4.04 HPV detected 16 or 18 results from a vaginal swab collected sample	**Practice point** Where an HPV detected 16 or 18 result is from a swab collected sample. Participants must be referred directly to colposcopy where a cytology sample will be taken at the colposcopy visit.
R4.05 HPV detected 16 or 18 and a cytology result suspicious of or definite for invasive cancer	**Practice point** Participants with a test result of HPV detected 16 or 18 and a cytology result suspicious of or definite for invasive cancer should be urgently referred to a colposcopist and seen within 10 working days from receipt of referral.
R4.06 Referral to colposcopy and support	**Practice point** Ask all participants / whānau whether they require assistance or support to attend their colposcopy appointment. Consider transport, cultural support and where appropriate offer referral to support to screening services.
R4.07 Topical estrogen prior to colposcopy	**Practice point** A short course of vaginal estrogen therapy is recommended in post-menopausal participants. It may also be useful for participants with vaginal atrophy associated with progestogen contraception or people using testosterone therapy. The recommended course of vaginal estrogen treatment is nightly for 3 weeks and should be stopped 2 nights prior to a cervical sample being taken. The reason for the use of vaginal estrogen should be explained (to reduce discomfort from the speculum, improve the diagnostic accuracy of colposcopy and any associated cytology and/or biopsy).

Figure 2: HPV 16 or 18 detected - Cervical screening pathway (clinician-collected or self-collected)



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HPV detected Other

HPV detected Other on vaginal swab

Participants with a vaginal swab collected sample that is HPV detected Other **should be recalled for a cervical sample** using a liquid-based cytology sample **within 6 weeks.**

Cytology is an important test used to triage those with HPV detected Other results, as it assists in determining the clinical pathway for participants. Approximately 5% of participants will have a high grade cytology following an HPV detected other.[1] If participants have a high grade cytology they will be seen earlier in the pathway.

Self-testing studies in Aotearoa New Zealand have shown that with a good informed consent process, shared decision making and early referral to Screening Support Services, most participants will attend for follow-up cytology and ongoing management.[2 3] It is also important to acknowledge that some participants may not attend for a follow-up cervical sample for cytology, after an HPV detected Other result.

For participants who have **not attended for follow-up cytology by 9 months'** efforts should be made to recall participants for a HPV vaginal swab test to determine whether the HPV has become not detectable.

The HPV test **should not be repeated earlier than 9 months** to provide an adequate period of time between testing to allow the HPV infection to resolve.

In certain circumstances it may be difficult to engage participants with ongoing cervical screening follow-up following a positive HPV detected Other result. Screen takers can discuss individual cases with colposcopy services where earlier review in colposcopy clinic may be warranted and is in the best interest of the participant.

HPV detected Other and negative, ASC-US or LSIL cytology

Participants with HPV detected Other and negative, ASC-US or LSIL cytology results are at lower risk of having precancerous cell changes than participants with HPV types 16 or 18. [1 4] Approximately 37-50% of HPV Other infections clear within 12 months [1 4] and the majority clear within 3 years. [5] Once these infections are no longer detected with HPV testing, participants are at very low risk high grade disease for at least five years. [5 6]

Follow up and modelling data from international studies and screening programmes including Australia have demonstrated that participants with persisting HPV detected Other and negative, ASC-US or LSIL cytology, can be managed more conservatively due to the lower risk of cancer. [1 7 8] This means that for participants with HPV detected Other and negative or low grade cytology, it is appropriate to delay referral for colposcopic assessment to allow the HPV infection time to resolve without treatment.

This approach avoids unnecessary colposcopies and the associated harms (such as over treatment and anxiety) for participants. Most cervical abnormalities caused by HPV detected Other infections will resolve without medical intervention. [1 7 8]

All participants with an HPV detected Other result and negative, ASC-US or LSIL cytology should have a repeat HPV test in 12 months. This can be a vaginal swab or a cervical sample.

Screen takers should explain the options available for a follow-up HPV test with participants. **It is important for screen takers** to discuss the potential need for an additional visit when the follow-up test is a vaginal swab**,** and the test is HPV detected Other as a cytology sample is recommended.

Approximately 40-50% of follow-up HPV tests will be not detected at 12 months [1 4 8] allowing a return to regular interval screening. Recent data from the UK and US indicate that this applies equally across all age groups. [5 8]

A change to the HPV detected Other pathway is the removal of the under/over 50 age category for participants with HPV detected Other on vaginal swab or cervical

sample with reflex cytology negative, ASC-US or LSIL cytology. Recent evidence suggests that participants over the age of 50 with persistent HPV detected Other and negative, ASC-US or LSIL cytology, do not have a higher risk of high grade disease or cervical cancer when compared to those under 50 years of age, therefore do not warrant earlier referral. [1 4 7-9] Participants aged 70-74 will also be managed on the same pathway and **it is important** a follow-up cytology is performed in this age group if a vaginal swab is used.

Management of participants with HPV test results at 12 months in the HPV detected Other pathway

Participants who have had a primary screen of HPV detected Other and negative, ASC-US or LSIL cytology should have a repeat HPV test in 12 months. Follow-up management of the 12-month result is dependent on the result and management is outlined below.

HPV not detected

If the 12-month repeat test result is HPV not detected, the participant should return to the regular interval screening.

HPV detected Other

A new recommendation If participants are overdue for screening by at least 2 years at their initial screen (with HPV detected other) and are aged 30 years and over with an HPV detected Other result again at 12 months they should be referred to colposcopy (vaginal swab or a cervical sample with reflex cytology - any result). Participants referred with a vaginal swab will have cytology performed at colposcopy.

For all other participants the following applies:

Participants with a vaginal swab sample that is HPV detected Other at 12 months **should be recalled for a cervical sample** using a liquid-based cytology **within 6 weeks.** Cytology is an important test used to triage those with HPV detected Other results, as it assists in determining the clinical pathway for participants. Approximately 5% of participants will have a high grade cytology following an HPV detected other. [1] Participants with HSIL cytology will be seen sooner at colposcopy.

Participants with a cervical sample with HPV detected Other and cytology which is

negative, ASC-US or LSIL should be recalled for another HPV test in a further 12 months.

HPV detected 16 or 18

If the follow-up HPV test result is HPV detected 16 or 18 referral to colposcopy should occur.

Management of participants with HPV test results at 24 months in the HPV detected Other pathway

Follow-up management of the 24-month test result is dependent on the result and management is outlined below.

HPV not detected

If the 24-month repeat test result is HPV not detected, the participant should be advised to return to regular interval screening.

HPV detected Other

If the 24-month repeat test result is HPV detected Other participants should be referred to colposcopy irrespective of the cytology result. If the participant had a vaginal swab a cytology will be performed at colposcopy.

Participants who are **2 years overdue** following their initial HPV detected Other test result and have a further HPV detected Other after 24 months they should be referred to colposcopy irrespective of the cytology result. The HPV detected Other may have been persistent for more than 24 months. If the participant had a vaginal swab a cytology will be performed at colposcopy.

HPV detected 16 or 18

If the 24-month repeat test result is HPV detected 16 or 18, the participant should be referred to colposcopy.

HPV detected Other and high grade cytology

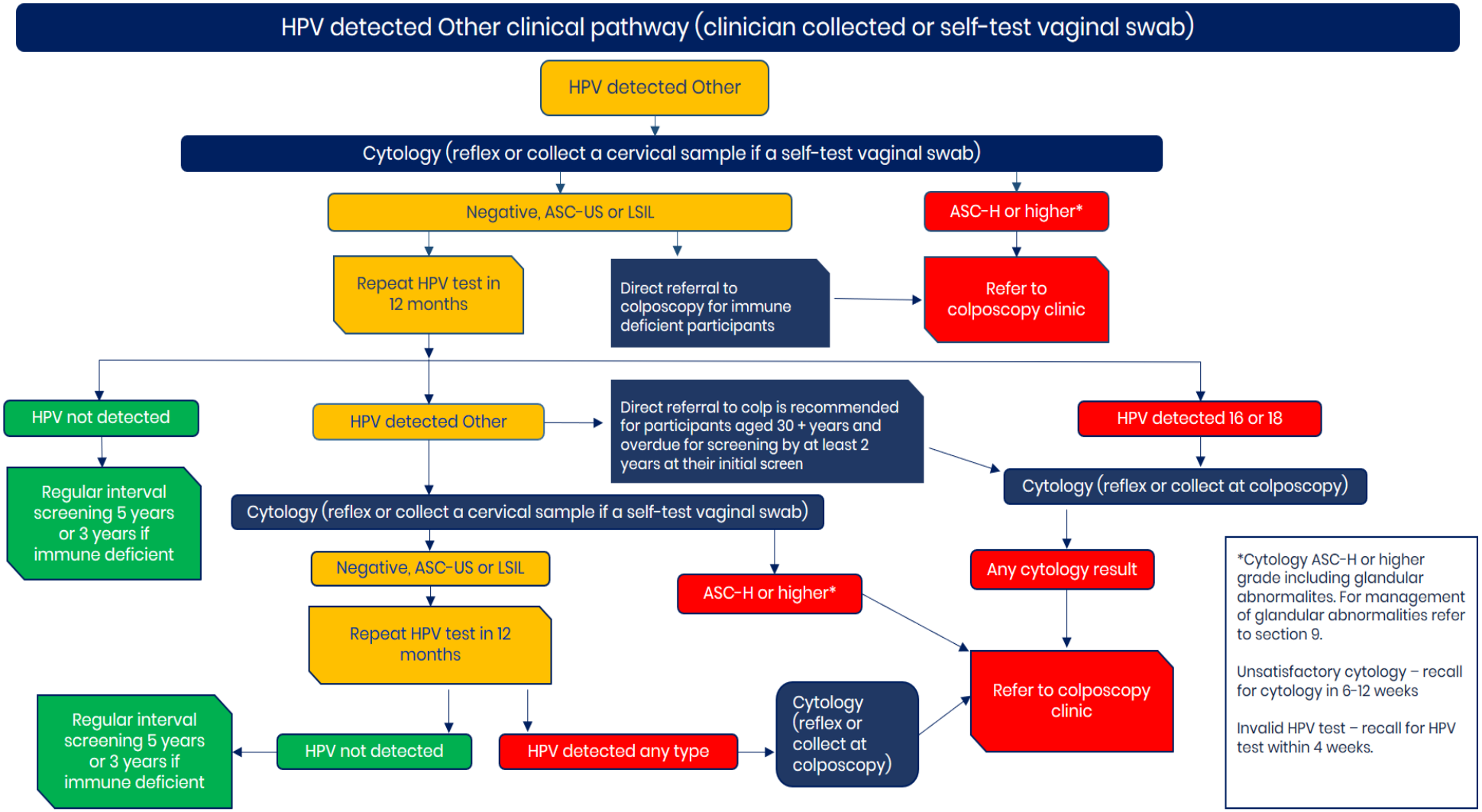
Participants with HPV detected Other and cytology reported as ASC-H, HSIL or any glandular abnormality including AIS are at higher risk of having high grade disease and should be referred directly to colposcopy when this occurs at any time on the HPV detected Other pathway [16]

- Those with cytology results of possible or definite invasive cancer must be urgently referred.
- Where the cytology reports atypical endometrial cells or endometrial cancer, the referral should be to gynaecology services, not to colposcopy, as long as there is no other co-existing reason for referral to colposcopy.

RECOMMENDATIONS – HPV DETECTED OTHER	
R4.08 HPV detected Other on a vaginal swab sample	**Practice point** Participants with vaginal swab-collected sample result of HPV detected Other should be recalled for a cervical sample for cytology within 6 weeks.
R4.09 Support for participants requiring follow-up cytology	**Practice point** Ask all participants/whānau whether they require assistance or support to attend for follow-up cytology. Consider transport, cultural support and where appropriate offer referral to Support to Screening Services.
R4.10 HPV detected Other on a vaginal swab result with no cytology result	**Consensus based recommendation** For participants who have not attended for follow-up cytology by 9 months' following an HPV detected Other primary screening result, efforts should be made to recall participants for an HPV test. It is acceptable to offer an HPV vaginal swab test to determine if the HPV test result has returned to not detected. The repeat HPV test should not be taken before 9 months to allow sufficient time for the HPV infection to resolve.
R4.11 Supporting participants where earlier colposcopy may be indicated due to individual /whānau circumstances	**Consensus based recommendation** Some participants will have circumstances that require extra support for ongoing cervical screening follow-up when HPV Other is detected. Screen takers can discuss individual cases with colposcopy services where earlier review in colposcopy clinic may be warranted, if it is in the best interests of the participant. Ask all participants/whānau whether they require assistance or support to attend their colposcopy appointment. Consider transport, cultural support and where appropriate referral to Screening Support Services.
R4.12 HPV detected Other and a cytology result of negative, ASC-US or LSIL	**Evidence based recommendation** Where participants have an HPV detected Other test result and a cytology result of negative, ASC-US or LSIL, they should have a repeat HPV test in 12 months.

R4.13 Repeat HPV test at 12 months (following HPV detected Other and a cytology result of negative or ASC-US/LSIL)	**Evidence based recommendation** If the 12-month repeat test result is HPV not detected, the participant should be advised to return to regular interval screening. If the 12-month repeat test result is HPV detected Other refer to the HPV detected Other flow chart for management. If the 12-month repeat test is HPV detected 16 or 18 refer to colposcopy.
R4.14 HPV detected Other and ASC-H, HSIL, or glandular abnormality on cytology	**Evidence based recommendation** Where participants have a test result of HPV detected Other and an ASC-H, HSIL, or any glandular abnormality on cytology, they should be referred to colposcopy. Those with an atypical endometrial cell cytology result should be referred to gynaecology services, unless there is a co-existing reason for referral to colposcopy.
R4.15 HPV detected Other and a cytology result suspicious of or definite for invasive cancer	**Evidence based recommendation** Where participants have a test result of HPV detected Other with a cytology result suspicious of or definite for invasive cancer, they should be referred to a colposcopist for urgent evaluation within 10 working days of from receiving the referral. Those with cytology reports of endometrial cancer should be urgently referred to gynaecology services, unless there is a coexisting reason for referral to colposcopy.
R4.16 Referral to colposcopy and support	**Practice point** Ask all participants/whānau whether they require assistance or support to attend their colposcopy appointment. Consider transport, cultural support and where appropriate offer referral to Support to Screening Services.
R4.17 Topical estrogen prior to repeat cervical sample or colposcopy	**Practice point** A short course of vaginal estrogen therapy is recommended in post-menopausal participants. It may also be useful for participants with vaginal atrophy associated with progestogen contraception or people using testosterone therapy. The recommended course of vaginal estrogen treatment is nightly for 3 weeks and should be stopped 2 nights prior to a cervical sample being taken. The reason for the use of vaginal estrogen should be explained to participants. (to reduce discomfort from the speculum and to improve the diagnostic accuracy of cytology).

Figure 3 HPV detected Other - Cervical screening pathway (clinician-collected or self-collected)



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