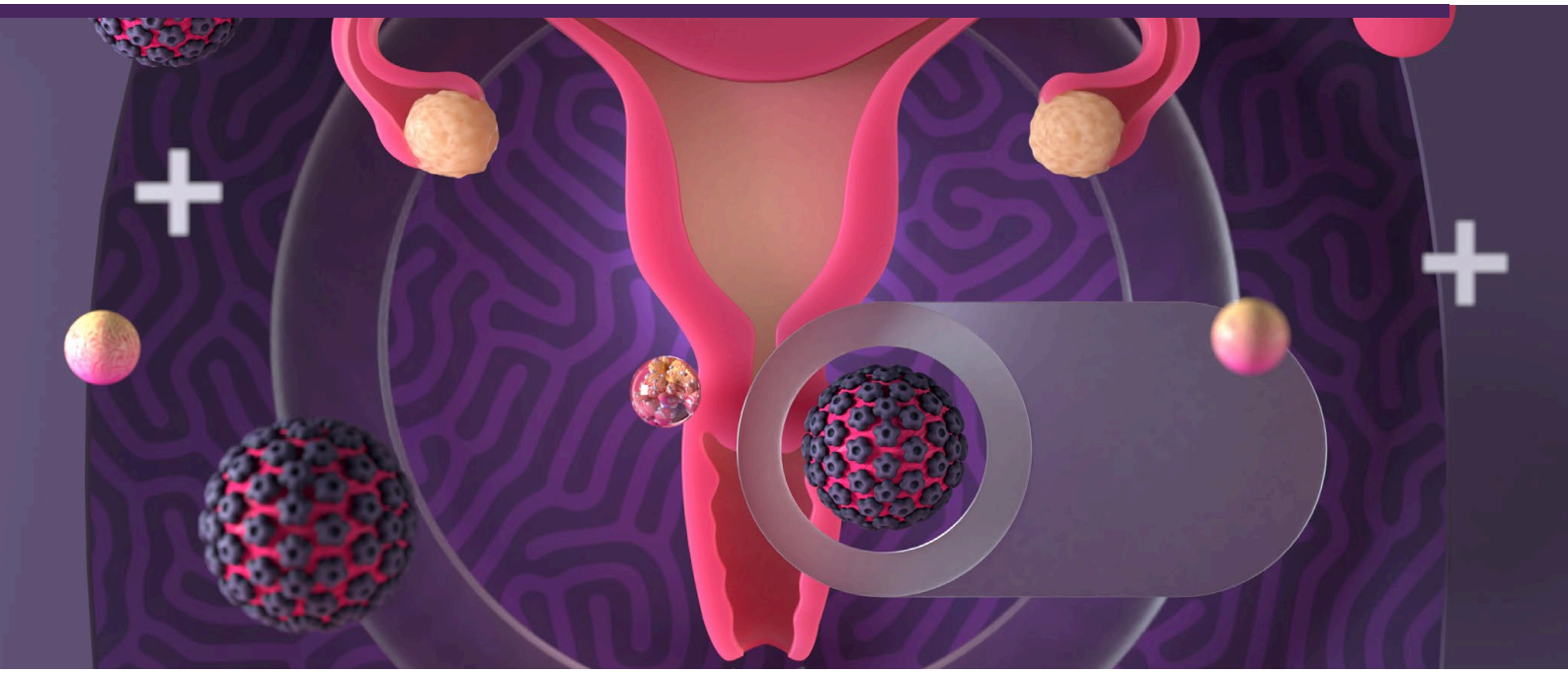

Cervical cancer – early detection and referral

The risk of cervical cancer is significantly reduced through HPV vaccination and cervical screening programmes, however, there are still an average of 171 females newly diagnosed with cervical cancer each year (from 2015 – 2020) in New Zealand. Upcoming changes to the cervical screening programme in New Zealand in 2023, including moving to HPV primary screening, are predicted to further reduce the burden of cervical cancer.

KEY PRACTICE POINTS

- Human papillomavirus (HPV) is the major cause of cervical cancer
- Up to 80% of people (including males) who are sexually active are infected with HPV at some stage in their life, however, for most people infection is transient and self-resolves. Persistent infection with high-risk HPV types can over time cause pre-cancerous cervical lesions that, if left untreated, progress to invasive cervical cancer.
- HPV vaccination prevents new HPV infections and is the most effective cervical cancer prevention strategy. Gardasil 9 is the currently recommended vaccine, funded for eligible females and males aged 9 – 26 years. It is most effective when administered prior to the onset of sexual activity but vaccinating those who have already commenced sexual activity is still recommended.
- Most females who develop pre-cancerous cervical lesions are asymptomatic and therefore cervical screening programmes are the best approach for detecting these abnormalities early
- Symptoms and signs of cervical cancer may include abnormal vaginal bleeding, unusual and persistent vaginal discharge, non-specific pelvic or low back pain or pressure, abdominal pain or pain during sexual intercourse; initiate further investigations if symptoms are reported irrespective of cytology results
- Cervical cytological analysis using liquid-based cytology (LBC) is the current method of cervical screening in New Zealand. Females with a cervix aged 25 – 69 years who have ever been sexually active are recommended to undergo cervical screening every three years:
  - Management is dependent on the cytology results; if high-grade lesions are identified, referral for colposcopy is indicated. See main text for further details on managing other cytology results.
  - If the cervix is visually abnormal during screening, refer to or discuss with a colposcopy service irrespective of the cytology result
- From July, 2023, HPV testing, which can be performed on a LBC sample or on a vaginal swab sample, will become the primary cervical screening test in New Zealand:
  - If any HPV types are detected, cytology is then performed (there is a direct referral to colposcopy option for those who test positive for HPV type 16 or 18) with management dependent on the results
- HPV testing is more sensitive than cytology and has a self-testing option using a vaginal swab. The vaginal swab sample can also be taken with the assistance of a clinician if preferred. The new screening interval for participants with normal results will be five years. HPV testing is expected to increase cervical screening attendance, further reduce the incidence and mortality from cervical cancer and improve equitable outcomes.

N.B. The term "female" is used in this article to describe the biological sex of the patient population who are at risk of cervical cancer. However, we acknowledge that this may not reflect the identity of all patients, which will include transgender boys or men, intersex and non-binary individuals. Also see footnote on Page 6, for terminology used in the National Cervical Screening Programme.

A future article will cover the follow-up and surveillance of a patient after curative-intent treatment for cervical cancer.

From 2023, the primary cervical screening test in New Zealand will change from liquid-based cytology to HPV testing. This article will be updated once the new cervical screening programme is established.

Cervical cancer is the third most common gynaecological cancer in New Zealand

Cervical cancer is now largely preventable through human papillomavirus (HPV) vaccination and cervical screening programmes. Since the implementation of these programmes in New Zealand, fewer people are being diagnosed with and dying from cervical cancer. However, there are on average 171 new diagnoses (6.2 per 100,000 females; from 2015 – 2020) and 53 deaths (1.6 per 100,000 females; from 2015 – 2018)* caused by cervical cancer each year.†[1,2]

* Mortality data are available for 2019, but are preliminary so have not been included. Mortality data for 2020 are not yet available.

† There are differences in published data. For consistency across the gynaecological cancer series, incidence and mortality data has primarily been obtained from the publication – **Cancer: Historical summary 1948 – 2020.**

Squamous cell carcinoma is the most common type of cervical cancer in New Zealand (approximately 70% of all cases), followed by adenocarcinoma of the glandular cells lining the cervix (approximately 20% of all cases).[3] Persistent HPV infection is necessary for the development of almost all cases of cervical cancer; other factors, however, also contribute to the incidence and progression (see: "HPV infection is responsible for almost all cases of cervical cancer").[4]

People are generally infected with HPV shortly after the onset of sexual activity, but for most people the infection is transient.[5] For those with persistent infection, progression to invasive cervical cancer is slow, with peak incidence between the ages of 25 and 44 years.[6–8] The five-year survival rate from cervical cancer in New Zealand between 2010 – 2014 (latest data available) was 67.4%.[9] Internationally, five-year survival rates vary widely but are generally better in high-income countries.[9] Cervical screening programmes are therefore essential to identify precursor lesions and to prevent the development of invasive cervical cancer (see: "The early detection of cervical cancer is possible through cervical screening programmes").

Incidence and mortality rates from cervical cancer have reduced over time

Since 1990, the overall incidence and mortality rates from cervical cancer in New Zealand have reduced from 13.9 and 5.5 per 100,000 females to 6.7 and 1.7 per 100,000 females in 2018, respectively (Figure 1).[1] The most recent data available (2020) show that incidence is still declining (5.7 per 100,000 females).[1] This has occurred primarily because of nationally

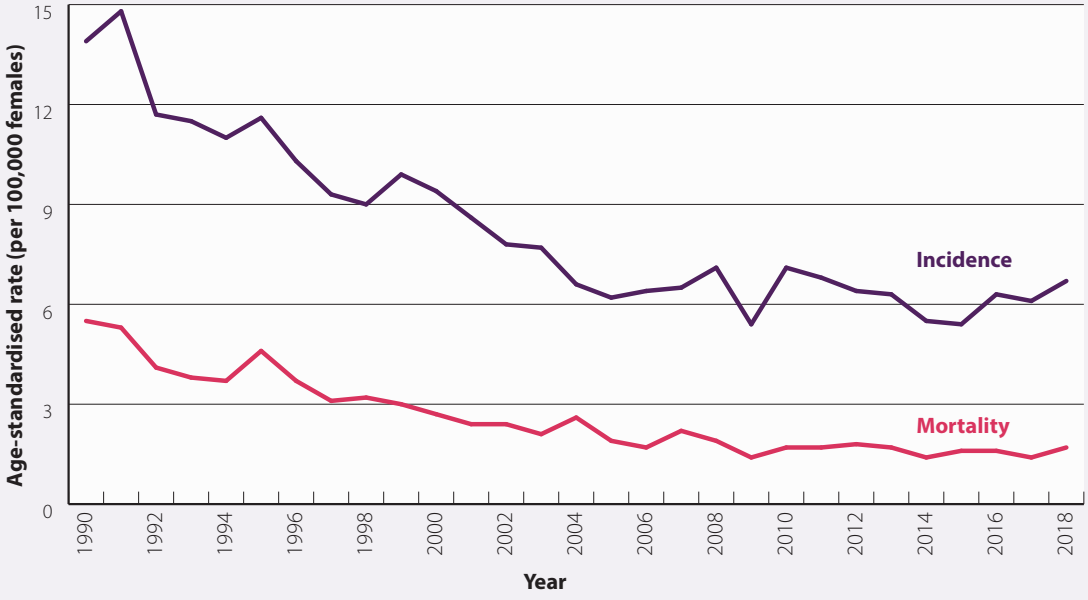

Figure 1. Age-standardised incidence and mortality rates (per 100,000 females) for cervical cancer between 1990 and 2018 in New Zealand.[1] N.B. Incidence data are available up to 2020 but have not been included in this graph for comparative purposes. Mortality data are available for 2019, but are preliminary so have not been included. Mortality data for 2020 are not yet available.

co-ordinated cervical screening (established in 1990) and HPV immunisation (established in 2008) programmes, and well-established diagnostic and treatment services in New Zealand. Other factors such as reduced rates of smoking and improvements in sexual practices, e.g. condom use/barrier contraception, may also have contributed.[10, 11]

Incidence and mortality rates from cervical cancer in New Zealand are similar to those in Australia and North America, e.g. Canada, but lower than those in Northern Europe, e.g. the United Kingdom.[12]

There are significant ethnic and socioeconomic inequities in cervical cancer incidence and mortality

Despite incidence and mortality rates from cervical cancer having reduced overall in New Zealand, Māori and Pacific peoples continue to have a higher incidence rate (Figure 2).[2] Māori are also more than twice as likely to die from cervical cancer than Europeans.[13] Cervical cancer is the second leading cause of death for Māori females aged 25 – 44 years.[14]

HPV infection is responsible for almost all cases of cervical cancer

HPV DNA is present in 99% of all cervical cancers, but infection alone in people with a competent immune system is not sufficient to cause invasive cervical cancer.[4, 10]

Many risk factors (see across) for developing cervical cancer are also related to an increased risk of HPV and can be explained largely by the degree of HPV exposure countered by the degree of participation in cervical screening and HPV immunisation. It is difficult to determine which risk factors are independent of HPV infection.

Risk factors for the development of cervical cancer, in addition to HPV infection, include:

- **Pre-cancerous cervical lesions.** Females treated for cervical intraepithelial neoplasia (CIN) have a two-to-three-fold increased risk of developing cervical cancer.[15]
- **History of HPV-related vulval or vaginal dysplasia**[16]
- **Immunosuppression.**[10, 16, 17] Immune deficiency is associated with an increased risk of HPV infection and an increased rate of progression of cervical cancer.
- **Low rates of cervical screening attendance**[16]
- **Low socioeconomic status**[10]
- **Younger age at sexual activity onset**[15, 16]
- **Increasing number of sexual partners or a high-risk sexual partner.**[15, 16] Females with more than six lifetime sexual partners are approximately three times more likely to develop cervical cancer compared to those with one sexual partner.[10]
- **History of sexually transmitted infections** (STIs).[16] Particularly chlamydia or genital herpes.[15]
- **Long-term oral contraceptive use.***[10, 17] The risk of cervical cancer increases in proportion to the duration of oral contraceptive use (1.9-fold for every five years of oral contraceptive use) and reduces after cessation.[15] It is unclear whether HPV exposure is a confounding factor.
- **Young age at first full-term pregnancy.**[15] Females who give birth before age 17 years have approximately three times the risk of developing cervical cancer than those who give birth after age 25 years.[10]

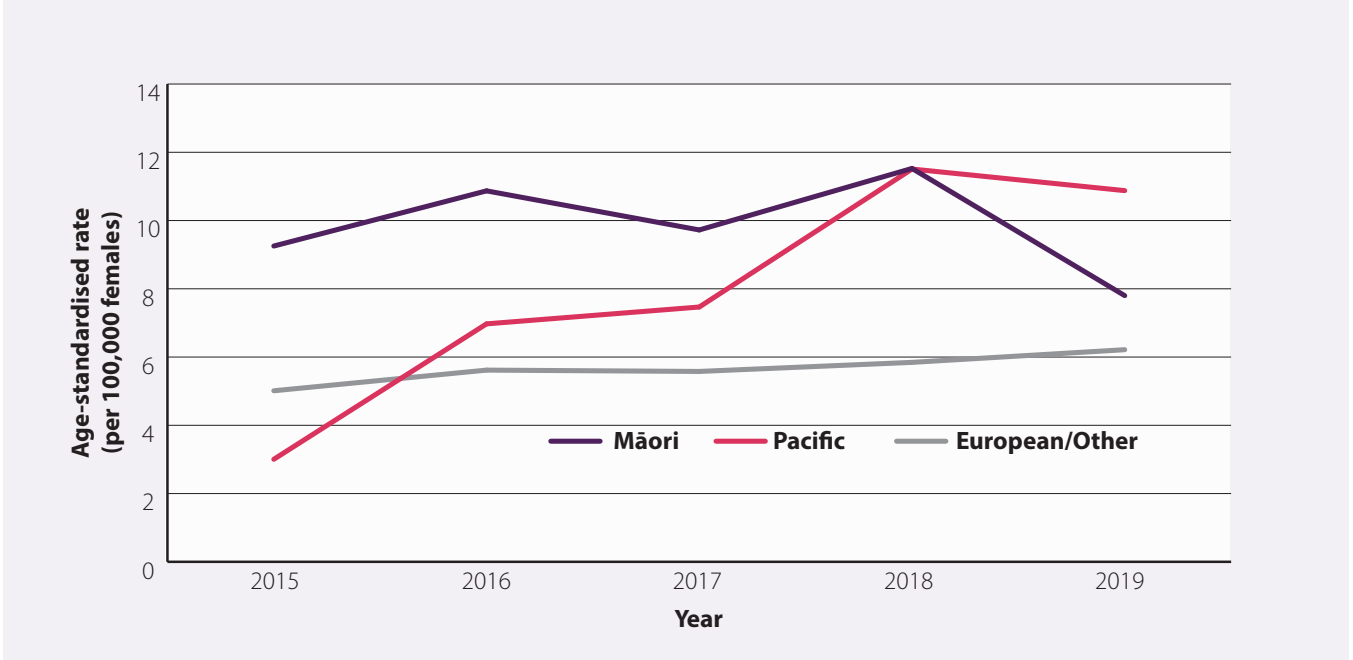

Figure 2. Age-standardised incidence rate (per 100,000 females) for cervical cancer by ethnicity between 2015 and 2019 in New Zealand.[2] N.B. Incidence data by ethnicity are not yet available for 2020.

- **Increasing number of full-term pregnancies.**[15, 17] Females with more than five full-term pregnancies are approximately twice as likely to develop cervical cancer than females with one to two full-term pregnancies.[10]
- **Smoking.**[16, 17] Smoking is an established co-factor (with HPV) for the development of pre-cancerous cervical lesions and cervical cancer. Females who smoke are approximately twice as likely to develop cervical cancer than females who do not smoke.[10] The risk of cervical cancer increases in proportion with the duration and quantity smoked and reduces with smoking cessation.
- ***In utero* exposure to diethylstilboestrol (DES).**† Increases the risk of CIN 2 or higher.[10]
- **Family history of cervical cancer.** This is not usually a significant factor, except for an association with some very rare genetic conditions.

* In contrast, intrauterine devices (IUD) have been shown to protect against progression to invasive cervical cancer.[10] The exact mechanism of protection is unknown, but a local cellular immune response from the IUD may help the body to clear the HPV infection.[10] Protection begins after less than one year of use and persists after the device has been removed.[10]

† DES was used by approximately 1,000 pregnant females in New Zealand between the 1940s and 1960s to reduce the risk of miscarriage.[18] Female offspring exposed *in utero* prior to 18 weeks' gestation have an increased risk of clear cell adenocarcinoma of the cervix (and vagina), high-grade intraepithelial lesions (CIN 2/3) and cervical cancer. As DES has not been used during pregnancy for more than 45 years, the problem is declining.[19]

Most HPV infections resolve spontaneously

HPV is spread through skin-to-skin contact, most commonly through sexual activity.[5] It is estimated that two-thirds of people (including males) become infected with HPV within three years of being sexually active, and up to 80% of people will be exposed to HPV at some stage in their lifetime.[5, 20]

There are over 200 types of HPV; 100 are relevant to the cervix. These are divided into high- and low-risk based on oncogenic potential.[8] For most people (90%), infection is transient and spontaneously resolves within six to 24 months, but for others, HPV infection may become latent or persistent.[4, 5, 10] Persistent infection with high-risk HPV types (see box) is generally asymptomatic but can lead to the development of cancers over time, including cervical, vulval, vaginal, anal, penile and oropharyngeal.[5]

High-risk HPV types 16 and 18 cause approximately 70% of all cervical cancers and up to 60% of precursor lesions.[11] Other high-risk types are 31, 33, 35, 39, 45, 52, 56, 58, 59 and 68. Low-risk types, particularly 6 and 11, are commonly associated with non-malignant lesions, e.g. genital warts.[5]

Cervical cancer progression. A small proportion of females with persistent infection with high-risk HPV types, develop pre-cancerous cervical lesions that can progress to invasive cervical cancer if left untreated (Figure 3).[4, 5] However, fewer than one-third of low grade pre-cancerous lesions progress to high-grade lesions and the majority of those do not progress to cervical cancer.[10] Regression of pre-cancerous cells to normal cells can also occur, usually within one to two years.[4] Progression to invasive cervical cancer is slow, taking up to 20 years, which provides multiple opportunities for the early detection of pre-cancerous cervical lesions through cervical screening programmes (see: "National Cervical Screening Programme").[5, 19]

Prophylactic HPV vaccination is the primary prevention strategy for cervical cancer

HPV vaccination can protect against the acquisition of new HPV infections; it does not reduce the progression of established cervical lesions.[5] It is estimated that 92% of cancers caused by HPV can be prevented by vaccination with Gardasil 9 if administered prior to HPV exposure.[19]

The HPV immunisation programme was first launched in New Zealand in 2008 (Figure 4). A retrospective population-based study (including 104,313 people) in New Zealand using data from 2010 – 2015 found that females aged 20 – 24 years who had at least one dose of the quadrivalent HPV vaccine (Gardasil 4) prior to age 18 years, had a 25% lower incidence of high-grade cervical cytology and 31% lower incidence of high-grade histology compared to those who were unvaccinated.[21]

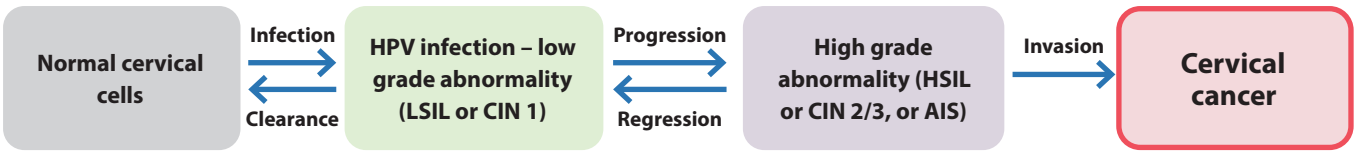

Figure 3. An overview of the development of cervical cancer from infection to invasion.

LSIL, low-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion; AIS, adenocarcinoma *in situ*

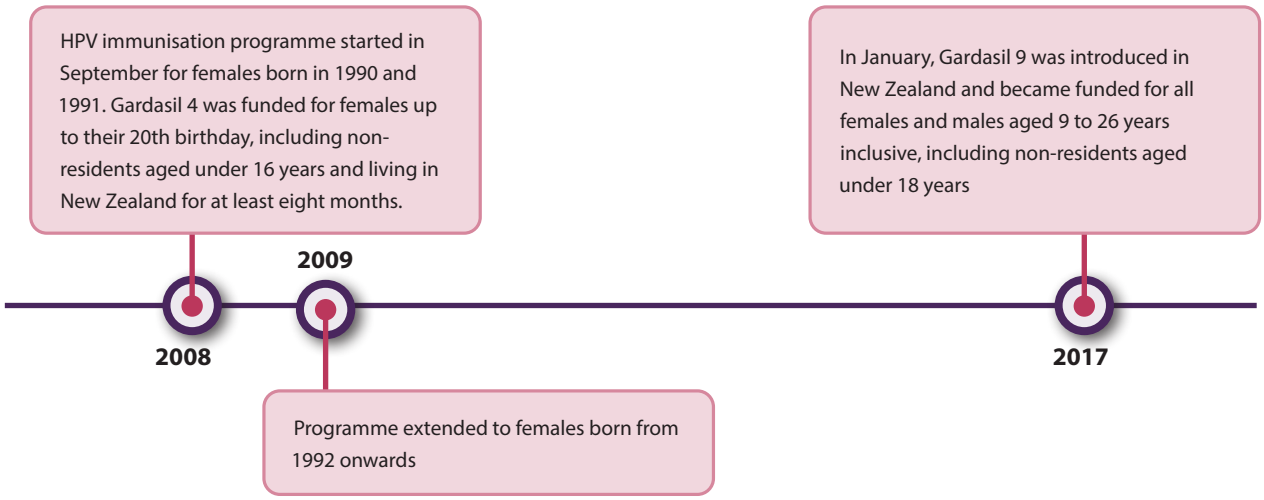

Figure 4. Timeline detailing significant events in the HPV immunisation programme in New Zealand.[22]

Gardasil 9 has been used in New Zealand since 2017 and protects against nine types of HPV (6, 11, 16, 18, 31, 33, 45, 52, 58); seven of which cause HPV-related cancers and two cause genital warts.[5] HPV vaccination is recommended for all females and males ideally before the onset of sexual activity, and is funded for eligible people aged 9 – 26 years inclusive*.[5] School immunisation programmes and general practices generally offer HPV vaccination to students in Year Eight (around age 12 years). The vaccine can be administered (not funded) to people aged 27 years and older if they have not been vaccinated before and are likely to benefit, e.g. people who are newly sexually active, men who have sex with men.[5]

Expert tip. Vaccinating people who have already commenced sexual activity is still recommended as even if they have been infected with one or several HPV types, there are 14 high-risk types associated with cervical cancer, and so it is unlikely that someone will have been infected with all of them.

N.B. Gardasil 9 is registered for use in females aged 9 – 45 years and in males aged 9 – 26 years. However, there are no theoretical concerns that the efficacy or safety of the vaccine in males aged up to 45 years will differ significantly from females of the same age or younger males.[5]

* If the course is started prior to the patients 27th birthday, the rest of the course is funded. For further information on funded indications, see: **https://www.health.govt.nz/publication/immunisation-handbook-2020**

The early detection of cervical cancer is possible through cervical screening programmes

Despite the HPV immunisation programme being effective at reducing the prevalence of HPV infection and the incidence of cervical cancer, vaccination cannot eliminate cervical cancer entirely as people may:[5]

- Not have been eligible for vaccination, did not opt to be vaccinated or did not complete the course*
  - Mostly, only people born after 1990 have been vaccinated; the vaccination rate among the eligible population (including males) born in 2008 (most recent data) was 56%; 75% of people had at least one dose.[23] Vaccination rates were highest among Asian peoples (62%), followed by European/Other (59%), Pacific peoples (52%) and Māori (50%).[23] Coverage needs to be 75 – 80% to achieve herd immunity.[24]
- Have been exposed to HPV prior to being vaccinated
- Have been infected with a high-risk type of HPV that was not covered by the vaccine (Gardasil 9 only covers seven of the 14 high-risk HPV types known to be associated with cervical cancer)
- Have been infected with a low-risk type of HPV that very rarely, can cause cervical cancer
- Have a non-HPV associated cervical malignancy

* In rare cases, people may not develop immunity despite being vaccinated[5]

Therefore, all eligible people including those who have been vaccinated against HPV, should undergo regular cervical screening to detect any pre-cancerous lesions and prevent progression to invasive cervical cancer.

National Cervical Screening Programme

Most females with pre-cancerous cervical lesions are asymptomatic and therefore, screening programmes are required to detect these pre-cancerous changes early (see box for symptoms and signs of invasive cervical cancer).[7,19] Since the National Cervical Screening Programme (NCSP) began in 1990, overall incidence and mortality rates from cervical cancer have reduced by approximately 50% and 60%, respectively (Figure 1).[20] Rates have declined among all ethnicities, particularly for Māori, however, inequities still exist.[3,20]

Current cervical screening relies on the microscopic analysis of cells taken from the cervix during a speculum examination, utilising liquid-based cytology (LBC). If the cervix is visually abnormal upon cell collection, patients should be referred for a colposcopy irrespective of the cytology report.[20]

The NCSP currently recommends three-yearly cervical cytology screening for females* aged between 25 and 69 years† who have ever been sexually active.[19] Also see "Cervical screening in special clinical circumstances", Page 7.

* The NCSP refers to the eligible screening population as "participants" and define this as anyone who is sexually active and has a cervix

† Prior to 2019, the start age was 20 years; people aged < 25 years who have already started cervical screening should continue to be recalled and managed in the same way as those aged 25 – 69 years. People aged ≥ 70 years who were unscreened or under-screened prior to age 70 years are recommended to have two consecutive normal cytology samples (taken 12 months apart) before ceasing screening.[19]

Cervical screening attendance has declined over time

Three-yearly cervical screening attendance in New Zealand has been steadily declining over time, with an accelerated rate of decline during the COVID-19 pandemic, from 76% of eligible people in 2008, to 67% in June, 2022.[27]

There are considerable inequities in cervical screening attendance; in June, 2022, the national three-year coverage was 57.7% for Asian, 55.7% for Pacific peoples and 54.9% for Māori, compared to 74.4% for European/Other.[27] People who live in low socioeconomic areas also have lower rates of attendance for cervical screening.[19] Low rates of cervical screening attendance is concerning as most cervical cancers in New Zealand occur in people who are not regularly screened.[19]

Reducing barriers to cervical screening

The following strategies may be used to enhance cervical screening attendance:[28, 29]

- Discuss or offer (if time allows) screening to people who are overdue when they present for any reason, i.e. opportunistic screening
- Ask patients how they would like to be contacted with reminders, and note this in their clinical record
- Provide culturally appropriate educational materials on the importance of cervical cancer screening in waiting or consultation rooms, e.g. **https://www.healthed.govt.nz/search?topic%5B0%5D=33&type=resource&mode=picture-view**
- Assess eligibility for funded or low-cost cervical screening
  - Priority groups for the NCSP are Māori and Pacific peoples who are due, and anyone who is overdue for screening or never screened. Check local HealthPathways for a full list of priority groups and funding initiatives in your region.
- Consider whether your practice could offer occasional dedicated times for people to attend for cervical screening, e.g. a monthly evening or weekend session, or a weekly morning or early evening slot. N.B. We acknowledge that this might not be achievable in the current COVID-19 environment.
- Take time to ask the patient if they have any questions or concerns about the cervical screening procedure. Not knowing what to expect or the fear of finding cancer can be a barrier to access for some people. Address any concerns and reassure patients as appropriate.

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Getting a good cervical sample

The role of lubricant. Use of lubricant can result in unsatisfactory cervical cytology results;[19] lukewarm water may be a suitable alternative. If a lubricant is required, apply a water-based product sparingly to the outer sides/exterior of the speculum blades, making sure to avoid the tip so that lubricant does not get into the liquid cytology vial.[25]

The role of vaginal oestrogen cream. A course of vaginal oestrogen can be offered prior to cytology testing for people who are post-menopausal, post-natal or breastfeeding, or for other people experiencing vaginal dryness, including transgender males. Vaginal oestrogen cream can reduce the discomfort of a speculum examination associated with vaginal dryness/atrophy, and can improve visualisation of the cervix, the quality of the cervical sample and diagnostic accuracy of liquid-based cytology.[8, 26] Instruct patients to insert the cream each night for two to three weeks prior to the test and to stop one to two days before the appointment.[8] N.B. Patients should also stop use of other vaginal applications, e.g. anti-fungal creams, spermicides, prior to the appointment.

N.B. Although bleeding has less of an impact on the quality of a cervical sample now that liquid-based cytology is used, the general advice is to avoid taking a sample during menstruation, if possible.

Cervical screening in special clinical circumstances

Pregnancy. Cervical screening is safe during pregnancy and should not be deferred until the post-partum period, particularly if the person:[19]

- Has never been screened
- Is overdue for screening
- Has abnormal screening history and is due for screening
- Is recommended to have a follow-up test

The post-partum period is not an ideal time for cervical screening as the transitional lack of oestrogen makes the cytology more difficult to interpret. Females who are post-natal or breastfeeding may experience vaginal dryness or atrophy due to lower oestrogen levels; consider a course of vaginal oestrogen cream if cervical screening is required.[19]

People aged older than 40* years with normal endometrial cells detected with cervical cytology. Endometrial cells are sometimes detected with cervical cytology, and this is not usually a concern (unless the cells are abnormal). However, given that in rare cases this may indicate endometrial cancer, further investigation is required for people aged older than 40 – 45 years.[19]

* Normal endometrial cells will soon be reported from the age of 45 years, rather than the current age of 40 years.[19] This change will be introduced when HPV primary screening commences and a new NCSP Register is used.

Immunodeficiency. Females who are immune deficient may require more frequent cervical screening than every three years due to evidence of an increased risk of persistent HPV infection and cervical lesions, and because established lesions may progress more rapidly.[19] Based on current evidence, people with immune deficiency can be divided into two groups with regard to cervical screening intervals:[19]

- **Annual screening is required** for people with HIV and those who have had a solid organ transplant due to definitive evidence of increased risk
- **Annual screening is recommended** for people who are immune deficient for other reasons such as a disease causing immune deficiency, those taking immunosuppressant medicines or with congenital (primary) immune-compromising disease

The evidence-base for those in the second group is thought to not be definitive enough to require (rather than recommend) annual screening and clinicians are advised to make an individualised decision for people in this group.[19] The guidance is considered to represent a cautious approach until further evidence is available.

The threshold for colposcopy for a person with immune deficiency and an abnormal cytology result should also be lower than for the general population.[19]

Reminder: Young people who have been sexually active and who have been immune deficient for more than five years should start cervical screening before age 25 years.[19]

Ensure an appropriate recall is set on your PMS for patients eligible for cervical screening who have immune deficiency. You can also contact the National Cervical Screening Register team (0800 506 050) to add immune deficiency as a medical condition on a patient's record which will flag them as requiring annual screening, otherwise the default recall will be three years.

For information on specific cervical screening recommendations for people with immune deficiency, see: **www.nsu.govt.nz/system/files/resources/final_ncsp-guidelines-for-cervical-screening-new-zealand-5_june_2020.pdf#page=50**

Hysterectomy. Cervical screening is recommended in some instances after hysterectomy, unless the hysterectomy was for benign reasons and the patient has a normal screening history.[19] For specific recommendations, see: **https://www.nsu.govt.nz/system/files/page/guideline_17_-_management_of_women_with_a_hysterectomy.pdf**

In utero* exposure to diethylstilboestrol. Offer annual cervical screening and referral for colposcopic examination.[19]

* See earlier note Page 4

Transgender and non-binary people. Transgender men and non-binary people with a cervix are recommended to participate in cervical screening programmes to the same extent as cisgender females.[31] Additional attention may need to be given to addressing concerns around the testing procedure, privacy and recalls. N.B. There is no evidence that use of testosterone modifies the risk of cervical cancer, however, long-term use may cause vaginal atrophy which can alter cytology wresults; some patients may wish to be prescribed a course of vaginal oestrogen cream prior to testing.[32]

Practice Tip. If you change a patient's gender to male in their clinical record, ensure they remain in the practice recall system for cervical screening and enrolled with the National Cervical Screening Programme.

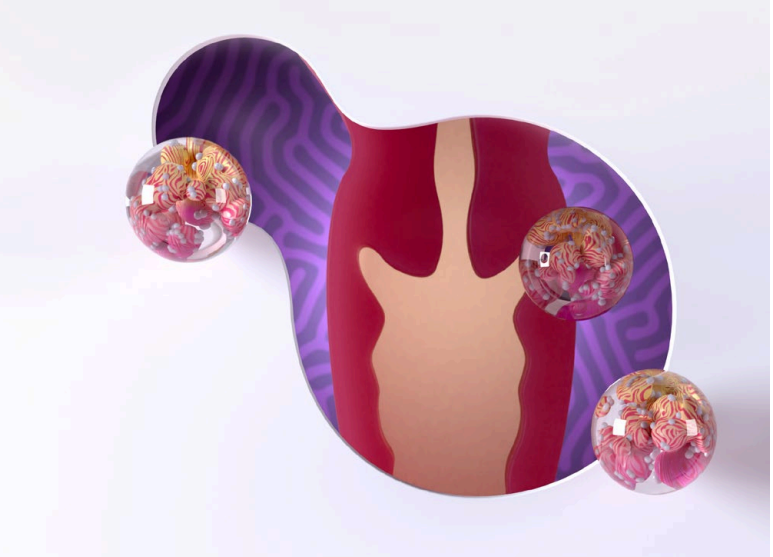
Invasive cervical cancer

Symptoms of cervical cancer can be subtle and may be attributed to other gynaecological conditions.[30] The presence of multiple symptoms and signs should raise clinical suspicion for cervical cancer:[7, 10, 15, 30]

- Abnormal vaginal bleeding, including inter-menstrual, post-menopausal or post-coital bleeding; bleeding is the most common symptom of cervical cancer
- Unusual and persistent vaginal discharge
- Dyspareunia
- Non-specific pelvic or low back pain or pressure
- Abdominal pain
- Loss of appetite, weight loss or fatigue
- Bladder changes, i.e. urinary tract infection, incontinence, haematuria
- Bowel changes, e.g. haematochezia
- Unexplained laboratory results, e.g. low haemoglobin or ferritin, high white blood cell count (N.B. Biochemical changes are often not present.)

In advanced cervical cancer, the combination of lower limb oedema, flank pain and sciatica suggests pelvic sidewall invasion.[16] Passage of urine or faeces through the vagina suggests invasion of the bladder or rectum.[16]

Perform a pelvic examination, including a cervical cytology test, on patients with suspicion of cervical cancer.[7, 15] Palpable inguinal or supraclavicular lymph nodes suggest advanced cancer.[15, 16] If the patient has symptoms or signs of cervical cancer or if the appearance of the cervix is abnormal, refer to or discuss with a colposcopy service, irrespective of the cytology report.[19] Check local HealthPathways for specific referral information.



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- Address any issues that may cause difficulties in taking the sample, e.g. initiate vaginal oestrogen cream for people who are post-menopausal, warm the speculum before insertion
- Minimise embarrassment or vulnerability by discussing ways that could make the patient more comfortable, e.g. bringing a support person, choosing their sample taker (gender, ethnicity), appropriate covering of the patient and pulling curtains around the bed to ensure privacy. Explaining each step of the process as it is performed can be helpful to make the patient more relaxed.
- Provide reassurance about confidentiality. Some people may not want to attend cervical screening because it acknowledges that they are sexually active. Reassure these patients that the consultation is entirely confidential and remind them that they do not need to disclose to others the reason for their appointment.

The cytology report is back; where to from here?

N.B. Clinical Practice Guidelines for Cervical Screening in New Zealand are currently being revised; this section will be updated to reflect these once the guideline is made publicly available.

Non-result (unsatisfactory sample)

Recall for repeat cytology in four to six weeks. Refer the patient to a colposcopy service after three consecutive unsatisfactory results.[19]

Negative for squamous or glandular intraepithelial cervical lesion or malignancy (i.e. a normal test result)

Recall for repeat cytology in three years. However, if this is the first test or more than five years have passed since the previous test, recall in 12 months.[19]

Low-grade cervical abnormality

Low-grade cervical abnormalities (i.e. atypical squamous cells of undetermined significance [ASC-US] or low-grade squamous intraepithelial lesion [LSIL]) are associated with a low risk of progressing to cervical cancer. These abnormalities indicate the presence of a viral infection that will resolve for the majority of people within two years; treatment is not usually required.[19] The management of a patient with a low-grade abnormality currently differs depending on their age (Figure 5).

Follow-up after colposcopy for a patient with a low-grade abnormality

If the results from colposcopy are normal, the patient will be referred back to primary care and a recall for repeat cytology should be placed at 12 and 24 months post-discharge from

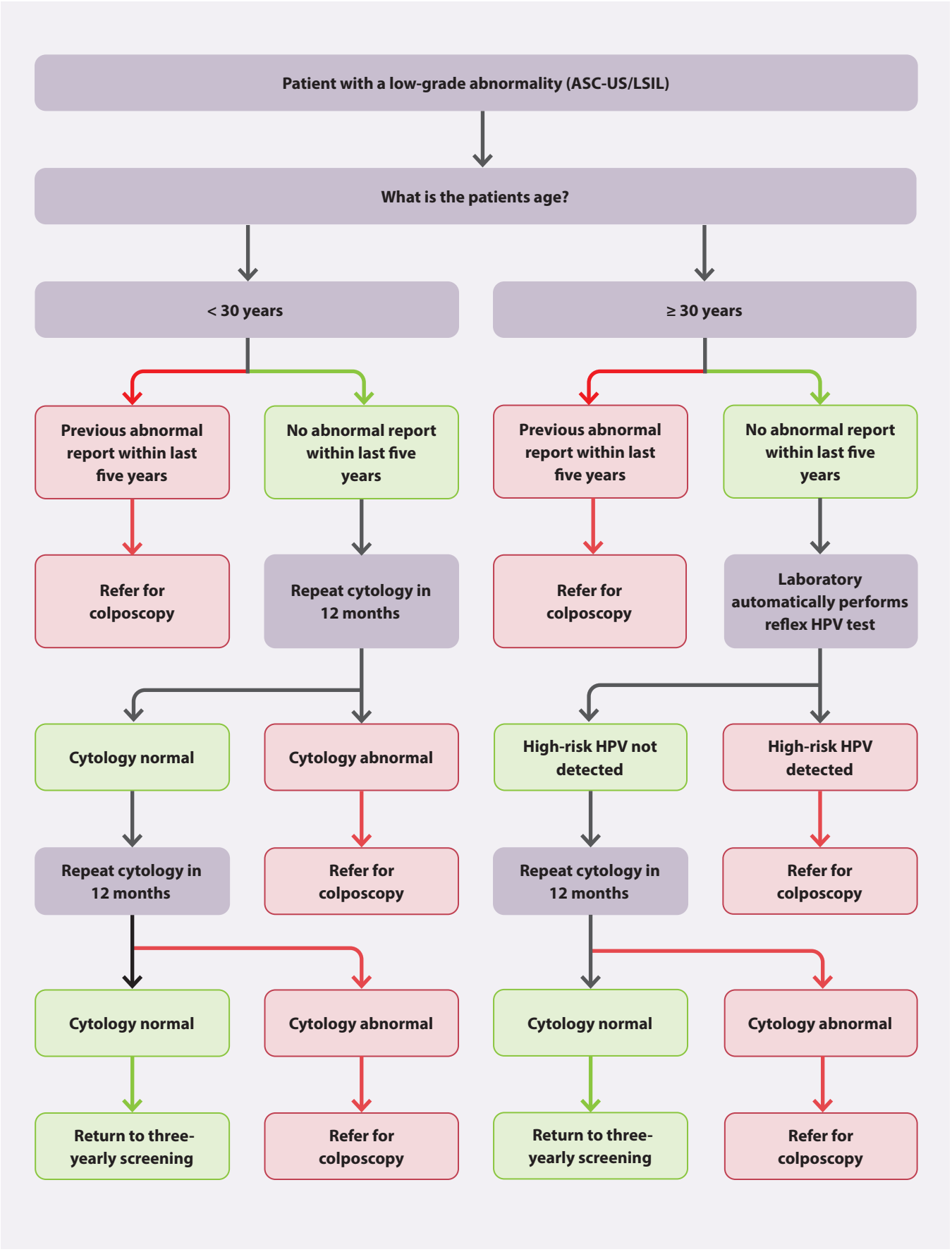


Figure 5. Management pathway for a patient with a low-grade (ASC-US or LSIL) cervical abnormality. Adapted from Ministry of Health, 2020.[19] N.B. A new guideline is under development. As information is likely to change when the guideline is released, this article will be revised when it is made publicly available.

ASC-US, atypical squamous cells of undetermined significance; LSIL, low-grade squamous intraepithelial lesion

colposcopy. If these subsequent cytology tests return:[19]

- Any abnormal result – refer back to a colposcopy service
- Normal cytology results – return to three-yearly cervical screening

If the results from colposcopy are unsatisfactory, the patient will have their cytology reviewed in secondary care and managed as required. If LSIL is confirmed from the cytology review, place a recall to ensure patients have had appropriate repeat tests (i.e. colposcopy and cytology ± HPV test) at 12 months.[19]

If the results from colposcopy are abnormal, a cervical biopsy will be taken. Patients with:[19]

- **A normal biopsy** will be managed on a case-by-case basis. Treatment is not generally indicated. Place a recall to ensure these patients have appropriate repeat tests (i.e. colposcopy and cytology ± HPV test) at 12 months.
- **LSIL (CIN 1)** on biopsy will not usually require treatment. These patients will be referred back to primary care; place a recall for repeat cytology at 12 and 24 months.
- **HSIL (CIN2/3)** on biopsy will undergo treatment and management in secondary care – see section below

High-grade cervical abnormality

People have an increased risk of cervical cancer if a high-grade cervical abnormality, e.g. high-grade squamous intraepithelial lesion (HSIL), is left untreated.[19] If results indicate HSIL (CIN 2/3), refer for a colposcopy.[19] A report of atypical squamous cells – HSIL cannot be excluded (ASC-H) requires colposcopy to determine whether a high-grade lesion is present or not.[19] Request urgent colposcopic assessment and annotate the referral with "high suspicion of cancer" for any patients with cytology results indicating HSIL with suspected invasive squamous cell carcinoma. See Figure 6 for details on the management pathway following colposcopic assessment of a patient with a high-grade lesion detected with cytology.

Follow-up after treatment for a high-grade cervical abnormality

Once a patient has successfully completed treatment for HSIL, they will be referred back to primary care for a test of cure. Recall patients at 6 and 18 months post-treatment for combined cytology and HPV testing ('co-tests'). If both test results are normal/negative on both occasions, the patient has successfully completed a test of cure and they can return to three-yearly cervical screening.[19]

If there are clinical concerns or the test(s) are positive at 6 or 18 months, re-refer for a colposcopy. Recall the patient annually for repeat cytology and HPV testing until two consecutive negative 'co-tests' are taken 12 months apart. When achieved, the patient can return to three-yearly cervical screening.[19]

Cervical glandular abnormality

Glandular lesions of the cervix, e.g. atypical glandular cells, adenocarcinoma in situ, are estimated to represent 15 – 20% of invasive cervical cancers.[19] Refer patients with cervical glandular abnormalities detected with cervical cytology for colposcopic assessment; patients will undergo treatment in secondary care if required.[19]

There are currently no New Zealand specific recommendations for the follow-up of people after treatment for a cervical glandular abnormality.[19] Australian guidelines recommend that those who have undergone complete excision with clear histological margins for adenocarcinoma in situ, have annual 'co-tests' with HPV testing and cytology until data are available to support cessation of testing.[8] If any of the results are abnormal, the patient should be re-referred for colposcopic assessment.[8]

N.B. Clinical Practice Guidelines for Cervical Screening in New Zealand are currently being revised and will include specific follow-up recommendations after treatment for a cervical glandular abnormality; this section will be updated to reflect these once the guideline is made publicly available

HPV testing to become the primary cervical cancer screening test from 2023

In line with best practice, the primary screening test for cervical cancer in New Zealand will change to HPV testing from July, 2023; the new pathway will be called HPV primary screening.[33] HPV testing offers up to 70% greater protection against the development of invasive cervical cancer, compared to cytology-based screening alone.[33]

The incidence and mortality rates from cervical cancer are expected to decline over time with HPV testing, however, a transient increase in both the incidence of cervical cancer and demand for colposcopy services is likely after the initial transition due to the higher sensitivity of the test.[34, 35] By 2035, the incidence and mortality rates from cervical cancer are expected to reduce by 32% and 25%, respectively, compared to 2018; this is equivalent to the prevention of 149 new diagnoses and 45 cervical cancer related deaths in New Zealand.[35]

An overview of HPV primary screening

A HPV test detects the presence of DNA from certain types of HPV that are known to cause cervical cancer.[34] This can identify people at risk for abnormal cell changes and therefore, those who require further testing.

The new method of obtaining a sample for HPV testing is with **a vaginal swab taken by either the patient (self-testing) or a healthcare professional**. Patients can, however, still opt for a clinician to perform a speculum examination and take a LBC sample for HPV testing if they prefer; cytology can then be performed on the LBC sample if the HPV test result is positive. All testing options, including self-testing, require

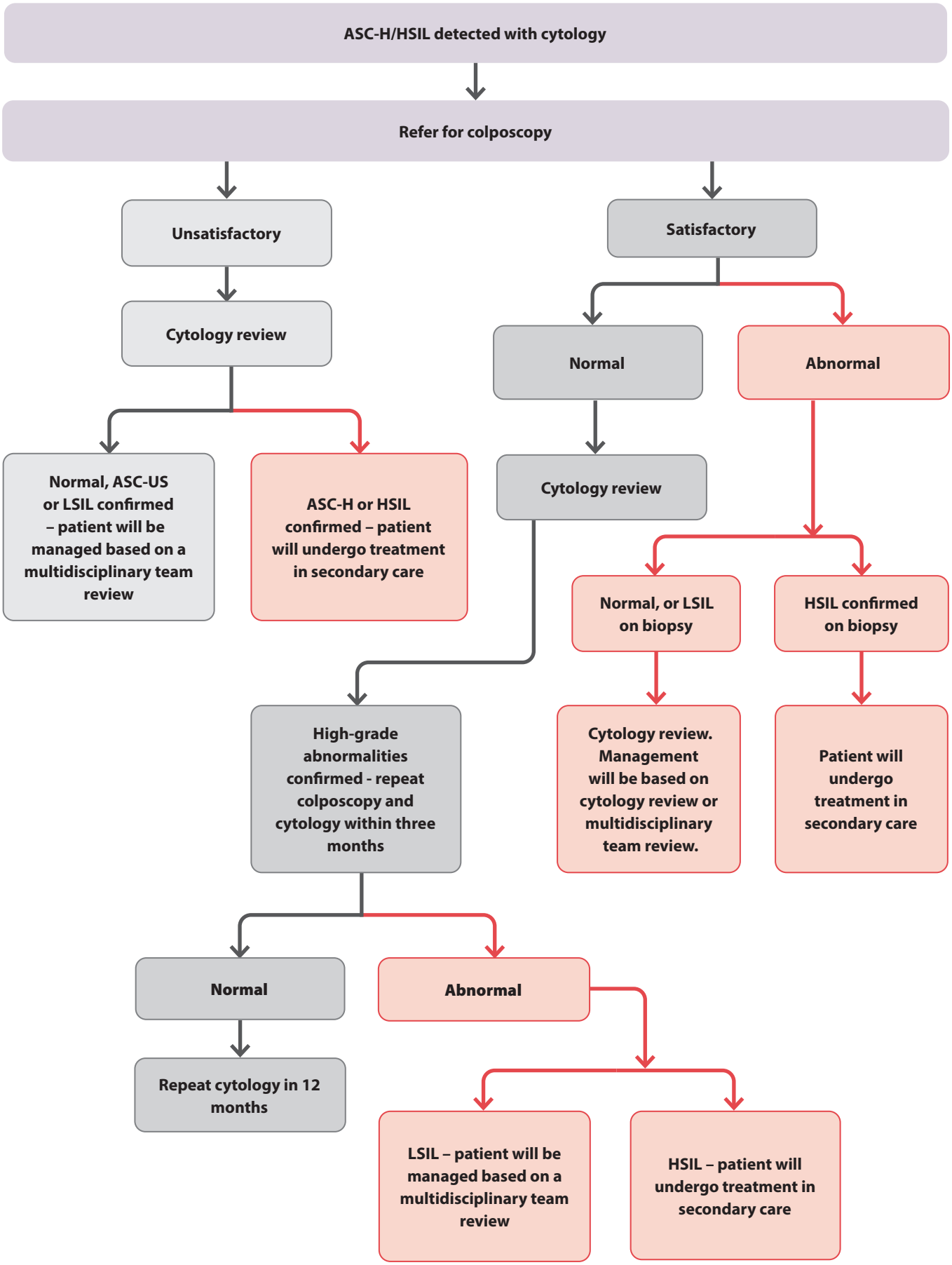


Figure 6. Colposcopic assessment of a patient with a high-grade cervical abnormality detected with cervical cytology. Adapted from Ministry of Health, 2020.[19] N.B. A new guideline is under development. As information is likely to change when the guideline is released, this article will be revised when it is made publicly available.

clinical oversight including a discussion about which method of sample taking is preferred by the patient (see: "How HPV testing will work").

Routine cervical screening will occur every five years.[34] When the cytology-based cervical screening programme transitions to HPV primary screening, patients should continue to be recalled and will have a HPV test at their next scheduled cervical screen. Five-yearly screens will commence once the patient has returned a negative test for HPV.[34] Table 1 details a comparison between cervical screening programmes.

How HPV testing will work

When the patient is due for their HPV test, an appointment with a general practitioner, nurse practitioner or practice nurse is required to discuss the test, including:

- Consent
- How the test works
- Whether the patient would benefit from a clinician-taken cervical sample with speculum examination, or whether a vaginal swab is preferred. Guidance for both healthcare professionals and patients will be available to help with this decision.
- Self-testing, including the benefits and risks (see below) and guidance on how to perform a self-swab
- What follow-up to expect if the result is positive

The patient may then take their own sample using a vaginal swab at the clinic or at another location (but must return the sample to the clinic), or have the clinician take a vaginal swab sample or a cervical sample with a speculum.

If a patient tests positive for HPV (approximately 10% of the population) from a vaginal swab, they then require a speculum examination and a cervical sample taken for liquid-based cytology, or in some cases, e.g. if HPV type 16/18 is detected, they can choose to be referred directly for a colposcopy (Figure 7).[34, 36] N.B. Follow-up management is then dependent on the results of cytology, refer to: "The cytology report is back; where to from here?", Page 8.

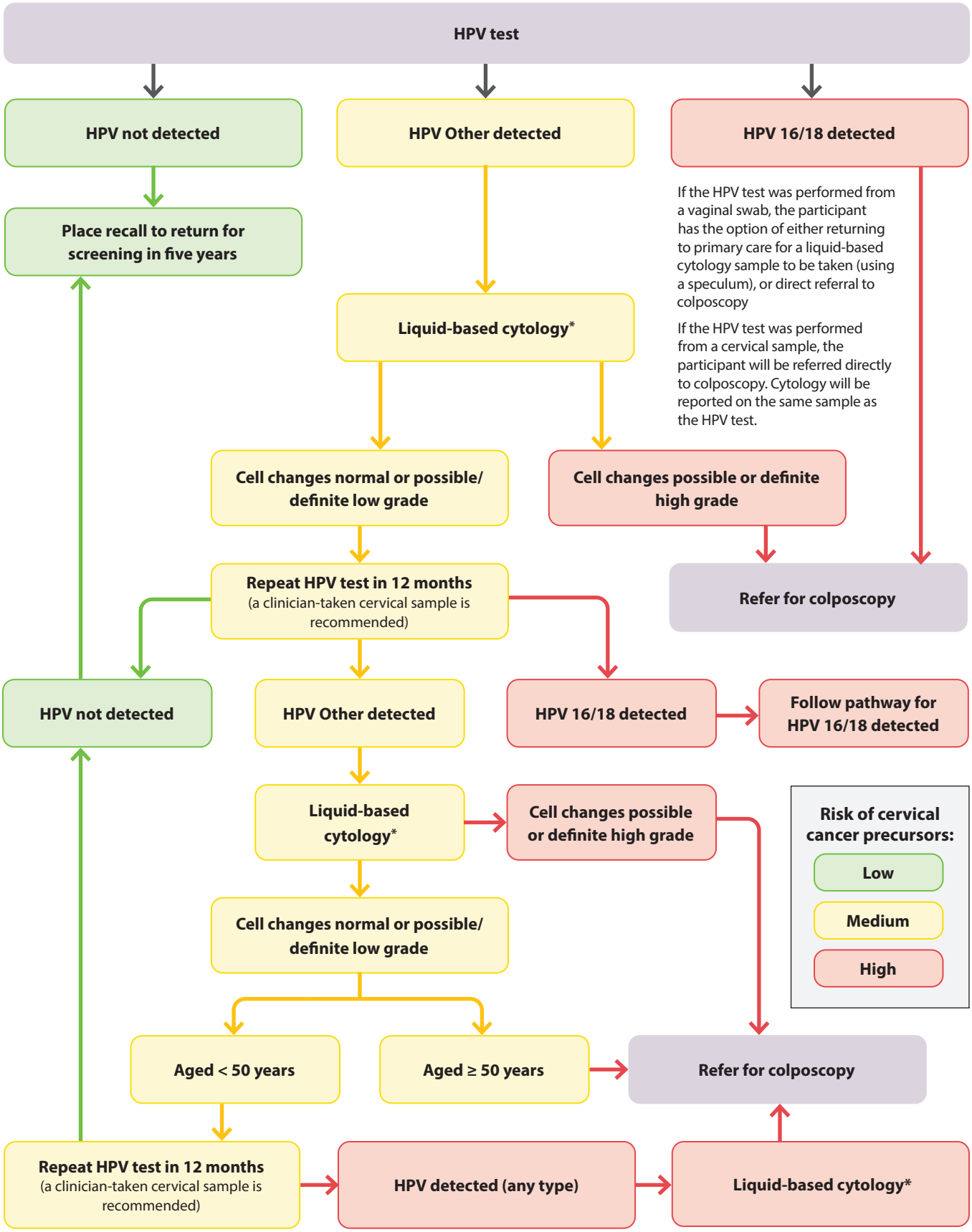
The benefits and risks of HPV self-testing

HPV self-testing has been shown to have equivalent accuracy for detecting HPV as a clinician-taken sample, and is expected to increase the uptake of cervical screening in those who have previously been reluctant to screen.[13, 36] HPV self-testing has the potential to reduce the equity gap by halving the number of Māori females who are under-screened or never screened.[13]

Although the option of self-testing is an important strategy to increase the uptake of cervical screening, there are still benefits to a clinician-taken sample. Compared to cytology-based cervical screening, risks of HPV testing include missed opportunities for the clinician to detect other health concerns such as STIs or abnormal pathology, and the patient not attending follow-up after a positive HPV result.[13, 36]

Table 1. Comparison between cervical screening programmes.[19, 34, 36]

	Current recommendations	Recommendations from July, 2023
Primary screening test	Cervical cytology	HPV test
Eligibility criteria	Females aged 25 – 69 years who have ever been sexually active	Females aged 25 – 69 years who have ever been sexually active Eligibility criteria is extended to age 75 years if the participant has been under-screened or never screened
Screening interval	Every three years	Every five years
Sample preparation	LBC of a cervical sample taken using a speculum by a clinician	A PCR test will be performed from one of the following samples: ■ A vaginal swab taken by the patient ■ A vaginal swab taken by a clinician ■ A clinician-taken (speculum) LBC sample N.B. If a LBC sample was obtained (during a speculum examination), the same specimen can be used for the analysis of both cytology and HPV. Cytology will be performed if HPV is detected.
Self-collection	Not available	Available
Aim of test	To identify pre-cancerous cervical cell changes	To identify the presence of any high-risk HPV DNA types, particularly 16 and 18



* Liquid-based cytology cannot be performed from a vaginal swab. If the HPV test was conducted from a vaginal swab, a return visit is required for a clinician-taken cervical sample with speculum examination.

Figure 7. Proposed HPV cervical screening test pathway for females who are asymptomatic in New Zealand. Adapted from Ministry of Health, 2021.[36] N.B. A new guideline is under development. As information is likely to change when the guideline is released, this article will be revised when it is made publicly available.

Regardless of the testing method, it is recommended that consultation with a clinician, including a physical examination should still be encouraged as good clinical practice and as a way to address opportunistic health issues or patient concerns.[36] Cervical screening may also be an appropriate time to ask about domestic partner abuse or harm, including sexual violence.

If the patient opts for self-testing, reinforce follow-up expectations if the HPV test result is positive and encourage them to return to primary care if they experience any gynaecological concerns.

A future article will cover the follow-up and surveillance of a patient after curative-intent treatment for cervical cancer

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