Moving to HPV testing for primary cervical screening: why, what, when and how

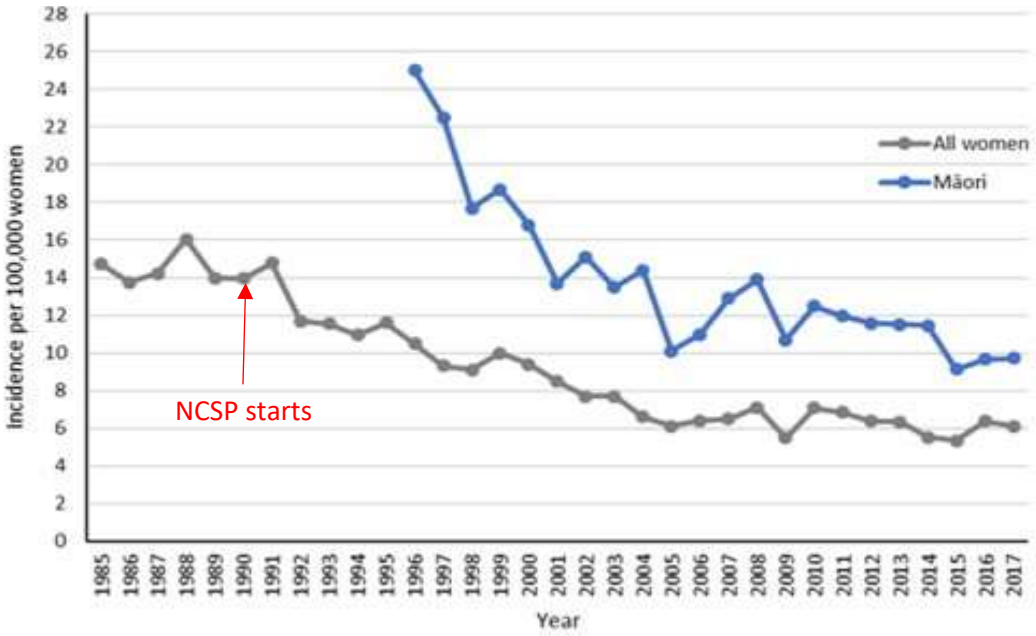
November 2022

This is expanded content from a Goodfellow webinar presentation September 2022, delivered by Dr John McMenamin, Primary Care Lead for the National Screening Unit, and further contributed to by Dr Margaret Sage, Clinical Lead - Pathology, for the National Cervical Screening Programme.

Changing incidence rates of cervical cancer, 1985-2017

- New Zealand's cervical cancer incidence rates fell for almost three decades after the NCSP commenced in 1990.
- There have been incidence reductions for All women and for Māori.
- While incidence rates reduced considerably for both groups, the gap between the higher rate for Māori compared with All women did not reduce up to 2017
- From 2005 to 2017, the overall rate for All women plateaued. This has happened all over the world.

Age-standardised cervical cancer incidence rates for Māori and All women, 1985 to 2017



Rates are per 100,000 women, age-standardised to the WHO Standard Population (all ages).

NCSP 2017 Annual Report

Cervical cancer is now largely preventable

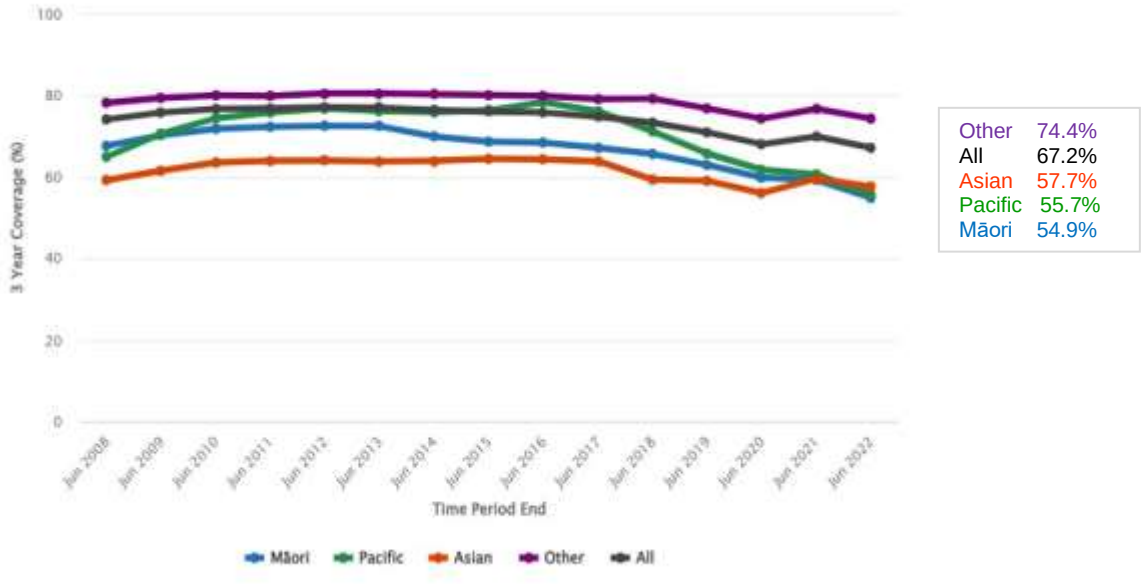
- HPV infection is common in the community, is usually asymptomatic and resolves without treatment, but persistent infection with high-risk types of HPV carries a risk of cervical cancer developing.
- Where diagnostic and treatment services are well established, immunisation rates and screening coverage both play a large role in determining cancer rates. (Smoking is also a known co-factor).
- There is no genetic reason why Māori and Pacific people have higher cancer rates.In New Zealand, low screening coverage usually means high cancer rates, with a few exceptions:
  - In people under-30, immunisation is lowering cancer rates despite low coverage.
  - The Asian population has low cancer rates despite low coverage.

Barriers to accessing immunisation and screening are key reasons limiting the effectiveness of the NCSP to reduce cancer rates in New Zealand.

Coverage by ethnicity

- Māori and Pacific participants now have about 55% screening coverage compared with 75% for European/Other women.
- The Asian population is a heterogenous population and while coverage rates are around 58%, cancer rates are low. The reasons are probably multiple and are not well understood.

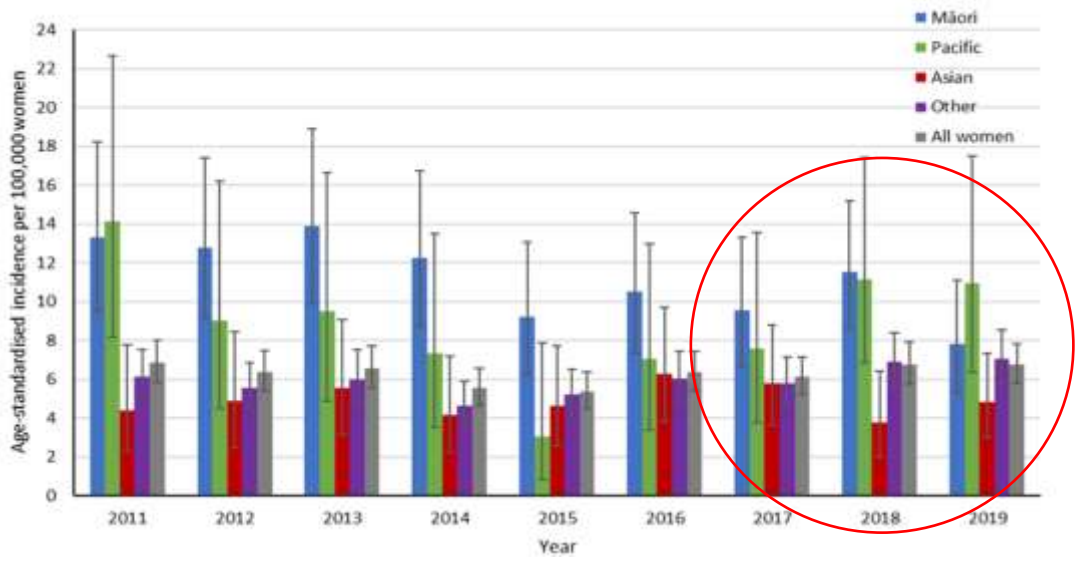
3-year coverage by ethnicity, New Zealand, ages 25 to 69, 15 years to June 2022



NCSP Coverage data

Māori and Pacific people are priority groups for the NCSP because of high and inequitable cancer rates.

Age-standardised cervical cancer rates 2011 to 2019, by ethnicity

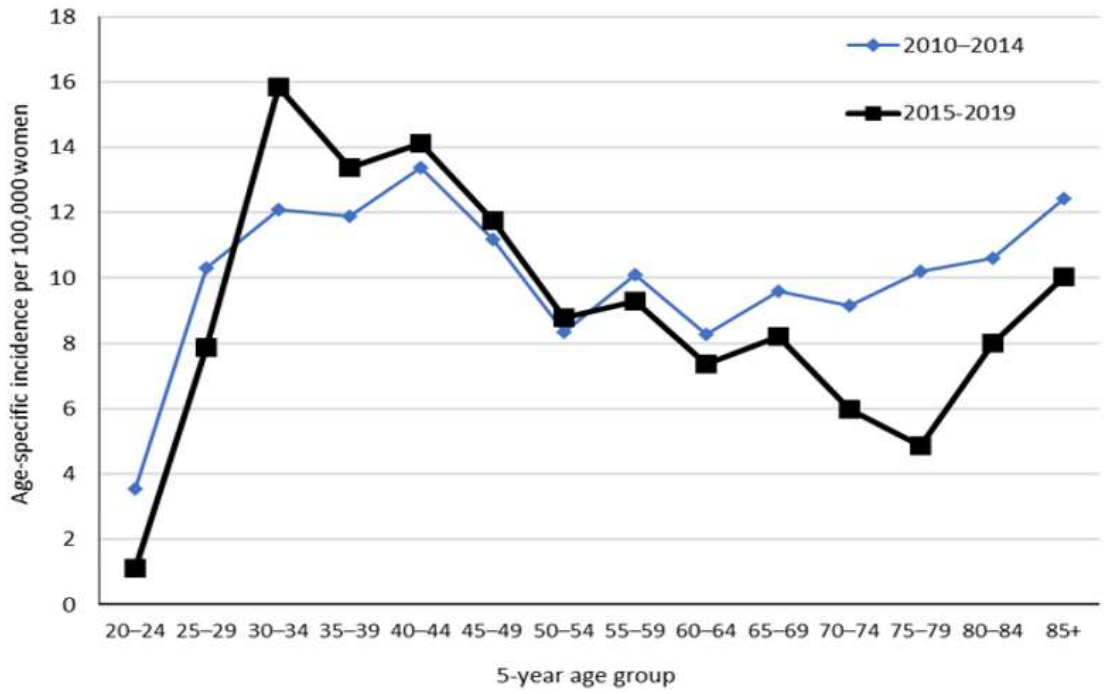


NCSP Incidence and Mortality report 2018-19

The changing age distribution of cervical cancer

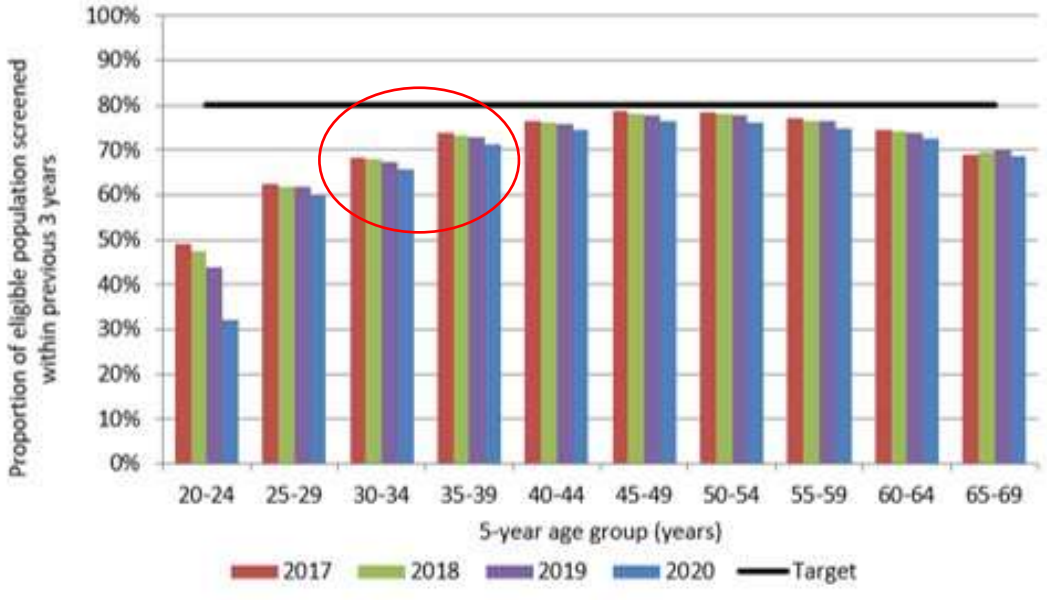
- In 2018 and 2019 about 185 new cases of cervical cancers occurred each year.
- About 60 people die from cervical cancer each year.
- In 2015-19, proportionately more cancers occurred in the 30 to 34 age range, with fewer cancers in women over 60, compared with 2010-2014 cancers.
- The graph below shows the age distribution of 5 years of cancers from 2010 to 2014 compared with the cancers that occurred in 2015 to 2019.
  - Cancer rates are rising for women aged 30 to 50, particularly for the 30-to-40-year age group (declining coverage rates are occurring in this age group and immunisation rates are low).
  - Cancer rates continue to fall for those 50+ years, particularly for those 65+ years. (These now older participants were very well screened in their younger years, partly because of the publicity about the Cartwright and Gisborne Inquiries).
  - Cancer rates are dropping for women under 30 because of immunisation.

Five-year average cervical cancer incidence rates, by age



NCSP Incidence and Mortality Report 2018 to 2019

3-year coverage by age (women screened in the previous 3 years as a proportion of hysterectomy-adjusted female population)



NCSP Monitoring Report 1 Jan – 31 Dec 2020

Unscreened and under-screened people are priority groups for the NCSP because of high cancer rates.

Why continue with cervical screening now?

- Regular screening greatly reduces your risk of cervical cancer (even if you have been immunised), and screening coverage closely reflects cancer rates.
- Analysis of all cases of invasive cervical cancer reported in New Zealand in 2013 to 2017* (n=747) showed that:
  - of women aged 25 to 69 with invasive cervical cancer only 12% were adequately screened, (i.e., had at least 2 cervical screening samples not more than 3 years apart in the 6 months to 7 years prior to diagnosis).
- COVID-19's impact on screening services has been significant as a result of lockdowns, people isolating and the desire to "stay home and stay safe".
- In particular there has been a COVID-19 impact on access to cervical screening services for Māori and Pacific people.

**Review of Cervical Cancer Occurrences in relation to Screening History in New Zealand for the years 2013-2017*
Report prepared for the NCSP. P Sykes et al. Department of Obstetrics & Gynaecology University of Otago – Christchurch

The WHO cervical cancer elimination strategy

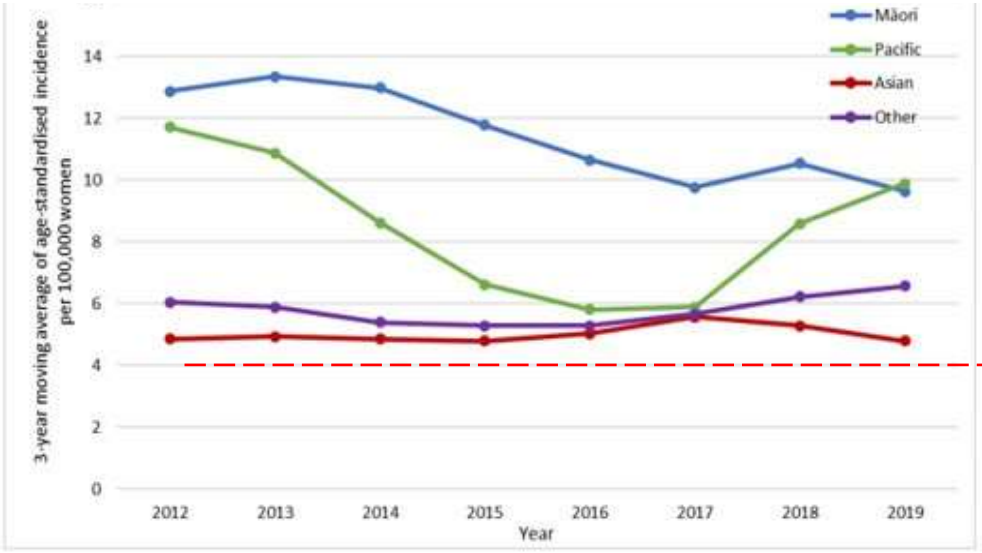
- In 2020 the World Health Organization launched a global strategy to accelerate the elimination of cervical cancer as a public health problem.
- Elimination does not mean getting down to zero cases. It means reaching an incidence rate of less than 4 cases per 100,000.
  - There are cases of cervical cancer unrelated to HPV and rarely, low-risk HPV viruses can cause cervical cancer – we won't prevent these by immunisation or by screening for high-risk HPV.

The three WHO targets for all countries for 2030:

Eliminating cervical cancer in New Zealand

- New Zealand currently has about 6-7 cases per 100,000 for All women but there is ethnic disparity, with higher rates for Māori and Pacific participants (about 10 cases per 100,000 for both) .
- The graph from the NCSP Incidence and Mortality Report for 2018-19 (available on the NCSP website), shows what's happening for different ethnicities using a moving 3-year average (see below). This is helpful to even out the way the numbers vary from year-to-year.
- There is a lot more work to do to get Māori and Pacific people down to the WHO threshold than there is for Other (non-Māori, non-Pacific and non-Asian) and Asian people so additional efforts and resources are needed for Māori and Pacific people.

New Zealand age-standardised cervical cancer incidence rates, 2011 to 2019, by ethnicity (3-year rolling average)



Other includes all non-Māori, Non-Pacific, and non-Asian.

NCSP Incidence and Mortality Report 2018-19

Encouraging regular screening is vitally important

- The NCSP's Māori social media marketing campaign to promote a safe return to cervical screening after the disruptions caused by COVID-19, went live in August.
- The campaign is called '**Hey, Let's Catch Up!**' and has been shared across Facebook and Instagram to raise awareness about cervical screening and to encourage wāhine and their whānau to return to the screening pathway.
- The campaign for Pacific peoples has also recently been launched to '**Sister to Sister'**.

https://youtu.be/xnisWv9vT

Supporting participation

- Primary and community health care efforts to encourage people to participate in screening are critically important to the success of the NCSP.
  - Front-line health workers and support to screen services are key to improving screening participation.
  - Local trusted relationships and partnerships are needed to support eligible people to become regular screening participants.
- Barriers to screening participation are already well identified: we need to work together as much as possible to find ways to overcome them.
- The NCSP is committed to meeting our Te Tiriti obligations by achieving equitable cervical cancer outcomes for Māori.

Our understanding about HPV has exploded

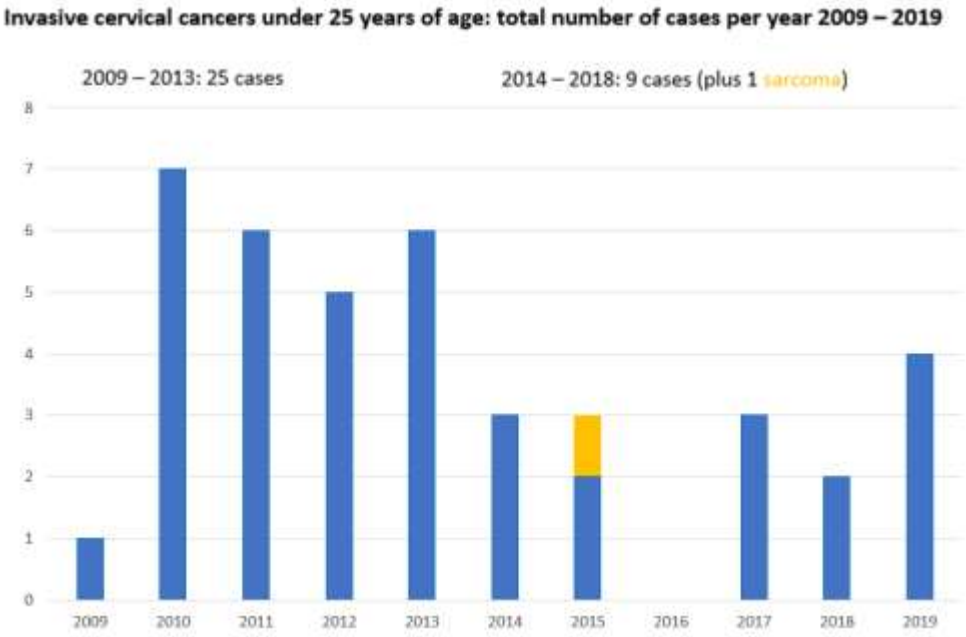
- More than 99% of cervical cancers are caused by Human Papillomavirus (HPV).
- 80% of people who have been or are sexually active are estimated to acquire an HPV infection at some point in their lives.
- Most people clear these asymptomatic infections without knowing they have had an HPV infection.
- The 2% of people who develop persistent HPV infections (2+ years) are those at risk of developing high-grade pre-neoplastic lesions, and potentially invasive cervical cancer if untreated.
- Symptoms often don't occur until there is a deeply invasive tumour.
- We need immunisation to prevent lesions developing and then screening to detect pre-invasive lesions that do develop.

Immunisation against HPV – vaccinations are working

The most important cervical cancer prevention strategy is vaccination

- Introduced in 2008, the New Zealand programme now offers funded immunisation for all gender groups from ages 9 to 26 years (inclusive).
- Vaccination against HPV-16 is particularly important for preventing penile, throat and anal cancers.
- In 2022, the WHO advised that 1 dose is as effective as 2 or 3 doses for preventing HPV-related disease.
- Gardasil-9 (since 2017) vaccinates against the 7 highest-risk HPV types that collectively cause 90% of HPV-related cervical cancers, plus two low-risk types that cause 90% of genital warts.
- 7 of the 14 High-risk HPV types are not in the vaccine, so vaccination isn't a substitute for screening.
  - Screening those who are vaccinated is still needed, to prevent cancers caused by the remaining 7 high-risk types.

- Cancers caused by “HPV-Other” high-risk types are still occurring because these types aren’t in Gardasil-4, and those in the screening age are currently predominantly vaccinated with Gardasil 4. this will change in future years.
- We are now seeing the impact of HPV vaccination on cancer rates for those under 30, particularly those under 25.
  - There were 25 cases of invasive cancer in under 25-year-olds in the 5-years from 2009 to 2013, compared with 9 cases (excluding 1 sarcoma unrelated to HPV) in the next 5-year period, from 2014-18 where on average there were about 2 cases of cervical cancer nationally in those under 25 years.



Screening for HPV

HPV testing is very sensitive, identifying the 10% of people in the population at risk of cervical lesions.

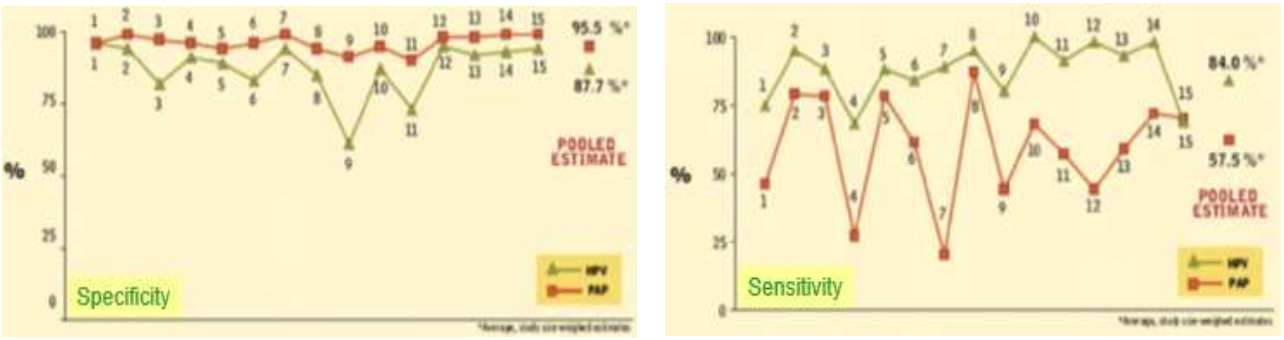
Cytology is better at identifying who has a cervical lesion by looking for cell changes, not for the presence of the virus; it works well as a second test for those who are HPV positive, to see who needs further investigation.

- Because HPV primary screening is such a sensitive test, one HPV negative result gives more assurance than one negative cytology test, so:
  - no need to keep doing two tests 12 months apart when participants commence screening
  - we can safely extend the screening interval to 5 years.
- one negative HPV test result for those in their late 60s/early 70s is sufficient before exiting screening.
- There is a very small number of cervical cancers that are not HPV related (most are adenocarcinomas) so symptoms of cervical cancer still need to be taken seriously, even if an HPV test is negative.

HPV testing is more sensitive than cytology

- 15 studies by reputable authors published in peer-reviewed journal articles between 1995 and 2004 all showed that HPV testing was more sensitive as a screening test than conventional cytology.
- There was also less variation in reporting performance with HPV testing compared with cytology.
  - This is to be expected because it is an objective automated test, whereas cytology relies on subjective visual interpretation.
  - Cytology was more specific than HPV testing in every study, i.e., cytology was better at sorting out who actually had a cervical abnormality and who didn't.
  - We would expect this because cytology detects abnormal cells whereas HPV testing detects the presence of HPV DNA.

Specificity versus sensitivity of HPV testing versus Cytology



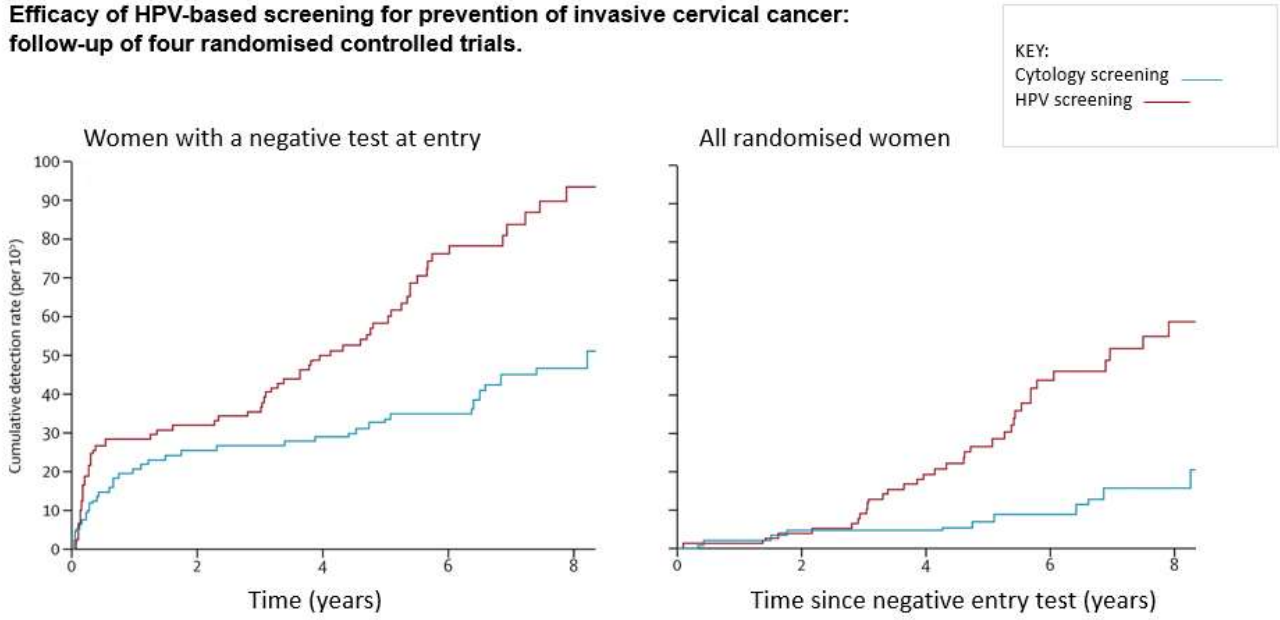
KEY:
HPV testing
Cytology (conventional)

HPV Today, 2005

HPV testing: a better primary screening test

- In 2014 Ronco et al published follow-up data from four large European trials, looking at invasive cancer rates in women screened and managed with HPV testing compared with cytology screening.
  - For all women screened, cumulative cancer rates were lower for women screened and managed on the basis of their HPV test results compared with women managed according to their cytology results, and the difference was greater with time.
  - For those who had negative tests at the start, there wasn't any difference in invasive cancer rates between HPV and cytology screening until about 3 years. After this a clear advantage for HPV screening emerged, again with a widening difference in successive years.

Efficacy of HPV-based screening for prevention of invasive cervical cancer: follow-up of four randomised controlled trials.



Ronco G et al. Lancet 2014;383:524-32

HPV primary screening results in lower invasive cancer rates compared with cytology screening.

Changes to primary screening July 2023: Impact on cancer rates

1. **An HPV primary screening test instead of cytology.**
   - This will reduce cancer rates even if no additional people were screened. This will happen both for vaccinated and unvaccinated participants.
2. **Offering the HPV test as a self-test will improve screening coverage.**
   - How the test is taken doesn't influence cancer rates per se, but if currently unscreened and under-screened people take up the self-test option and follow through to treatment if they have positive results, then even greater disease reductions will be achieved.

The decision to move to HPV Primary Screening is based on international evidence and modelling using New Zealand data. The modelling predicts this will reduce the incidence of cervical cancer in both vaccinated and unvaccinated participants.

HPV primary screening options from July 2023

- Primary cervical screening will change to a Human Papillomavirus (HPV) test.
- This new screening method will test for the presence of HPV, the cause of 99% of cervical cancers.
- Self-testing will be an option for all: done in the clinic, at home, or at other community sites, (universal mail-out will not occur in first phase of programme).
- Clinical oversight is required in order to explain the test, the role of the NCSP Register, manage results and arrange follow up.
- The screening interval following a negative HPV test will change to 5 years.

Empowering choice

- Participants can choose how to have their screening test: either take it themselves OR have a clinician take it for them.
- They will be able to:
  - choose to self-test using a swab, in a location of their choice
  - opt for a clinician to take the HPV test using a swab
  - choose for the clinician to take a liquid-based cytology (LBC) sample (using a speculum), which can be used for HPV testing, and for cytology if required.
- Participants need to be reassured that a self-test is just as effective as a clinician-taken sample at detecting the presence of HPV.*

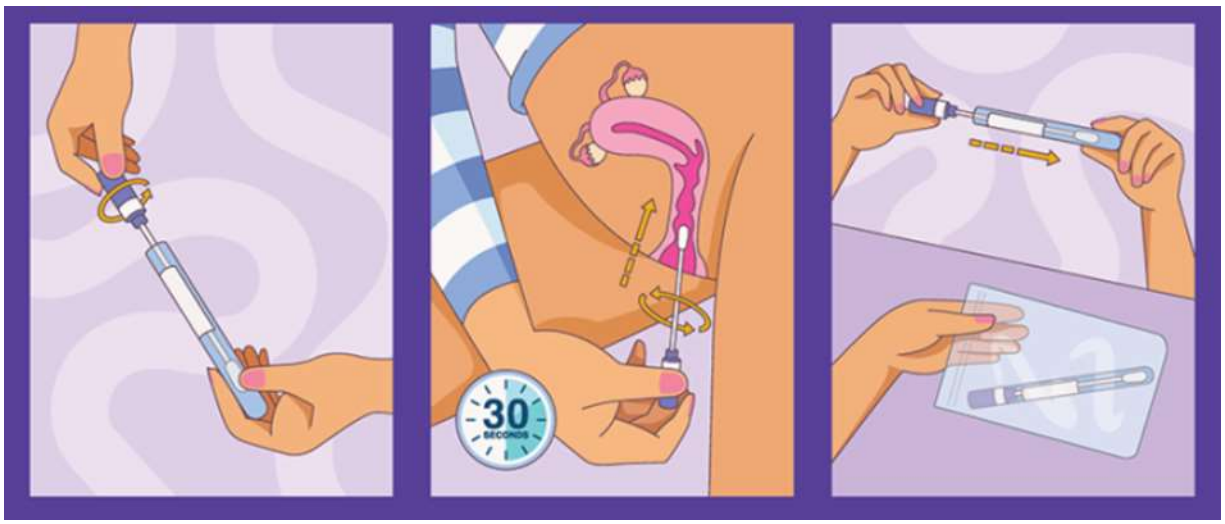
Detecting cervical precancer and reaching under-screened women by using HPV testing on self-samples: updated meta-analyses Marc Arbyn et al. BMJ 2018;363: k4823 | doi: 10.1136/bmj.k4823

HPV screening options: self-test

- Self-taken sample for HPV testing.
- Vaginal swab used.
- Requires an informed consent process with clinical oversight.
- If HPV is detected – a clinician-taken LBC sample is then required for cytology.
- A swab-collected sample can only be used for HPV testing, not cytology.
  - If cytology is needed, a return visit for a clinician-taken LBC sample (using a speculum) will usually be required.

Explaining the HPV self-test

- Information will be available to explain to women how to take the test.
- The test is a vaginal swab (i.e., there's no need to find the cervix).
- The participant may self-test in a location of their choice.
- Self-testing requires informed consent with clinical oversight.
- The participant can alternatively choose to have a clinician (nurse or doctor) take the sample using a swab.



HPV screening options: clinician-taken

- A clinician can use a swab to take a sample for HPV testing – this will be treated by the labs as a self-test, OR
- a clinician can use a speculum to take an LBC sample from the cervix.
  - If a swab sample is taken and cytology is then required (e.g., the HPV test is positive) a return visit will be needed so that an LBC sample can be taken for cytology, as a swab sample can't be used for a cytology test

If HPV is detected on an LBC sample - cytology will be performed on the same sample if the HPV test is positive, as an LBC sample can be used to test for HPV, cytology or both using the same sample

Choosing between screening options

	PROS	CONS
Self-testing: taken by self	Personal control of the process Privacy Comfortable as no speculum Possible to take it at a place other than a medical clinic	Possible anxiety about 'doing it properly' Possible anxiety about effectiveness No clinical examination May have to return for a clinician-collected sample if need cytology
Self-testing: taken by a clinician	More confidence that taken properly Some clinical examination (cervix not visualised) Comfortable as no speculum May suit some disabilities	Less private than taking it yourself Mostly taken at a medical centre May have to return for a clinician-collected sample if need cytology
Usual Clinician-collected sample using a speculum	Full clinical examination with cervix visualised Confidence and trust in an established method Don't have to return if need cytology	Discomfort from speculum exam More intrusive Whakamā Mostly take at a medical centre May trigger past bad experiences

Participants need to be **fully informed** of these options so they can make a **personal choice**.

New clinical management pathways

Swab collected sample
(self-test or clinician-assisted)

- HPV not detected – 5-year screening interval.
- HPV 16/18 detected – the option of returning to primary care for a cytology sample OR direct referral to colposcopy, where the cytology sample will be taken.
- HPV Other detected – cytology sample required:
  - Low-grade cytology – repeat HPV Test in 12 months.
  - High-grade cytology – referral to colposcopy.

Clinician-taken LBC sample

- HPV not detected – 5-year screening interval.
- HPV 16/18 detected – direct referral to colposcopy. Cytology will be reported on the same sample as the HPV test.
- HPV Other detected – cytology on the same sample shows:
  - Low-grade cytology – repeat HPV Test in 12 months.
  - High-grade cytology – referral to colposcopy.

The pathway after primary screening

- An HPV test tests for 14 high-risk HPV types, but the 14 types are not all of equal risk.
- HPV types 16 and 18 cause 70% of cervical cancers, so if these types are found participants will be referred to colposcopy.
  - If the HPV test was performed on an LBC sample, cytology will be performed on the same sample.
  - If the HPV test was a swab sample (self or clinician-collected), there is another choice option in the pathway for those who are HPV 16/18 positive, either:
    - Return to primary/community health care for a clinical examination and an LBC (speculum) sample for cytology. The cytology result will then be available to assist the colposcopist, OR
    - proceed directly to colposcopy where cytology will be taken at colposcopy.
- People with high-risk HPV which is not type 16 or 18 need cytology. This will identify who:
  - can be safely followed with repeat HPV testing and cytology (low-grade or normal cytology),
  - needs to be referred to colposcopy (high-grade cytology).
- The pathway has been influenced by the experience in Australia:
  - It was found that for those under 50 years of age with HPV non-16/18 and low-grade cytology, it was best to allow 2 years for resolution of the HPV infection rather than referring everyone who was still HPV positive at the first 12-month repeat test to colposcopy. This reduced referrals to colposcopy as significantly more infections resolved in the second 12 months without intervention.

A new NCSP Register

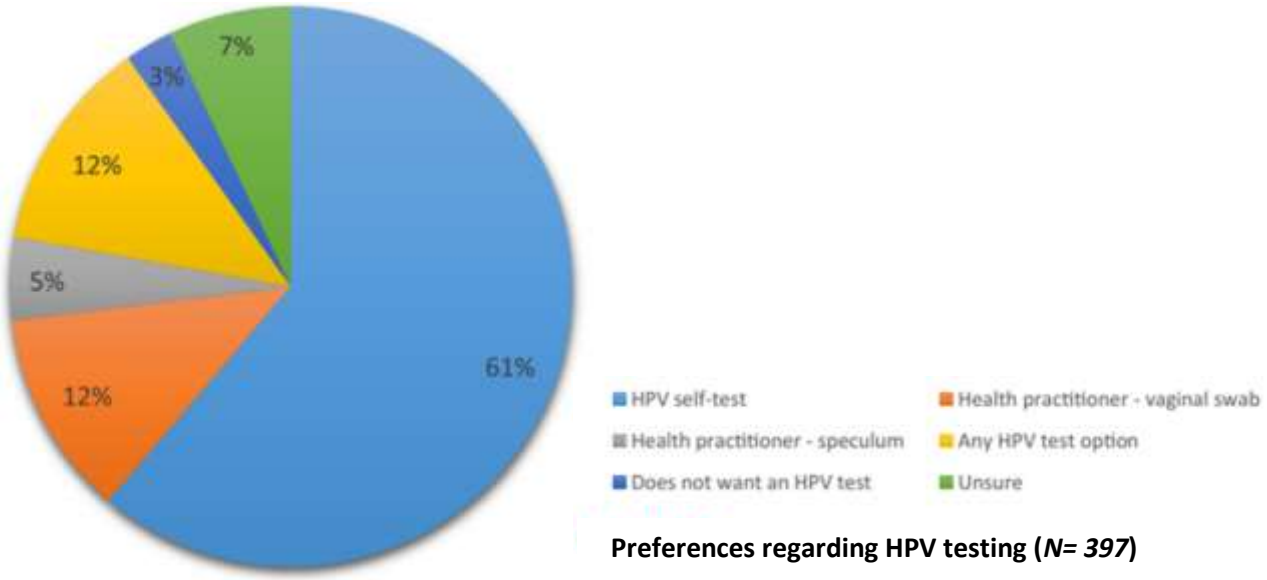
- The new NCSP Register will be population-based, sourced from NHI data.
- It will include both those already enrolled in the NCSP and those who are unenrolled, with an opt-off option.
- The Register will be accessed by many more health professionals to support participants on their screening journey.
  - There will be direct look-up access for primary/community healthcare, with improved reporting and monitoring capability.
- Two new major functions will be:
  - centralised notification (the first notification for someone starting screening)
  - recall (when someone already in the programme is notified that their next screen is due).

Reduced barriers for under-screened indigenous populations

In New Zealand research 73% of the under-screened indigenous population said they were likely/very likely to self-test. Reasons given included:

- Easier.
- More comfortable.
- Less intrusive.
- Brilliant.

Acceptability of self-taken vaginal HPV sample among an under-screened indigenous population



Preferences regarding HPV testing (*N= 397*)

More people will screen

- Participants will be automatically enrolled for HPV primary screening.
  - Everyone eligible will be invited to join, with an 'opt-off' option.
- Because the test is less invasive and can be done at a location of their choice, more people are expected to engage with screening.
- This is particularly true for groups such as Māori and Pacific, where there are cultural barriers to the speculum-based test.
- Increasing participation in these groups will be a major step forward in achieving equitable outcomes.

Confidence in longer screening interval

- The screening interval following a negative HPV test will change to 5 years compared to the current 3 years.
- If the HPV virus is not present, the screening interval can be safely extended to 5 years after the negative test. This is because of the greater reassurance that a negative HPV test provides compared with a negative cytology test.
- The risk of cancer 3 years after a negative cytology test is about the same as 5 years after a negative HPV test.

Key messages

- HPV testing is a better primary screening test than cytology.
- The new test is more sensitive, simpler and more acceptable.
- About 10% will have high risk HPV detected, requiring follow-up (cytology or colposcopy).
- The new Register will enable clinicians to track screening histories and recommended follow-up.

Anyone currently due for screening should **continue to have cytology screening on time** prior to July 2023, rather than waiting for the new test.