BJOG: An International Journal of Obstetrics & Gynaecology

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BJOG An International Journal of Obstetrics and Gynaecology

RESEARCH ARTICLE OPEN ACCESS

Human Papillomavirus (HPV) Screening With Universal Access to Vaginal Self-Testing: Outcomes of an Implementation Trial

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Received: 17 September 2024 | **Revised:** 13 March 2025 | **Accepted:** 21 March 2025

Funding: This work was supported by a grant from Te Whatu Ora Health New Zealand (Provider No. 469329/Contract No. 374890/00). The study design included evaluation of the implementation of a clinical pathway proposed by Te Whatu Ora Health New Zealand; however, the sponsor had no input into the collection, analysis and interpretation of data or in the writing of the report. Permission was sought from Te Whatu Ora Health New Zealand prior to submission of this article for publication; however, permission was granted and no changes were made to the publication.

Keywords: cervical cancer screening | colposcopy | health inequity | human papillomavirus | self-testing | vaginal swab

ABSTRACT

Objective: Determine the feasibility of high-risk human papillomavirus (HPV)-based cervical screening that included the option of a vaginal swab HPV test (*vaginal self-test*).

Design: Implementation trial.

Setting: 17 primary care practices.

Population or Sample: People due for a cervical screening test.

Methods: Participants could choose a clinician-taken *cervical test* or a *vaginal self-test* (undertaken in clinic or at home), unless a cervical co-test (HPV and cytology) was clinically indicated.

Main Outcome Measures: Proportion of participants who had (a) a *vaginal self-test*, (b) an HPV-detected result and (c) HPV detected on a *vaginal self-test* and returned for further investigation.

Results: 3121 people were enrolled. Participation rates were high for people of all recorded ethnicities. A *vaginal self-test* was undertaken by 95% (2954/3121, 95% confidence interval [CI] [93.8, 95.4]) of people. HPV was detected in 12.9% (404/3121, 95% CI [11.8, 14.2]) of people. 95% (384/404, 95% CI [92.5, 97.0]) of people with HPV detected had follow-up cytology or colposcopy. 2.6% (82/3121, 95% CI [2.1, 3.2]) had HPV 16/18 detected, all of whom attended colposcopy. Cytology triage was completed for 92% (276/301, 95% CI [88.0, 94.3]) of people with non-16/18 HPV types (*HPV other*) detected on a *vaginal self-test.* This varied by ethnicity and screening history.

Conclusion: This study confirms the feasibility of cervical screening with the universal option of a *vaginal self-test* and demonstrated a clear preference for the *vaginal self-test*. Challenges remain in relation to equitable provision of cytology triage. Ongoing programme monitoring is imperative.

Trial Registration: Australia and New Zealand Clinical Trial Register. ANZCTR Reference number: ACTRN12622000699763 (https://anzctr.org.au/)

1 | Introduction

High risk human papillomavirus (HPV) screening is the most effective screening modality for cervical cancer prevention [1, 2]. Most screening programs in high income countries have utilised a clinician-taken cervical liquid-based cytology sample (*cervical test*) as the primary screen, testing for HPV and utilising a reflex cytology test for triage when HPV is detected [3, 4]. More recently, it has been recognised that the HPV vaginal swab polymerase chain reaction (PCR) test (*vaginal self-test*) offers similar sensitivity and specificity to the *cervical test* [5]. It has also been demonstrated that the *vaginal self-test* is more acceptable and accessible to many people, particularly those who are under-screened [5–8]. Other test modalities have been explored including urine tests [9]. A number of established HPV screening programs have introduced the option of the *vaginal self-test*; however, in most high income countries, the *cervical test* remains predominant [3, 4]. The vaginal swab HPV test, often referred to as self-sampling, has been called the'self-test' n Aotearoa New Zealand (NZ) following consumer consultation.

The NZ National Cervical Screening Programme (NCSP) commenced in 1990, and cervical cancer incidence approximately halved to 6.4 per 100 000/year by 2006 [10]. However, since then cervical cancer rates have remained largely stable. Lower screening coverage for Māori and Pacific peoples (NCSP August 2023 coverage rates: Māori 56%, Pacific 56%, NZ European 75%) [11] result in higher cervical cancer incidence (WHO age standardised rate (2017–2021): Māori 9.1/100 000/year, Pacific 8.4/100 000/year, NZ European 6.2/100 000/year) [10]. Elimination of these inequities is a major goal of the cervical screening program [12]. Cervical screening in Aotearoa NZ is partially funded. Full funding is available for priority groups including Māori and Pacific.

In November 2023, the NCSP replaced cytology testing with HPV testing as the primary screening tool. As a *vaginal self-test* is more acceptable than a *cervical test* for many, including Māori and Pacific people [6, 13], the intention was to commence the new HPV screening programme providing the choice of a *vaginal self-test* or a clinician-taken *cervical test*.

The aim of this implementation study was, prior to the nationwide roll-out, to determine the feasibility of HPV screening with the choice of a *vaginal self-test* or a clinician-taken *cervical test* in a range of primary care practice environments across three regions of Aotearoa NZ.

This study was approved by the NZ Southern Health and Disability Ethics Committee (Ethics ref.: 2022 FULL 12546, 1 July 2022).

2 | Methods

The study was designed in consultation with primary care providers and regional Māori advisors. Māori and Pacific steering groups assisted in ensuring an equity focus. Primary care practices were selected in three regions (Whanganui, Capital and Coast and Canterbury) of Aotearoa NZ. The regions were selected to offer a range of urban, rural and socioeconomic settings and a diversity of ethnicities typical of Aotearoa NZ. In view of known screening inequities, we aimed to overrepresent Māori.

2.1 | Outcome Measures

Primary outcome measures were the proportion of participants who had

- a *vaginal self-test*,
- an HPV detected result and
- HPV detected and completed cervical cytology triage or colposcopy, as indicated.

Secondary outcome measures included the proportion of the estimated eligible population screened by ethnicity, the primary outcome measures by demographic variables, the successful method of invitation, screen location (home or clinic), completion of test of cure (TOC) recommendations and the high grade histology detection rate.

2.2 | Sample Size Calculation

The sample size was calculated to ensure we could estimate, with reasonable precision, the proportion of people with HPV detected on a *vaginal self-test* who were not reached for follow-up investigations. This outcome measure was chosen because non-return for follow-up was a potential safety risk and, because only a proportion of the overall cohort was expected to have HPV detected, this was the primary objective which needed the largest overall sample to provide a reasonable estimate. Assuming 60%–70% of patients opted for a *vaginal self-test* [6, 14], we estimated that 3000 people would need to be recruited to obtain 1800 *vaginal self-tests*. We estimated 12% of HPV *vaginal self-tests* would have HPV detected [4], and thus we would observe 216 people with HPV detected from 1800 *vaginal self-tests*. If the true failure to return rate was 2% or greater than, in a sample size of 195 people or more, there is a 98% probability that at least one failure to return would be observed.

2.3 | Primary Care Practice Selection

The screen eligible population for all practices across the three regions was estimated based on figures provided to primary care by the NCSP. We aimed to recruit 1000 people from each region. In the Whanganui region, all five practices were selected in consultation with local Māori providers. In Canterbury and Capital and Coast, one practice per region was selected randomly from practices with a higher than

population-level number of eligible Māori people; one practice per region was randomly selected from practices with a higher than population-level number of eligible Pacific people. Remaining practices were randomly selected from all practices.

2.4 | Recruitment

People were eligible for the study if they were enrolled in a participating practice and were eligible and due or overdue for a cervical screening test. Patients were ineligible if, at the time of screening, it was 4 months or more prior to their due date. Participating practices were asked to invite all eligible people to participate in the study utilising their usual invitation methods, including letter, text messaging, telephone calls and opportunistic invitation. Practices were also asked to record the invitation method that led to recruitment to the study for each participant. Following informed consent, demographic data including self-reported ethnicity was recorded in a study-specific database by the health practitioner. Other study-relevant quantitative data was extracted from medical records, the NCSP Register and Ministry of Health National Health Index.

Ethnicities were reported and prioritised as recommended by Manatū Hauora Ministry of Health [15]. These are Māori, Pacific, Asian and European, plus, due to small numbers, an aggregated group of ethnicities which includes Middle Eastern, Latin American and African (MELAA). The estimated eligible populations by ethnicity were available for Māori, Pacific, Asian and Other (European and MELAA groups combined).

As part of the formal informed consent process, all participants were provided with written information and were able to discuss their screening test options with their doctor or nurse. They were informed that unless there was a clinical indication for a *cervical test*, they had the choice of an HPV screening test either as a *vaginal self-test* or a clinician-taken *cervical test*. Additionally, people had the option of the *vaginal self-test* being performed in the clinic or at home. Written information stated that the *vaginal self-test* and a *cervical test* offered similar accuracy, but that following an HPV-detected *self-test*, a cervical cytology test may be required.

The study participant information sheet (https://blogs.otago.ac.nz/hpv/participant-information-sheet/) and culturally responsive engagement brochures were developed in conjunction with the study Māori and Pacific Steering groups.

The current indications for cervical co-testing include test of cure (TOC) following a prior high-grade abnormality, follow-up of adenocarcinoma in situ and the investigation of symptoms. Those who were due to have a TOC or who were due for a screening test but were symptomatic were able to take part in the study. Both were advised to have a clinical examination and a *cervical test* for HPV and cytology (co-test).

Practices had a six-month period of active recruitment, and invited persons had up to 3 months to complete their screening test following an invitation.

2.5 | Clinical Pathway

All HPV tests were performed using the BD onclarity HPV assay (Becton Dickinson Limited, USA) as per manufacturers recommendations. This test is validated for vaginal swab and liquid based cervical samples and detects HPV types 16 and18 (HPV 16/18) and 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68 (*HPV other*). Clinician-taken *cervical tests* utilised a cervical brush and a SurePath vial. Participants utilising the *vaginal self-test* were given standardised pictorial instructions and asked to insert a FLOQswab into the vagina and rotate for 10 s (https://blogs.otago.ac.nz/hpv/files/2022/09/Self-test-instruction-sheet.pdf). The dry swab was then replaced into the specimen tube and transported to the laboratory. Following an 'HPV not detected' result, participants were advised that their next screen would be at the usual screening interval. Following an 'HPV detected' result, reflex cytology would be performed if a *cervical test* had been taken. If a *vaginal self-test* had been utilised, people were asked to undergo cervical cytology. All people with HPV 16/18 detected were referred to colposcopy regardless of the cytology test. Those with *HPV other* detected were referred to colposcopy if the subsequent cytology test result was abnormal (i.e., atypical squamous cells of uncertain significance [ASC-US] or worse). Those with *HPV other* detected and normal cytology test results were recommended to return for a repeat cervical screen in 12 months.

People who did not participate in the study were able to access cervical screening utilising a liquid-based cervical cytology test. Only accredited screen takers ('smear-takers') were permitted to take clinical responsibility for screening tests. Test results were communicated to participants in the usual manner by the screen taker. To ensure safety, the study team monitored recommendations and provided clinical advice when required.

2.6 | Data Analysis

Study data were collected and managed using REDCap (Research Electronic Data Capture) [16]. Data included demographic data, screening history, invitation method, screening-related encounters and clinical results.

Analyses were conducted using STATA [17]. A 2-sample test of proportions was used to compare proportions. A corrected median test was used to compare time intervals. Adjusted (multivariable) odds ratios with 95% confidence intervals (CI) were calculated using Logistic regression (logit-binomial). In Aotearoa NZ, Māori are the tāngata whenua (indigenous people) and are the reference group for analysis. 95% CIs are reported where appropriate. Percentages are rounded to the nearest percent with the exception of HPV detection rates, 95% CIs and percentages $<1\%$, which are reported to 1 decimal place.

Where cytology results were reported, low-grade cytology was defined as atypical squamous cells of undetermined significance (ASC-US) or low-grade squamous intraepithelial lesion (LSIL). High-grade cytology was defined as atypical squamous cells—cannot exclude high-grade (ASC-H), atypical glandular cells or worse. Where histology results were reported, low-grade histology was defined as HPV effect, CIN grade 1 (CIN1). High-grade histology was defined as high-grade cervical Intraepithelial

neoplasia grade 2 and 3 (CIN2 and CIN3), glandular cervical Intraepithelial Neoplasia (cGIN) and cervical carcinoma.

3 | Results

3.1 | Participating Practices

17 primary care practices in three regions of Aotearoa NZ took part in the study. Based on NCSP lists, the population eligible for screening over 6 months in these practices was estimated to be 4006. See Table S1. By prioritised ethnicity, 22% (866/4006) of the eligible population were recorded as Māori, 5.7% (230/4006) Pacific and 15% (603/4006) Asian peoples.

3.2 | Recruitment and Participation

$N = 3308$ people were consented to the study. See Figure 1 Recruitment and clinical pathway flowchart. However, 106 (3%) people were excluded because they were not due for a screening test (i.e., > 4 months early) and 81 people were excluded because, following consent, they did not complete a screen. 80 of these people were among the 744 who had been sent or given a *vaginal self-test* kit to complete at home.

Ultimately, 3121 people from the three regions (1019, 1112 and 990 people) were eligible for a screening test, completed a cervical screen and were included in analyses.

The demographics of the included population are documented in Table 1. The median age of study participants was 45 years (range 21–70 years, interquartile range [IQR] 34–56 years). Age distribution by ethnicity is included in Table S2. By prioritised ethnicity [15], 24% (741/3121) participants were Māori, 5.8% (181/3121) were Pacific peoples, 15% (473/3121) were Asian, 2.6% (81/3121) were MELAA, 52% (1634/3121) European and 0.3% (11/3121) had no ethnicity reported. Where reported, 50% (1527/3053) of participants resided in areas of higher socioeconomic deprivation (Quintiles 4 and 5).

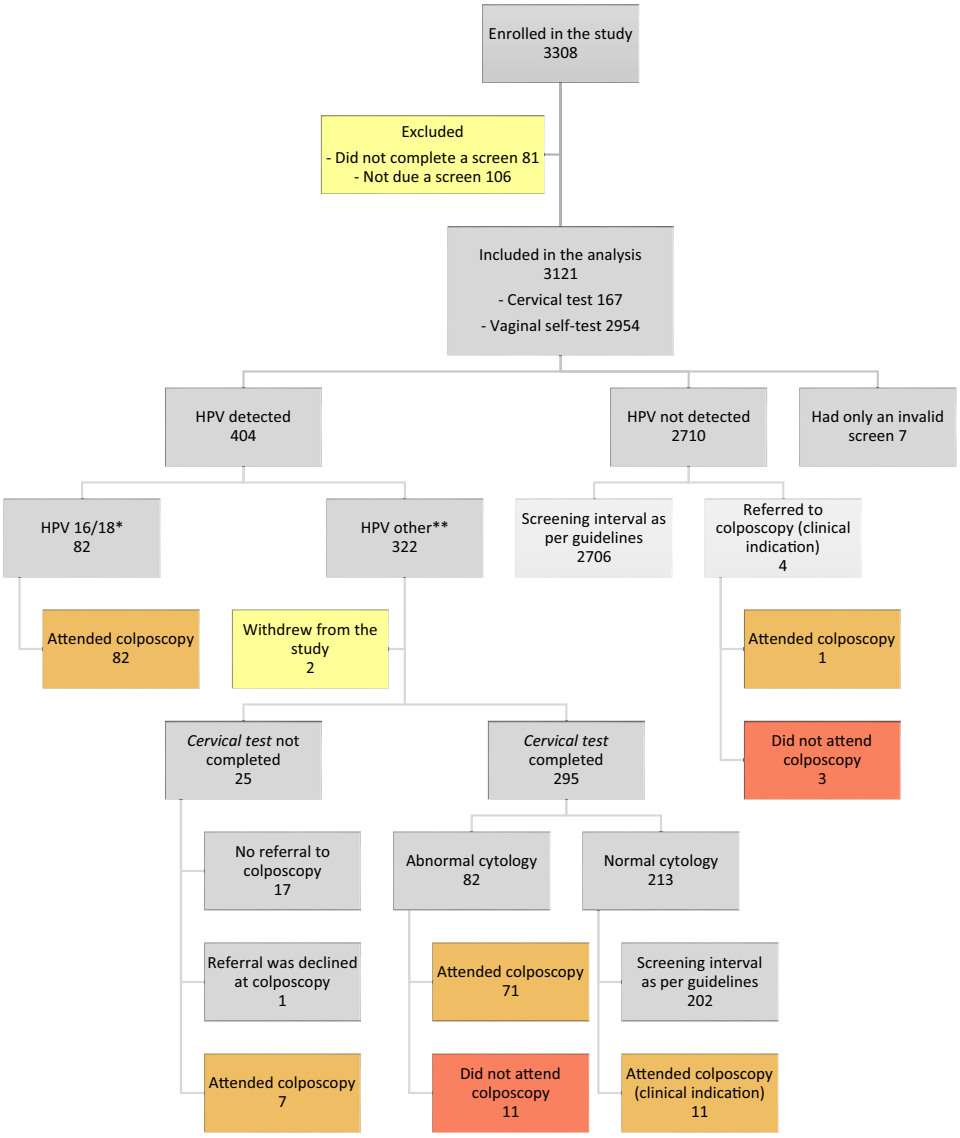

FIGURE 1 | Recruitment and clinical pathway flowchart. *HPV 16 and/or HPV 18 detected with or without *HPV other* types detected. *High risk HPV types detected excluding HPV16 or HPV 18 detected.

TABLE 1 | Baseline demographics by prioritised ethnicity.

Prioritised ethnicity	Median age (IQR)	Median NZDep Index (IQR)[a]	Proportion with no screening history	Median months overdue for screening (IQR)[b]	Proportion on a short-interval recall[c]	Total
Māori	44 (33–55)	4 (4–5)	7% (50/741)	8 (2–29)	32% (223/691)	741
Cervical test	37 (29–50)	4 (4–5)	3% (1/30)	8.5 (2.5–14.5)	59% (17/29)	30 (4%)
Vaginal self-test	45 (33–55)	4 (4–5)	7% (49/711)	8 (2–29)	31% (206/662)	711 (96%)
Pacific	42 (32–52)	5 (4–5)	13% (24/181)	12.5 (3–41.5)	36% (56/157)	181
Cervical test	29 (27–35)	4 (3–5)	33% (2/6)	110 (57–141)	75% (3/4)	6 (3%)
Vaginal self-test	43 (32–53)	5 (4–5)	13% (22/175)	12 (3–40)	35% (53/153)	175 (97%)
Asian	40 (33–49)	3 (1–4)	30% (143/473)	6 (1–16)	33% (110/330)	473
Cervical test	35 (31–40)	3 (2–4)	17% (7/41)	5 (3–15)	56% (19/34)	41 (9%)
Vaginal self-test	41 (34–50)	3 (1–4)	31% (136/432)	6 (1–16)	31% (91/296)	432 (91%)
MELAA	39 (33–48)	3 (1–4)	16% (13/81)	8.5 (1–20)	40% (27/68)	81
Cervical test	33 (28–34)	2 (1–4)	0% (0/7)	2 (0–16)	57% (4/7)	7 (9%)
Vaginal self-test	39 (33–49)	3 (2–4)	18% (13/74/)	9 (2–21)	38% (23/61)	74 (91%)
European	49 (36–59)	3 (1–4)	5% (82/1634)	5 (0–17)	24% (372/1552)	1634
Cervical test	40 (32–50)	2.5 (2–4)	5% (4/82)	3 (0–14)	54% (42/78)	82 (5%)
Vaginal self-test	49 (37–59)	3 (1–4)	5% (78/1552)	5 (0–17)	22% (330/1474)	1552 (95%)
Not reported	48 (32–58)	3 (2–5)	18% (2/11)	7.5 (3.5–33.5)	33% (3/9)	11
Cervical test	58 (58–58)	4 (4–4)	0% (0/1)	41 (41–41)	100% (1/1)	1 (9%)
Vaginal self-test	47 (32–53)	3 (2–5)	20% (2/10)	5 (3–26)	25% (2/8)	10 (91%)
All ethnicities	45 (34–56)	4 (2–5)	10% (314/3121)	6 (1–21)	28% (791/2807)	3121
Cervical test	37 (31–46)	3 (2–4)	8% (14/167)	5 (1–17)	56% (86/153)	167 (5%)
Vaginal self-test	46 (35–57)	4 (2–5)	10% (300/2954)	6 (1–21)	27% (705/2654)	2954 (95%)

Abbreviations: IQR, Interquartile range; MELAA, Middle Eastern, Latin American, or African; NZDep Index, Socioeconomic index quintile ranges.
[a]Excludes 68 people with no Socioeconomic index reported.
[b]Excludes 314 people with no screening history recorded in the NCSP register and 12 people under specialist care.
[c]Short-interval recall of < 3 years (e.g., following a previous cervical abnormality or 12-month follow up after their first ever cytology). Excludes 314 people with no screening history recorded in the NCSP register.

Based on the estimated eligible population, 78% (3121/4006, 95% CI [76.6, 79.1]) of people were screened. By ethnicity, 86% (741/866, 95% CI [83.0, 87.8]) of Māori were screened, 79% (181/230, 95% CI [72.8, 83.8]) of Pacific peoples were screened, 78% (473/603, 95% CI [74.9, 81.7]) of Asians were screened, and 75% (1726/2307, 95% CI [73.0, 76.6]) of other ethnicities (European and MELAA groups combined) were screened. See Table S1 for further detail.

10% (314/3121) of people had no cervical screening history recorded with the NCSP. 25% (80/314) of these were < 28 years old and 50% (156/314) were Asian or MELAA [18].

Participants who had a cervical screening history were a median of 6 months overdue for screening (mean 20 months, IQR: 3–304). 26% (195/741) of Māori, 34% (61/181) of Pacific and 19% (310/1634) of European participants were more than 24 months overdue. See Table 2.

65% (2016/3121) of people had been on a 3-year routine screening pathway, 25% (779/3121) had been on a short interval recall (e.g., following a previous cervical abnormality or 12-month follow up after their first ever cytology), and 0.4% (12/3121) had not been discharged from specialist care but were overdue for a screening test.

People who had been on a short interval recall screen were a median of 17 months overdue (IQR: 3–268 months). People who were on a routine screen pathway were a median of 4 months overdue (IQR: 3–265 months).

Data on method of invitation was provided from 11/17 practices. 53% (1094/2052) of people were recruited opportunistically when attending the practice for another reason. When not opportunistic, the most successful invitation method was a text from the primary practice (54% 513/958).

3.3 | Type of Cervical Screen

An HPV *vaginal self-test* was utilised by 95% (2954/3121, 95% CI [93.8, 95.4]) of people. Of people who chose the *vaginal self-test*, 77% (2260/2954, 95% CI [74.9, 78.0]) undertook the test in the clinic, while 22% (647/2954, 95% CI [20.4, 23.4]) of people were given or sent a *self-test* kit to complete at home. Location was not reported for 2% (47/2954, 95% CI [1.2, 2.1]).

The remaining 5% (167/3121, 95% CI [4.6, 6.2]) of participants undertook a *cervical test*. The reason for a *cervical test* was recorded as (more than one answer could be selected): Requested by clinician 38% (63/167, 95% CI [30.3, 45.5]), symptoms 37% (62/167, 95% CI [29.8, 44.9]), previous high-grade abnormality 63% (105/167, 95% CI [55.1, 70.2]), requested by patient with no clinical indication 15% (25/167, 95% CI [9.9, 21.3]). Overall, < 1% (25/3121, 95% CI [0.5, 1.2]) of people on the study selected the clinician-taken *cervical test* with no clinical indication.

82 people were recruited while on the TOC clinical pathway. Only 46% (38/82, 95% CI [35.3, 57.7]) of people eligible for TOC undertook a *cervical test* as the initial screen. However, 32% (14/44, 95% CI [18.6, 47.6]) of the people on the TOC pathway who had a *vaginal self-test* returned for cytology when requested.

3.4 | HPV Tests

Of 3121 people who had an HPV test, 23 (0.7%, 95% CI [0.4, 1.1]) had an invalid screen, of whom 16 had a subsequent valid screen.

HPV was detected in samples from 12.9% (404/3121, 95% CI [11.8, 14.2]) of people. HPV genotypes detected were: *HPV other* 11.1% (346/3121, 95% CI [10.0, 12.2]), HPV 16 2.0% (62/3121, 95% CI [1.5, 2.5]) and HPV 18 0.7% (21/3121, 95% CI [0.4%, 1.0]). This included 23 people who had HPV 16 or 18 and *HPV other*, and one person who had HPV 16, HPV 18 and *HPV other*. HPV test result by prioritised ethnicity and test type is reported in Table 3.

The proportion of people with HPV detected on a *cervical test* was 15.0% (25/167, 95% CI [9.9, 21.3]) and on a *vaginal self-test* was 12.8% (379/2954, 95% CI [11.6, 14.1]).

Likelihood of having HPV detected was associated with younger age (binary logistic regression odds ratio [OR] 0.82 per 10 years of age, 95% CI [0.76, 0.90], $p < 0.001$), being on short interval recall (OR 1.52 compared with being on routine recall, 95% CI [1.20, 1.93], $p < 0.001$), and having no recorded screening history (OR 1.49 compared with being on routine recall, 95% CI [1.04, 2.16], $p = 0.03$). Pacific and Asian people were at lower risk of having an HPV detected compared to Māori (the reference group) (Pacific OR 0.45, 95% CI [0.26, 0.78], $p < 0.001$, Asian OR 0.48, 95% [CI 0.33, 0.70], $p < 0.001$). No other differences by ethnicity compared to the reference group were noted. See Table S3.

3.5 | Further Investigations Following an HPV Detected

404 people had HPV detected and 95% (384/404, 95% CI [92.5, 97.0]) had follow-up cytology or colposcopy (or both). Two people withdrew from the study after having *HPV other* detected on a *vaginal self-test*.

3.5.1 | Cytology

Cervical cytology was completed by 62% (47/76, 95% CI [50, 73]) of people who had an HPV 16/18 detected on a *vaginal self-test*. This was similar by ethnicity, but all were referred to and attended colposcopy. Of the people with *HPV other* detected on a *vaginal self-test*, 92% (276/301, 95% CI [88.0, 94.6]) completed

TABLE 2 | Proportion of participants by cervical screening history and prioritised ethnicity.

Prioritised ethnicity	No prior screen recorded	Under specialist care	Due	6–23 months overdue	24–59 months overdue	60+ months overdue	Total
Māori	50 (7%)	2 (0.3%)	303 (41%)	191 (26%)	115 (16%)	80 (11%)	741
Pacific	24 (13%)	1 (0.6%)	53 (29%)	42 (23%)	33 (18%)	28 (15%)	181
Asian	143 (30%)	3 (0.6%)	159 (34%)	106 (22%)	43 (9%)	19 (4%)	473
MELAA	13 (16%)	—	27 (33%)	26 (32%)	10 (12%)	5 (6%)	81
European	82 (5%)	5 (0.3%)	801 (49%)	436 (27%)	185 (11%)	125 (8%)	1634
Not reported	2 (18%)	1 (9%)	4 (36%)	1 (9%)	2 (18%)	1 (9%)	11
Total	314 (10%)	12 (0.4%)	1347 (43%)	802 (26%)	388 (12%)	258 (8%)	3121

Note: Due = Up to 4 months prior to screening due date, up to 6 months after screening due date. Overdue = 6 months or more after screening due date.
Abbreviation: MELAA, Middle Eastern, Latin American, or African.

TABLE 3 | HPV detected (total response[a]) by prioritised ethnicity.

Prioritised ethnicity	HPV detected (total response)[a]						
	HPV 16	HPV 18	*HPV other*	Any HPV	HPV not detected	Only invalid results[b]	Total
Māori	20 (2.7%)	7 (0.9%)	104 (14.0%)	123 (16.6%)	614 (82.9%)	4 (0.5%)	741
Pacific	—	—	16 (8.8%)	16 (8.8%)	164 (90.6%)	1 (0.6%)	181
Asian	6 (1.3%)	2 (0.4%)	40 (8.5%)	46 (9.7%)	427 (90.3%)	—	473
MELAA	1 (1.2%)	1 (1.2%)	8 (9.9%)	9 (11.1%)	72 (88.9%)	—	81
European	35 (2.1%)	11 (0.7%)	178 (10.9%)	210 (12.9%)	1422 (87.0%)	2 (0.1%)	1634
Ethnicity not reported	—	—	—	—	11 (100.0%)	—	11
Total number[b]	62 (2.0%)	21 (0.7%)	346 (11.1%)	404 (12.9%)	2710 (86.8%)	7 (0.2%)	3121

Abbreviations: HPV, High risk HPV; MELAA, Middle Eastern, Latin American, or African.
[a]People may have more than one genotype detected.
[b]Excludes 20 invalid, failed, or unlabelled samples if the person came back for a repeat sample that was valid.

triage cytology. There was variation by ethnicity (Table S4). Of note, 85% (79/93, 95% CI [76.0, 91.5]) of Māori with *HPV other* detected through a *vaginal self-test* were reached for cytology triage. Proportionally, fewer people with *HPV other* on a *vaginal self-test* sample who were more than 24 months overdue were reached for triage (83%, 57/69, 95% CI [71.6, 90.7]) compared to those who were due (97%, 116/120, 95% CI [91.7, 99.1]) (Pearson $chi^2(1) = 11.17$, $p = 0.001$). See Table S4.

Cytology outcomes are described in Table S5. High-grade cytology was reported in 11% (6/53) of those with HPV 16/18 detected (95% CI [4.3, 23.0]) and 8% (24/295) with *HPV other* detected (95% CI [5.3, 11.9]). None (95% CI [0, 4.6]) of the 79 cytology samples for people with HPV not detected were high grade.

An additional 2% (7/301) of people (4 European and 3 Māori) with *HPV other* detected attended colposcopy without cytology triage for clinical reasons.

3.5.2 | Colposcopy

6% (187/3121, 95% CI [5.2, 6.9]) of people were referred and 172 people attended colposcopy (100% [82/82, 95% CI [95.6, 100]] who had HPV 16/18 detected and 86% [90/105, 95% CI [77.5, 91.8]] who had *HPV other* detected). A satisfactory histological biopsy was taken for 72% (124/172, 95% CI [64.8, 78.7]) of people. High-grade histology was confirmed in 15% (26/172, 95% CI [10, 21]) of people. This included 10% (8/82, 95% CI [4.3, 18.3]) of people with HPV 16/18 detected and 6% (19/322, 95% CI [3.6, 9.1]) of people with *HPV other* detected. One case of cervical cancer was diagnosed. No cervical glandular abnormalities were identified, but 1 case of endometrial cancer was identified incidentally by abnormal cytology following an *HPV other vaginal self-test*. See Table S6.

4 | Discussion

4.1 | Main Findings

This study demonstrated the feasibility of universal self-testing in this population. The high recruitment rate across Māori, Pacific, Asian and European ethnicities combined with the high proportion of people that were overdue a screen indicates that a *vaginal self-test* is acceptable and may help reduce screening inequity.

In this study, when people were offered a *vaginal self-test* as an alternative to a speculum-based cervical sample in a primary care setting with a healthcare practitioner, 95% of people chose a *vaginal self-test*. 12.9% of people had HPV detected, including 2.6% who had HPV 16 or 18. All participants with HPV 16/18 detected attended colposcopy, and 92% of people with *HPV other* detected on a *vaginal self-test* had triage cytology. Six percent of people completed a colposcopy appointment, and 1% had a cervical high-grade histology or cancer detected.

The main logistical issues were the equitable uptake of cytology triage in people with *HPV other* detected and the delivery of cervical co-tests for people on the TOC pathway. Practices were unable to reach 15% of Māori for cytology triage. In addition, triage cytology was less likely to be completed for those more than 2 years overdue. Identification of those due for a TOC and delivery of a co-test for these people represented a challenge as the role of the *vaginal self-test* for TOC is not yet established [19]. 46% of those eligible for TOC initially completed a co-test. Despite prompting, some participants did not return for cytology.

4.2 | Strengths and Limitations

This implementation study introduced HPV screening that incorporated the offer of a *vaginal self-test* for people undergoing cervical screening tests and involved a wide range of general practice environments. Engagement with the study was excellent. Over 78% of the estimated eligible population were screened and there was evidence that uptake by Māori (86%) was higher. We note the relatively high proportion of Asian people who had not been previously screened in Aotearoa NZ—likely representing an immigrant population who also took part [18]. It is likely factors associated with the conduct of this study in addition to test availability may have influenced screening uptake including Involvement of Māori and Pacific steering groups, consultation with local providers, and the enthusiasm of the participating practices. The estimated coverage in our study is limited by the short time frame and the lack of data we recovered on

people who did not take part in our study and cannot be directly compared with national screening coverage data.

While the general practices that participated in the study covered a wide range of demographics, this can only be considered a limited representation of the Aotearoa NZ population. There will be a range of confounders that may introduce bias for which we did not control. We note that Pacific peoples were underrepresented in our eligible population. As recruitment for this study was undertaken through general practices, this did not include people who were not enrolled in general practice. There are other opportunities for screening recruitment outside of the general practice environment for which the *self-test* may be particularly applicable.

The rescreening of people with HPV detected in the absence of a high grade abnormality after 12 months is not included in this report. Monitoring of this aspect of the programme is important as previously the NCSP has been unable to completely or equitably screen those requiring a short interval rescreen [20].

4.3 | Interpretation

There are very few examples worldwide where the introduction of HPV screening has included the universal offer of self-testing. As such, this implementation study in Aotearoa NZ is unique. The size of this study and the range of general practice environments engaged mean it is likely the study offers a good indication of the impact of the introduction of HPV screening in Aotearoa NZ as a whole. It may also be applicable to other cervical screening programmes.

The preference for the *vaginal self-test* in this study was clear. Some people who preferred the option of a *cervical test* may not have enrolled in the study. The nature of the invitation and the information people are given is likely to influence people's choices. Participants were informed that the *vaginal self-test* was as accurate as the clinician-taken *cervical test*, and health practitioners discussed the advantages and disadvantages of the tests with each participant. A survey of participants revealed a strong preference for the *self-test* and emphasised the importance of choice and the ease and comfort of the test [21]. A survey of participating health practitioners also revealed much enthusiasm and anticipation for access to the *vaginal self-test*, as it was seen as a highly acceptable and convenient way to deliver screening [22].

A large proportion of participants were recruited opportunistically when it may not have been practical or convenient to perform a *cervical test*. We note the success of an opportunistic *vaginal self-test* and the significant role of home testing, as have been reported by other authors [23, 24]. A survey of participants indicates that the option of a home test is important to ensure maximum participation [21, 25].

Cost may also influence a person's choice of test. In Aotearoa NZ, although screening is subsidised for high-priority people, many are charged for their cervical screen. In this study, the majority of participants (71%) were not charged regardless of test choice. However, those that were charged approximately 10 New Zealand dollars more if a *cervical test* was performed. See Table S7.

The results of this study are consistent with the *vaginal self-test* being associated with improved equity of access to cervical screening. Making the offer of the *vaginal self-test* universal removes the need to identify under-screened individuals and offers people the choice of a more acceptable test. Numerous studies have demonstrated increased uptake for under-screened people with the *vaginal self-test* [7, 13, 26]. We note the increased uptake when a universal offer of self-testing was made within the Swedish screening program during the COVID pandemic [23]. While this study is performed in Aotearoa New Zealand, it is likely the option of self-testing would be feasible and increase the accessibility of cervical screening and reduce inequity for many other under-screened populations worldwide. Achieving equity involves numerous components and requires active engagement from underserved populations. It is crucial to ensure that individuals with abnormal screening outcomes receive proper follow-up care and investigation. New program recommendations include colposcopy for all people with HPV 16/18 detected and for those with *HPV other* and high-grade cytology. Six percent of people screened in this study were referred to colposcopy. This would fall to 4% if people with *HPV other* and low-grade cytology are rescreened in 12 months as per current guidelines [27]. Combined with a high-grade histology detection rate of approximately 1%, the outcome of HPV-based screening appears similar to that of the Aotearoa NZ cytology-based program [20]. Although HPV screening may be associated with similar positive predictive value to cytology programs [28], rapid uptake of HPV testing is likely to result in increased colposcopy demand [29]. Significant heterogeneity regarding the specificity of self-testing for the detection of CIN2+ has been reported dependent on the test methodology [5, 30, 31]. Lower specificities are likely to be associated with a further increase in demand for colposcopy.

This study was not designed to compare the accuracy of *vaginal self-tests* and *cervical tests*. The underlying justification for universal self-testing is that cervical and vaginal HPV testing offer similar sensitivity for cervical precancerous lesions. While recent metanalyses and other studies show this to be the case [5, 31, 32], a recent *self-test* study [33], which was associated with a lower than expected detection of abnormalities indicates the importance of validated HPV screening methodologies, ongoing research, and the monitoring of cervical screening programs [31].

5 | Conclusion

This study confirms the feasibility of cervical screening with the universal option of the *vaginal self-test*. While this appears to enable more equitable participation in screening, ensuring the safe follow-up of all women with an HPV detected test remains a challenge. In order to ensure safety, ongoing monitoring of the Aotearoa NZ screening programme is essential.

Author Contributions

P.S. and C.I. have directly accessed and verified the underlying data reported in the manuscript. All authors had full access to all the data in the study and accept responsibility to submit for publication. All authors meet the four criteria for authorship as specified in the ICMJE recommendations: P.S. contributed to the conceptualisation, funding acquisition,

investigation, methodology, project administration, formal analysis and writing – original draft and writing – review and editing. C.I. contributed to the funding acquisition, investigation, methodology, project administration, data curation, formal analysis and writing – original draft and writing – review and editing. R.B. contributed to the funding acquisition, investigation, methodology, project administration, data curation and writing – review and editing. J.N. contributed to the investigation, methodology, project administration and writing – review and editing. J.M., L.M., B.H., M.G., B.L., S.T.W., A.T. and A.M. contributed to the funding acquisition, investigation, methodology and writing – review and editing. J.W. contributed to the funding acquisition, investigation, methodology, data curation and writing – review and editing.

Acknowledgements

We wish to acknowledge and thank all study participants, Māori Steering Committee, Pacific Advisory Group, National Cervical Screening Programme, Canterbury Health Laboratories, Health and Research Collaborative (Whanganui), participating primary care practices, Pegasus Health, Tū Ora Compass Health, Screen South and for cultural support from Kathy Simmons, Sala Temo, and Mana Wāhine. Open access publishing facilitated by University of Otago, as part of the Wiley - University of Otago agreement via the Council of Australian University Librarians.

Ethics Statement

This study was approved by the NZ Southern Health and Disability Ethics Committee (Ethics ref.: 2022 FULL 12546, 1 July 2022), site locality approvals in place.

Conflicts of Interest

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: C.I., R.B., J.N., J.W., L.M., B.H., J.M., M.G., S.T.W., A.T. and B.L. received funding from Te Whatu Ora Health New Zealand for salary for work associated with this study. L.M. received funding from the Royal New Zealand College of General Practitioners, Research and Education Committee and the Wellington Faculty for a summer research student stipend for work associated with this study. M.G. received funding from Te Whatu Ora Health New Zealand and Health Research Council of New Zealand for separate research projects on the implementation of HPV self-testing. R.B. received consulting fees from Te Whatu Ora Health New Zealand for advising the working group for the National Screening Unit that wrote the Educational resources for those involved in cervical screening in Aotearoa NZ. B.L. received funding from the NZ Health Research Council and Te Whatu Ora Health New Zealand to carry out trials related to HPV self-testing and Point of Care testing and research on maternal child health, was a Member of the Maternal Birth Injuries Expert Advisory Group (ACC), a member of the National Cervical Screening Action and Advisory group, and a member of the He Hono Wahine advisory group to the Royal Australian and New Zealand College of Obstetrics and Gynaecology (RANZCOG), and was provided the loan of two Gene Xpert machines from Cepheid to carry out research (Cepheid provided no other funding and had no influence or part in the research).

Data Availability Statement

The de-identified data that support the findings of this study may be available on request from the corresponding author, subject to ethical approval and Māori data sovereignty considerations. The data are not publicly available due to Māori data sovereignty and ethical restrictions.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.