

Trends in the diagnosis of high-grade cervical abnormalities in young women in the post-vaccination era

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ABSTRACT

BACKGROUND: Most cervical cancers are associated with human papillomavirus (HPV) types 16 and 18. In 2008, New Zealand commenced a quadrivalent HPV (virus-like particles of types 6, 11, 16 and 18) vaccination programme.

AIM: Document trends in number of colposcopy referrals and number and grade of cervical abnormalities diagnosed in women (20–24 years) referred to three large colposcopy clinics over time.

METHOD: Retrospective analysis of colposcopy clinic data.

RESULTS: The dataset included 5,012 episodes from 4,682 women. In Auckland (2013–2017), there was a 38% decrease in colposcopy referrals and 55% decrease in cervical intraepithelial neoplasia grade 2 (CIN2) or worse diagnoses. In Waikato (2011–2017), there was an 8% decrease in referrals and 22% reduction in CIN2 or worse diagnoses. In Canterbury (2011–2017), there was a 24% decrease in referrals and 49% reduction in CIN2 or worse diagnoses. Across all centres, the decrease in cervical intraepithelial neoplasia grade 3 (CIN3) or worse diagnoses was marked and more consistent than in CIN2 diagnoses. However, while the proportion of biopsies reported as CIN3 or worse decreased in non-Māori (24% in 2013 vs 16% in 2017, nptrend $z=-4.24$, $p>|z|<.001$), there was no change in Māori women (31% in 2013 vs 29% in 2017, nptrend $z=-0.12$, $p>|z|= .90$).

CONCLUSIONS: We observed a decreased number of CIN diagnoses in young women over time, with a particularly large drop in the number of CIN3/AIS/CGIN diagnoses. However, compared to non-Māori, Māori women having biopsies are more likely to have CIN3 or worse and there was a smaller reduction in the total number of Māori women diagnosed with CIN2 or worse.

In 2008, the quadrivalent HPV vaccine (containing HPV virus-like particles of types 6, 11, 16 and 18) was introduced to the New Zealand National Immunisation Schedule. HPV types 16 and 18 are associated with around 70% of all cervical cancers and about 50–60% of high-grade cervical precancerous abnormalities (CIN2/3).^{1,2} HPV types 6 and 11 are associated with 90% of anogenital warts.³

When introduced, fully subsidised HPV vaccination was first offered to New Zealand young women born in 1990 and 1991. A catch-up programme was then offered to girls and young women aged 9–20 years.⁴ From 1 January 2017 onwards, HPV immunisation became funded for everyone aged 9–26 years, including boys and young men.⁴ HPV vaccination coverage in New Zealand has increased from 39% (for all three HPV

doses) for the cohort born in 1990 to 67% (for all three HPV doses) for the cohort born in 2003.⁵

International research has demonstrated a decrease in vaccine-type HPV infections and the number of high-grade cervical cell abnormalities in young women following HPV vaccine introduction compared to pre-vaccine introduction^{6–11} and in HPV-vaccinated compared to unvaccinated women.^{12–16}

The New Zealand National Cervical Screening Programme (NCSP) was established in 1990 and until very recently recommended regular three-yearly cervical screening for women aged 20–69 years.¹⁷ The incidence of cervical cancer in New Zealand has decreased from 10.5 per 100,000 women in 1996 to 5.5 per 100,000 women in 2014 for all ethnicities.¹⁸ For Māori women, rates have decreased from 25 to 10.8 per 100,000 women over the same time period.¹⁸ Women born in 1990 turned 20 and became eligible for cervical screening in 2010.

Many countries are currently reconsidering cytology-based cervical screening programs.¹⁹ Australia, among other countries, has already transitioned to five-yearly primary HPV screening for women aged 25–74 years.¹⁹ New Zealand increased the commencement age for cervical screening from 20 to 25 years in November 2019 and plans to commence HPV primary screening in 2021.²⁰ The justification for increasing the commencement age comes from local²¹ and international^{22,23} screening data and research showing that screening women aged 20–24 does not reduce the incidence of cervical cancer in these women.

Women in New Zealand aged under 25 have high incidences of cervical abnormalities but information regarding them will greatly diminish when they cease to be screened. Furthermore, there is little published information regarding the trends of change in cervical abnormalities in women under 25 in New Zealand, since the vaccination programme started.

This study's aims were to document, in a vaccine-eligible population of women aged 20–24 years, any change over time in (a) colposcopy referrals and (b) the number of histologically confirmed high-grade CIN (CIN2 and CIN3). A secondary aim was to investigate any differences over time

regarding histologically confirmed high-grade CIN in Māori women compared to non-Māori.

Methods

Ethical approval for this retrospective audit was received from the University of Otago Human Research Ethics Committee (approved 24 August 2017, reference number HD17/033). Data were collected from the databases of three major colposcopy clinics serving three district health boards (DHBs) in New Zealand: National Women's Health, Auckland City Hospital, Auckland (Auckland), Waikato Hospital, Hamilton (Waikato) and Christchurch Women's Hospital, Christchurch (Canterbury). At each centre, data was exported from Gynaecology Plus colposcopy databases (Version 7, Solutions Plus, Auckland, New Zealand, <http://www.solutionsplus.co.nz/index.php/gynaecology-plus/>). Exported data included the woman's date of birth, ethnicity, referral indication, referral cervical cytology sample grade, number of visits, histological biopsy results (if applicable) and type of treatment (if applicable). The age attributed to each woman was the age she was when she attended her first visit. Each woman was attributed a single ethnicity using the NCSP priority order: Māori, Pacific, Asian, European/Other, ie, a woman identifying as New Zealand European and Māori, is counted as Māori.²⁴

Data was episode-based, with an episode including data from all visits, starting from being referred, to colposcopy, through to discharge. Following discharge, a woman could have another abnormal cervical cytology sample and be re-referred, which would then mark the start of second episode. It was possible to export the self-reported vaccination status for a subset of women from the Canterbury cohort; however, the option to extract vaccination status was not available from Auckland and Waikato at the time of data extraction.

All episodes were included in the colposcopy referrals analysis, but only episodes from women referred following an abnormal cervical cytology sample were used to examine the trend of histologically confirmed high-grade CIN (CIN2 and CIN3)

changes over time. Women with clinical symptoms or an abnormal appearing cervix, vulva or genital tract may also be referred to colposcopy in the absence of abnormal cytology. However, the vast majority of women referred without abnormal cytology will not have CIN or any other significant cervical abnormalities. Referral patterns for women without abnormal cytology may vary and it was considered that inclusion of these women may lead to a misleading bias.

It is possible that occasionally no histological samples are taken following referral for an abnormal cervical cytology sample or the histological sample is deemed to be unsatisfactory. These episodes cannot contribute to the trends of histologically diagnosed CIN, but the number of episodes in which this occurs will be provided for completeness.

The time-period for which data was extracted was in a non-calendar year format from 1 November 2010 to 31 October 2017 for Waikato and Canterbury. For Auckland data was extracted from 1 November 2012 to 31 October 2017. This was done to maintain consistency in the data parameters obtained as previous to this Auckland was using a different system. All women who had been referred and had their first attended visit within these respective time frames for each colposcopy clinic, and were between 20 and 24 years of age at their first attended visit, were included in the data. Using non-calendar years allowed maximal utilisation of available data and the most recent data up till late 2017. For brevity, years are specified based on the 'year ending' when referring to each year, eg, the 12 months between 1 November 2012 and 31 October 2013, is referred to as 2013.

Cervical glandular intraepithelial neoplasia (CGIN) and adenocarcinoma in situ (AIS) were grouped with CIN3 for analysis. For completeness, low-grade CIN changes (CIN1) and microinvasive or invasive carcinoma were also included in analyses. The main endpoint of this study was the highest (worst) histologically confirmed diagnosis per episode contributed by each woman. It was possible for a woman to contribute more than one episode (ie, the patient may be re-referred following discharge), but she could only contribute one outcome per episode. The number of

low-grade CIN (CIN1), and high-grade CIN (CIN2 and CIN3/AIS/CGIN) diagnoses per year served as indicators of trends.

The number of episodes with each grade of cervical cell abnormality was determined for each centre (and for combined centres) each year and change over time in CIN diagnoses was investigated using a non-parametric test for trend across ordered groups as implemented in STATA (nptrend StataCorp. 2013. Stata Statistical Software: Release 13. College Station, TX: StataCorp LP). Significance level was set at $\alpha = .05$

Results

The dataset included 5,012 episodes from 4,682 women. Of this dataset 4,460 episodes from 4,209 women were used to examine the trend of histologically confirmed high-grade CIN (CIN2 and CIN3) changes over time as these episodes came from women referred following an abnormal cervical cytology sample. The remaining 552 episodes (from 473 women) were excluded from the high-grade CIN trend analysis due to referral for other reasons including clinical reasons (eg, pelvic pain, abnormal bleeding, abnormal appearing cervix, suspicious symptoms or vaginal and vulval inflammation, metaplasia and atrophy). Of the episodes excluded from the high-grade CIN trend analysis, there was no biopsy taken in 280 (51%), there was a low-grade or normal biopsy result in 227 (41%), CIN2 was diagnosed in 25 (5%), and CIN3 or AIS was diagnosed in 20 (4%). There were no cervical carcinoma diagnoses in the excluded episodes.

Auckland

One thousand one hundred and sixty-five episodes (from 1,126 women) were recorded at National Women's Health, Auckland City Hospital, Auckland (2013–2017). There was a 38% decrease in total referrals over time (292 episodes in 2013 vs 182 episodes in 2017).

One thousand and sixty-four episodes (from 1,036 women) were referrals following an abnormal cervical cytology sample. There was one cervical carcinoma diagnosis. See Appendix for the histology results for all women.

There was a 45%, 55%, and 54% reduction in the number of CIN1, CIN2 and CIN3/AIS/CGIN diagnoses over time, respectively (see

Figure 1). However, there was a transient increase in CIN1 diagnoses in 2016. Overall (2013–2017), there was a 50% reduction in CIN1 or worse diagnoses over time and a 55% reduction in total CIN2 or worse diagnoses over time.

Waikato

One thousand four hundred and eighteen episodes (from 1,295 women) were recorded at Waikato Hospital (2011–2017). There was an 8% decrease in total referrals over time (221 episodes in 2011 vs 204 episodes in 2017).

One thousand two hundred and ninety episodes (from 1,192 women) were referrals following an abnormal cervical cytology sample. There was one cervical carcinoma diagnosis. See Appendix for the histology results for all women.

The number of CIN3/AIS/CGIN diagnoses increased from 2011 to 2014, following which there was a 50% decrease in diagnoses between 2014 and 2017 (see Figure 2). The number of CIN1 and CIN2 diagnoses remained relatively consistent, other than a transient decrease in CIN 1 diagnoses in 2015. Overall (2011–2017), there was a 16% reduction in total CIN1 or worse diagnoses and a 22% reduction in total CIN2 or worse diagnoses.

Canterbury

Two thousand four hundred and twenty-nine episodes (from 2,261 women) were recorded at Christchurch Women’s Hospital (2011–2017). There was a 24% decrease in total referrals over time (367 episodes in 2011 vs 278 episodes in 2017).

Two thousand one hundred and six episodes (from 1,981 women) were referrals following an abnormal cervical cytology sample. There were five cervical carcinoma diagnoses. See Appendix for the histology results for all women.

Overall CIN diagnoses increased from 2011 to 2012 and then began to decrease, with a 74% decrease in CIN3/AIS/CGIN diagnoses and 36% decrease in CIN1 diagnoses between 2012 and 2017 (see Figure 3). The number of CIN2 diagnoses were relatively stable over time with a transient increase in diagnoses in 2016. Overall (2011–2017), there was a 38% reduction in total CIN1 or worse diagnoses and a 50% reduction in total CIN2 or worse diagnoses.

Impact of HPV vaccination in Canterbury

HPV vaccination status was known for 823 episodes from 752 women (367 unvaccinated and 385 vaccinated) referred

Figure 1: Number of CIN diagnoses by grade (2013–2017) at National Women’s Health, Auckland City Hospital, (Auckland) in women aged 20–24 years referred following an abnormal cervical cytology sample.

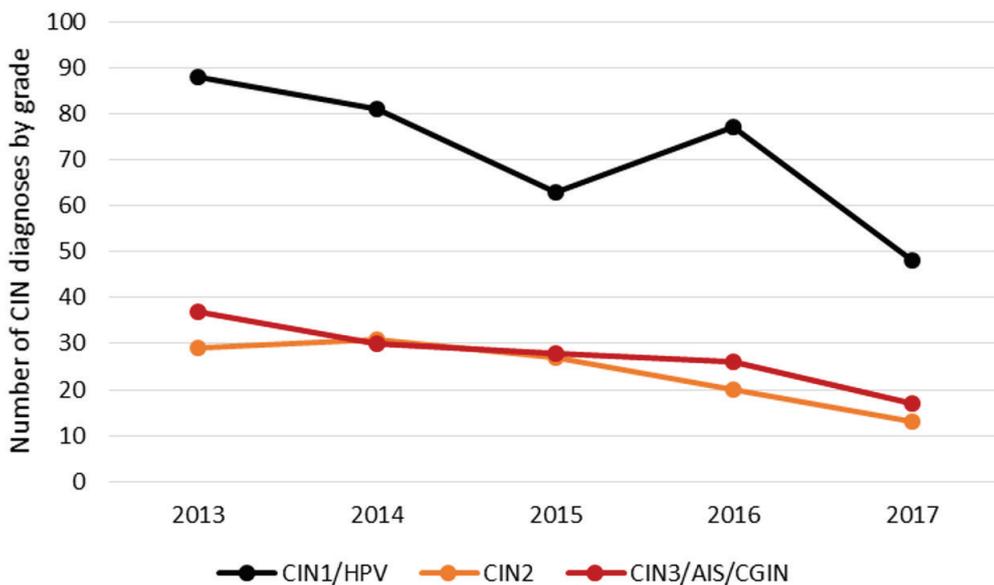
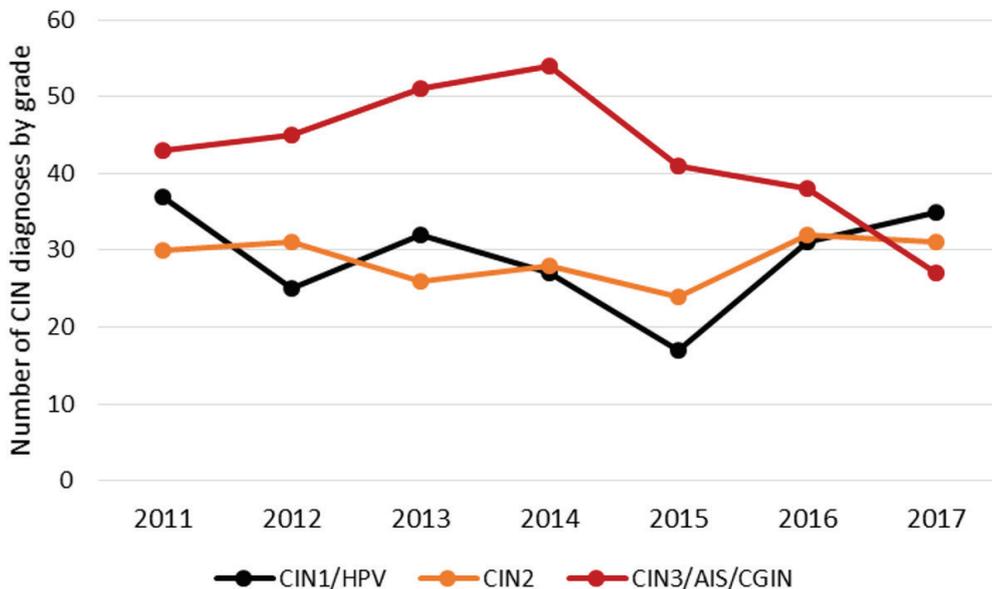


Figure 2: Number of CIN diagnoses by grade (2011–2017) at Waikato Hospital in women aged 20–24 years referred following an abnormal cervical cytology sample.



following an abnormal cervical cytology sample (See Table 1).

Of the 823 episodes where vaccination status was known, 789 had a satisfactory histological biopsy, of which 382 (48%) episodes were for unvaccinated women and 407 (52%) were for vaccinated women. CIN3

or worse was diagnosed in a significantly higher proportion of episodes for unvaccinated women than vaccinated women (31% vs 19%, $X^2=15.18$ $p<.001$). There was no evidence of a difference in the proportion of CIN2 episodes for unvaccinated and vaccinated women (29% vs 24%, $X^2=2.64$ $p=.104$).

Figure 3: Number of CIN diagnoses by grade (2011–2017) in women aged 20–24 years at Christchurch Women’s Hospital (Canterbury).

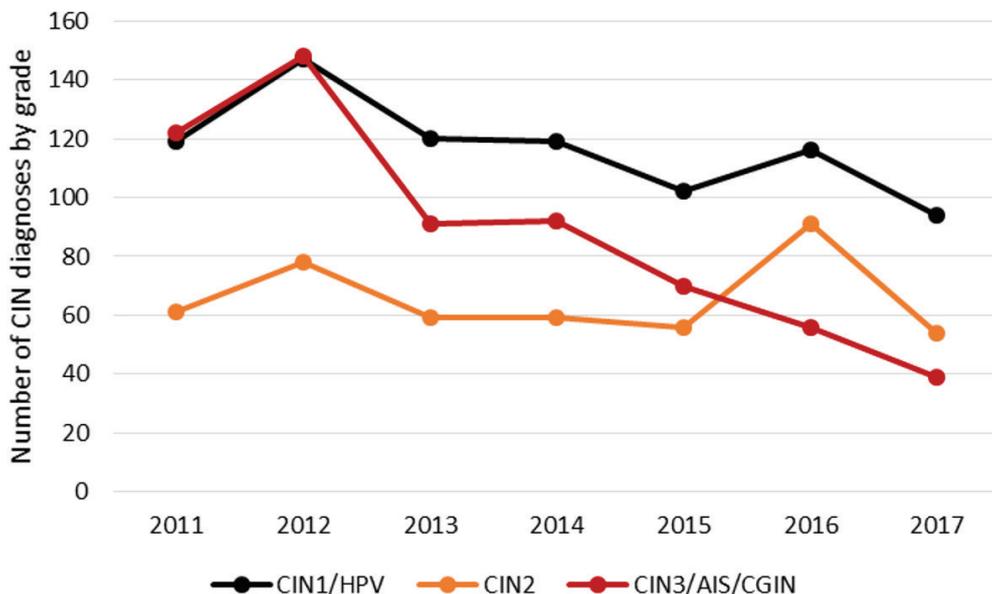


Table 1: Number of episodes and contributing women by vaccination status.

Vaccination status	Number of women
Vaccination status known	752
• Unvaccinated	367
• Vaccinated	385
• Vaccinated—complete	241
• Vaccinated—incomplete	25
• Vaccinated—number of doses not reported	119

There was weak evidence that CIN1 or better was diagnosed in a higher proportion of episodes for vaccinated women than unvaccinated women (52% vs 45%, $X^2=3.68$ $p=.055$).

Impact of ethnicity

Ethnicity was not recorded for 302 episodes from 282 women across the three centres (2013–2017). These episodes were excluded from ethnicity analyses.

Four hundred and fifty-six episodes from 409 Māori women were recorded at the three centres (2013–2017). There was a 27% decrease in total referrals for Māori women over time (108 in 2013 vs 79 in 2017). Four hundred and eighteen episodes from 379 Māori women were referrals following an abnormal cervical cytology sample. Of these episodes, 359 had a satisfactory histological biopsy. See Appendix for the histology results for Māori vs non-Māori women.

Three non-Māori women and no Māori women were diagnosed with cervical carcinoma following an abnormal cytology sample (2013–2017). Between 2013 and 2017, Māori women had a 58% reduction in CIN1, no reduction in CIN2 and a 33% reduction in CIN3 or worse. This pattern appears different in non-Māori women who had a more marked reduction in CIN3 or worse (48% decrease) but less reduction in CIN1 (13% decrease). The number of high grade CIN diagnoses by grade (2013–2017) in women aged 20–24 years by ethnicity is shown in Figure 4.

If we consider CIN3 or worse as a proportion of all satisfactory biopsies, overall Māori women had a higher

proportion of CIN3 or worse than non-Māori (29% vs 23%, $X^2=5.69$, $p=.02$).

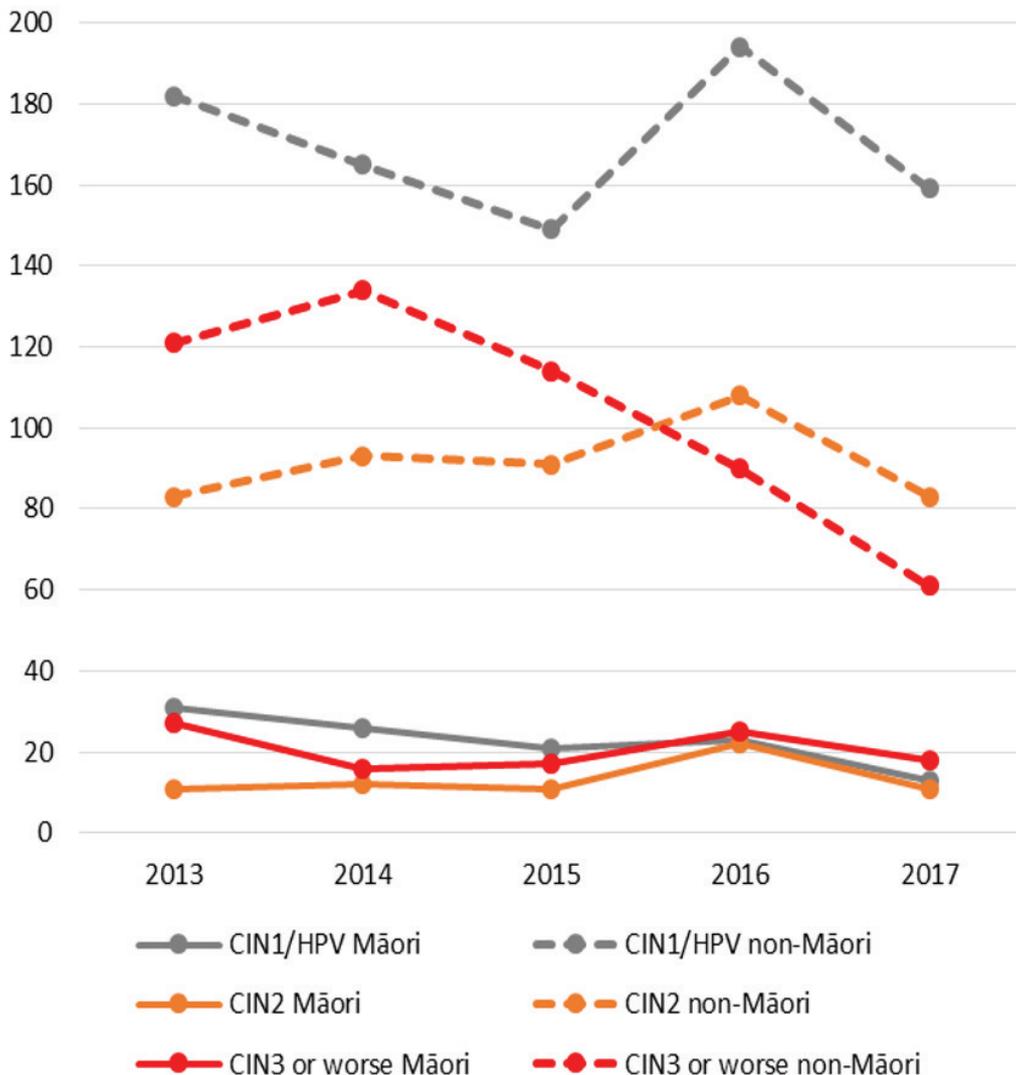
Furthermore, for Māori women there was no change over time in CIN3 or worse diagnoses as a proportion of all satisfactory biopsies (31% in 2013 vs 29% in 2017, $nptrend\ z=-0.12$, $p>|z|=0.90$). In contrast, in non-Māori women there was a decrease over time in CIN3 or worse diagnoses as a proportion of all satisfactory biopsies (24% in 2013 vs 16% in 2017, $nptrend\ z=-4.24$, $p>|z|<0.001$).

Impact of smoking

Smoking status was recorded for 61% of women (2,323 episodes from 2,110 women) across the three centres (2013–2017). Where smoking status was recorded, 30% (563/1,892) of referrals following an abnormal cervical cytology sample self-reported smoking. Overall, smoking rates decreased over time (35% in 2013 vs 25% in 2017, $z=-3.93$, $p>|z|<.001$). Women who smoked were more likely to be diagnosed with CIN3 or worse than women who did not smoke (32% vs 21%, $X^2=23.3$ $p<.001$).

A higher proportion of Māori women self-reported smoking than non-Māori women (55% vs 26%, $X^2=85.5$ $p<.001$). Smoking rates decreased over time in non-Māori women (28% in 2013 vs 23% in 2017, $z=-2.79$, $p>|z|=0.005$). However, although smoking rates also appeared to decrease over time in Māori women (62% in 2013 vs 47% in 2017), trend analysis did not reach significance ($z=-1.65$, $p>|z|=0.099$). See Appendix for a figure showing the proportion of women who self-reported smoking (2013–2017) by ethnicity.

Figure 4: Number of CIN diagnoses by grade (2013–2017) in women aged 20–24 years by ethnicity.*



*Excludes n=258 women where ethnicity was unknown.

Discussion

In this study, we describe the changes over time in the number and type of cervical abnormalities diagnosed in women (aged 20–24 years) in three large public hospital colposcopy clinics following the introduction of a national HPV vaccination programme. We observed in all three clinics a reduction in women diagnosed with high-grade abnormalities (CIN2 or worse). The reduction was particularly marked and consistent for CIN3 or worse. In comparison, changes in CIN1 and CIN2 varied between clinics and, overall, the reduction was less marked.

The changes observed in our study are consistent with data from NCSP reports. Nationally, histologically confirmed high-grade CIN for 20–24-year-old women

decreased between 2011 and 2017.²⁵ This decrease is expected in the context of the introduction of HPV vaccination. Using data from the vaccination registry and the NCSP, we have previously demonstrated that vaccinated women had a 31% reduced cumulative incidence of high-grade abnormalities but only a 15% reduction of low-grade abnormalities when compared to non-vaccinated women.²⁶

In this study, as laboratories reporting to these colposcopy clinics routinely differentiate between a histological diagnosis of CIN2 and CIN3 in young women we were able to report these occurrences separately. It is notable in this study that the reduction of CIN3 is more marked and consistently observed in all three clinics, whereas the pattern of CIN2 diagnoses over time was

more similar to CIN1. This would suggest that a greater proportion of CIN3 diagnosis are due to HPV 16 or 18 than CIN2.

While we do not have HPV typing data for this study, previous studies examining HPV genotypes found in high-grade cervical disease have reported a prevalence of types 16 and/or 18 of 40–53% in CIN2 and 58–75% for CIN3 lesions.^{2,27} Other oncogenic types (excluding types 16 and 18) have been shown to be more prevalent in CIN2 compared to CIN3.²⁷ Furthermore, studies indicate that CIN3 lesions associated with HPV 16 occur at a significantly younger age compared to lesions associated with other high-risk HPV infections.^{28,29} Thus, vaccination may be more effective at preventing CIN3 disease than CIN2 disease, especially in young women.

As expected in the sub-population of women where vaccination status was known, the proportion of women with CIN3 or worse was lower in vaccinated women than in unvaccinated women, indicating a protective effect of vaccination. It is likely, however, that the decreases in CIN3 or worse observed are not just due to reductions in vaccinated women. It is also likely that a reduction of prevalent HPV 16 and 18 in the community has resulted in a reduction of HPV 16/18 in non-vaccinated women via the herd effect. We have previously described a reduction of HPV 16 in young women with CIN2 regardless of vaccination status.³⁰ Other populations have demonstrated reductions in vaccination HPV types in non-vaccinated women belonging to vaccination eligible cohorts.^{31–33}

An important observation of the study was that the proportion of satisfactory biopsies that were CIN3 or worse was greater in Māori women and this proportion decreased over time in non-Māori women but did not change in Māori women. We hypothesise that this inequity is due to reduced vaccination rates for Māori women in this cohort. New Zealand Ministry of Health data on vaccination coverage is published for birth cohort years 1990 to 2003 and women are grouped as either Māori, Pacific, Asian or Other. The 'Other' category is comprised predominantly of New Zealand European women.⁴ Compared to 'Other' women, HPV vaccination coverage for Māori was lower in earlier birth cohorts (ie, those born in 1990

[23% vs 47%] to 1993 [47% vs 54%]). Other research examining the pre-vaccination HPV type prevalence between Māori and non-Māori women with high-grade cytological abnormalities, found no significant difference between Māori and non-Māori regarding the prevalence of HPV 16 and/or 18.³⁴ In addition, data matching between the NCSP register and the vaccination registry revealed that the cumulative incidence of high-grade CIN was dependent on vaccination status but did not vary between Māori and European women.²⁶ Reassuringly, Māori have had either similar or slightly higher vaccination coverage compared to 'Other' women for birth cohorts from 1994 onwards so hopefully this inequity will not persist.

A confounding risk factor is smoking. Although our data is incomplete, smokers had a higher proportion of CIN3 or worse than non-smokers and Māori women were more likely to report being smokers.

The study limitations include its retrospective nature, some missing data, and the involvement of only some colposcopy units, which although large and cover demographically different populations, may not provide findings that accurately reflect trends in the entire New Zealand population.

The three clinics showed large variation particularly regarding trends in the numbers of CIN1. We have no clear explanation of these trends. We acknowledge the quadrivalent HPV vaccine introduced in New Zealand, includes vaccination against types 6 and 11 which may cause low-grade but not high-grade abnormalities, and we have little information regarding the regional epidemiology of these virus types. It is of note that the denominator of the referral populations cannot be accurately described and the proportion of women with screen-detected abnormalities from each DHB that are referred to that clinic stratified by age is undocumented. It is therefore difficult to compare the trends seen in three different clinics.

Referral patterns may vary between DHB and also over time. However, approximately 10% of colposcopies nationwide are performed in private practice and it has stayed at this proportion over the years, hence it is unlikely to have influenced trends over time in our study.²⁵

Public colposcopy clinics in each DHB have remained the same for the duration of our study period.²⁵ In addition, there have been no systematic changes that we are aware of that are likely to have changed referral patterns over this time. However, there is inter-observer variation in the reporting of cervical cytology and histology, which may influence histology findings; this is somewhat reflected in the differing positive predictive value of abnormal smears reported in different laboratories as seen in the NCSP monitoring reports.²⁵

An important confounding variable is that screening rates for 20–25-year-olds have decreased between 2013 and 2017, nationally. Using the NCSP's interactive screening coverage app,³⁵ we are able to observe that from 2011 to 2017 there has been a decrease of 9.8% in three-yearly screening coverage, nationally. This decrease has not been uniform as screening rates remained relatively stable from 2010 to 2015 (53,000–54,000 satisfactory cervical cytology samples per annum) but subsequently dropped to 51,000 per annum in 2016 and dropped further to 48,000 per annum in 2017, nationally.²⁵ Per DHB there has been a 5.5%, 6.7% and 9.9% decrease in screening coverage for Auckland, Waikato and Canterbury, respectively.³⁵ These reductions in screening rates undoubtedly explain a proportion of the reductions we observed but are unlikely to explain the different reductions depending on CIN grade. Unfortunately, we are unable to account for ethnicity-related changes in screening rates in young women.

The population of women aged 20–24 years has been steadily increasing in each of the DHBs during our study period,³⁵ hence we can exclude the scenario of a decreasing population as a contributing reason for a decrease in the number of CIN lesions.

HPV vaccination status was not known for a substantial proportion of women in our study across all years but especially for women referred prior to 2013. In addition, for women referred prior to 2013, a very low proportion were known to be vaccinated. Both reporting of vaccination status and the proportion of women who were vaccinated increased from 2013 onwards. However, missing vaccination status data,

especially in earlier years, does limit the power of our analyses.

This study adds to the information describing the impact of the National HPV vaccination programme. Overall, the drop in cervical abnormalities in this age group have been modest. This is likely a result of relatively low HPV vaccination coverage in New Zealand, the limited time since the introduction of the vaccination programme, and type-specific coverage of the vaccine. A meta-analysis demonstrated the dose-response link between vaccination coverage and the reduction in cervical disease.⁶ This is supported by studies showing that populations with a higher vaccination coverage such as Australia and Scotland show a reduction in cervical disease spanning all three CIN types.^{6,14,16} In contrast the impressive reduction of CIN3 or worse abnormalities is an indication of the effectiveness of the vaccination programme in reducing the occurrence of these precancerous abnormalities.

These data demonstrate that following the introduction of the HPV vaccination programme in 2008 there has been a subsequent marked decrease in young women with CIN3 or worse. As women under 25 years with CIN2 are no longer routinely treated, this translates to a major reduction in the requirement for destructive cervical treatments in this age group. In time, a decrease in CIN3 is also likely to result in a reduction in the incidence of cervical cancer provided cervical screening rates can be maintained. From 2017, HPV vaccination became fully funded for males and females, aged 9–26.⁴ Also available from 2017 onwards is a second-generation nonavalent HPV vaccine (Gardasil-9; Merck), which includes the addition of the next five most prevalent oncogenic HPV types. Together, the seven high-risk types covered by this nonavalent vaccine are associated with 90% of cervical cancers, thus providing more benefit than the quadrivalent vaccine. This should herald a greater reduction in the incidence of cervical disease.³⁶

It is of concern that, in this study, CIN3 or worse was observed in a higher proportion of Māori women compared to non-Māori women. In addition, the reduction in CIN3 or worse does not appear to be shared

equally with Māori women. As the NCSP no longer recommends screening for women under age 25, this inequity can no longer be explored. It would appear essential that access to screening is prioritised for young Māori women and that, for screen eligible women, pre-invasive and invasive disease rates are carefully monitored.

In conclusion, over time we observed a decreased number of CIN diagnoses with a particularly large drop in the number

of CIN3/AIS/CGIN. However, compared to non-Māori women, Māori women having cervical biopsies are more likely to have CIN3 or worse and there was a smaller reduction in the total number of Māori women diagnosed with high-grade disease. We hypothesise that the overall decreases are largely due to the prevention of infections with HPV 16 and 18 as a result of HPV vaccination. Further measures need to be taken to reduce inequities for New Zealand women.

Appendix

Appendix Table 1: Histology results at National Women’s Health, Auckland City Hospital, (Auckland) per year for young women referred following an abnormal cervical cytology sample.

	2013	2014	2015	2016	2017	Total	% change 2013–2017
No biopsy or unsatisfactory biopsy	69	47	36	50	40	242	-42%
Normal or benign*	51	47	27	43	38	206	-25%
CIN1/HPV	88	81	63	77	48	357	-45%
CIN2	29	31	27	20	13	120	-55%
CIN3/AIS/CGIN	37	30	28	26	17	138	-54%
>Stage 1a1 carcinoma	1	0	0	0	0	1	-100%
Total episodes	275	236	181	216	156	1,064	-43%

*Includes normal, cervicitis, inflammation only, squamous metaplasia.

Abbreviations: CIN1/HPV – cervical intraepithelial neoplasia grade 1 or human papillomavirus effect, CIN2 – cervical intraepithelial neoplasia grade 2, CIN3 – cervical intraepithelial neoplasia grade 3, AIS – adenocarcinoma in situ, CGIN – cervical glandular intraepithelial neoplasia.

Appendix Table 2: Histology results at Waikato Hospital per year for young women referred following an abnormal cervical cytology sample.

	2011	2012	2013	2014	2015	2016	2017	Total	% change 2011–2017
No biopsy or unsatisfactory biopsy	47	27	36	45	17	32	35	239	-26%
Normal or benign*	46	49	62	41	40	46	61	345	+33%
CIN1/HPV	37	25	32	27	17	31	35	204	-5%
CIN2	30	31	26	28	24	32	31	202	+3%
CIN3/AIS/CGIN	43	45	51	54	41	38	27	299	-37%
Stage 1a1 carcinoma	1	0	0	0	0	0	0	1	-100%
Total	204	177	207	195	139	179	189	1,290	-7%

*Includes normal, cervicitis, inflammation only, squamous metaplasia.

Abbreviations: CIN1/HPV – cervical intraepithelial neoplasia grade 1 or human papillomavirus effect, CIN2 – cervical intraepithelial neoplasia grade 2, CIN3 – cervical intraepithelial neoplasia grade 3, AIS – adenocarcinoma in situ, CGIN – cervical glandular intraepithelial neoplasia.

Appendix Table 3: Histology results at Christchurch Women's Hospital per year for young women referred following an abnormal cervical cytology sample.

	2011	2012	2013	2014	2015	2016	2017	Total	% change 2011-2017
No biopsy or unsatisfactory biopsy	19	20	12	13	6	10	16	96	-16%
Normal or benign*	15	16	14	12	18	22	15	112	0%
CIN1/HPV	119	147	120	119	102	116	94	817	-21%
CIN2	61	78	59	59	56	91	54	458	-11%
CIN3/AIS/CGIN	122	148	91	92	70	56	39	618	-68%
Invasive adenocarcinoma	1	0	0	0	0	0	0	0	-100%
Stage 1a1 carcinoma	0	1	0	0	0	0	0	1	0%
>Stage 1a1 carcinoma	1	0	2	0	0	0	0	3	-100%
Total episodes	338	410	298	295	252	295	218	2,106	-36%

*Includes normal, cervicitis, inflammation only, squamous metaplasia.

Abbreviations: CIN1/HPV – cervical intraepithelial neoplasia grade 1 or human papillomavirus effect, CIN2 – cervical intraepithelial neoplasia grade 2, CIN3 – cervical intraepithelial neoplasia grade 3, AIS – adenocarcinoma in situ, CGIN – cervical glandular intraepithelial neoplasia.

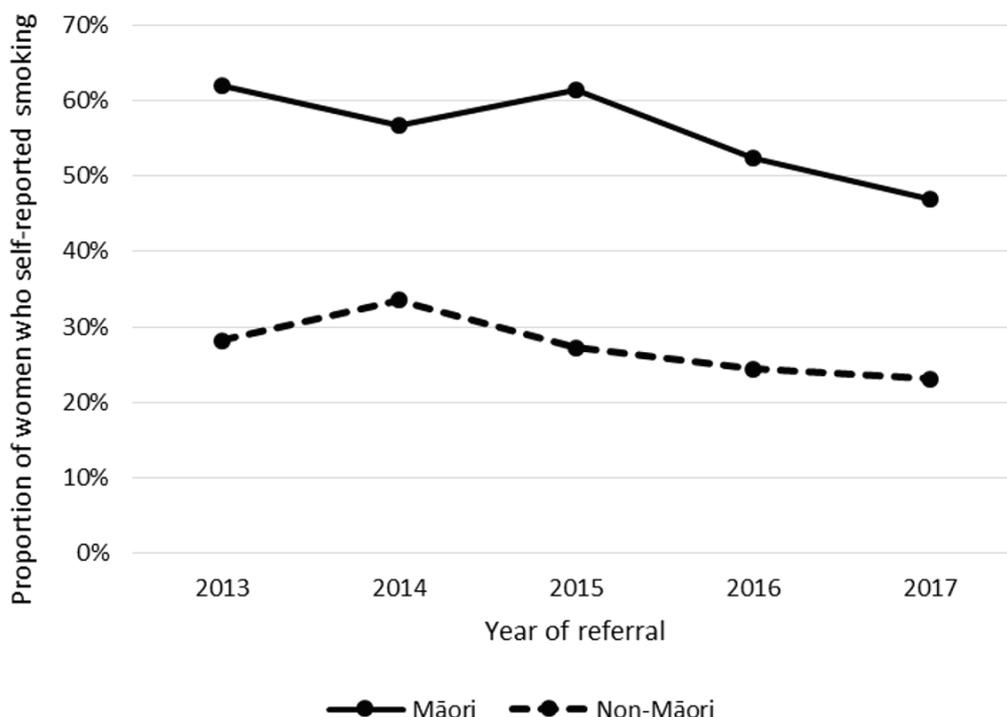
Appendix Table 4: Histology results for young Māori versus non-Māori women* referred following an abnormal cervical cytology sample.

		2013	2014	2015	2016	2017	Total	% change 2013-2017
No biopsy or unsatisfactory biopsy	Māori	15	11	11	15	7	59	-53%
	Non-Māori	99	90	48	74	76	387	-23%
Normal or benign^	Māori	17	11	10	17	20	75	+18%
	Non-Māori	108	82	72	89	90	441	-17%
CIN1/HPV	Māori	31	26	21	23	13	114	-58%
	Non-Māori	182	165	149	194	159	849	-13%
CIN2	Māori	11	12	11	22	11	67	0%
	Non-Māori	83	93	91	108	83	458	0%
CIN3/AIS/CGIN	Māori	27	16	17	25	18	103	-33%
	Non-Māori	118	134	114	90	61	517	-48%
>1a invasive carcinoma	Māori	0	0	0	0	0	0	0%
	Non-Māori	3	0	0	0	0	3	-100%
Total	Māori	101	76	70	102	69	418	-32%
	Non-Māori	593	564	474	555	469	2,655	-21%

*Excludes women where ethnicity was unknown (n=258) ^ Includes normal, cervicitis, inflammation only, squamous metaplasia.

Abbreviations: CIN1/HPV – cervical intraepithelial neoplasia grade 1 or human papillomavirus effect, CIN2 – cervical intraepithelial neoplasia grade 2, CIN3 – cervical intraepithelial neoplasia grade 3, AIS – adenocarcinoma in situ, CGIN – cervical glandular intraepithelial neoplasia.

Appendix Figure 1: Proportion of women who self-reported smoking in those aged 20–24 years referred following an abnormal cervical cytology sample (2013–2017) by ethnicity.*



*Excludes n=258 women where ethnicity was unknown and n=1,191 where smoking status was unknown.

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