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Impact of the human papillomavirus (HPV) vaccine on genital wart diagnoses at Auckland Sexual Health Services

Jeannie Oliphant, Nicky Perkins

Abstract

Aim To review cases of genital warts diagnosed at Auckland Sexual Health Service (ASHS) and to document any change following the introduction of the human papillomavirus (HPV) vaccination. The national HPV immunisation programme, using the quadrivalent vaccine Gardasil, commenced on 1 September 2008. The publically funded programme provides for the ongoing vaccination of girls in year 8 with an initial catch-up programme for young women born after 1 January 1990 until the end of 2010. Monitoring rates of diagnosis of genital warts should provide the earliest clinical indicator of a population response to the vaccine.

Method The proportion of new clients attending ASHS who were diagnosed with genital warts from 1 January 2007 to 31 December 2008 was compared to the proportion diagnosed from 1 January 2009 to 30 June 2010.

Results 40,793 new clients attended the ASHS between 2007 and June 2010 and genital warts were diagnosed in 3125 (7.7%). Genital warts were diagnosed in 9.2% of new clients in 2007 decreasing to 6.6% for the first 6 months of 2010. Analysis of the subgroup of clients under the age of 20 years, found genital warts in males decreased from 11.5% in 2007 to 6.9% in 2010 while in females the rates decreased from 13.7% to 5.1% over the same time period. In comparison, the rates decreased from 7.5% in 2007 to 5.9% in 2010 for females aged 20 years and over. Thus there was evidence of a significant difference, in the pre to post vaccination era, in the proportion of female clinic visits for genital warts in those aged less than 20 years and those aged 21 years or older (p=0.02) and further a borderline significant difference for males aged less than 20 years (p=0.05).

Conclusion A significant decline in the incidence of genital warts in the target population suggests an early response to the HPV vaccination programme with some evidence of an effect for males aged less than 20 years.

There are approximately 40 different genotypes of the Human Papilloma Virus (HPV) that can be found in the genital tract. The high risk oncogenic types 16 and 18 account for about 70% of all types found in cervical cancer.[1]

Types 6 and 11 are the cause of more than 90% of genital warts and co-infection with high risk types is common.[2] It is expected that a vaccine providing protection against types 16 and 18 will have the potential to reduce the impact of cervical cancer in New Zealand (NZ) and it has been called the single most important advance in the prevention of cervical cancer since the introduction of cervical cytology.[3]

Both the bivalent vaccine Cervarix® which protects against types 16 and 18 and the quadrivalent vaccine Gardasil® providing protection from HPV types 6, 11, 16 and 18

are licensed in NZ and were options for the NZ vaccination programme. Governments in Australia and the United Kingdom have opted to utilise the quadrivalent and bivalent vaccines, respectively, in their own HPV vaccination programmes, while the NZ Ministry of Health has selected the quadrivalent vaccination for use here in NZ.

Genital warts are the exophytic lesions of anogenital epithelium that develop following infection with genital HPV types, mostly 6 and 11.[2] Rates of infection are high following the initiation of sexual activity, even with the first ever sexual partner.[4]

The self-reported cumulative incidence of genital warts from members of the Dunedin Multidisciplinary Health and Development Study by age 21 years was 6.9 % for females and 4.7% for males.[5] A diagnosis of genital warts was associated with significantly higher levels of distress, anxiety and depression in a UK study.[6] Current treatments which utilise a range of local destructive methods or immunological therapy can cause significant discomfort and may necessitate frequent health provider visits over a prolonged period of time.

While rare (4 per 100,000), recurrent respiratory papillomatosis in infancy is a condition associated with high morbidity and results from vertical transmission of HPV types 6 and 11.[5,7,8] Potentially, with an ongoing vaccination programme that includes protection against HPV types 6 and 11, this could become a vaccine preventable disease.[7,8]

The impact of a quadrivalent HPV vaccination programme on incident HPV-related disease should be seen first in the changing rates of genital wart diagnoses rather than decreases in cervical cancer rates, as the time to development of genital warts after infection with HPV types 6/11 is a matter of months rather than years or even decades.[8] Thus, the incidence of genital warts could decrease quite rapidly following the introduction of a national immunisation programme if vaccination rates are high enough.[7]

Our aim was to determine if rates of diagnosis of genital warts had changed at Auckland Sexual Health Service (ASHS) following the introduction of the NZ national HPV immunisation programme.

Method

A retrospective review was undertaken examining the proportion of new clients attending the ASHS who were diagnosed with genital warts between 1st January 2007 and 30th June 2010. The ASHS is a regional service covering a large, urban, multicultural population. It covers three district health boards (DHBs) namely Auckland, Waitemata and Counties Manukau and operates four clinics across Auckland in north, south, west and central Auckland. Patients access these clinics by self referral or referral from other health providers and services are free of charge.

Genital warts are not a notifiable infection in NZ but clinicians at the ASHS routinely enter a diagnosis code for new clients or a new diagnosis in a patient seen previously by the service. Demographic data is routinely collected for all new clients.

The NZ HPV immunisation programme using the quadrivalent HPV vaccine was started on the 1st September 2008 with the school-based arm of the vaccination programme commencing in February 2009. The publically funded programme targets girls in year 8 of school (approximate ages 11–12 years) with an initial catch up programme until the end of 2010 for young women born on or after 1 January 1990, that is up to the age of 20 years.

The vaccine is offered free of charge through general practitioners and community immunisation groups in addition to the school-based programmes. There is no publically funded vaccination programme for boys although it is possible for males to purchase the vaccine privately, with the

manufacturers recommending use between the ages of 9 through to 15 years. Data on vaccination coverage was obtained from the HPV programme coordinator, Auckland District Health Board (ADHB).

The cumulative HPV vaccination coverage per DHB of young women from 1 September 2008 through to 30 June 2010 by year of birth:

- 1997 cohort: Auckland 20%, Counties Manukau 20%, Waitemata 17%.
- 1992–1996 cohort: Auckland 25%, Counties Manukau 32%, Waitemata 20%.
- 1990–1991 cohort: Auckland 38%, Counties Manukau 32%, Waitemata 33%.

The denominator for estimating percentage coverage is the estimated eligible population. Data from the first year of the school-based vaccination programme show that for the Auckland DHB alone, 51.7% of eligible students (enrolled in years 8, 12 and 13) were vaccinated by the end of the school year in 2009. Data from the other two DHBs for the school-based programme was not available.

Statistical analysis was performed with SAS (version 9.2) software. A Poisson regression was run including an age category, month of visit and a variable indicating whether the time was pre or post vaccine introduction in the model. The outcome was the number of first-visits diagnoses of genital warts within these subcategories with the log of the total number of first clinic visits in the sub category included as an offset.

To overcome the changing age of the women who would have been eligible for vaccination those aged between 20 and 21 years of age at the time of their visit were not included in the analysis, as some but not all of these women would have been eligible to receive the vaccine.

Although the vaccine was introduced on 1 September 2008 the time cut off point for pre and post vaccine was taken as the end of 2008 as few women could have had full protection for the vaccine prior to this time. This model was run separately for females and males to see if any change observed in females was reflected in male rates.

Results

Over the time period from 1 January 2007 to 30 June 2010, 40,793 new clients attended the ASHS and genital warts were diagnosed in 3125 (7.7%). The number of clients diagnosed with genital warts by year is shown in Table 1 and the risk ratios for genital wart diagnoses per quarter for two time periods, pre and post HPV immunisation programme with the time division being the end of 2008 is shown in Table 2.

Table 1. Number and percentage of first-visit clients diagnosed with genital warts by year and for the first six months of 2010

Variables	2007 Number (%)	2008 Number (%)	2009 Number (%)	2010 (6 months) Number (%)
All	917 (9.2)	897 (7.6)	876 (7.0)	435 (6.6)
Male	491 (9.6)	461 (7.7)	488 (7.8)	241 (7.7)
Female	426 (8.7)	436 (7.6)	388 (6.2)	194 (5.7)
Female >20 years	292 (7.5)	282 (6.2)	255 (5.4)	152 (5.9)
Female <20 years	134 (13.7)	154 (12.5)	133 (8.5)	42 (5.1)
Male >20 years	450 (9.5)	413 (7.5)	439 (7.6)	227 (7.7)
Male <20 years	41 (11.5)	48 (10.4	49 (10.2)	14 (6.9)
Number of clients	9988	11751	12493	6561

Table 2. Comparison of the change in risk ratios per quarter in the pre and post vaccine time periods between the two age groups: <20 and >21 years of age

Variables	Risk ratio Pre vaccine	Risk ratio Post vaccine	P value
Female <20 years	0.98 (0.93–1.02)	0.87 (0.82–0.93)	0.02
Female >21 years	0.95 (0.92–0.99)	0.98 (0.94–1.03)	
Male <20 years	1.02 (0.94–1.10)	0.91 (0.82–1.02)	0.05
Male >21 years	0.96 (0.93–0.98)	1.02 (0.99–1.06)	

The data in Table 1 illustrates a clear reduction in the percentage of first-visit female clients aged less than 20 years diagnosed with genital warts from pre to post vaccine time periods. There was a similar but smaller reduction in the percentage of males aged less than 20 years over the same time period.

There was a significant (p=0.02) reduction in the change in risk ratios per quarter pre and post vaccination for women aged less than 20 compared to those aged over 21 years, and there was a borderline significant (p=0.05) reduction for males in the same age groups. See Figures 1 and 2.

Figure 1. Proportion of genital wart diagnoses per first visit over time in months from 1 January 2007 for females

(Categories: 1 and 3 pre and post vaccine <20 years; 2 and 4 pre and post vaccine >21 years; *Proportions predicted from the Poisson model)

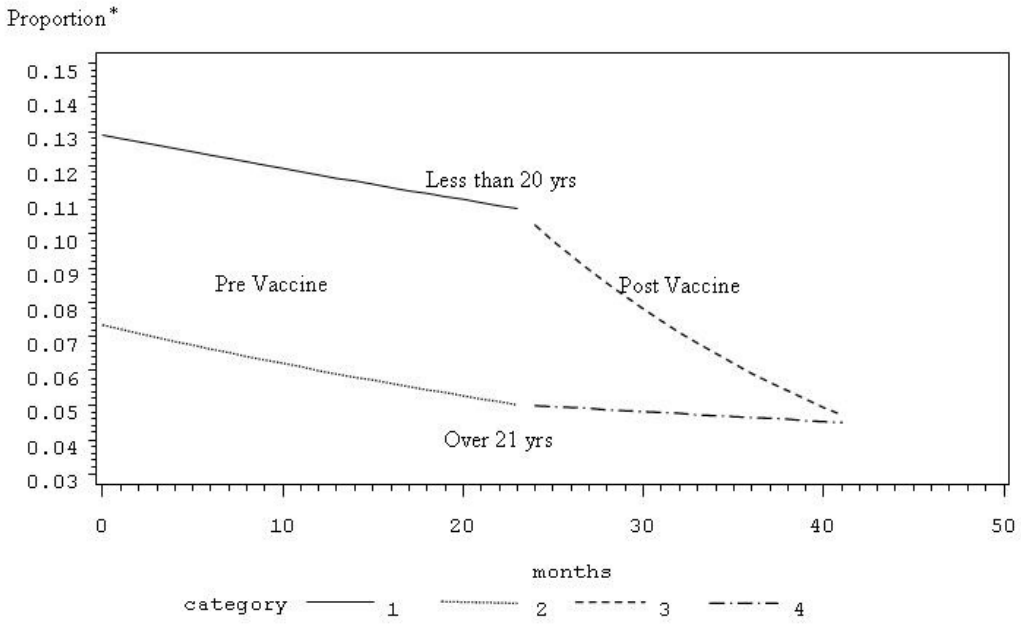
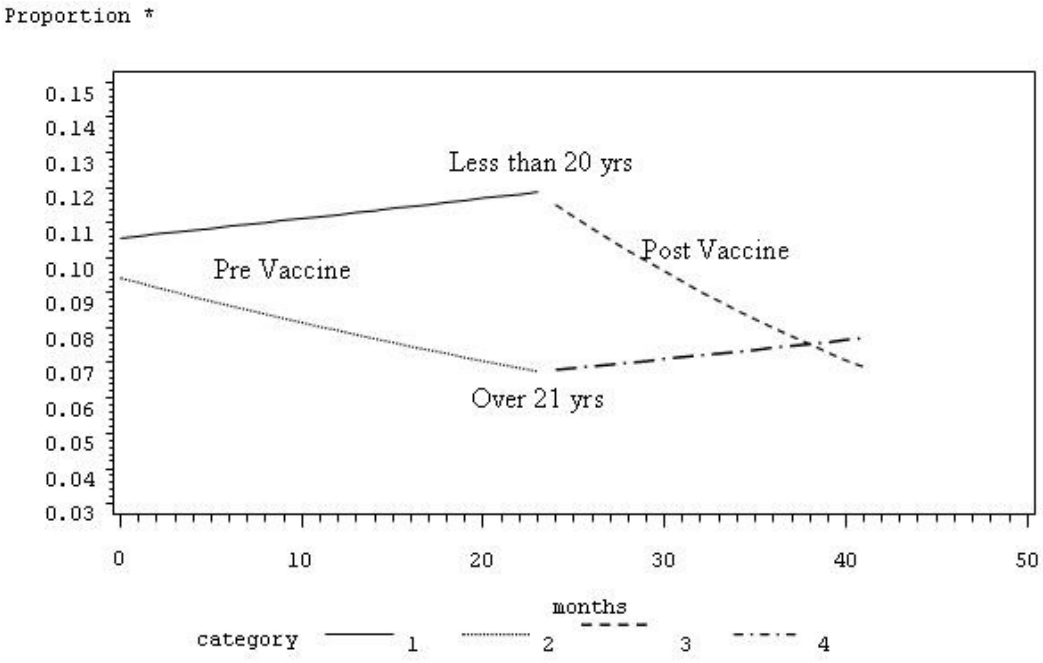


Figure 2. Proportion of genital wart diagnoses per first visit over time in months from 01/01/2007 for males
(Categories: 1 and 3 pre and post vaccine <20 years; 2 and 4 pre and post vaccine >21 years; *Proportions predicted from the Poisson model)



Discussion

These findings suggest an early response to the HPV immunisation programme, despite the relatively low levels of reported vaccine coverage and provide evidence for the vaccine being effective at a population level in NZ.

The 13% decrease per quarter (RR 0.87), in the proportion of genital warts diagnosed after the commencement of the HPV vaccination for women aged less than 20 years demonstrates a smaller reduction than that observed in Australia. Published data from the Melbourne Sexual Health Centre (MSHC) noted a 25.1% decrease per quarter (30.5% to 19.3%, $p<0.001$) in the proportion of women aged less than 28 years presenting with genital warts to their service, after the introduction of the their HPV vaccination programme.[9]

The Australian HPV publically funded immunisation programme started in April 2007, utilising the quadrivalent vaccine, providing immunisation to 12–13 year old girls in a school-based programme with an initial catch up programme for 13–18 year old young women and free primary care vaccination of women up to the age of 26 years.[10]

Looking at vaccine coverage rates in the school-based programmes of the two countries, in the State of Victoria from the start of the school programme in April

2007 through to the end of the school year in 2007 between 69% to 75% of enrolled school girls were vaccinated in years 7, 10, 11 and 12.[10]

Comparing this to data from the school-based vaccination programme in the Auckland DHB area during the school year in 2009, 51.7% of eligible students (in years 8,12 and 13) were vaccinated. The higher vaccination rate in the State of Victoria may help to explain the highly statistically significant decrease in genital warts seen at MSHC as compared to the more modest reduction seen at the ASHS.

The ASHS data also demonstrates a borderline statistically significant decrease in the proportion of genital warts diagnosed for young men aged less than 20 years. It is possible that some of this decrease is due to young men paying to have the vaccination privately. However the significant costs of this make it unlikely that vaccination would account for the majority of the effect. It is more likely that a decrease in the prevalence of infection for young women is impacting on the incidence in young men, suggesting that sexual coupling is tending to occur predominantly between similar aged cohorts. MSHC data noted a reduction in genital wart diagnosis in heterosexual but not homosexual men,[9]again supporting reduced sexual transmission of HPV as a result of female vaccination.

The current eligibility criteria for funded vaccination in NZ do not provide equitable cover for all people in NZ at increased risk of HPV-related disease. Men who have sex with men (MSM) are at significantly elevated risk of HPV-related anal cancer[11] and are unlikely to receive any substantial herd immunity benefit from the current vaccination programme in NZ. Extending the programme to all boys in year 8 at school is the strategy most likely to provide protection for MSM in NZ as selective vaccination would require young men to identify their sexuality to health care providers preferably before initiation of sexual activity.[12]

The study has several limitations. Firstly, over the time period of the study the number of first visits for young people aged less than 20 years at ASHS increased substantially. However, provided that the characteristics of this client population such as mean age have not changed significantly over the study period then this should not affect the individual risks of having acquired an HPV infection.

An important potential confounding factor to consider is the increased prescribing of topical imiquimod for genital wart treatment since late 2008 with PHARMAC permitting prescribing under special authority. It is possible that this resulted in more people receiving treatment for genital warts in primary care and therefore different referral patterns to ASHS from the community.

This study did not look for changing proportions of self referral versus community referral over the time period, although it is difficult to see how this would preferentially affect a younger client group. If anything it might be expected that genital warts diagnosis would decrease in the older group with more financial resources to seek treatment in primary care. Further the continuing decline in the proportion of clients with genital warts diagnosed from 2009 to 2010 is not explained by the use of imiquimod.

This study only examines data from one sexual health clinic, so it is possible that the results may not be able to be generalised to the whole population, although ASHS being an Auckland regional service does therefore provide a service for

approximately a third of the total NZ population. While genital warts is not a notifiable disease and is usually diagnosed without confirmatory pathology, sexual health clinics routinely collect data on diagnoses and can provide an appropriate site for genital wart surveillance.

The ASHS data suggests that the HPV immunisation programme is having a significant impact on the prevalence of genital warts in young women and to a lesser extent young men in NZ. This would support the continued use of the quadrivalent vaccine and consideration should be given to the funded use for boys to aid in the prevention of other non-cervical HPV-related diseases.

Competing interests: None.

Author information: Jeannie Oliphant, Sexual Health Registrar; Nicky Perkins, Sexual Health Consultant: Auckland Sexual Health Service, Greenlane Clinical Centre, Auckland.

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Correspondence: Jeannie Oliphant, Auckland Sexual Health Service, Greenlane Clinical Centre, Private Bag 92024, Auckland, New Zealand. Fax: +64 (0)9 6309783; email: jeannieo@adhb.govt.nz

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