Evaluation of the National Human Papillomavirus Vaccination Program

FINAL REPORT

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Contents

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Abbreviations

ABS	Australian Bureau of Statistics
ACIR	Australian Childhood Immunisation Register
ACT	Australian Capital Territory
ADRS	Adverse Drug Reaction System
AEFI	Adverse event following immunisation
AIHW	Australian Institute of Health and Welfare
AMLA	Australian Medicare Local Alliance
APC	Annual percentage change
CALD	Culturally and linguistically diverse
CI	Confidence interval
ERP	Estimated resident population
GEP	Gardasil Expert Panel
GP	General practitioner
HGA	High-grade abnormality
HPV	Human papillomavirus
ICD-10-AM	International Statistical Classification of Diseases and Related Health Problems, 10th edition, Australian modification
JIC	Jurisdictional Immunisation Coordinator
LGA	Local Government Area
MedDRA	Medical Dictionary for Regulatory Activities
MS	Multiple sclerosis
NCIRS	National Centre for Immunisation Research and Surveillance
NCSP	National Cervical Screening Program
NHVPR	National HPV Vaccination Program Register
NIP	National Immunisation Program
NPEV	National Partnership Agreement on Essential Vaccines
NSW	New South Wales
NT	Northern Territory

PBAC	Pharmaceutical Benefits Advisory Committee
QLD	Queensland
RR	Rate ratio
SA	South Australia
SES	Socioeconomic status
STI	Sexually transmissible infection
TAS	Tasmania
TGA	Therapeutic Goods Administration
VAERS	Vaccine Adverse Events Reporting System (USA)
VE	Vaccine efficacy
VIC	Victoria
WA	Western Australia
WHO	World Health Organization

Executive summary

Background

Human papillomavirus virus (HPV) may result in lesions that include cutaneous warts, genital warts, cancers, respiratory papillomatosis, and cervical and other anogenital tract abnormalities. HPV is responsible for a significant disease burden worldwide. Australia was the first country to implement a fully funded National HPV Vaccination Program which commenced from April 2007. The vaccine currently used in the National HPV Vaccination Program is the quadrivalent vaccine Gardasil® (CSL Biotherapies/Merck & Co. Inc.). The continuing component of the program targets females 12–13 years old with 3 doses of the vaccine routinely offered through state/territory school-based vaccination programs. There were two catch-up phases for the female-only program between July 2007 and December 2009. These targeted 13–17-year-old females through school-based vaccination programs as well as 18–26-year-old females through general practice and in community settings. In February 2013, the National HPV Vaccination Program was extended to males aged 12–13 years with a catch-up program for males aged 14 and 15 years delivered over 2 years until the end of 2014.

Aims

To understand the strengths and weaknesses of program implementation, measure vaccination coverage and adverse events following immunisation (AEFI), and assess the impact of this program on the epidemiology of high-grade cervical abnormalities and genital warts.

Methods

This evaluation was based on the standard National Centre for Immunisation Research and Surveillance (NCIRS) immunisation program evaluation framework, developed for previous immunisation program evaluations. This framework consists of these major components: process evaluation, vaccination coverage, adverse events following immunisation and impact on disease burden.

Both the original female program that commenced in 2007 and the extension of the program to males in 2013 were included in most aspects of this evaluation, including the process evaluation, analysis of adverse events and impact on genital warts. Vaccination coverage was only assessed for females because, at the time of the evaluation, eligible males had not completed all 3 doses of the vaccine.

Process evaluation

Process evaluation was through interviews with a sample of key stakeholders involved in program implementation. A literature review of existing published evaluations was undertaken and surveys were developed based on gaps in the literature. Key stakeholders participated via an online survey and semi-structured telephone interviews. The surveys and interviews covered stakeholders' experience of aspects of the program implementation including communication and resources; program planning and rollout; service delivery; data collection and reporting; strengths and challenges of the program; and recommendations for future national immunisation programs. In addition, National Cervical Screening Program managers at state and territory level completed an online survey about their organisations' involvement in the HPV vaccination program and its impact on their activities.

Vaccination coverage

Coverage was calculated as the number of doses notified divided by estimated resident population (ERP), expressed as a percentage. Notified doses are valid doses counted by their implied dose number (dose number allocated according to total doses recorded on the National HPV Vaccination Program Register [NHVPR] for that individual and as per Chief Medical Officer [CMO] guidelines for acceptable dose intervals), as at the date of data extraction from the NHVPR. Mid-year Australian Bureau of Statistics (ABS) ERPs for females were used as the denominator. For the female catch-up program, ERPs for 2007 were used.

Stratifying variables used in the analysis were age, socioeconomic status (SES) by the ABS 2006 Socio-Economic Indexes for Areas (SEIFA) Index of Relative Disadvantage, and remoteness using the Remoteness Structure of the Australian Standard Geographical Classification published by the ABS using area of residence of the vaccinee at the Local Government Area (LGA) level.

Providers were grouped into two types: general practice providers and non-general practice providers. Non-general practice providers include councils, state/territory health departments and other community-based immunisation providers such as Aboriginal Medical Services and Family Planning Services.

Indigenous status is a non-mandatory field for reporting and was deemed to be of adequate completeness for analysis for the catch-up program cohorts in the Northern Territory and Queensland.

For assessment of timeliness, the proportion completing the course within 6 or 12 months of receiving their first dose of vaccine (recommended schedule for vaccination is 0, 2, 6

months) was estimated for each calendar year, with the denominator being persons recorded as receiving the third of 3 valid doses within that year (i.e. completing the full course).

A secondary analysis was undertaken using Medicare enrolment data for females as the denominator, which was provided as at 30 June 2007 at the LGA level. Coverage was calculated by age group (12–17 years and 18–26 years) and by geographical area. Spatial analysis was performed using ESRI ArcMap 10.3.

A secondary analysis was also undertaken using 'episode dose number', which is the dose number reported by the provider, instead of the implied dose number.

Adverse events following immunisation

De-identified information on all AEFI reports to the Therapeutic Goods Administration (TGA) and stored in the Adverse Drug Reaction System (ADRS) database were released to NCIRS. All the data associated with HPV vaccines from 1 April 2007 to 30 June 2013 were analysed to summarise Australian passive surveillance data for HPV-related adverse events and to describe reporting trends. The denominator data for HPV vaccine doses from the NHVPR were available from 1 April 2007 to 31 December 2011. Data were analysed in two periods: 1 April 2007 to 31 December 2012 and 1 January 2013 to 30 June 2013.

Reporting rates were calculated for the period 1 April 2007 to 31 December 2011. For subsequent periods, numbers and proportions of AEFI by age groups and jurisdictions are presented.

A summary of vaccine safety issues associated with use of HPV vaccine in Australia, including a timeline of adverse events issues raised, was also compiled.

Disease impact

Disease impact was assessed using two sources of routinely collected data: 1) high-grade cervical abnormalities data from the *National Cervical Screening in Australia* reports, and 2) hospitalisations with one or more codes associated with genital warts from the National Hospital Morbidity Database (NHMD) of the Australian Institute of Health and Welfare (AIHW).

For high-grade cervical abnormalities, data were analysed using an ecologic design comparing the pre-vaccine period (2004–2007) with 2008–2011. High-grade abnormalities (HGA) were defined as lesions coded as cervical intraepithelial neoplasia of grade 2 (CIN 2) or 3 (CIN 3), adenocarcinoma in situ or endocervical dysplasia.

The annual rate of females attending screening was assessed according to age using ABS census data as the denominator. The population was adjusted to include only females with an intact uterus and cervix using age-specific hysterectomy fractions derived from the NHMD.

Data on numbers of females screened and numbers of HGAs detected from 2004 to 2011 (2004–2007, 2008–2011 and individual years) were tabulated by age groups (<20, 20–24, 25–29, 30–34 and 35–69 years) and by jurisdiction. Trends in the rate of HGAs detected were examined. Absolute rates, rate ratios (RR) and 95% confidence intervals (CI) were used to quantify changes.

For analysis of genital wart hospital admissions, the included period was 1 July 1999 to 30 June 2011. The NHMD is a comprehensive population-based dataset of routinely collected admissions data from all public and private hospitals in Australia. All admissions for genital warts (including those where genital warts was not the principal diagnostic code) were eligible. Trends in age-specific admission rates, defined by age groups eligible for the National HPV Vaccination Program from 2007, were compared for periods before and after program implementation.

Results

Process evaluation

Key stakeholders all agreed that implementation of the National HPV Vaccination Program was successful, for both the original female and the extended male program. Respondents reported that the extension of the HPV Vaccination Program to include adolescent males was less difficult to implement than the initial female program. However, some issues were raised about the initial female program. These included the very short lead-time to organise 3 doses for a large cohort of adolescent females within the school year and the late availability of information resources. At that time, there was the added factor of community concerns about vaccine safety, adverse events and the perception that vaccinating against a sexually transmitted infection may encourage an early sexual debut in adolescent girls.

Most program managers and providers (n=14) observed that the male program was well accepted. Reasons for acceptance included the establishment of the female program on the National Immunisation Program (NIP), the expectation that the vaccine would be extended to include males, greater knowledge of HPV and reduced parental concerns around a vaccine related to sexual health. Lessons learnt from the female program were applied when extending the program to males including development of comprehensive and accessible

information resources and establishment of enhanced surveillance activities for adverse events.

Under the National Health Care Agreement, the states and territories are responsible for providing service delivery of the HPV vaccination program while the Commonwealth is responsible for purchasing the vaccine. While recognising their responsibilities under the National Health Care Agreement, jurisdictional managers raised the lack of additional funding to support service delivery as the main issue they faced when implementing the extended program for males. This was contrasted with the provisions made by the Commonwealth for service delivery at the start of the female program. With the inclusion of males, the National HPV Vaccination Program now involves delivering 3 doses of vaccine to a large cohort of students within the limited timeframe of the school year. It was noted that adding males to the program placed additional pressure on jurisdictional capacity in terms of staff levels and liaisons with the school sector. The rollout of both the female and male programs was made more difficult by time pressures due to short lead-times from the announcement (especially so for the female program) and the late availability of information resources.

Stakeholders expressed a need for improved communication mechanisms to share dosage information between the school-based program and providers who deliver missed doses outside the school setting.

Despite these challenges, stakeholders expressed strong support for running the HPV vaccination program as a school-based program and noted the advantages of the program in reaching adolescents and achieving good uptake of the HPV vaccine.

Vaccination coverage

As recorded on the NHVPR, coverage achieved in the female HPV vaccination catch-up program was substantial, with national coverage of 66/58/47% for doses 1/2/3, respectively, in the 12–26-year-old cohort overall. Actual coverage is undoubtedly higher, given the need for parental or patient consent to record doses on the NHVPR and likely under-notification of doses from providers outside of the school-based program. Providers outside schools were particularly important for women aged 18–26 years in 2007, among whom a population-based mobile phone survey found self-reported coverage to be 20/15/10% higher for doses 1/2/3, respectively, than that reported on the NHVPR, with a validation substudy able to verify 86% of self-reported doses.

Within the school cohorts, coverage for 12–17-year olds (2007) was 83/78/70% for doses 1/2/3, respectively. Monitoring of coverage in the 15-year-old cohorts over time suggests

relatively stable coverage. There was and is some variation in coverage achieved by jurisdictions suggesting more effective delivery in some states/territories than others. Also notable is the difference between dose 1 and dose 3 coverage, highlighting the need for attention to barriers to completing the course.

In contrast to the uptake of cervical screening in adult women, the school-based delivery of HPV vaccination achieves almost equivalent uptake by socioeconomic status, with only a 5% difference between 3-dose coverage in areas of lowest and highest SES (and a <1% difference for 1-dose coverage). Similarly, coverage is relatively equal by area of residence. Although data interpretation is limited primarily due to uncertainty surrounding denominator estimates, data from the Northern Territory and Queensland suggest lower coverage rates in Indigenous catch-up cohorts of school age. Data quality was not adequate to allow estimates of Indigenous coverage in other jurisdictions.

Assessment of the impact of using Medicare enrolment data instead of ABS ERP estimates on coverage estimates from the catch-up program found that, overall, a small increase in coverage would result (about 0.5% in school cohorts and 2% in adult females). A third dose assumption applied to the catch-up program also improved 3-dose coverage estimates by a small amount (from 47% to 51% for the 12–16-year-old cohort overall.) The corresponding adverse impact on dose 1 and 2 coverage when provider-allocated dose numbering was used suggests that provider-reported dose number is not likely to be significantly more accurate than dose number assigned in date order by the NHVPR.

Coverage measures at age 15 years between 2007 and 2012 demonstrate that stable coverage of over 70% is being achieved over time.

Adverse events following immunisation

The ADRS database included a total of 2,460 AEFIs reported following receipt of HPV vaccine during the period 1 April 2007 to 30 June 2013. The highest annual number of cases (n=765; 31%) was reported in 2007 in the context of initial implementation of the school-based National HPV Vaccination Program and catch-up program for young adult females commencing in April 2007. The number of reported AEFIs reduced substantially in the following years (from 765 in 2007 to 160 in 2012). As would be expected, the total number of reported AEFIs increased in 2013 (n=615) following the commencement of male vaccinations in February 2013 and the implementation of enhanced AEFI surveillance activities for both males and females in February 2013. Of the 615 AEFIs reported in 2013, 341 were in males and 273 in females.

Over a period of almost 5 years, from 1 April 2007 to 31 December 2012, a total of 1,845 reports of AEFI following receipt of HPV vaccine were received by the TGA. Of the 1,845 reports, 82% (n=1,505) were following administration of HPV vaccine alone. The most commonly reported AEFIs included headache (21%; n=381), nausea (16%; n=293) and dizziness (15%; n=273). Other reactions reported included fever (13%; n=231), syncope (11%; n=201), injection site reactions (10%; n=191), pruritus (9%; n=163) and urticaria (8%; n=155). A total of 16 cases of anaphylactic reaction were reported (1% of reports). The criteria for serious AEFI were met for 129 events (7%), including 6 cases of life-threatening events; no deaths were reported.

As expected, the enhanced surveillance implemented prior to the introduction of the male program in February 2013 resulted in a higher number of HPV AEFI reports; however, the majority of these were mild and consistent with those expected. The most frequently reported reactions included syncope (48%; n=296), presyncope (11%), nausea and dizziness (8% each), headache (6%), vomiting and pyrexia (5% each).

Overall, the majority of AEFIs reported following implementation of the National HPV Vaccination Program for females and males were mild and transient. These national surveillance data provide evidence supporting the good safety profile of the HPV vaccine and are consistent with data from international spontaneous reporting systems.

Disease impact

High-grade cervical abnormalities

A decline in the rate of HGAs detected per 1,000 women screened was observed between 2004 and 2011 in females aged <20 years. In the first full year of the program (2008), the rate of HGA was 10.8 (95% CI: 10.0–11.6) per 1,000 females screened, an 18% (95% CI: 11–25%) reduction from the rate during the pre-vaccine period (2004–2007) of 13.1 (95% CI: 12.7–13.6) per 1,000 females screened. The rates further declined in 2009, by 33% (95% CI: 26–39%), and in 2010, by 41% (95% CI: 34–47%), compared to the pre-vaccine period. The most pronounced decline occurred in the most recent post-vaccine year (2011): the rate was 46% (95% CI: 40–51%) lower than the rate during the pre-vaccine period.

In females aged 20–24 years, who would have been aged 16–20 years in 2007, a significant reduction in the HGA rate, compared to the pre-vaccine period rates, was first observed in 2011 (RR=0.87; 95% CI: 0.83–0.90).

Anogenital warts

There were 39,350 eligible hospitalisations (24,811 in females; 14,539 in males) for genital warts over the study period. Substantial decreases in hospitalisation rates were observed

from mid-2007 in females aged 12–17 years, and from mid-2008 in both females and males aged 18–26 years. In females aged 12–17 years, the estimated annual decline was 44.1% (95% CI: 35.4–51.6%) from mid-2007 to 2011. Among persons aged 18–26 years, the declines were 31.8% (95% CI: 28.4–35.2%) and 14.0% (95% CI: 5.1–22.1%) since mid-2008 in females and males, respectively. The overall observed reduction in coded hospitalisations in 2010–2011, compared to 2006–2007, was 89.9% (95% CI: 84.4–93.4%) for females aged 12–17 years, 72.7% (95% CI: 67.0–77.5%) for females aged 18–26 years and 38.3% (95% CI: 27.7–47.2%) for males aged 18–26 years.

Among hospitalisations in jurisdictions for which Indigenous status could be analysed, there were 322 in Indigenous females and 11,590 in females not identified as Indigenous in the 15–24 years age group. The reduction in hospitalisations that included a genital warts code in the post-vaccine period was similar for Indigenous females (86.7%; 95% CI: 76.0–92.7%; N=185 in this age group) and other Australian females (76.1%; 95% CI: 71.6–79.9%). Numbers of Indigenous males were too small for meaningful analysis.

Although there have been several previous reports on genital wart diagnoses before and after the introduction of quadrivalent HPV vaccine into Australia's NIP, this is the first at national level, based on hospitalisations coded as related to genital warts in both public and private hospitals. The marked decline identified in admissions involving a diagnosis of genital warts in young females and young males in Australia is consistent with other evidence from Australia reporting that the program had a rapid and substantial impact on genital warts in young people. These data add to earlier evidence of indirect benefits to males from the female vaccination program and provide the first indication that the impact of HPV vaccine in young Indigenous females is similar to that in other Australian females.

Strengths and limitations of data sources in the evaluation

Data sources used in the evaluation of the National HPV Vaccination Program have inherent strengths and limitations with respect to determining the impact of the vaccine program on the burden of disease. A strength is the availability of hospitalisation data for genital warts coded using the ICD-10-AM (International Statistical Classification of Diseases and Related Health Problems, 10th edition, Australian modification) system which are consistent over time (before and after the vaccination program), available nationally and reasonably specific. However, there is considerable lag in data availability, data on immunisation status are not available, and admissions represent only a small proportion of the disease burden as genital warts are mostly managed in general practice and sexual health clinics and hospitalisations represent the majority of severe cases. Also, in females, HGA detection may vary between states and territories due to random variation with small populations; underlying differences in HPV exposure or persistence (due to different sexual behaviours or mixing patterns due to

age structures or geography or cofactors such as smoking); or decline in screening rates; or differences in the completeness of histology reporting from laboratories to the registers; or differences in the quality of specimen collection, processing and interpretation.

Coverage estimates from the NHVPR are likely to under-estimate actual levels of coverage. Key challenges remaining include better measurement of Indigenous coverage, an ability to accurately monitor ongoing coverage by school populations rather than age, closing the gap between dose 1 and dose 3 coverage, ensuring the doses delivered in general practice are notified to the NHVPR and lifting 3-dose coverage.

For AEFI, there are a diverse range of approaches to passive surveillance employed by jurisdictions across Australia. This leads to differences in the quality, accuracy and timeliness of AEFI reports and the potential for discrepancies in aggregated data. The reforms to the existing system suggested in the Horvath Review of 2011 would assist in improving existing AEFI surveillance in Australia.

Conclusion

The HPV vaccine has been successfully incorporated into Australia's NIP. The implementation process was viewed as successful by all stakeholders, but a number of areas for potential improvement were identified by stakeholders, especially with respect to lead-time between the announcement and start of the program and early availability of information resources. The available data on high-grade cervical abnormalities and genital warts show that the routine school-based program has substantially reduced the burden of high-grade cervical abnormalities and genital warts in the vaccine-eligible group and also provided substantial indirect disease reduction in population groups not targeted for HPV vaccine. This is reflective of the rapid uptake of the HPV vaccine such that more than half of Australia's young adult females (aged <30 years) are currently fully vaccinated. The NHVPR is providing an effective way to improve coverage over and above jurisdictional systems, as evidenced by responses to overdue dose reports and vaccination history statements. More reliable notification of Indigenous status to the NHVPR is needed to allow a comprehensive calculation of coverage for Indigenous adolescents. The reported AEFI were predominantly mild and transient in nature and the vaccine has a safety record comparable with other more established vaccines on the NIP. Stakeholders did not raise any major issues around reporting of AEFI. Continued monitoring of coverage, AEFI and disease epidemiology is needed to determine if these results can be sustained or improved in the future, particularly in light of the extension of the program to males in early 2013.

CHAPTER 1. Introduction

Background

Human papillomaviruses (HPVs) are non-enveloped, double-stranded, epitheliotropic DNA viruses with an icosahedral capsid. HPVs are designated as specific types according to sequence variation in the major genes; there are more than 40 types that infect the mucosal epithelium of males and females. Some HPV types, including types 16, 18, 31, 33, 35, 45, 52 and 58, are designated as 'high-risk' as they are causally associated with the development of cancer of the cervix as well as some anal, vaginal, vulval, penile, and head and neck cancers. Other HPV types, including types 6, 11, 40, 42, 43, 44, 54, 61, 70, 72, 81 and 89, have been classified as 'low-risk' and are predominantly associated with non-malignant lesions such as genital warts.[1]

The most common mode of transmission of HPV infection is through close skin-to-skin or mucosa-to-mucosa contact.[2] The primary route for anogenital transmission of HPV is sexual intercourse; perinatal transmission of HPV is also possible, though this occurs infrequently.[3] HPV infections are transient and asymptomatic, with only a small proportion of persistent infections progressing to disease.[4] Dependent on the infecting HPV type, infection may result in lesions that include cutaneous warts, genital warts, cervical and other anogenital tract abnormalities and cancers, and respiratory papillomatosis.[5]

HPV infection rates vary greatly between geographic regions and population groups, but it is estimated that up to 79% of women worldwide will be infected with HPV at some point in their lives.[6] HPV infection rates are highest among young women, usually peaking soon after the age when most young women become sexually active.[7] A woman's lifetime number of sex partners is the most important predictor of HPV acquisition. In a study of monogamous women, 48% acquired HPV infection within 3 years of becoming sexually active despite only having one partner.[8]

Australia has one of the lowest rates of incidence and mortality from cervical cancer in the world.[9] In 2008, there were 9 new cases of cervical cancer per 100,000 women of all ages, and in 2007, the age-standardised mortality rate from cervical cancer was 2 deaths per 100,000.[10] These are the lowest rates observed to date. Cervical cancer in Australia now occurs predominantly in unscreened or under-screened women. Indigenous women have more than double the risk of developing cervical cancer and a mortality rate over 5 times that of non-Indigenous women.[10,11] HPV types 16 and 18 are responsible for the largest burden of cervical cancers and for over 80% of HPV-typed cancers of the anus, penis, and head and neck.[12] Of the low-risk genital HPV types, types 6 and 11 cause approximately 95% of genital warts.[13] An Australian serosurvey from 2006 found 24% of females and 18% of males aged 0–69 years were seropositive to at least one of the four HPV types 6, 11, 16 and 18;[14]

however, fewer than 60% of women, and an even lower proportion of men, who are infected with HPV develop antibodies.[4]

The population incidence of benign HPV-associated lesions, such as anogenital warts, is much higher than the incidence of HPV-associated cancers. In Australia, the estimated annual incidence of anogenital warts in 2000–2006 was 206 per 100,000 in males and 231 per 100,000 in females. The age group of peak incidence was 25–29 years for men (rate 740 per 100,000) and 20–24 years for women (rate 861 per 100,000). In Australia, 4.0% of men and 4.4% of women aged 16–59 years reported ever being diagnosed with genital warts.[15]

The National Cervical Screening Program's regular Pap testing allows the early detection and treatment of HPV-related cervical abnormalities prior to the development of cervical cancer. Every year in Australia, Pap testing detects low-grade cervical abnormalities in about 92,000 women and high-grade cervical abnormalities in a further 50,000 women. The incidence of both low- and high-grade abnormalities peaks in women aged 20–24 years.[10]

Successfully applied molecular biology techniques have underpinned the development of two prophylactic HPV vaccines. The bivalent vaccine (Cervarix®, GlaxoSmithKline) contains virus-like particles (VLPs) of HPV types 16 and 18;[16] the quadrivalent vaccine (Gardasil®, CSL Biotherapies/Merck & Co. Inc.)[14] contains VLPs of HPV types 16, 18, 6 and 11. The primary vaccination course consists of 3 doses over 6 months though the need for a booster has not yet been established. Overall, seroconversion occurs in 99–100% of those vaccinated and vaccination protects against 90–100% of persistent infections and cervical abnormalities caused by HPV types in the vaccine.[17,18] The duration of immunity is not yet known though current evidence suggests it is at least 5 years;[19] long-term studies are ongoing.

Human papillomavirus vaccination in Australia

From June 2006, the quadrivalent HPV vaccine, Gardasil® (CSL Biotherapies/Merck & Co. Inc.),[20] was registered for use in females aged 9–26 years with the bivalent HPV vaccine, Cervarix® (GlaxoSmithKline),[16] registered in March 2007 for females aged 10–45 years. From mid-2010, the registered indication for Gardasil® in Australia was extended to females aged 45 years and males aged 9–26 years.[21]

Australia was the first country to implement a funded national HPV vaccination program with Gardasil® added to the National Immunisation Program (NIP) from April 2007.[22] The continuing component of the National HPV Vaccination Program targets females aged 12–13 years with 3 doses of the vaccine routinely offered through state/territory school-based

vaccination programs. Arrangements for catch-up vaccination differ between jurisdictions. Approaches include vaccine offered at subsequent school visits, dedicated catch-up clinics at the end of the school year and vaccine available at the local general practice.[23] There were two catch-up cohorts for the female-only program between July 2007 and December 2009. These targeted 13–17-year-old adolescent females through school-based vaccination programs as well as 18–26-year-old adult females through general practice and in community settings.[22] The National HPV Vaccination Program Register (NHVPR) was established to record vaccine delivery and allow monitoring and evaluation of the program.[24]

In November 2011, the Pharmaceutical Benefits Advisory Committee (PBAC) recommended extension of the NIP listing of Gardasil® to include ongoing administration to males aged approximately 12–13 years in a school-based program, with a catch-up program for two cohorts (all males in the two school-years above the ongoing cohort), delivered over 2 years.[25] In July 2012, the Australian government announced that these recommendations would be supported by NIP funding with the program to commence from the 2013 school year.[26]

CHAPTER 2. Process evaluation

Aims

To describe National HPV Vaccination Program implementation in 2007 for females and 2013 for males and identify strengths, challenges and satisfaction of key groups implementing the program.

Methods

A mixed methods approach was used in the process evaluation. This included a review of published literature, a review of stories in the Australian media, and an online survey and interviews with key stakeholders involved in the implementation of the National HPV Vaccination Program. Key stakeholders from each state and territory participated in a structured online survey and a semi-structured telephone interview. In addition, National Cervical Screening Program managers from each jurisdiction completed an online survey.

Literature review

A literature review of the peer-reviewed literature was undertaken to identify published studies and reports of evaluations of HPV vaccination programs that included Australia.

Review of Australian media

Regular searches of the Australian print and electronic news media for articles and reports on the male and female HPV vaccination programs were made between 2010 and 2013. In addition, a search of the Factiva database was conducted for the years 2006 to 2009 for Australian newspaper articles and electronic media reports on the rollout and implementation of the female HPV vaccination program.

The main messages were analysed for content of positive and negative messages around the program. Positive messages included factual information around program implementation as well as promotional and supportive editorials, opinions and ‘good news’ stories. Negative messages include information about adverse events as well as critical editorials or opinions and negative reader correspondence.

Recruitment of key stakeholders

Purposive sampling was used to recruit a sample that included key stakeholder groups and jurisdictions. A sampling matrix was used to ensure representativeness across these areas and set the quota of participants required for each stakeholder group (see **Appendix 2.1**). Key stakeholders interviewed included state and territory immunisation program managers, regional state/territory immunisation coordinators, school-based vaccination coordinators,

representatives of Medicare Locals, general practitioners and practice nurses. An expert from the NHVPR, surveillance officers from the Therapeutic Goods Administration (TGA) and a representative from the Australian Government Department of Health were also interviewed.

Immunisation program managers were invited from each state and territory and all agreed to participate. Other stakeholders were either approached directly or were referred by other participants (respondent-driven sampling).

Stakeholder interviews

Key stakeholder interviews were conducted between July and October 2013 to gain an in-depth understanding of program implementation as well as strengths and challenges of the program implementation. A structured interview questionnaire was developed by staff at the National Centre for Immunisation Research and Surveillance (NCIRS) based on previous national immunisation program evaluations (see **Appendix 2.2**). The questionnaire included open and closed questions on the following topics:

- Communication and resources
- Program planning and rollout
- Ongoing service delivery
- Collaboration across sectors
- Data collection and reporting
- Strengths and challenges of the program
- Recommendations for implementing future national immunisation programs.

The interview questionnaire was modified to ensure the questions were relevant for each key stakeholder group (e.g. school-based coordinators, immunisation program managers). Prior to the interview, key stakeholders were sent the questionnaire by email to allow collection of relevant information for discussion at the interview. Most interviews were audio-digitally recorded with the consent of the respondent. Where consent for recording was not given, detailed notes were taken. Responses were professionally transcribed and drafts sent back to participants for respondent validation with amendments and additions incorporated into the final interview transcripts.

Stakeholder online survey

An online questionnaire was developed to survey respondents' experiences and perceptions of aspects of the National HPV Vaccination Program using a series of rating tasks and short answer questions. Topics in the online survey included:

- Usefulness of communication resources
- Perceived acceptance of each component of the National HPV Vaccination Program by parents, students, schools and providers
- Experiences of the rollout of the female and male programs
- Overall value and success of the program.

Most questions involved using a five-level ordinal response scale to allow respondents to rate their strength of agreement with a series of statements. The scale had categories of response from strongly negative opinions to strongly positive (i.e. 'Strongly disagree', 'Disagree', 'Neutral', 'Agree' and 'Strongly Agree'. The online survey was chosen as a more efficient method to collect responses to a series of rating questions rather than via the telephone interview. Once they had agreed to participate in the evaluation, respondents were sent a link to the online survey to complete either before or after the telephone interview. Any respondent who had not completed the online survey was sent up to two reminders within the month following his/her interview, after which it was assumed the respondent did not wish to participate in the online survey. Respondents could complete the survey up until its close at the end of October 2013.

Survey of National Cervical Screening Program managers

A separate online survey was also developed for managers of the National Cervical Screening Program in each jurisdiction. The survey included questions on the involvement of each jurisdiction's cervical screening program in the National HPV Vaccination Program and the managers' perceptions of the impact of the vaccination program on the National Cervical Screening Program. Managers or coordinators of the National Cervical Screening Program were approached by email or phone and invited to participate. Those who agreed were sent a link to the online survey.

Results

Jurisdictional program implementation 2013 to 2014

All jurisdictions commenced vaccinating adolescent males from February 2013 through school-based vaccination programs. However, the strategies for rolling out the extended National HPV Vaccination Program varied between the jurisdictions. Reasons for these variations included differences in the commencement age in high school, jurisdictional capacity, funding constraints and existing commitments that had been planned prior to the announcement of the program. The schedule for each jurisdiction is summarised in **Table 2.1**.

Table 2.1. School-based HPV vaccination schedule by jurisdiction, 2013 to 2015

Jurisdiction	2013 Females	2013 Males	2014 Females	2014 Males	2015 Females	2015 Males
ACT	Year 7	Year 7*	Year 7	Year 7 Year 9*	Year 7	Year 7
NSW	Year 7	Year 7 Year 9	Year 7	Year 7 Year 9	Year 7	Year 7
NT	Year 7	Year 7 Year 9	Year 7	Year 7 Year 9	Year 7	Year 7
QLD	Year 8	Year 8 Year 10*	Year 8	Year 8 Year 10*	Year 8	Year 8
SA	Year 8	Year 9	Year 8	Year 8 Year 9	Year 8	Year 8
TAS	Year 7	Year 7 Year 9	Year 7	Year 7 Year 9	Year 7	Year 7
VIC	Year 7	Year 7 Year 9	Year 7	Year 7 Year 9	Year 7	Year 7
WA	†	Year 8 Year 9‡ Year 10‡	Year 8	Year 8	Year 8	Year 8

* Males aged 15 years offered the vaccine as part of the catch-up program in 2013 and 2014.

† Western Australia moved the HPV vaccination program from primary school (Year 7) to high school (Year 8) in 2013. As a result females in Year 8 in 2013 had already been vaccinated in Year 7 in 2012. Therefore no large scale vaccination program for females in Year 8 was needed in 2013. In 2013 catch-up doses were offered to females in Year 8 who had missed HPV doses in 2012. Vaccination of Year 8 females commenced in 2014.

‡ Western Australia offered the catch-up program to males aged 14 to 15 years in 2013. The catch-up program was completed in 2013 as eligible males aged 15 years in 2014 had already received the vaccine in 2013.

Strategies for the catch-up of missed doses and reaching all eligible adolescent males in the catch-up program differed between jurisdictions. These strategies are summarised in **Table 2.2**.

Table 2.2. Missed doses and catch-up program by jurisdiction*

Jurisdiction	Missed doses	Male catch-up (aged 14–15 years) 2013–2014
ACT	At general practice Catch-up doses are only available at the end of the school year.	Males in Year 9 offered the vaccine through the school vaccination program in 2013 and 2014. Males aged 15 years in 2013 who were not in school grade being vaccinated were eligible to receive the free HPV vaccine at general practice.
NSW	At the next scheduled school visit or at general practice Doses can be completed until end of Year 8 at scheduled school visits.	Year 9 males who miss a dose at school are required to complete their doses at general practice. Males aged 15 years in 2013 who are not in school grade being vaccinated are eligible to receive the free HPV vaccine at general practice.
NT	At community health clinics and general practice	In remote areas catch-up is offered to all adolescent males between the ages of 12 and 15 years. Males aged 15 years who are not in Year 9 in 2013 are eligible to receive the free vaccine at general practice, Aboriginal Medical Service or community clinic.
QLD	At school clinics and general practice Eligible adolescents can complete the 3 doses by the end of the following calendar year.	Males aged 15 years in 2013 who are not in school grade being vaccinated are eligible to receive the free HPV vaccine at general practice.
SA	At council clinics	Males aged 15 years who are in Year 10 in 2013 are eligible to receive the free vaccine at general practice.
TAS	At council clinics, general practice	Males aged 15 years in 2013 who are not in school grade being vaccinated are eligible to receive the free HPV vaccine at general practice.
VIC	At council clinics, general practice Can continue in the school-based program after catch-up of missed dose. Eligible adolescents are aged 12–13 years or boys 14–15 years.	Adolescent males aged 14–15 years are eligible to complete the 3 doses of free vaccine at council clinics and general practice until the end of December 2014.
WA	At school, community clinics, general practice	The vaccine is offered to males aged 13–15 in Years 8, 9 and 10 in 2013. The male catch-up program will be completed in 2013 and in 2014 HPV will be offered to males and females in Year 8 only.

* Source: Key stakeholder interviews, jurisdiction documents and websites.

Existing literature on the implementation of the Australian National HPV Vaccination Program

Nine published journal articles and reports that included some form of evaluation of the implementation of the Australian National HPV Vaccination Program were found in a literature search of relevant databases. A brief description of the type of study and findings of each evaluation is provided in **Table 2.3**.

The published evaluations focused on the community catch-up program for young women and the school-based program for adolescent females. Two of the studies were Australia-wide but focused only on the community catch-up program for young women.[27,28] The other Australian evaluations focused on the school-based program for adolescent females but were specific to one jurisdiction or region.[29-33] The stakeholders sampled in the different studies included schools, students, parents, immunisation providers and jurisdictional managers.

The existing literature on evaluations of the HPV program in Australia found that immunisation providers were generally positive about delivering the program and that the program was generally accepted by parents, adolescent females and schools.[27,28,34,35] Issues for parents and adolescent females were availability of appropriate information and knowledge, concerns about vaccine safety and side effects.[29,34] Scheduling and organising vaccination day, vaccination setting and disruption to classes were issues for schools.[29,35] Vaccination setting and managing anxiety among adolescent girls were important issues for immunisation nurses.[29,30] Effective consent strategies were seen by many stakeholders as central to a successful program. (See **Table 2.3** for more detailed summaries of published findings.)

There has however, not been any published Australia-wide process evaluation of the implementation of either the full female program or the more recent extension of the program to include adolescent males.

The current process evaluation takes an Australia-wide approach, focusing on both the male and female stages of the National HPV Vaccination Program. The relevant stakeholders interviewed for the evaluation are the program managers and service providers responsible for aspects of the delivery of the program.

Table 2.3. Summary of existing literature on the evaluation of HPV vaccination programs

Authors	Source & Year	Location	Study design	Scope	Participants	Results
Leask J, et al.[28]	Vaccine 2009	Australia	Qualitative interviews with key informants including immunisation program managers, coordinators and providers	Community catch-up for women aged 18–26 years	State/territory immunisation program managers, program coordinators from Divisions of General Practice, general practitioners, practice nurses, Aboriginal health workers, (n=24)	Participants were positive about the vaccine and the program and perceived that the catch-up program was generally well accepted by young women and the community. Concerns with program implementation included short timing of rollout, political imperatives driving implementation and the cost to public funds. Early information resources were provided by the vaccine supplier. Implementation was seen as successful and fitted into existing general practice systems, though uptake by young women was not optimal. Inter-sectoral links were strengthened as a result of the program although segregation between private and public providers was evident.
Brotherton JM, et al.[27]	Sexual Health 2010	Australia	National survey of general practitioners on their experiences in delivering the community catch-up program	Community catch-up for women aged 18–26 years	GP providers (n=320)	GP participants were positive about their role as vaccine providers. The program was easily incorporated into existing systems. GPs thought that the program would have positive health benefits for Australia. The majority (57%) agreed that uptake of the vaccine for women would have been better if the community catch-up had started at the same time as the school-based program. A large minority of GPs expressed concern about the late set-up of the NHVPR (41%) and 30 % felt confused by changes to eligibility for young women aged 27 years. The $6 incentive payment for vaccine notification was considered important by 44% of GPs.

Authors	Source & Year	Location	Study design	Scope	Participants	Results
Cooper-Robbins SC, et al.[33]	Vaccine 2010	New South Wales	Explore knowledge about HPV and HPV vaccination in 12–13-year-old girls post program implementation Semi-structured focus groups and interviews conducted with adolescent girls and their parents	School-based program for adolescent females aged 12–13 years and school-based catch-up for females aged 13–18 years for HPV vaccination program	Parents and girls	Parents and girls had low levels of knowledge about HPV and expressed desire for more information and preferences for how that information should be provided. Lack of available information for girls contributed to confusion and low levels of knowledge. Since consent was only required from parents this also contributed to a lack of knowledge among girls. Girls in Year 7 expressed a need for age-appropriate information and more information in class so they could be better informed before receiving the vaccine. Accurate information and high levels of knowledge are crucial for safe sexual health behaviours and uptake of screening for cervical cancer.
Reeve C, et al.[31]	CDI 2008	Rural Queensland	Routinely collected administrative data	Adolescent girls school-based catch-up (Years 10–12) HPV vaccination program	Administrative data on eligible girls	Timely return of signed consent forms from parents is a major issue. Lower consent rates for Years 8–10 may affect the ongoing program delivery for Year 8 girls. GP delivery of school-based program allows easy catch-up of missed doses at GP surgery.
Queensland Government[35]	Evaluation of the school-based vaccination program, 2010	Queensland	Online survey of vaccine service providers, focus groups of parents and students, CATI interviews with school principals or representatives	Process evaluation of girls school-based catch-up (Years 9–12) HPV vaccination program	Vaccine service providers (n=86), parents (n=32), school principals (n=56), students (n=32)	Parents and students reported positive experiences with the program. Parents recommended more reminders and more information and better records. Students recommended more information, more reassurance and privacy during clinic. Service providers were mostly satisfied with the program implementation and communication with schools. A minority (18%) suggested that data reporting is too cumbersome. The majority of schools rated the program as good. Return of consent forms, informing parents and disruption to classes were the main issues raised by a minority of principals.

Authors	Source & Year	Location	Study design	Scope	Participants	Results
Cooper-Robbins SC, et al.[34]	Vaccine 2011	International	Systematic review of published evaluations	Process evaluations of international school-based vaccination programs for various vaccines	Published papers (n=14); four articles involved HPV programs	Findings were general for all school-based vaccination programs. In the four studies on HPV, reasons for parental refusal included insufficient information about vaccine, concerns about safety, lack of perceived need and impact on sexual behaviour. Appropriate information for all stakeholders and consent strategies are important factors for successful program implementation of school-based programs generally.
Kent H, et al.[30]	Sexual Health 2010	Victoria	Mail-out survey of immunisation nurses	Process evaluation of girls school-based HPV program (2008–2009)	Immunisation nurses (n=159)	Physical layout of the vaccination setting was the most important issue for nurses (41%). Nurses suggested improvements for the school-based HPV vaccination program included better education of parents and girls (85%), attention to vaccination setting (35%) and better consent processes (19%).
Cooper-Robbins SC, et al.[29]	Sexual Health 2010	Sydney	Qualitative interviews with parents and teachers, focus groups with nurses and students	Process evaluation of girls school-based HPV program (2008–2009)	Students (n=130), parents (n=38), teachers (n=10), immunisation nurses (n=7)	Successful programs were related to good preparation prior to vaccination day, involvement of coordinating teacher, school commitment, scheduling the time and place of vaccinations to suit school timetable, managing anxiety in girls, managing consent process and record keeping.
Watson M, et al.[32]	ANZJPH 2009	South Australia	Process evaluation	South Australian Government evaluation of the implementation of the girls school-based HPV program	SA jurisdictional health officers	Service is delivered through local government. There were issues with short timeframes for the rollout including vaccine supply and setting dates for school visits. Dates for 2007 were already set. This created issues for delivering the 3-dose schedule within the school year. Sensitive communication was needed to allay concerns and misinformation; therefore, the message focused on reducing cancer. Two schools refused on religious grounds. Anti-vaccine activity, mass psychogenic illness and adverse media attention created community concerns around the vaccine. Social media can amplify rumours and adverse information.

Summary of media reports on the National HPV Vaccination Program

Implementation of the female program 2007 to 2009

A search of the Factiva database returned 435 articles from the Australian print and electronic media between January 2007 and December 2009, the period covering the implementation of the school-based program for adolescent females and the period of school-based catch-up for adolescent females up to 18 years of age and the community catch-up program for young women. The community catch-up program finished in 2009 while the school program for adolescent females aged 12–13 years continued on as a routine part of the NIP.

The types of media reporting on the National HPV Vaccination Program during 2007 to 2009 is shown in **Table 2.4**. Reporting was dominated by the print media. Major newspapers and regional newspapers accounted for the majority of items.

Table 2.4. Distribution of selected Australian print and electronic news media on the National HPV Vaccination Program, 2007 to 2009, by type of media

Media type	Number of reports
Major newspapers and magazines	176
Regional papers	135
AAP news bulletins	46
Medical media	30
Radio/television	18
Other media	14
Popular	12
Other wire	4
Total	**435**

A summary of the proportion of articles and reports in each year 2007 to 2009 with positive or negative content is shown in **Table 2.5**. This list of 435 articles and reports is not exhaustive but provides an indication of the number and tone of reports in the Australian media at the time of the implementation of the female catch-up program.

Table 2.5. Distribution of selected Australian print and electronic news media on the National HPV Vaccination Program, 2007 to 2009, by message content

	2007	2008	2009	Grand Total
Negative	38 (16.4%)	20 (21%)	10 (9%)	68 (15.6%)
Positive	194 (83.6%)	77 (79%)	96 (91%)	367 (83.9)
Total	232	97	106	435

Table 2.5 indicates that there was frequent media reporting around the female program in 2007, the first year of the rollout. The number of reports declined substantially in subsequent years.

The majority of media stories (84%) were rated as positive, most of which were reporting of the rollout over the period. The rate of negative reports did not change over the 3 years covering rollout to the end of the female catch-up program.

Many regional and metropolitan newspapers presented discussions on negative aspects of the program in a positive light. For example, incidents of fainting were often reported in terms of reassurance from experts or politicians. Parents were encouraged to continue vaccinating their daughters. Many of the strongest negative messages came from readers' correspondence.

Themes

There were a number of major themes that changed across the course of the school-based program. The positive and negative themes discussed in the media by year from 2006 to 2013 are listed in **Appendix 2.3**.

Australian innovation

In the first half of 2006, there were a number of stories around the HPV vaccine as an Australian world-first innovation and the nomination of researcher Ian Frazer as Australian of the Year.

School-based program and community catch-up rollout

In 2007, many regional and metropolitan papers reported the rollout of the school-based program in each of their own localities. The rollout was discussed in positive terms and these reports accounted for a substantial proportion (40%) of the positive media stories sourced for 2007.

Adverse events

In 2007, there were some reports on adverse events, which accounted for about 30% of negative media stories accessed in 2007. By late 2008, however, newspapers were reporting that Gardasil® was safe and that fears around allergy and adverse events were unfounded.

Vaccine may promote teenage promiscuity

In 2007, there were both positive and negative reports around the introduction of the vaccine and the issue of female sexual activity. There were a small number of media stories about schools and parents refusing the vaccine due to fears of promiscuity and some editorials

advocating refusal on moral grounds. There were also a number of reports and articles arguing that concerns around sexual activity and the vaccine was not a major issue in Australia.

Community catch-up deadline

Many regional papers advertised the looming deadline for the community catch-up program for young women throughout 2008 and in late 2009.

Advocating for vaccine for males

From 2006 onwards, there were media reports advocating for access to the vaccine for males.

Decrease in genital warts and high-grade cervical lesions

During 2010–2012, there were only a few media stories which focused on vaccine effectiveness, particularly the reduction in incidence of genital warts and high-grade cervical lesions.

Implementation of the male program 2013

In 2013, the media covered the start of the extended program for males. However, after the start of the male program, there was very little media attention either positive or negative. This contrasted with the female program in the years 2007 to 2009, where the media followed particular themes over the course of the program, for example, announcing the start of the female school-based program, region by region, in 2007 through to reminding women of the looming deadline for the end of the community catch-up program in 2009.

Stakeholder interviews

HPV program stakeholder sample

Thirty stakeholders involved in implementation of the National HPV Vaccination Program participated in the evaluation interviews/questionnaires. Twenty-seven of these were interviewed by phone and two provided written responses to the questionnaires.

Participation was voluntary, so the mix of roles held by key stakeholders in the final sample differed slightly from the original sampling matrix (see **Table 2.6** and **Appendix 2.1**). Several stakeholders had experience in a number of roles associated with implementation of the National HPV Vaccination Program (e.g. Medicare Local coordinator/practice nurse, regional immunisation coordinator/council-based provider). The depth of experience among the key stakeholders created a rich source of information for the evaluation.

Table 2.6. Stakeholders by role held in the National HPV Vaccination Program

	Interviewed (N=30) n	Online survey (N=20) n
Department of Health Immunisation Branch	1	–
Chief Health Officer	1	–
State/territory immunisation program managers*	11	8
General practice (nurse, GP)	3	3
Medicare Locals	4	3
Australian Medicare Local Alliance (AMLA)	1	–
School-based vaccination providers/coordinators	5	5
Regional immunisation coordinators	2	1
Therapeutic Goods Administration	2	–

* In three jurisdictions, a jurisdictional immunisation nurse coordinator was interviewed with the immunisation program manager.

Twenty key stakeholders completed the online survey. Respondents from the TGA did not complete the online component as the survey was not directly relevant to them. In a number of instances, more than one stakeholder was interviewed from one organisation (e.g. two respondents from the same Medicare Local) and only one respondent from that organisation completed the online survey. Therefore the number of online survey responses was fewer than the number of interviews.

The final sample had representatives from all states and territories (see **Table 2.7**).

Table 2.7. Sample of key stakeholders by jurisdiction

Jurisdiction*	Interview (N=29) n	Online survey (N=20) n
ACT	2	1
NSW	5	4
NT	3	2
QLD	5	5
SA	2	2
TAS	2	1
VIC	4	3
WA	3	2

* Excludes the Department of Health, TGA and the AMLA

The majority (65%) of key stakeholders had been working in immunisation and vaccine-preventable diseases for more than 10 years.

Most respondents had been involved in multiple aspects of the National HPV Vaccination Program (see **Table 2.8**).

Table 2.8. Key stakeholder participation in the National HPV Vaccination Program

Component of National HPV Vaccination Program	Online survey (N=19) n (%)
Planning and initial rollout of the female program (commencing 2007)	12 (60)
Ongoing school-based program for adolescent females aged 12–13 years	16 (80)
School-based catch-up for adolescent females aged 13–17 years (from 2007 to 2009)	16 (80)
Community catch-up program for young adult females aged 18–26 years (from 2007 to 2009)	12 (60)
Planning and initial rollout of the male program (commencing 2013)	16 (80)
School-based program for adolescent males aged 12–15 years	15 (75)
Other	2 (15)

National Cervical Screening Program manager sample

A further seven respondents from state and territory cervical screening programs completed the online survey for National Cervical Screening Program managers.

Planning and rollout

Survey results

Table 2.9 shows the results from the online survey questions on the adequacy of the lead-time from the announcement of funding of the program until the start of the program for aspects of program planning for the original female program and the extended male program. Less than half of respondents agreed or strongly agreed that the period from the announcement of the funding of the female HPV vaccination program to the start of the program was adequate in relation to program planning (30%), coordination (35%), developing information resources (30%), communicating with schools and parents (30%), provider education (35%) and the set-up of data collection (20%). A large proportion of respondents (10–20%) were neutral on these issues.

Respondents generally thought that more adequate lead-time was given between the announcement of the extension of the program for males and the start of the male program than was given for the female program. At least 50% of respondents agreed that the period from the announcement of the funding of the male program to the start of the program was adequate for aspects of planning and coordination, provider education (65%) and the set-up of data collection (65%). However, only 40% of respondents agreed that the interval

between the announcement and start of the male program was adequate to develop information resources. A large majority of respondents agreed that there was adequate time for vaccine supply (75%) and safety planning (70%) for the male program, compared with 50% and 40%, respectively, for the female program.

Table 2.9. Distribution (%) of responses to statements on the adequacy of lead-time for planning and rollout

	Strongly disagree	Disagree	Neutral	Agree	Strongly agree
The period from the announcement of the funding of the female HPV vaccination program (November 2006) to the start of the program (April 2007) was adequate for:					
Planning	20	30	20	25	5
Coordination	15	35	15	30	5
Vaccine/supply delivery	10	25	15	45	5
Vaccine safety planning	10	30	20	35	5
Developing information resources	15	40	15	25	5
Communication with schools/parents/students	20	30	20	25	5
Provider education	10	45	10	30	5
Set-up of data collection	25	35	20	15	5
The period from the announcement of the funding of the male HPV vaccination program (July 2012) to the start of the program (February 2013) was adequate for:					
Planning	10	20	20	45	5
Coordination	15	20	15	45	5
Vaccine/supply delivery	5	5	15	70	5
Vaccine safety planning	5	10	15	65	5
Developing information resources	5	40	15	35	5
Communication with schools/parents/students	10	25	15	45	5
Provider education	5	25	5	60	5
Set-up of data collection	5	15	15	60	5

Table 2.10 shows the distribution of responses to statements on the rollout of the extended program for males. The majority of respondents agreed that rollout of the extended program for males was able to take good advantage of the existing female program for all aspects of planning and implementation. Twenty per cent of respondents, however, disagreed that the existing female program assisted with the development of communication resources and communicating with parents and students about the extended program. The majority of respondents agreed that including both males and females in the National HPV Vaccination

Program had advantages over the previous female-only program in all aspects of planning and implementation.

Table 2.10. Distribution (%) of responses to statements on the rollout of the extended program for males

The rollout of the male HPV vaccination program was able to take good advantage of the existing female program in terms of:

	Strongly disagree	Disagree	Neutral	Agree	Strongly agree
The rollout of the male HPV vaccination program was able to take good advantage of the existing female program in terms of:					
Planning	6	6	6	61	22
Coordination	6	–	6	67	22
Vaccine/supply delivery	–	-	5	75	20
Developing information resources	5	15	10	50	20
Communication with schools/parents/students	5	15	10	50	20
Provider education	–	10	20	50	20
Including both boys and girls in the National HPV Vaccination Program has advantages over the previous female-only program in terms of:					
Planning	–	–	25	50	25
Coordination	–	–	22	50	28
Vaccine/supply delivery	–	5	30	40	25
Developing information resources	–	–	25	50	25
Communication with schools/parents/students	–	–	20	55	25
Provider education	–	–	25	45	30

Table 2.11 summarises responses to statements on the delivery of 3 doses of HPV vaccine. Half the respondents agreed that the 3-dose schedule of the HPV vaccine created difficulties for adolescent females in the school-based program and 60% agreed that delivering 3 doses created difficulties for the community catch-up program for young adult females.

The majority of respondents agreed that the return of consent forms, absenteeism on vaccination days and the scheduling of other school activities adversely affected vaccination coverage in their jurisdiction or region.

Table 2.11. Distribution (%) of responses to statements on the delivery of 3 doses of HPV vaccine

	Strongly disagree	Disagree	Neutral	Agree	Strongly agree
The 3-dose schedule of the HPV vaccine created difficulties for:					
Adolescent girls in the school-based program	10	20	20	35	15
Young women in the community catch-up program	10	10	20	25	35
Achieving vaccination coverage of the 3 HPV doses was adversely affected in my jurisdiction/region by:					
School attendance rates	5	25	30	35	5
School absenteeism on vaccination day	5	10	15	60	10
Scheduling of other school activities/classes	5	15	25	50	5
Inadequate notification of students/parents	5	30	30	30	5
Return of consent forms	5	20	5	50	20

The majority (65%) of respondents agreed that the National HPV Vaccination Program in his/her jurisdiction/region provided adequate advice/information to adolescent females and young adult females about the need for cervical screening (results not tabled). Half of the respondents disagreed that they were concerned that HPV vaccination will reduce the uptake of cervical screening.

A small proportion (10%) of respondents agreed that the concurrent rollout of the National Rotavirus Program made the rollout for the female HPV program more difficult.

The majority (90%) of respondents agreed that the National HPV Vaccination Program in his/her jurisdiction was providing HPV vaccination in an efficient way to adolescent males and females.

Respondent interviews

Announcement of the extended National HPV Vaccination Program to include males

The jurisdictions were expecting the program to be rolled out to adolescent males following the positive recommendation of the HPV vaccine Gardasil® for males by the PBAC in November 2011.

Nearly all immunisation program managers mentioned that there had been preliminary consultations between the Australian Government Department of Health and the jurisdictions, via the Jurisdictional Immunisation Committee teleconferences and meetings

early in 2012, around the possible extension of the National HPV Vaccination Program to males.

> *"We were advised through the Jurisdictional Immunisation Committee and National Immunisation Committee in early 2012 that there was a probability that the HPV program would be funded and available for boys in 2013."*

Most immunisation program managers, however, noted that no firm date had been proposed for the rollout at these early discussions and that the first confirmation they received was on the day of the ministerial announcement of government funding for the extended program. This was followed by official notification to the states and territories.

Most managers expected the announcement but some expressed surprise that the announcement had come so quickly and the rollout was happening so soon. Managers understood that jurisdictions were going to be kept somewhat in the dark prior to a ministerial announcement. Managers felt, however, that this approach to launching the program did not help with implementing the rollout in terms of jurisdictional budgets and planning. Most managers (60%) indicated a need for greater transparency and consultation between the Australian government and the jurisdictions around the timing of the announcement of the program.

Those immunisation program managers who could recall commented that the notification of the original female program had similarly been via the media announcement in 2006.

> *"The confirmation came through the media release. I believe that's the case. That was the case with the girls' program as well."*

Many of the school-based vaccination providers and regional immunisation coordinators also remembered first hearing of the extension of the National HPV Vaccination Program to males through the media release. Official notification to providers and coordinators came from the state or territory health departments. Some school-based coordinators and regional immunisation coordinators had no clear recollection of how they were officially notified.

Initial rollout of the National HPV Vaccination Program for adolescent males

Most immunisation program managers felt that the 6-month lead-time between the announcement in July 2012 and the start of the program in February 2013 was, in principle, adequate and better than the previous lead-time for the female program. Six months was the lead-time that jurisdictions had campaigned for in initial discussions with the Australian Department of Health around the extended male program.

"I think the lead-time, I mean it was 6 months, that's a good amount of time. And that's what I suppose the states and territories have always said to the Commonwealth that we'd need at least 6 months."

However, most immunisation program managers thought the effective lead-time was a lot shorter than 6 months. The main reasons for this were the need to find funding and time in the school calendar.

The Australian Department of Health acknowledged that the lead-time for the rollout of the program for adolescent males was short. A lead-time of 12–18 months would ideally allow all aspects of the program to be planned and implemented smoothly, especially when setting up or modifying a vaccine register.

Commonwealth funding to the states and territories for immunisation service delivery is rolled into the National Healthcare Agreements and under the National Partnership Agreement on Essential Vaccines (NPEV) states and territories are responsible to fund the service delivery of the HPV vaccine.[36] The announcement of the extension of the HPV vaccination program to males arrived after some jurisdictions had already allocated their health budgets for 2013 - immunisation program managers had to negotiate with their jurisdictions over funding the program and could not plan to roll out the program until the level of funding was established.

"And even though we were preparing on the assumption that we would be starting in 2013 without funding and nurses to actually administer it we were a bit stymied for the first couple of months. We knew we'd start it but we couldn't go ahead and prepare everything in case the [jurisdiction] government said, 'well no we're not going to do it'."

Most stakeholders would also have liked more lead-time to accommodate the summer school holidays. Many jurisdictions needed to finalise dates and develop and deliver consent materials to schools for distribution prior to the summer break. Furthermore, jurisdictions were already negotiating school dates for the 2013 vaccination program when the announcement of the extended program was made in July 2012.

Although the lead-time for the rollout of the male program was tight, it was acknowledged as more workable than the shorter lead-time that had been available for the female program.

"From an operational point of view the lead-time was okay in the end but very condensed, especially towards the end."

Funding

The Australian government's role in extending the National HPV Vaccination Program to males was to fund and procure the vaccine, create and distribute communication resources, expand the National HPV Vaccination Program Register to record doses for males, and establish enhanced surveillance of adverse events following immunisation with HPV. Organising and funding of the delivery of the program was the responsibility of the states and territories. These arrangements are consistent with the Commonwealth and state and territory responsibilities set out in the National Partnership Agreement on Essential Vaccines (NPEV) which provides the framework for funding arrangements that support implementation of the NIP.

The NPEV does not provide funding for delivery activities associated with vaccination programs within states and territories, including school-based programs. Funds for service delivery have been incorporated in the National Health Reform Agreement payments which are made under the National Healthcare Agreement.

Strengths of the funding model

One immunisation program manager observed that Australia was a world leader in funding the HPV vaccine on a population level. Some immunisation program managers and school-based vaccination providers commended the Australian government for extending the funded program to include adolescent males.

> *"I think the strengths are that [it has] been acknowledged that there is value in giving it to boys and that the Commonwealth have put the funding to ensuring that it happens."*

Challenges of the funding model

The majority of immunisation program managers discussed funding of service delivery for the rollout of the extended HPV vaccination program for adolescent males as a major challenge (n=7). Immunisation programs had to compete with other priorities for funding within their jurisdictional health services. Some jurisdictions felt the strain of funding the extended program for males more than other jurisdictions. For some jurisdictions there was an appreciable opportunity cost of delivering the extended HPV vaccination program for adolescent males. Funding for the delivery of school-based vaccination programs has not kept pace with costs in some jurisdictions.

> *"The biggest challenge is resources and funding. Everybody's competing for funding in the health services, and public health is always the poor people. Health services do not allocate sufficient funding to resource immunisation programs."*

One school-based coordinator from South Australia noted that adequate funding of service delivery was important for the long-term sustainability of the program. Local government and other providers cannot be expected to keep supporting programs without funding.

Despite the funding model agreed to in the NPEV many, but not all, jurisdictional program managers expressed disappointment that the Commonwealth had not provided extra funding support for service delivery of such a large school-based program. There had been some expectation of Commonwealth funding support for service delivery with the rollout of the male program as there had been for the rollout of the female program.

Several immunisation program managers discussed the need for a better model for funding the service delivery of the National HPV Vaccination Program.

The Australian Department of Health recognised that the announcement of the male program was made after jurisdictions had allocated their budgets and appreciated the efforts of the jurisdictions to accommodate the extended HPV vaccination program into their existing budget allocations to ensure the program was implemented.

Amendments to policies and guidelines

The extension of the National HPV Vaccination Program to include males did not require major amendments to policies by the Australian government or in most jurisdictions.

Amendments that were mentioned by New South Wales, the Australian Capital Territory and Victoria included changes to protocols, standing orders for nurses, eligibility policies and reviewing tenders for the purchase of vaccines.

In 2007, at the start of the female program, the Commonwealth funded the states and territories to purchase their own vaccines. From 2009, under the NPEV, the Commonwealth progressively moved to directly purchasing vaccines for use by the states and territories.[36] Under the agreement, the role of states and territories is to assist with advice and procurement of tenders for the purchase of vaccines. With the announcement of the extension of the HPV program to adolescent males the Commonwealth took over the purchase and supply of the HPV vaccine for the last of the jurisdictions still purchasing its own HPV vaccine under transitional arrangements.

In Queensland, Tasmania, Western Australia and the Australian Capital Territory the original National HPV Vaccination Program for females and the later extension of the program to include males has provided the impetus for changes to their school-based vaccination program schedules and delivery. For example, at the start of the male program, Western Australia brought forward by 1 year plans to move the school-based program from primary to

high school (see section below on school-based programs for more details for each jurisdiction.)

Vaccine safety plan

The TGA and the Immunisation Branch of the Australian Government Department of Health implemented a safety plan of enhanced surveillance of adverse events following immunisation for the rollout of the male program. During the implementation of the female program, there was some concern that information about unexpected events (e.g. the mass psychogenic illness in Victoria, the anaphylaxis cluster in NSW and the claims of a link between Gardasil® and multiple sclerosis) was not rapidly collated centrally and shared early enough.

The main aim of the safety plan was to ensure that the TGA and jurisdictions were notified early of any unexpected adverse events with the male program.

The safety plan involved enhanced surveillance of four conditions: anaphylaxis; generalised allergic reaction; loss of consciousness (simple faints, faints with injury, faints with convulsion); and any condition requiring emergency department attendance or hospitalisation.

The enhanced surveillance of adverse events involved more rapid reporting from the states/territories to the TGA and a weekly collation of summary data by the TGA shared with the Immunisation Branch and the jurisdictions and discussed at regular teleconferences. Teleconferences were held weekly until the completion of the first dose of vaccine in all jurisdictions. Since no unexpected safety signal was detected during the first dose, meetings were then held monthly.

Strengths of the safety plan

The male program was the first program with such a comprehensive safety plan for early detection of signals for adverse events.

The safety plan was put in place in time for the rollout of the male program.

Weekly meetings ensured that the Australian Government Department of Health and jurisdictions were informed early of any potential or perceived safety signal and could be well prepared for any follow-up action and media attention.

The TGA and the Australian Government Department of Health were prepared to rapidly detect and act upon any expected and unexpected adverse events following immunisation in the male program.

> *"We had those processes set up and running at the start of the program. I think the safety planning was a real strength."*

Communication from jurisdictions to their stakeholders

The jurisdictions had a diverse range of stakeholders who they were responsible to inform about the extension of the program to males. This included stakeholders directly involved in the program such as local government, the education sector and immunisation nurses. They also informed a broad range of other areas of the health sector, such as remote and regional health services, Aboriginal Medical Services, public hospitals, general practice and Medicare Locals.

The jurisdictions informed other stakeholders at different levels in each sector, from briefing the state or territory Minister of Health, meeting with representatives of the Education Department, Catholic and independent school sectors, and directly informing individual school principals and parents.

Communication activities included letters, faxes, emails, teleconferences, face-to-face meetings, media releases, articles in newsletters and information posted on state/territory health department websites. Early direct notification of organisations and individuals involved in the HPV vaccination program was seen as key to effective communication.

Communication with private practice

The Australian government communicated with all GPs about the extended program for males via a letter from the Chief Medical Officer and through an announcement in the RACGP Friday Facts.

Respondents involved with general practice thought, however, that because the National HPV Vaccination Program was currently a school-based program there had been a lack of communication with general practice around the extension of the program to include males. As one Medicare Local respondent observed:

> *"There has been a real lack in communication with how the boys' program has been rolled out, we haven't had nearly as much information as when the girls program was rolled out and I know that it was a larger catch-up that they were doing [for females] but there just hasn't been much [for males], I think it's all been very much school based".*

In contrast with the initial female program providers in general practice were more engaged with the male program.

> *"One positive thing about it was it was active promotion to the community to involve your general practitioner and so, you know, the GPs felt engaged."*

Information resources

Survey results

In the online survey respondents were asked to rate the usefulness of the HPV-related information resources created by the Australian Government Department of Health, jurisdictions and other organisations.

Table 2.12. Key stakeholders' rating of usefulness of information resources

Resource	Don't know/Not aware†	Not at all useful	Not very useful	Useful	Very useful
	%	%	%	%	%
Department of Health HPV website	–	5	10	60	25
Department of Health fact sheet for professionals	–	5	10	60	25
Department of Health resources for schools	25	–	20	40	15
Department of Health HPV resources for students	30	–	20	35	15
Department of Health HPV resources for parents	30	–	10	35	25
Department of Health HPV resources for Aboriginal and Torres Strait Islander students/parents	25	–	10	40	25
Department of Health HPV resources for culturally and linguistically diverse students/parents	35	–	10	35	20
NCIRS HPV fact sheet for providers	5	–	10	35	50
NCIRS HPV fact sheet for patients	20	–	15	35	30
State/territory-based health department information	15	5	5	20	55
Medicare Local/GP Division information	40	10	10	30	10
Medical media (e.g. Medical Observer)	50	5	15	20	10
Pharmaceutical company website	40	10	15	30	5
Pharmaceutical company promotional material	20	10	20	35	15
Vaccine product information	–	10	10	45	35
Cancer Council information	20	5	–	35	40
Peer-reviewed publications	45	5	5	20	25
Newspapers/radio/television	15	5	30	30	20
Social media (e.g. Facebook, Twitter)	60	10	20	10	–

† 'Don't know/Not aware': Respondents were either not aware of or not familiar with the resource.

Table 2.12 summarises respondents' ratings for each resource. The Australian Government Department of Health website was the current site that includes information resources for both females and males. Respondents could follow links to the relevant websites to check the exact resource materials being evaluated.

Respondents were aware of and made use of HPV-related information from a wide range of sources.

All respondents were aware of the Australian Government Department of Health HPV website and the fact sheet for professionals and 85% of respondents found these resources useful or very useful.

One quarter of respondents were not aware of the HPV resources developed by the Australian Government Department of Health for Aboriginal and Torres Strait Islander students/parents and 35% were not aware of the language resources for culturally and linguistically diverse (CALD) students and parents. However, of those respondents who knew of the Indigenous or CALD resources, the majority found the resources to be useful or very useful.

Other resources that were rated as most useful by respondents were the information provided by their state or territory health departments, the NCIRS HPV fact sheet for providers and information provided by the Cancer Council.

Half the respondents reported they were not aware of any information or promotional material on HPV in the medical media and 40% of respondents were not aware of any promotional material provided by Medicare Locals or GP Divisions.

Respondent interviews

National information resources developed by the Australian Government Department of Health

Prior to the start of the male program, the Government consulted with the jurisdictions to agree to a set of key messages for use in the development of national and local level communication resources. Draft materials were circulated to all jurisdictions for comment. The consultation process around key messages allowed jurisdictions to go ahead and develop their own information resources even though the national resources were delayed.

Information resources developed by jurisdictions/regions

Most jurisdictions did not develop extensive information resources for the extension of the National HPV Vaccination Program to include adolescent males. Instead, they depended on the national communication resource materials developed by the Australian Government Department of Health.

The most important resources developed by most jurisdictions for the extended HPV program were the revision and adaption of their consent forms and the accompanying fact sheets on HPV to include information for males.

The other major activity that jurisdictions undertook was updating web-based information on jurisdiction websites to ensure that information on HPV was readily accessible and up-to-date for females and males. Other resources developed at the jurisdiction level included advice packs for immunisation providers and New South Wales translated its consent forms into languages other than English. Because in 2013 Western Australia was running a male-only program (since females in Year 8 had been vaccinated in 2012), the state had to adapt the national resources for adolescent males only.

Immunisation program managers thought it was important that the jurisdiction and national communication resources had a consistent message around HPV and vaccination.

> *"We developed our messages using the key national messages for consistency which placed emphasis on other cancers more common in males."*

Some immunisation program managers thought that the Australian Government Department of Health resources for the extended program did not provide enough detail of HPV as a sexually transmitted infection. Therefore, some of the jurisdictions' fact sheets and websites include more detail on HPV and sexual transmission.

Immunisation program managers recalled that jurisdictions had developed more of their own resources for the initial female program than they had for the male program. Jurisdiction resources for the initial female program included information pamphlets, posters and Indigenous-specific resources, including consent forms for remote communities.

School-based vaccination providers and regional immunisation coordinators used resources provided by the Australian Government Department of Health or the jurisdiction. Few resources were developed at the local level, although one immunisation program manager mentioned vaccination day posters developed by staff.

Some stakeholders, both in the school-based program and private practice, recalled relying on messages and materials from the vaccine manufacturer and Cancer Council for the female program.

Strengths of communication and resources

Respondents mostly had positive opinions of the information resources developed by the Australian Government Department of Health for the extended program in adolescent males. The Australian Government Department of Health had consulted early with the jurisdictions when preparing the materials, especially around key messages. Two immunisation program

managers commented that using a market research company to assist in developing information materials for the extended program was a good approach. The information resources produced were useful.

> *"They had a good website, they had good resources that could be used. I think they did a really good job with them and it just seemed like a very broad and thorough communication strategy."*

Respondents noted that up-to-date use of information technology and developing eye-catching materials was a strength of the Australian Government Department of Health's communication strategy for the extended program for males.

> *"We're seeing the role of the internet and Facebook and information technology has increased so much in that short space of time, so I think they're a lot more savvy with their approach."*

Respondents also observed that with the extended program for males the Australian Government Department of Health had developed a more proactive communication strategy, using evidence-based messages to avert potential negative community attitudes and misinformation. The Australian Government Department of Health had also developed better lines of communication with schools and, generally, the communication program had worked; parents were reading the information and consenting to vaccinate their children.

Challenges of communication and resources

Many immunisation program managers and school-based coordinators agreed that the national information resources had been prepared too late for distribution before or at the start of the program rollout. This was the case both for the original female program and the extended male program.

To immunisation program managers, the late arrival of information resources was a problem as information materials were needed early to allow for better preparation of the program rollout and to provide consistent messages about HPV and vaccination.

> *"The material must be ready 6 months in advance of the year starting in a school-based program so that we can all use it and know that consistent messages are used."*

Late arrival of the national resources was also seen to waste jurisdiction resources due to the duplication of materials. Resources were less likely to be used at all if they arrived late.

> *"The girls' stuff all came out late, which is another reason why we tend not to use Commonwealth materials."*

One practice nurse considered that the original female resources had been too wordy and that nurses had still needed to explain the message to females in their practices.

Two respondents from South Australia and the Australian Capital Territory mentioned logistic problems with distributing the national resources through schools. Sending materials directly was an issue because schools did not distribute them, especially when they arrived after the start of the school year. It was also impractical for providers to carry all the information resources to vaccination days along with the vaccines and consent materials.

Several stakeholders thought that since the community could now be more easily reached via the internet and phone messages than was possible 5 years ago, distributing paper-based information resources was not as critical as it had been at the start of the female program and could be superseded by electronic media.

Not all immunisation program managers considered that the market research approach to developing materials had been useful. Two stakeholders mentioned they preferred to use the Immunise Australia Program website for information resources rather than the HPV Program website and one suggested the HPV website should be integrated into the Immunise Australia website.

Communicating messages about HPV

A unique aspect of the National HPV Vaccination Program was communicating messages around sexual transmission of the virus. This created both challenges and opportunities for sexual health messages. One regional immunisation coordinator remarked that with the start of the female program immunisation nurses had received more questions from adolescent girls about sexual health, which was initially a challenge but also ultimately a good outcome.

Several respondents saw value in the original message of a vaccine against cervical cancer, as it targeted a specific disease and it was a less controversial message to sell to parents of young adolescent females. Many respondents, however, thought the original message to females should have more fully explained the link between HPV, sexual transmission and cancer.

A large proportion of respondents commented that the original emphasis on a cervical cancer vaccine made it more difficult to explain why the program was being extended to adolescent males.

> *"I don't think just the actual vaccine on the day getting all these kids in and jabbing them is any more challenging just because you've put the boys in. It's getting parents and schools and students to understand why it's a good vaccine for a boy because it was so much 'we're going to cure cervical cancer'."*

Role of media

Respondents had very different perceptions of the role of media in promoting the National HPV Vaccination Program, possibly due to differences in media attention across jurisdictions. There was negative attention from the media at the start of the female program, which affected the initial community acceptance of the program for females. This adverse media attention was largely absent for the announcement and rollout of the extended program for males. One respondent noted that although there had been negative media around the female program, it had not stopped a good uptake of the vaccine.

However, several stakeholders also discussed the role of media in the positive promotion and communication of the National HPV Vaccination Program.

Several school-based coordinators recalled there had been some positive promotional announcements on radio and in magazines for the female program, in particular around the female community catch-up in general practice.

Another school-based coordinator had also noticed positive promotion of the program by the media coverage of the rollout of the male program.

> *"Quite a bit in the media recently especially just before the male program was introduced they had quite a few documentary type programs and talkback programs."*

Respondents suggested that the media could be better used to promote the program, either at the local level through local papers or through wider coverage such as glossy magazines.

The Australian Government Department of Health observed that the safety plan of enhanced surveillance of adverse events allowed the Department and the jurisdictions to be forewarned to handle any media attention for the male program regarding safety concerns.

Role of vaccine company

Some respondents from private practice and Medicare Locals and one immunisation program manager mentioned the information provided by the vaccine pharmaceutical company as a positive aspect of the original female program, although not all private providers used the pharmaceutical company information.

The information from the pharmaceutical company was seen as important to fill the initial gap in information at the start of the female program but was not so important once the national resources became available.

> *"I can remember that most of the information did come from drug reps. I can remember being bombarded by drug reps and not much information coming from [jurisdiction health department]."*

Besides providing information the vaccine company actively promoted the engagement of general practice in the female program.

One school-based coordinator and one immunisation program manager also mentioned using vaccine company market research findings for the male program. However, a respondent from private practice considered that the relative lack of promotion of the male program by the vaccine company contributed to less awareness of and engagement with the male program by general practice providers.

Service delivery

Respondents did not recall any major issues with vaccine supply, cold chain or administration. Two school-based coordinators noted that the single doses were convenient but came with excessive packaging.

School-based programs

Immunisation program managers in several jurisdictions credited the National HPV Vaccination Program for providing the impetus for changes to the jurisdiction's delivery of the school-based vaccination program.

In Queensland, the female HPV vaccination program brought the state and Australian government into the school-based program, which was formerly run solely by local councils.

Western Australia was planning to move the school-based vaccination program to high school in line with the education department decision to move Year 7 into high school in 2014. However, the move of the school-based vaccination program from primary to high school was fast tracked to start in 2013, a year earlier than planned, to coincide with the start of the extended HPV vaccination program for males. This provided Western Australia with an opportunity to focus on the vaccination of males only in 2013, because females in Year 8 at high school in 2013 had already been vaccinated against HPV in Year 7 at primary school in 2012.

In the Australian Capital Territory, the female program resulted in the establishment of a dedicated school immunisation team. Formerly school vaccinations were given by maternal and child health nurses. Collaboration with schools has improved since the start of the female program.

In Tasmania, the male program was the impetus for accelerating the review of the whole school-based program, including moving the program from primary to high school, more direct communication with schools, and developing consistent consent forms across the state.

Collaboration between the health and education sectors

In most jurisdictions, the collaboration between the schools sector and the school-based programs was relatively robust. However, some jurisdictions mentioned that the relationship was more fragile and the extended male program created some pressure. Stakeholders were aware that the success of the program depended on the goodwill of the education sector. Therefore improving communication strategies with the education sector was important for ongoing success of the program.

Some of the initiatives jurisdictions were undertaking to improve the collaboration between the health and education sectors included formal research into inter-sector collaboration, liaison between Medicare Locals and the education department on strategies to improve the return of consent forms, surveying schools on the progress of the school-based program and the jurisdictional health department communicating with schools directly rather than indirectly through local government.

The approach by the Australian Government Department of Health was to communicate with schools and distribute information resources to schools through existing mechanisms in each jurisdiction, for example, through Public Health Units. Some jurisdictions, however, requested that the Australian Government Department of Health communicate directly to schools due to the short timeframe allowed for the rollout.

Strengths of the school-based program

A large proportion of stakeholders (n=10) including immunisation program managers, regional and school-based coordinators, private providers and Medicare Locals mentioned delivering the HPV vaccine through the school-based program in Australia as a major strength of the National HPV Vaccination Program.

Australia has a good international reputation for delivering school-based vaccination programs.

> *"Internationally I think Australian delivery of school-based programs is very impressive."*

Delivering school-based programs was seen by immunisation program managers as the most efficient way to reach large numbers of adolescents and achieve the best coverage possible and more cost effective than delivering through general practice.

> *"Well I think that a school-based program is by far the best, to reach large numbers of students. If you relied on parents visiting their GP they'd probably never get there."*

The majority of immunisation program managers mentioned school-based vaccination programs as a strength of their state or territory. Most immunisation program managers felt

that school-based programs were well established in their jurisdictions and they feel that the state/territory owns the school-based programs. States and territories have knowledgeable, experienced staff and the jurisdictions are motivated and able to deliver a quality program.

> *"[We have] knowledge about how to go and do it. We've done it before, we know how to do it, it's just a matter of pointing us in the right direction."*

With school-based programs, immunisation program managers felt that the jurisdiction had more direct control over the quality of the program so it could deliver an optimal quality service. This includes providing flexibility for adolescents to go to another service if needed.

Delivering HPV vaccination in schools was an advantage as the school-based program is well accepted by schools and parents and a good way to reach the targeted age groups.

> *"Parents … they're totally in tune with there being a school-based program as well."*

Challenges to the school-based program

School absenteeism, return of consent forms, scheduling vaccination days and delivering 3 doses at the right intervals during the school calendar year were major challenges for delivering the HPV vaccine through the school-based program.

Several stakeholders mentioned that adding more vaccines to the school-based program was an imposition on schools. A bigger program also places extra burden on school-based immunisation providers. The increased work load makes it more difficult for staff to manage the vaccination day setting and increases the risk of errors.

A number of stakeholders mentioned that improving uptake for both males and females remains a challenge. Immunisation program managers were interested in understanding the reasons for incomplete coverage through the school-based program and how to improve uptake.

> *"I did want this year to look at, well if we get 85% of dose 1, where are the other 15% going?"*

Several jurisdictions had strategies in place to ensure that as many adolescents as possible were vaccinated through the school system as a way to optimise uptake and track missed doses. Strategies to ensure vaccinations were performed at school included limiting access to vaccinations in general practice and allowing catch-up of missed doses at the next scheduled school vaccination day.

Rollout of the catch-up program for males aged 15 years

The original announcement of the male catch-up program was for males in Year 9 in 2013 and 2014.[26] The PBAC determination was a 2-year catch-up program for males in the 2-year

age group above the ongoing cohort (i.e. up to 15 years old). Program delivery was based on the most appropriate school year for eligible males.[37] All jurisdictions, however, ensured that eligible males aged 15 years in 2013 who were not in the targeted school year could access the free vaccine outside school through community clinics or general practice.

Challenges to the catch-up program

The difference in coverage provided by the male and female catch-up programs was mentioned by four respondents. Eligibility for the male catch-up program was considered too restricted and extending vaccination to all high school males would have improved coverage. Restricting the eligibility age was also thought to disadvantage individuals who find it difficult to vaccinate on time due to life circumstances. In contrast, the whole-of-school catch-up for the female program achieved better coverage and immunisation program managers reported community and parent interest in broadening the age eligibility for the free vaccine for males.

> *"In fact, if we'd run this program like we did the female program, that is up to Year 12, we would have had an excellent uptake, because many parents rang and complained because their sons were in year 11 and year 12, and missed out."*

A large proportion of stakeholders, however, also perceived that adolescent males aged 15 years in the catch-up program were a group where it might be difficult to achieve good coverage. Females in the older age groups in the catch-up program had similarly been harder to reach.

> *"This was a vaccine into a totally new cohort. Now 14 to 15 year olds are really difficult in school. It's a difficult age, as a parent might attest, and so we weren't quite sure how it would go."*

Several immunisation program managers also mentioned that the catch-up programs posed a challenge in terms of the extra number of adolescents to vaccinate and the poorer uptake among older age groups.

Jurisdiction know-how and capacity

Several immunisation program managers and school-based coordinators emphasised the key role of expertise and commitment of their jurisdictions in delivering a successful program, especially given the constraints of time, funding and capacity faced in implementing the program for adolescent males.

Strengths of jurisdiction know-how and capacity

Running the school-based program was the main key jurisdictional strength discussed by immunisation program managers. Integral to a successful school-based program was having a committed workforce with a wealth of experience and expertise to run the program.

Jurisdiction staff are knowledgeable and show initiative in implementing the program. Examples include developing strategies to obtain optimal levels of consent and putting in the effort to reach people from CALD backgrounds.

Immunisation program managers described how their jurisdiction invests time in developing and maintaining staff capacity. Where local councils delivered the program, good collaborations between jurisdiction health departments and local government councils was seen as key to providing a quality program.

School-based providers expressed confidence and satisfaction in delivering the program in a timely and responsive way.

The jurisdictions had access to knowledgeable spokespersons who were able to address community concerns about adverse events early in the female program.

Challenges to jurisdiction know-how and capacity

Immunisation program managers felt that while expertise, staff initiative and commitment was integral to the success of the school-based program, there was a limit to how far jurisdictions could go in delivering the program without further resources.

Immunisation program managers expressed the opinion that the program happened because of the dedication of the jurisdiction to overcome obstacles and that there had been a risk that the program may not have been successfully implemented. A lot of work by the jurisdiction went into resources, contracts and, for the female program, procurement of vaccines.

> *"We weren't resourced additionally to roll this particular program out, and so I guess you could see that as a challenge and making sure that it all went according to plan and luckily it did."*

Western Australia and South Australia successfully adopted strategies to roll out the HPV vaccination program for adolescent males within their funding and capacity constraints while still providing full coverage to all eligible adolescents over the course of 2013 and 2014.

The female and male catch-up programs were big programs that stretched jurisdiction staff and funding and meant finding extra vaccination days at schools.

Some jurisdictions reported difficulty in finding staff for delivering the extended school-based program. Staff turnover in remote areas was also a challenge to the ongoing delivery of the program.

One school-based coordinator mentioned that the extra data collection and recording of dosage data and enhanced adverse events surveillance for the HPV program places a further burden on staff.

Commonwealth/state and territory partnership

Acknowledging some significant project limitations for the implementation of both the female and male programs (i.e. the timeframe required to implement both programs), the Australian Government Department of Health considered the partnership between the Australian government and state and territory governments to be collaborative and productive. The Jurisdictional Immunisation Committee was an effective mechanism for consultation with states and territories and the Commonwealth was encouraged by the willingness states and territories demonstrated to ensure both the female and male programs could be implemented within the pre-determined timeframe.

In reflecting on both the female and male phases of the program, however, many respondents thought there was room for improvement in the collaboration and communication between the states, territories and the Australian government. In particular, state and territories expressed a need to be given more flexibility to deliver the program within their resource constraints.

Program for Indigenous adolescents

Several key stakeholders from Queensland, Western Australia and the Northern Territory discussed their experiences with programs to vaccinate Indigenous young men and women.

These stakeholders' accounts have been supplemented by notes from meetings by the National Aboriginal and Torres Strait Islander Immunisation Network (NATSIIN) that discussed the implementation of the National HPV Vaccination Program for Indigenous adolescents.

Recording Indigenous status

All jurisdictions now record Indigenous status on HPV vaccination consent forms. However, reporting of Indigenous status to the NHVPR is not always complete.

Vaccine uptake and coverage in young Indigenous men and women

Access to remote communities and mobile populations potentially affects coverage. However, stakeholders working with remote Indigenous communities reported that they were successfully reaching eligible young males and achieving good uptake of the vaccine.

> *"Aboriginal Medical Services [AMS's] have a school program that is doing very well… they are not missing many children."*

"Low school retention rates are not affecting coverage, children not at school are captured at home, Aboriginal Health Workers run the program."

One school-based provider observed there was good acceptance of the HPV vaccination program by Indigenous parents and communities.

"Most Aboriginal boys and families are very keen to get their boys vaccinated."

Jurisdictions with remote Indigenous communities had strategies to reach young people in those communities. This included a dedicated nurse educator in the Northern Territory. The HPV vaccination program is often run outside school through community clinics. Adolescents in remote communities are actively followed up by community clinic staff.

"We have to work with the nurse or an Aboriginal health worker to find the young men because they often don't come into the clinic very often."

Other remote area health staff, such as sexual health teams and women's health clinicians, were often enlisted to promote the program in remote communities.

Barriers to vaccinating Indigenous young men in remote communities included long distances between communities, mobility of young Indigenous men, following up for 3 doses, fridge breakdowns and staff turnover.

Medicare Local staff in the Northern Territory and Queensland noted that it is Indigenous adolescents in urban locations rather than in remote communities who are the ones missing out on the vaccine, especially transient populations.

"With the remote area usually the healthcare worker would go and grab them from the community and a lot of the girls that were coming down to [Town] to do their education a lot of them missed out on a few."

Providers from the Northern Territory, Queensland and Western Australia described strategies to reach Indigenous adolescents in urban areas outside the school setting or the community health centre, for example, visiting shopping centres to catch-up females aged 15–17 years.

GPs and practice nurses who were interviewed all reported that Indigenous status was well recorded on practice records. However, they did not have any particular strategies to reach Indigenous adolescents; instead they identified all eligible patients by age, not Indigenous status. Several stakeholders mentioned that their Medicare Locals were active in promoting HPV vaccination to Indigenous young people through outreach services and Aboriginal Medical Services.

Indigenous communication resources

There was a lack of resources specifically for Indigenous parents and young women at the start of the female program so some jurisdictions developed their own.

> *"I am pretty sure [jurisdiction] developed some Indigenous specific like a flyer to go [on outreach days] just to explain what was going on and just really simple language."*

Stakeholders have been using the resources for Indigenous parents and students developed by the Australian Government Department of Health for the extended HPV program that includes males. The Australian Government Department of Health collaborated with jurisdictions in the development of these resources.

The Indigenous resources were seen as sometimes too wordy for remote Indigenous people. Several stakeholders mentioned the need for resources in simple language for some Indigenous communities. The Australian Government Department of Health developed oral recordings on HPV vaccination in 20 Indigenous languages. The use of oral resources were seen by stakeholders as a useful way to reach some groups of Indigenous parents and students.

Stakeholders working with Indigenous communities thought that including a sexual health message in messages to Indigenous parents and young people was important. Several stakeholders mentioned that the sexual health message was missing from the available information resources.

The needs of Indigenous people are diverse so some benefit from special information resources and some prefer to use 'mainstream' resources.

> *"Our Aboriginal team took a whole pile of information out to the celebrations at places and all that sort of jazz and most parents said, 'Oh no, no, we've already got all the normal information from school. It's all good' sort of thing."*

Strengths and challenges of Indigenous resources

Stakeholders commended the Australian Government Department of Health for the development of resources specific to Indigenous people with the extended HPV vaccination program.

> *"It's a real positive initiative by the Commonwealth that they have put so much time and effort into creating resources which are available for use by Indigenous groups."*

The written resources for Indigenous parents/young people were, however, considered too wordy for some people from remote communities.

The verbal resources in Indigenous languages are very well received. As one remote GP noted,

> *"This is a great initiative. It's great to finally have some health information in [Language]."*

One respondent commented that the comics produced for young Indigenous men and women should have included a message that HPV was a sexually transmitted infection. Stakeholders acknowledged sexual health messages for young adolescents can be controversial and sensitive, especially in Indigenous communities, and delivering messages in a culturally sensitive way was an ongoing challenge. Stakeholders involved in Indigenous programs, however, felt it was important to give a clear and succinct message to Indigenous people and there is an ongoing need for consultation around Indigenous information and materials.

Culturally and linguistically diverse populations

The majority of stakeholders (n=12) were not aware of or involved in specific programs to target adolescents and parents from CALD backgrounds. Most of the work done with CALD adolescents and parents involved one-on-one follow-up of consent by school nurses, which could be very resource intensive. This involved providing access to materials in other languages and in some cases providing interpreter services.

> *"It was very demanding on staff resources to get messages to culturally diverse groups because it was more on a one-to-one basis and included ringing parents up, using interpreters, going to meet parents in schools, so it was very resource intensive, but we did it."*

Seven stakeholders mentioned using language resources developed by his/her own jurisdiction, including translated consent forms and information sheets, oral language resources and interpreter services. Three stakeholders stated they relied on the language resources provided on the national HPV website.

Many stakeholders did not consider further outreach to CALD parents and students as necessary because the return of consent forms was high across most cultural groups. Informed consent was mentioned as an issue for some CALD parents as children may be translating HPV information and some CALD parents have poor literacy even in their native language.

One immunisation program manager and one private provider mentioned that the school-based program did not suit the needs of some new arrivals. In regions with high numbers of refugees or other new arrivals there were some initiatives run by general practice or through

council clinics to arrange catch-up vaccinations for new arrivals to supplement the school-based program.

Data

National HPV Vaccination Program Register

The NHVPR was established as part of the National HPV Vaccination Program and commenced operations in June 2008.[38] The NHVPR collects reports of HPV doses for the purpose of notifying individual vaccination status to patients, parents and providers and for reporting population coverage.

Jurisdictions are responsible for notifying doses to the NHVPR for school-based programs. The method of reporting school-based dosage data to the NHVPR differs across jurisdictions. In some jurisdictions, school-based HPV vaccine doses are reported directly to the NHVPR at the local level, for example, by the school-based coordinators or local government. In other jurisdictions, school-based coordinators report doses to a jurisdictional immunisation database and the jurisdiction sends the data on to the NHVPR.

Doses given in general practice are faxed directly to the NHVPR using a reporting form available on the NHVPR website or are recorded directly online via a secure portal. In some jurisdictions, GPs send reports to the jurisdiction database for forwarding to the NHVPR.

Most jurisdictions reported that they calculate coverage using their own vaccination databases. A minority relied on coverage reports from the NHVPR. Immunisation program managers raised a number of issues around calculating coverage.

Determining the denominator was reported as difficult because of variations in eligibility for the vaccine, which may depend either on age or school year. In addition, 3 doses are administered over time and adolescents can complete doses outside the eligible age range or school year. Using school enrolments as a denominator can be imprecise. Cross-jurisdiction school enrolments can skew the denominator. Jurisdiction databases do not always include doses given in general practice so jurisdiction coverage data are not complete.

The Australian Government Department of Health reported no issues for the extension of the NHPVR to include doses for adolescent males.

General practice and the NHVPR

Many stakeholders discussed the barriers for private practice around reporting to and using the NHVPR. Medicare Locals reported that they needed to constantly encourage providers in general practice to report doses to the NHVPR. Jurisdictions expressed some frustration around the lack of reporting of dosage information to the NHVPR by general practice.

Stakeholders generally perceived there was a lack of transparency in the two-way sharing of information between the school-based program and private practice to help coordinate and track catch-up doses.

Stakeholders in the school-based programs thought that in the current program general practice immunisation providers did not administer enough HPV vaccinations to remember to report to the NHVPR. This perception was corroborated by GPs and practice nurses who reported that they did not use the NHVPR frequently enough to stay up to date with the log-on and reporting procedures. It was thought that reporting to the NHVPR by general practice had been better during the female community catch-up program when general practice was administering more doses. Turnover of practice nurses had contributed to less familiarity with reporting to the NHVPR in the current program for males and females.

Stakeholders in the school-based programs noted that some GPs, practice nurses and providers in community catch-up clinics misunderstood the reporting procedures to the NHVPR and expected that HPV doses would be automatically uploaded to the NHVPR from their practice software as is the case with the Australian Childhood Immunisation Register (ACIR).

> *"So they don't know that they're not … they think they're transmitting their data and they're not. It's a bit of a system breakdown in that sense."*

One respondent from private practice reported that the NHVPR was of limited use for checking HPV doses as providers often cannot find patient records of school-based vaccinations on the NHVPR, and patients could not recall the number and timing of previous doses when presenting in general practice for catch-up doses.

> *"So right now and even back then, it's a black hole so far as whether kids have had them or not."*

Immunisation program managers also reported being unable to reliably track doses given in general practice on the NHVPR.

Therefore, the reporting and access to up-to-date dosage information in general practice for the current male and female program was perceived as an impediment to the catch-up of missed doses both for GPs and school-based providers.

Many respondents discussed the complications around reporting via multiple databases potentially leading to lost dosage information. Privacy considerations and cross-state movement of adolescents and families prevented easy exchange of information between jurisdictions and between jurisdiction health departments and general practice.

The late set-up of the NHVPR in 2008 was seen as a barrier to recording doses at the start of the female program. For private practice, the NHVPR did not compare favourably with the ACIR which is a comprehensive database that is used frequently by general practice for multiple vaccines and allows direct uploading of data from the practice computer. Many respondents thought that an expanded ACIR database to include adolescent doses would overcome some of the pitfalls associated with the current dosage reporting process.

Program acceptance

Survey results

Table 2.13 summarises respondents' perceptions of the acceptance of the National HPV Vaccination Program. Almost all respondents agreed that the school-based program, both for adolescent males and females aged 12–13 years, was well accepted by schools, parents, students and providers. Although most respondents agreed that the catch-up program for adolescent males aged 14–15 years was well accepted, there was a small proportion of respondents who thought the male catch-up program was not well accepted, especially by students. There was less perceived acceptance of the community catch-up by young females aged 18–26 years. Only half the respondents agreed that the community catch-up was well accepted by the target group of young adult females. Please also see **Appendix 2.4** for summary of strengths and challenges.

Table 2.13. Acceptance of the National HPV Vaccination Program (n=20)

	By schools %	By parents %	By students %	By providers %
The school-based program for boys aged 12–13 years is well accepted:				
Don't know	5	–	–	–
Strongly disagree	–	–	–	–
Disagree	–	–	–	–
Neutral	–	10	20	5
Agree	60	45	50	30
Strongly agree	35	45	30	65
The school-based catch-up program for boys aged 14–15 years is well accepted:				
Don't know	5	–	–	–
Strongly disagree	–	–	–	–
Disagree	5	5	10	5
Neutral	–	15	15	5
Agree	65	50	55	40
Strongly agree	25	30	20	50
The school-based program for girls aged 12–13 years is well accepted:				
Don't know	10	5	5	5
Strongly disagree	–	–	–	–
Disagree	5	5	5	5
Neutral	–	–	5	–
Agree	40	40	35	20
Strongly agree	45	50	50	70
The school-based catch-up program for adolescent girls aged 13–17 years was well accepted:				
Don't know	10	5	5	5
Strongly disagree	–	–	–	–
Disagree	5	5	5	10
Neutral	5	–	15	–
Agree	65	65	50	35
Strongly agree	15	25	25	50

The community catch-up program for young women aged 18–26 years was well accepted:	By young women %	By providers %
Don't know	15	15
Strongly disagree	–	–
Disagree	15	5
Neutral	20	5
Agree	40	50
Strongly agree	10	25

Respondent interviews

Strengths and challenges of program acceptance

Stakeholders recalled that a major challenge of the National HPV Vaccination Program for adolescent females and young women was the initial acceptance of the program by the community and parents.

At the start of the female program, parents were apprehensive about a new vaccine. There was a lack of knowledge by women about HPV and the link to cancer. It was also the first vaccine that was overtly to do with sexual health (although some respondents mentioned that, in fact, hepatitis B vaccine was the first vaccine for a sexually transmissible infection [STI]). Targeting young females during the period of sexual development in adolescence seemed to be controversial. Parents were concerned that vaccinating their daughter against a sexually transmissible disease may encourage early sexual activity in their daughters.

Acceptance of the program was adversely affected by negative messages from anti-vaccine groups who were quite active at the start of the female program. A number of respondents also mentioned the negative media attention around vaccine safety and perceived adverse events, in particular the media focus on episodes of mass psychogenic side effects.

> *"The female program experienced a lot of negative media coverage by the anti-vaccine groups, which really didn't do the program any good."*

However, stakeholders perceived that the acceptance of HPV vaccination for adolescent females has increased over time and that HPV vaccination was now normalised as just another of many good vaccines accepted as part of the school-based vaccination schedule. Reasons for this included greater community awareness of the relationship between HPV and genital warts and cancer. Millions of doses of vaccine have been delivered through the female program so there is more familiarity with the vaccine and the female program had been going long enough for its success to be evident in terms of safety and clinical outcomes.

Respondents generally agreed that the success of the adolescent female program created a positive message for implementing the male program.

Acceptance of the male program

Most immunisation program managers agreed that there was acceptance and support for the extension of the National HPV Vaccination Program to include adolescent males, both by the immunisation program managers themselves and in their assessment of community attitudes.

Immunisation program managers thought that extending the program was a sensible and natural progression from the female-only program and they commended the Australian government for acknowledging the value of the vaccine for adolescent males.

Stakeholders noted that there was no community backlash for the adolescent male program and the good uptake of the vaccine by adolescent males was an indication of community acceptance of the program.

Early apprehension in the female program around a new vaccine, adverse events and early sexual activity were not seen with the extension of the program to adolescent males.

Respondents remarked that community attitudes to the announcement of the male program contrasted with the initial reaction to the female program.

This was explained by three inter-related factors:

- There was greater awareness and acceptance of the female program over time. The girls paved the way for boys, acting like a pilot for the rollout of the program for adolescent males.
- It was more acceptable to promote an STI vaccine for adolescent males.
- A gender neutral program increases the program's acceptability.

Girls paved the way for boys

Respondents thought that the Australian government and jurisdictions were able to build on lessons learnt from the female program. The male program was easily added to the ongoing female program.

> *"We were already doing the girls so adding the boys in wasn't that much of a problem, once we get past the catch-up phase."*

Systems were put in place for any anticipated adverse events with the male program.

Lessons learnt from the female program also helped in delivering the male program to remote communities.

It was thought that the wider community was now familiar with the female program and there was more community knowledge of HPV infection and its consequences.

> *"… so the girls sort of had to break through the barrier and then the boys have just been a 'walk in the park'."*

The evidence for the clinical effectiveness of the HPV vaccine from the female program was mentioned as one of the best reasons for extending the program to males.

"The abnormal smears … have gone down. I'm not surprised. That's what it's supposed to do, so I'm impressed that it's doing what's supposed to happen. I suppose that's the main comment and I think it's great that boys are being done and I always thought boys should be done."

Immunisation program managers thought the success of the female program had created community expectations that the program would be extended to adolescent males. Parents were asking about when the program for adolescent males would start and once commenced parents were asking for vaccination for their sons in Years 11 and 12.

Stakeholders recalled that the expectation of the extension of the program to adolescent males was reflected in the media.

"… like the media attention around the boys was a wonderful thing, 'we are now getting it for boys'."

Greater acceptability of HPV vaccine as an STI vaccine for adolescent males

A second theme around acceptability of the male program was that HPV as a vaccine for a sexually transmissible infection was not such an issue for boys as for girls. Respondents observed that around the issue of the vaccine and perceived sexual activity, parents seemed more protective of their adolescent girls than their adolescent boys.

"… but for the boys, I mean, you know, clearly people are more than happy to know that their boys are having sex and can be protected."

Several respondents, however, noted that with the greater acceptance of the female program there had already been a decrease in community concerns around the vaccine and sexual activity among young adolescent females.

"I think it is much more accepted now and I think [with the girls] as well with the boys, there is not the sex thing as much."

Gender neutral program increases its acceptability

Most immunisation program managers thought that including both genders in the program was logical. It was a more consistent approach that provided equity for males and females and increased the acceptability of the program.

"I think probably the major strength in that is that there's now a consistent approach including males and females. So it didn't just target the girls. So I think it makes it a more acceptable program now that it includes both males and females."

Several immunisation program managers noted that a gender neutral program was less value laden and removed the focus from vaccinating females only. This both reduced the

burden placed on women to prevent HPV in the population and it reduced the community focus on HPV vaccination as 'encouraging promiscuity' among young girls, which was a prominent discourse with the female program, especially at the beginning.

As a sexually transmitted disease, it made sense to vaccinate both genders and some respondents thought that this should have been the approach from the start.

Some respondents also thought that including both adolescent males and females allowed a sexual health message to be emphasised in the promotion of the vaccine.

One respondent noted that a universal program would protect potentially vulnerable individuals without targeting and stigmatising them.

> *"It will certainly have a great benefit for young gay men and probably older gay men as well as they get older but without having to sort of deal with the fact that this vulnerable group are being targeted in any way."*

It is simpler to communicate with the community and schools that the vaccination is for all adolescents. A school-based program is also simpler to deliver if everyone is included rather than dividing classes.

One school-based coordinator also noted that including adolescent males in the National HPV Vaccination Program would likely improve male uptake of other school-based vaccines and improve males' general health education.

From the providers' perspective, there are economies of scale in vaccinating larger cohorts of male and female students in each school.

Success of the program

The Australian Government Department of Health and the jurisdictions generally considered the National HPV Vaccination Program to be a successful program. Throughout their interviews, respondents expressed positive opinions and sentiments about the value and success of implementing the National HPV Vaccination Program, both the original female and the extended male program.

> *"What changes would you make to a program that really has been very successful?"*

Indicators of success included Australia's reputation for delivering school-based vaccination programs, a safe effective vaccine and a generally smooth rollout of the extended program.

> *"I think the program has progressed really well."*

Key stakeholder recommendations

Stakeholders were asked if they had any recommendations for planning/implementing future national immunisation programs. Below is a summary of the recommendations raised by interviewed stakeholders. Some of these recommendations suggest changes or improvements to program delivery. Some of the recommendations can be taken as comments and observations that endorse and express support for current implementation practices. (See also **Appendix 2.4**.)

Lead-time

- Although 6 months was an agreed lead-time from announcement to rollout, for school programs a lead-time of 8–9 months is in fact needed to allow for the summer school holidays.
- The Australian Government Department of Health should be preparing information resources such as factsheets and websites before the announcement of the program so that they are immediately available at the start of program.
- Advance notice allows governments to be more strategic and be able to make rapid decisions.
- Avoid political announcements for better timing of rollout.

Funding and capacity

- More funding assistance was required from the Australian government for the delivery of the school-based program.
- School-based programs are run by the states/territories and therefore need some Australian government assistance with funding.
- Local councils need more resources to deliver the program and educate the community.

School-based program

- Need to come up with ways of improving the uptake in the older age groups, for example, finding ways to ensure that older students are there on vaccination day.
- It is effective to vaccinate the younger age cohorts in the first year of high school when uptake is better.
- A whole-of-high-school catch-up for the male program would improve coverage and equity of access to the vaccine.
- Additional staff are needed to plan, run and evaluate the growing school-based program.

- Research is needed on building successful models of collaboration between the health and education sectors.
- Pressures on staff on vaccination day need to be carefully managed to avoid putting staff at increased risk of making errors due to an excessive workload.
- GPs need more access to more timely, reliable data about doses received by patients through the school-based program, to allow better catch-up of missed doses in general practice.

Communication and resources

- Resources need to be available early to take to schools and to convey a consistent message.
- More collaboration is needed between the Australian Government Department of Health and the states and territories in developing the messages and resources prior to the rollout of the program.
- More collaboration is needed between the Australian Government Department of Health and general practice and Medicare Locals in the development of communication resources.
- National information resources should highlight and explain the role of local councils in delivering the program and catch-up doses, rather than just referring to GPs.
- There need to be more consistent messages to providers.
- Information and communication strategies should continue to target parents as they are the ones who give consent.
- Mass media may be a more effective way to promote the program, rather than sending paper-based material to schools.
- Keep using the National HPV website as a good resource.
- Social media and SMS reminders are a good way to communicate and should be used more in future communication strategies.
- Bright and engaging presentation of information is important.
- The HPV website should have more content on the need for cervical screening and the sexual transmission of the virus.
- There remains a need to reach people from CALD backgrounds. Although the HPV website has information in 21 languages, there is still a need to develop a greater variety of resources in languages other than English.

- Immunisation is not a substitute for sexual health services. The promotion of HPV immunisation and its benefits should be part of an integrated sexual healthcare message.
- Indigenous people from urban and remote locations can be very different from each other and need different resources and messages tailored to their particular circumstances.
- More resources in simple language are needed for Indigenous people from remote communities.
- Indigenous recorded language messages, however, take up time in general practice consultations so there is a need to evaluate the effectiveness of Indigenous audio language resources.

Cervical Screening Program manager survey results

Table 2.14 shows the percentage of National Cervical Screening Program managers/coordinators who had used selected National HPV Vaccination Program resources. All respondents were aware of the National HPV Vaccination Program website. All but one respondent had used the resources on the website for HPV vaccination information. Only one respondent had used the HPV website for cervical screening information. The other HPV vaccination information resources most frequently used by National Cervical Screening Program managers were the jurisdiction health department websites. Jurisdiction websites and peer-reviewed publications were used by the majority of respondents for cervical screening information, followed by Cancer Council information and media.

Table 2.14. National Cervical Screening Program managers' use of information resources

Resource	Did not use	Used for cervical screening information	Used for HPV vaccination information	Don't know/Not aware
	%	%	%	%
Department of Health National HPV Vaccination Program website	14	14	71	–
Department of Health HPV fact sheet for health professionals	29	–	29	43
Department of Health HPV resources for schools	57	–	14	29
Department of Health HPV resources for students	43	–	29	29
Department of Health HPV resources for parents	43	–	43	14
Department of Health HPV resources for Aboriginal and Torres Strait Islander students/parents	57	–	14	29
Department of Health HPV resources for CALD students/parents	57	–	14	29
NCIRS HPV fact sheet for providers	43	–	14	43
NCIRS HPV fact sheet for patients	43	–	14	43
State/territory-based health department information	14	57	71	–
Medicare Local/GP Division information	57	14	–	14
Medical media (e.g. Medical Observer)	57	29	14	–
Pharmaceutical company website	57	–	14	14
Pharmaceutical company promotional material	57	–	14	14
Vaccine product information	43	29	29	–
Cancer Council information	43	43	29	–
Peer-reviewed publications	29	57	29	–
Newspapers/radio/television	43	43	29	–
Social media (e.g. Facebook, Twitter)	57	29	–	–

Note: Percentages can add to more than 100.

The majority of National Cervical Screening Program managers did not recall receiving any official notification of the National HPV Vaccination Program for females in 2006/2007. Two managers mentioned the media as the main source of notification and one stated that the program manager at the time had received official notification by telephone and email and information brochures.

Most National Cervical Screening Program managers did not recall receiving official notification of the extension of the HPV vaccination program to include males in 2012/2013.

One mentioned first hearing through the ministerial media release and another recalled being notified at a Australian Government Department of Health managers meeting in 2012.

Table 2.15. Distribution (n, %) of National Cervical Screening Program managers' level of agreement on statements relating to the National HPV Vaccination Program and cervical screening outcomes

	Strongly disagree	Disagree	Neutral	Agree	Strongly agree	Don't know/Not sure
Young women who are immunised against HPV may be LESS likely to undertake appropriate cervical screening due to perceptions of greater protection by the vaccine.						
n	0	0	0	4	3	0
%	–	–	–	57.1	42.9	–
Young women who are immunised against HPV may be MORE likely to undertake appropriate cervical screening due to greater awareness of cervical cancer and screening.						
n	2	3	0	0	1	1
%	28.6	42.9	–	–	14.3	14.3
Inadequate or poor knowledge/understanding by young women about the need for cervical screening has contributed to a recent national decline in screening rates among young women.						
n	0	0	1	3	3	0
%	–	–	14.3	42.9	42.9	–
The recent decrease in national cervical screening rates among young women is part of a declining trend among women generally that existed prior to the implementation of the National HPV Vaccination Program.						
n	1	1	0	3	1	1
%	14.3	14.3	–	42.9	14.3	14.3
Recent research and debate has created uncertainty among women about the optimum intervals for cervical screening tests.						
n	0	1	1	3	1	1
%	–	14.3	14.3	42.9	14.3	14.3
The National HPV Vaccination Program in my jurisdiction provides adequate advice/information to adolescent girls and young women about the need for cervical screening.						
n	0	1	1	1	1	3
%	–	14.3	14.3	14.3	14.3	42.9
My organisation actively promotes the National HPV Vaccination Program.						
n	0	2	1	1	3	0
%	–	28.6	14.3	14.3	42.9	–
I am concerned that HPV vaccination will reduce the uptake of cervical screening by young women.						
n	0	2	1	2	2	0
%	–	28.6	14.3	28.6	28.6	–
Overall, HPV vaccination will have positive health consequences for Australia.						
n	0	0	0	2	5	0
%	–	–	–	28.6	71.4	–

Table 2.15 summarises the distribution of respondents' level of agreement on factors potentially affecting cervical screening rates. There was strong agreement that HPV vaccination would reduce rather than increase cervical screening rates in young women. Cervical Screening Program managers also generally agreed that inadequate or poor knowledge/understanding by young women about the need for cervical screening has contributed to a recent national decline in screening rates in this group. Cervical Screening Program managers were not all certain that the National HPV Vaccination Program was promoting cervical screening sufficiently in their jurisdictions. The majority agreed that their own cervical screening program was actively promoting the National HPV Vaccination Program, although two respondents disagreed that their jurisdictions were actively promoting the vaccination program. The majority agreed that they were concerned that the vaccination program would reduce cervical screening rates. All respondents, however, agreed that the National HPV Vaccination Program will have positive health consequences for Australia.

CHAPTER 3. Vaccination coverage

Introduction

As part of the National HPV Vaccination Program, Australia established the National HPV Vaccination Program Register (NHVPR, also referred to as 'the Register' in this chapter). The Register is underpinned by legislation and records doses of HPV vaccine given in Australia, primarily as part of the HPV vaccination program but also vaccinations in females and males received electively outside of the Program's recommended age range. This enables monitoring of coverage in the population and supports the completion of the 3-dose vaccine course by advising providers and vaccine recipients if a vaccine course is incomplete. It also ensures that a permanent accessible record of vaccination is retained in the long term, facilitating evaluation of the vaccination program through linkage to health outcomes data and enabling vaccine recipients to be advised if a booster dose of vaccine is ever required.[39]

The Register commenced operations in mid-2008. Data about doses administered prior to this (April 2007, when the program commenced, onwards) was also sought from providers. All school-based program providers retained records of these doses and uploaded them to the Register retrospectively. Consent forms used in the school-based program include consent to provide the record to the Register. Parents/students can choose to opt out but the rates of doing so are thought to be extremely low. Coverage data for school-administered doses should therefore be virtually complete. In contrast, notification from general practice and other community providers is not universal, with verbal consent required at the time of vaccination and a variety of methods of notification available (mail, fax, secure web portal upload of single dose or multiple doses in a form or spreadsheet or as extracted from commonly used practice management software systems). To facilitate notification during the females catch-up program, the Australian government paid general practitioners an incentive of $6 per dose notified.[39]

As at mid-2013, the Register held records of the administration of over 5.3 million doses of HPV vaccine, with >97% of these for females. This chapter aims to assess the HPV vaccination coverage achieved by the National HPV Vaccination Program using data held on the Register. It considers coverage in females vaccinated through the program through reviewing:

1. The coverage achieved among cohorts vaccinated in the catch-up program during 2007–2009, by age group, state of residence, area of residence/rurality, socioeconomic status (SES) and Indigenous status
2. Coverage by age 15 achieved in the ongoing routine cohorts vaccinated at age 12–13 years, over time and by state of residence

3. Proportion of doses administered by general practice and non-general practice providers by age group, state of residence and over time
4. Timeliness of course completion
5. Methodological considerations
    a. What is the effect on coverage estimates of using Medicare enrolment data instead of Australian Bureau of Statistics (ABS) population estimates?
    b. What is the effect on HPV coverage estimates of making a 'third dose assumption'?

Methods

Coverage was calculated as the number of doses notified divided by estimated resident population (ERP), expressed as a percentage.

Numerator

Notified doses are valid doses counted by their implied dose number (i.e. dose number allocated according to total doses recorded on the Register for that individual and as per CMO guidelines for acceptable dose intervals), as at the date of data extraction from the Register.

Denominator

Mid-year ABS ERPs for females were used as the denominator. For the female catch-up program, ERPs for 2007 were used.

Stratifying variables

'Age' is age as at ERP date.

The ABS 2006 Socio-Economic Indexes for Areas (SEIFA) Index of Relative Disadvantage was used to measure socioeconomic status among females aged 12–13 years in 2007 (same age and delivery method as the ongoing cohorts) in quintiles, using the area of residence of vaccinee at the Local Government Area (LGA) level.

Remoteness was classified using the Remoteness Structure of the Australian Standard Geographical Classification published by the ABS, using the area of residence of the vaccinee at the LGA level. This analysis focused on females aged 12–13 years in 2007 (same age and delivery method as the ongoing cohorts).

The Register groups providers into two types: general practice providers and non-general practice providers. Non-general practice providers include councils, state/territory health departments and other community-based immunisation providers such as Aboriginal Medical Services and Family Planning Services.

Indigenous status is a non-mandatory field for reporting to the Register and was deemed to be of adequate completeness for analysis for the catch-up program cohorts in the Northern Territory and Queensland. Experimental ABS population estimates by single year of age for the Northern Territory and Queensland, based on the 2006 census, were used to estimate the number of Indigenous females. The number of non-Indigenous females was estimated by subtracting these estimates from ABS ERP estimates.

For assessment of timeliness, the proportion completing the course within 6 or 12 months of receiving their first dose of vaccine (recommended schedule for vaccination is 0, 2, 6 months) was estimated per calendar year for vaccinees who had received the third of 3 valid doses within that year (successfully completing the full course of the HPV vaccine).

Methodological analyses

A secondary analysis was undertaken using Medicare enrolment data for females as the denominator, which was provided as at 30 June 2007 at the LGA level. Coverage was calculated by age group (12–17 years and 18–26 years) and by geographical area. Spatial analysis was performed using ESRI ArcMap 10.3.

A secondary analysis was also undertaken using 'episode dose number', which is the dose number reported by the provider, instead of the implied dose number. In this analysis, if a provider(s) reported different doses with the same dose number (e.g. multiple doses assigned as dose 2), only one dose 2 was counted for that vaccinee but the other doses were not assigned (i.e. no higher dose numbers and, if no dose 1 was reported no dose 1, were allocated). Dose 3 results are presented consistent with the 'third dose assumption' method used by the ACIR when calculating coverage for vaccines with multiple doses (i.e. when dose 3 is reported by a provider the assumption is made that previous doses were actually given, whether or not they were reported to the ACIR).

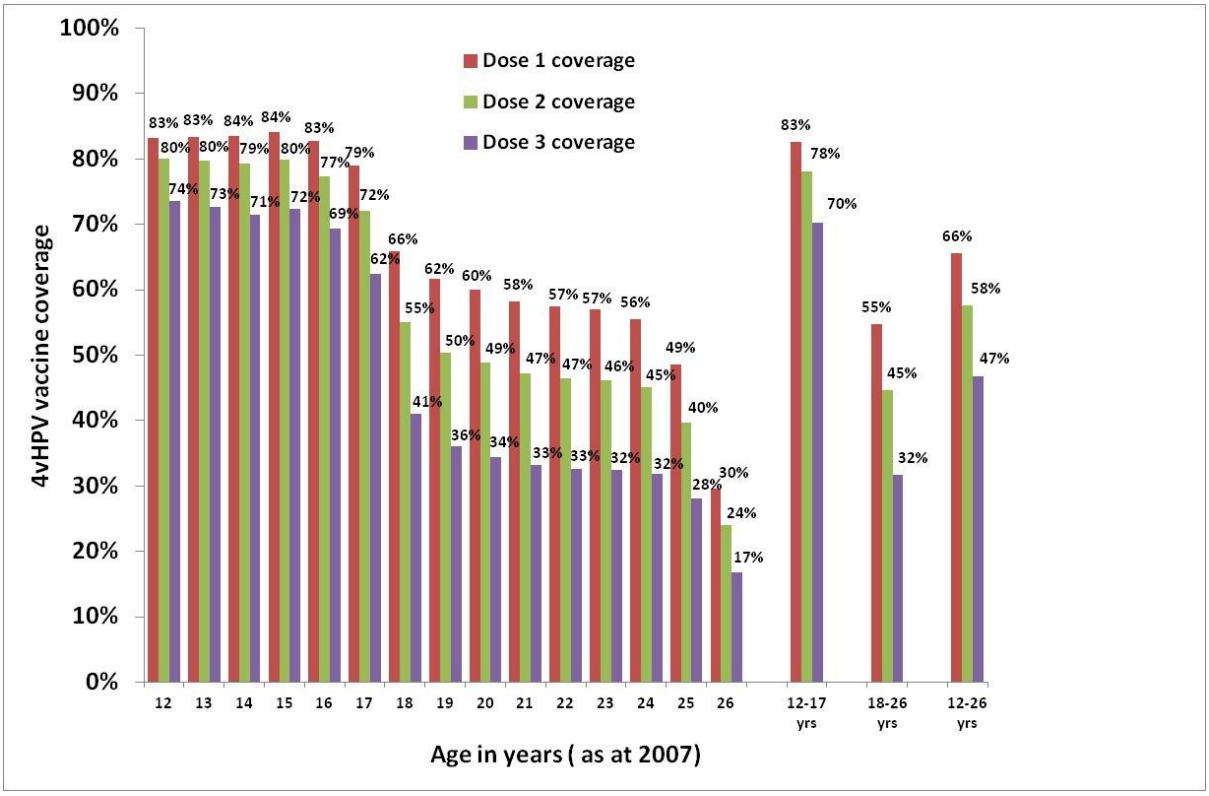
Results

Female catch-up program: National coverage by age

Figure 3.1 illustrates the notified coverage for females in the target age group, 12–26 years in 2007, by dose number. Overall, coverage in the cohort is estimated at 66/58/47% for doses 1/2/3, respectively. Notified coverage is highest in the school-based program, peaking

for dose 1 at 84% in those aged 14–15 years and for dose 3 at 74% in 12-year olds, and declines with age in females 18–26 years. There is a difference of around 10% in notified coverage with dose 1 compared to dose 3 in the school cohorts and a larger discrepancy (>20%) among adult females.

Figure 3.1. National HPV vaccination coverage for females aged 12–26 years in mid 2007, by dose number*



* As notified to the National HPV Vaccination Program Register, Australia (Data as held at September 2011)

Coverage by age and jurisdiction of residence

Table 3.1 details coverage by year of age, dose number and state of residence for females aged 12–17 years in 2007 (i.e. school-based catch-up cohorts). Notified HPV vaccination coverage for females aged 12–17 years nationally was 83/78/70% for doses 1/2/3, respectively. The highest 1-dose coverage achieved by jurisdiction was in 13-year olds in the Australian Capital Territory (91%) and in 12-year olds in the Northern Territory (92%). Both the Australian Capital Territory and Victoria recorded the highest 3-dose coverage for the 12–17-year-old cohort overall at 75%.

Table 3.1. National HPV vaccination coverage (%) for females aged 12–17 years in mid 2007, by dose number and jurisdiction of residence*

Jurisdiction (total doses)	Dose	Coverage (%) by age as at mid-2007 (years)						
		12	13	14	15	16	17	12–17
ACT N=32,319	D1	89	91	89	88	87	85	88
	D2	87	87	85	83	81	79	84
	D3	79	80	77	76	72	68	75
NSW N=628,101	D1	82	83	83	85	82	80	82
	D2	79	79	79	81	77	74	78
	D3	73	73	72	75	70	65	71
NT N=23,036	D1	92	88	82	86	87	81	86
	D2	87	83	77	81	80	73	80
	D3	81	76	70	74	72	63	73
QLD N=402,516	D1	84	84	85	86	85	80	84
	D2	80	79	81	81	79	71	79
	D3	73	72	72	73	71	58	70
SA N=137,085	D1	82	84	83	82	81	78	82
	D2	79	80	79	77	75	70	77
	D3	70	73	70	67	65	59	67
TAS N=42,084	D1	79	77	79	81	74	72	77
	D2	75	71	72	74	66	62	70
	D3	68	64	63	65	57	52	62
VIC N=490,586	D1	87	86	86	87	87	84	86
	D2	84	83	82	83	82	79	82
	D3	79	76	74	75	75	71	75
WA N=173,206	D1	77	78	78	75	72	64	74
	D2	73	74	73	69	66	56	68
	D3	66	65	64	61	56	46	60
National N=1,928,933	D1	83	83	84	84	83	79	83
	D2	80	80	79	80	77	72	78
	D3	74	73	71	72	69	62	70

* As notified to the NHVPR at 30 June 2011

As shown in **Figures 3.1a and 3.1b**, in the 12–15-year-old cohorts coverage gradually increased between 2007 and 2008 with marked increases corresponding with timing of vaccination of individual cohorts in the most populous states. In contrast coverage increased rapidly in the first year of the program among 16- and 17-year olds, with most of the vaccination completed by the end of 2007, reflecting that all jurisdictions targeted these cohorts in the first year (**Figures 3.1c and 3.1d**).

Figure 3.1a. Increase in national HPV vaccination coverage over time, 2007 to 2009, for females aged 12–13 years in 2007, by dose number and age, as notified to the National HPV Vaccination Program Register

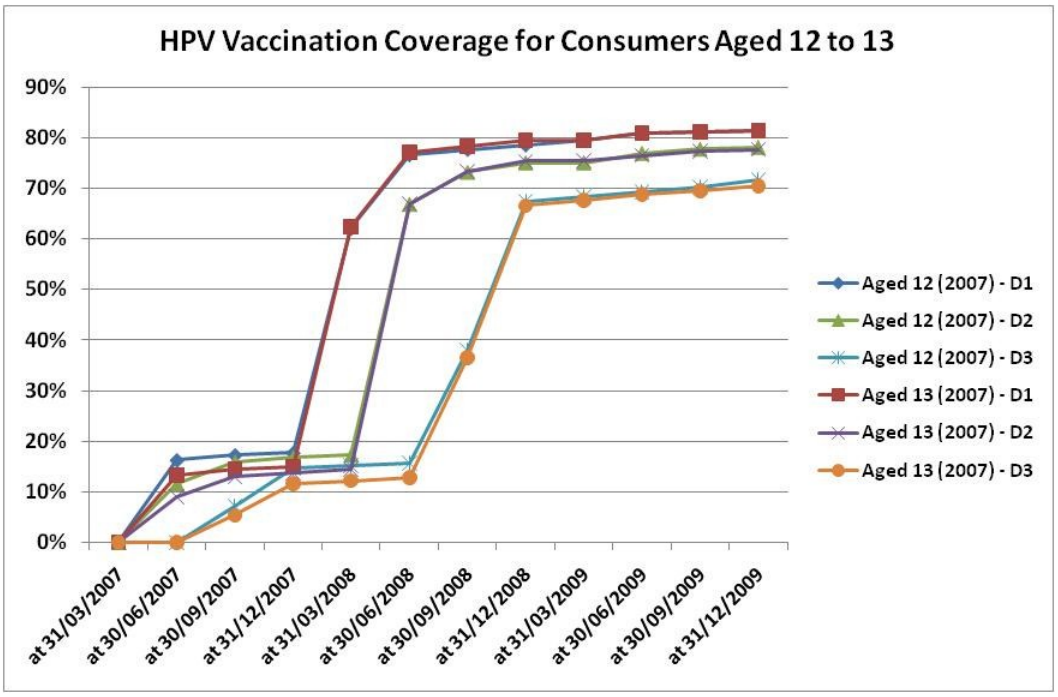


Figure 3.1b. Increase in national HPV vaccination coverage over time, 2007 to 2009, for females aged 14–15 years in 2007, by dose number and age, as notified to the National HPV Vaccination Program Register

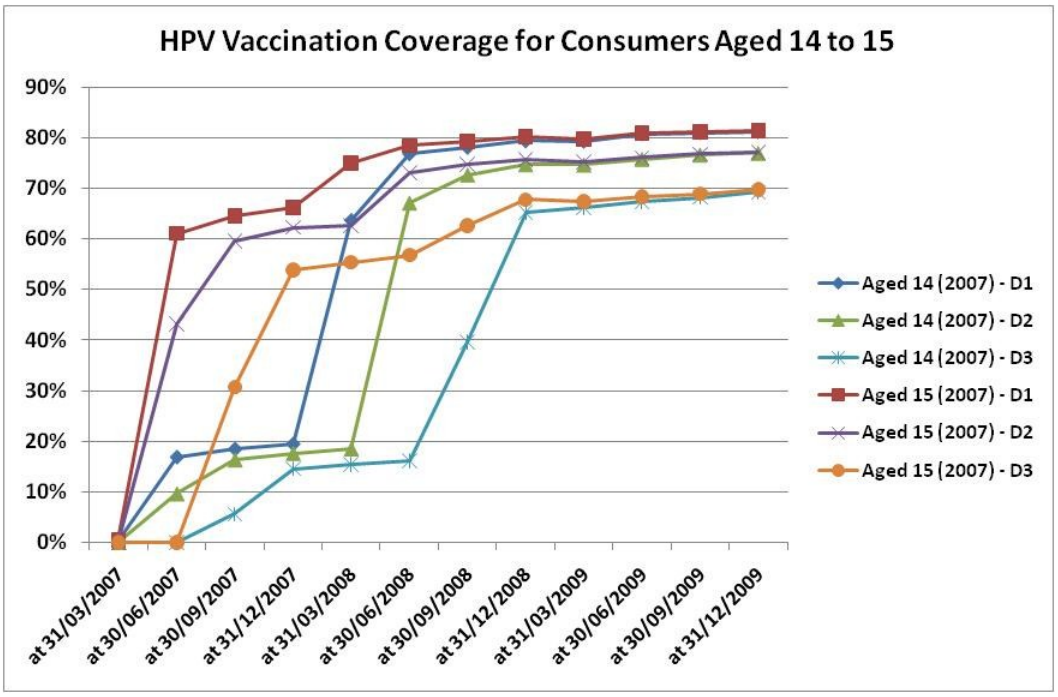


Figure 3.1c. Increase in national HPV vaccination coverage over time, 2007 to 2009, for females aged 16 years in 2007, by dose number and age, as notified to the National HPV Vaccination Program Register

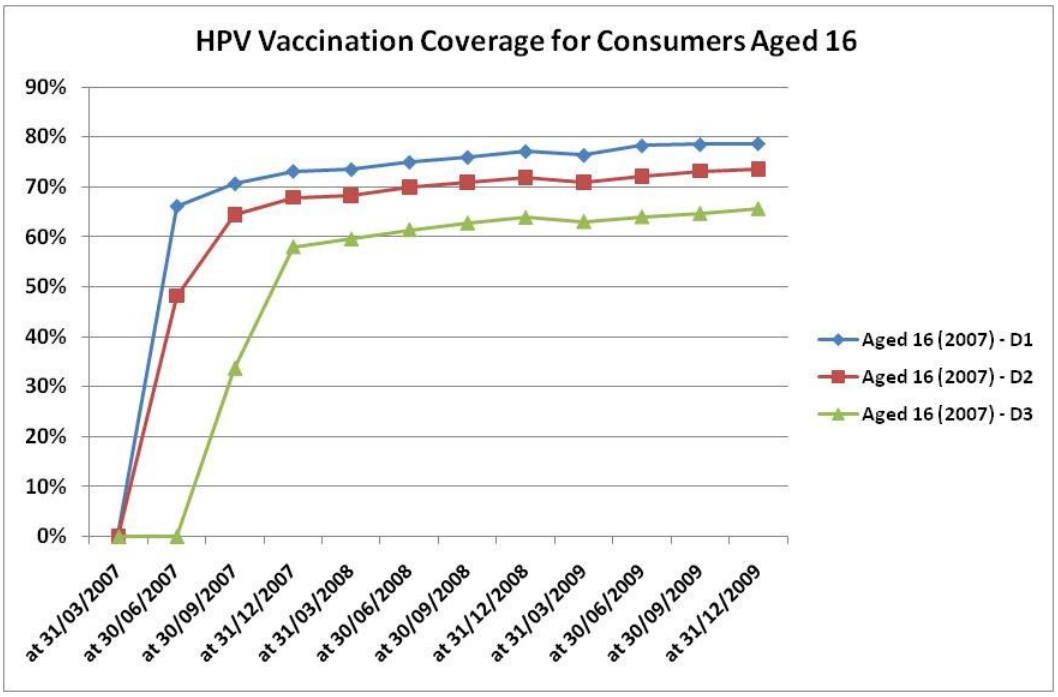


Figure 3.1d. Increase in national HPV vaccination coverage over time, 2007 to 2009, for females aged 17 years in 2007, by dose number and age, as notified to the National HPV Vaccination Program Register

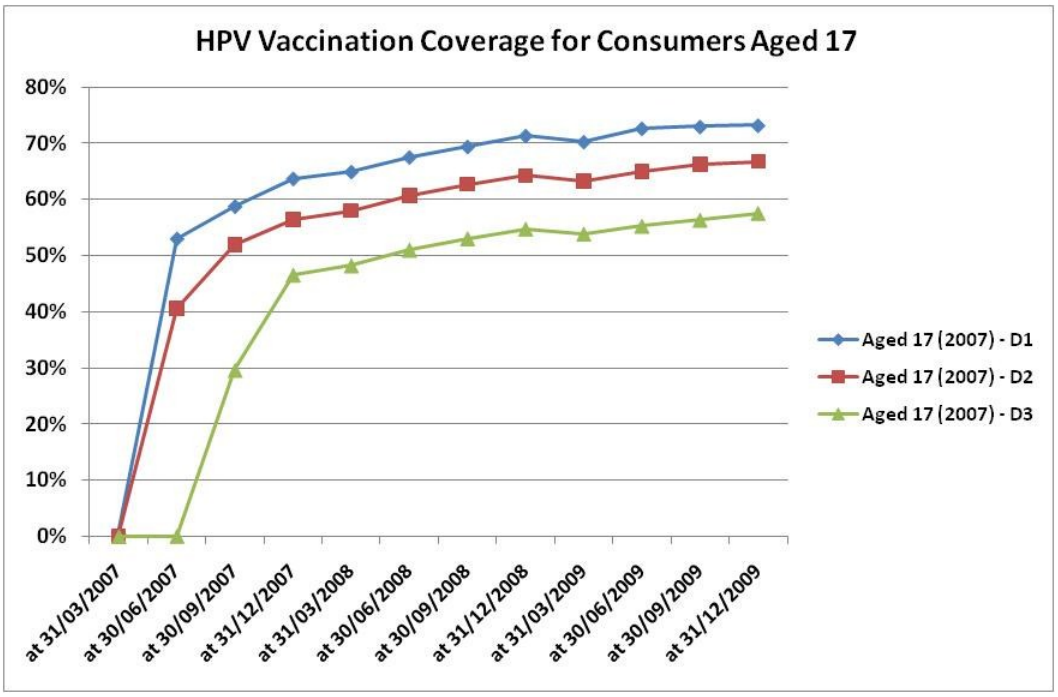


Table 3.2 details coverage by year of age, dose number and state of residence for females aged 18–26 years in 2007 (i.e. community based catch-up cohorts). National notified

coverage for females aged 18–26 years was 55% for dose 1, 45% for dose 2 and 32% for dose 3. Females aged 26 years in 2007, only half of whom were eligible for vaccination given that the general practice/community program started in July 2007 and women who had already turned 27 were ineligible to commence the course, had substantially lower notified coverage than other ages. Coverage for females aged 18–25 years is therefore slightly higher at 59/47/34% for dose1/2/3, respectively. The highest 1-dose coverage achieved by state was in 18-year olds in Queensland (76%). Victoria recorded the highest 3-dose coverage for the 18–26-year-old cohort overall at 37%.

Table 3.2. National HPV vaccination coverage (%) for females aged 18–26 years of age in 2007, by dose number, age and state or territory of residence*

Jurisdiction (total doses)	Dose	Coverage (%) by age as at mid-2007 (years)									
		18	19	20	21	22	23	24	25	26	18–26
ACT N=33,066	D1	64	59	56	58	58	56	54	46	31	53
	D2	54	48	45	47	45	45	43	39	26	43
	D3	41	35	31	33	33	33	33	29	19	32
NSW N=474,102	D1	60	55	53	52	50	50	49	43	26	48
	D2	49	43	41	40	39	38	38	34	20	38
	D3	37	30	29	27	27	26	26	24	15	27
NT N=20,826	D1	74	69	69	64	66	64	61	48	22	59
	D2	63	54	55	50	53	51	48	40	18	47
	D3	49	40	41	34	38	37	35	29	13	34
QLD N=394,872	D1	76	74	72	68	67	67	66	58	33	64
	D2	63	61	60	56	56	55	55	47	26	53
	D3	40	38	37	36	35	36	35	29	13	33
SA N=132,837	D1	69	67	64	61	60	60	59	52	32	59
	D2	57	55	52	50	49	49	49	43	26	48
	D3	42	39	36	35	34	34	34	31	18	34
TAS N=37,326	D1	65	60	63	60	59	57	54	48	31	56
	D2	55	49	51	49	48	47	45	40	25	46
	D3	43	36	38	36	35	35	33	30	18	34
VIC N=470,004	D1	70	63	62	60	60	60	58	52	35	58
	D2	61	53	52	50	50	50	48	44	29	48
	D3	49	41	39	37	37	38	37	34	23	37
WA N=155,461	D1	58	56	55	54	53	52	51	41	25	50
	D2	47	46	44	43	43	41	41	33	20	40
	D3	35	34	32	31	31	30	30	25	15	30
National N=1,718,494	D1	67	62	61	59	58	57	56	49	30	55
	D2	55	50	49	47	46	46	45	40	24	45
	D3	41	36	34	33	32	32	32	28	17	32

* As notified to the NHVPR at 22 March 2011.

Coverage by remoteness

As reported in Barbaro and Brotherton,[40] among females aged 12–13 years in 2007, coverage of the HPV vaccine was relatively uniformly spread across Australia's major cities, regional and remote areas for each dose received, although rates for 3 doses dropped off more markedly in the remote areas (**Table 3.3**). The rate for dose 1 coverage was highest in the very remote areas of Australia (88.5%), 5.1% higher than the rate in major cities (p<0.001). Areas in the outer regional class had the lowest uptake rate at 82.4%. Similarly, for dose 2 the highest coverage rate was in the very remote class (81.8%), while the other four remoteness classes had similar rates (78.2% to 80.2%). The proportion fully vaccinated was highest in the major cities (73.6%) and was up to 3% lower across other remoteness classes to 71.4% in the Very Remote class (rate ratio [RR] 0.97; p=0.01). The areas classified as remote recorded the lowest rate for both dose 2 and dose 3 coverage.

Table 3.3. National HPV vaccination coverage for females aged 12–13 years in 2007, by remoteness*

	Dose 1 % (95% CI)	Dose 2 % (95% CI)	Dose 3 % (95% CI)
Major cities	83.4 (83.3–83.6)	80.2 (80.0–80.4)	73.6 (73.4–73.8)
Inner regional	82.6 (82.3–83.0)	79.1 (78.7–79.4)	72.1 (71.8–72.5)
Outer regional	82.4 (82.0–82.8)	78.8 (78.3–79.3)	72.0 (71.5–72.5)
Remote	83.0 (82.0–84.1)	78.2 (77.0–79.3)	70.1 (68.8–71.4)
Very remote	88.5 (87.2–89.8)	81.8 (80.2–83.3)	71.4 (69.5–73.2)

* Data as at December 2011.

Coverage by socioeconomic status

Among females aged 12–13 years in 2007, HPV vaccination coverage stratified by socioeconomic status was relatively uniform. Nationally, 83.9% received the first dose of the vaccine in high SES areas, compared to 83.1% in low SES areas (RR 0.99; p<0.001) (**Table 3.4**). The difference in coverage by socioeconomic status was slightly greater for 2 doses, although still relatively small, with 81.2% coverage in high SES areas compared to 79.1% in low SES areas (p<0.001). The SES gradient was most pronounced when observing completed vaccination, with the rate in the low SES areas 4.1% below that in high SES areas (71.5% versus 75.6%; p<0.001) (**Table 3.4**).

Table 3.4. National HPV vaccination coverage for females aged 12–13 years in 2007, by socioeconomic status*

	Dose 1 %(95% CI)	Dose 2 %(95% CI)	Dose 3 %(95% CI)
Quintile 1: High SES	83.9 (83.6–84.3)	81.2 (80.9–81.5)	75.6 (75.2–75.9)
Quintile 2	83.3 (83.0–83.6)	79.4 (79.1–79.8)	72.9 (72.6–73.3)
Quintile 3	83.3 (83.0–83.6)	79.9 (79.6–80.3)	73.0 (72.6–73.3)
Quintile 4	83.0 (82.7–83.3)	79.4 (79.1–79.7)	72.6 (72.2–72.9)
Quintile 5: Low SES	83.1 (82.8–83.5)	79.1 (78.8–79.4)	71.5 (71.2–71.9)

* Data as at December 2011.

Coverage by Indigenous status

For vaccinations given during the female catch-up program, notification of Indigenous status to the Register was of insufficient completeness for reporting except in Queensland and the Northern Territory.[41] **Table 3.5** and **Table 3.6** show comparative estimates of coverage by Indigenous status in Queensland and the Northern Territory, respectively, for cohorts aged 10–26 years in 2007. These should be interpreted with caution, given the uncertainty in the accuracy of the denominator data and possible under-reporting of Indigenous status in the numerator. The data show a lower rate of vaccination in Indigenous females of school age in both jurisdictions. The Northern Territory estimates suggest slightly higher rates of dose 3 coverage in young adult Indigenous females, resulting in higher overall dose 3 coverage for 12–26-year-old Indigenous females than for non-Indigenous females.

Coverage by age 15, over time and by state of residence

Due to the varying age of administration of routine HPV vaccination (with children of varying ages in the first year of high school across the country), age 15 is a useful set point for comparing the coverage in the routine cohorts across jurisdictions. Age 15 is the recommended age for international comparisons from the World Health Organization (WHO). **Figure 3.2** illustrates 3-dose coverage by age 15 in jurisdictions over time (data given in **Table 3.7**). Coverage has remained relatively stable over time. Slightly lower coverage is reported for these cohorts at age 15 compared to at earlier ages given the increasing denominator population over time due to net immigration. **Figure 3.3** illustrates the coverage achieved and the varying age at vaccination of the 15-year-old 2011 cohort by jurisdiction. The figure clearly shows these variances in age of administration, with South Australian coverage at age 12 below 5%, while Northern Territory coverage for 12-year olds stands at over 60%. Some earlier vaccination at age 11 occurs in the Northern Territory and

in Tasmania, where some councils have routinely vaccinated girls in the final year of primary school.

Table 3.5. Notified HPV vaccination coverage (%) by Indigenous status and age in 2007, Queensland, Australia*

	DOSE 1 COVERAGE (%)				DOSE 2 COVERAGE (%)				DOSE 3 COVERAGE (%)			
Age at 30 June 2007 (years)	Indigenous	non-Indigenous	Difference	All	Indigenous	non-Indigenous	Difference	All	Indigenous	non-Indigenous	Difference	All
12	80.4	84.7	–4.3	84.4	71.7	80.8	–9.1	80.2	58.0	73.2	–15.2	72.3
13	78.9	84.2	–5.3	83.9	69.2	80.1	–10.9	79.4	56.0	72.0	–15.9	71.0
14	83.8	85.9	–2.2	85.8	71.7	81.2	–9.5	80.6	57.1	72.9	–15.9	72.0
15	80.5	86.4	–5.9	86.1	69.0	81.6	–12.6	80.8	53.5	73.7	–20.2	72.4
16	81.5	86.1	–4.7	85.9	69.2	79.9	–10.7	79.3	54.4	71.0	–16.6	70.0
17	77.5	80.8	–3.3	80.6	62.8	71.6	–8.8	71.1	46.9	57.6	–10.7	57.0
18	70.7	75.8	–5.0	75.5	52.6	63.2	–10.5	62.6	32.6	40.5	–7.9	40.1
19	68.3	74.2	–5.9	73.9	52.4	61.1	–8.7	60.7	33.2	38.5	–5.4	38.3
20	66.8	72.0	–5.1	71.7	52.2	59.9	–7.6	59.5	33.3	37.4	–4.0	37.2
21	60.9	68.8	–7.9	68.4	46.1	56.7	–10.6	56.2	28.7	36.0	–7.3	35.7
22	60.0	67.7	–7.6	67.4	48.1	55.7	–7.7	55.4	28.1	35.3	–7.2	35.0
23	60.8	67.1	–6.3	66.8	47.7	55.5	–7.8	55.2	28.5	35.7	–7.2	35.4
24	59.4	66.4	–6.9	66.1	47.5	55.3	–7.8	55.0	31.1	35.0	–3.9	34.9
25	50.0	58.0	–7.9	57.7	36.8	47.8	–11.1	47.4	22.7	28.6	–5.9	28.4
26	23.2	32.9	–9.7	32.6	18.6	26.3	–7.7	26.0	10.1	13.4	–3.3	13.3
Total	69.4	73.7	–4.3	73.5	57.5	65.0	–7.5	64.6	41.4	49.2	–7.8	48.8

* Data as at December 2010. Experimental ABS population estimates used as the denominator.

Table 3.6. Notified HPV vaccination coverage (%) by Indigenous status and age in 2007, Northern Territory, Australia*

	DOSE 1 COVERAGE				DOSE 2 COVERAGE				DOSE 3 COVERAGE			
Age at 30 June 2007 (years)	Indigenous	non-Indigenous	Difference	All	Indigenous	non-Indigenous	Difference	All	Indigenous	non-Indigenous	Difference	All
12	80.7	99.9	–19.2	91.5	76.0	96.2	–20.2	87.3	70.6	89.0	–18.4	80.9
13	77.5	96.4	–18.9	88.0	72.7	91.1	–18.5	82.9	64.9	84.9	–20.0	75.9
14	75.0	88.0	–13.0	82.6	70.5	82.4	–11.9	77.4	64.8	73.4	–8.6	69.8
15	78.1	90.9	–12.8	85.4	72.4	86.8	–14.4	80.6	64.7	80.2	–15.6	73.6
16	77.9	93.2	–15.3	86.6	73.2	85.1	–11.9	80.0	65.5	76.0	–10.5	71.5
17	69.7	89.9	–20.2	80.8	63.8	78.8	–15.0	72.0	56.0	68.0	–12.0	62.5
18	74.0	73.8	0.2	73.9	68.1	58.1	10.0	62.4	59.2	40.4	18.8	48.4
19	69.1	68.3	0.7	68.6	59.3	49.1	10.2	53.2	51.2	31.0	20.2	39.2
20	65.5	71.1	–5.6	68.8	57.4	52.0	5.4	54.3	48.3	34.5	13.8	40.2
21	55.5	69.7	–14.2	63.7	47.8	51.4	–3.6	49.9	39.0	29.3	9.7	33.4
22	60.9	68.5	–7.7	65.5	53.1	52.2	0.9	52.5	43.2	33.2	10.0	37.1
23	58.0	67.1	–9.1	64.0	50.8	51.7	–0.9	51.4	43.7	33.0	10.7	36.6
24	55.7	62.7	–7.0	60.4	48.9	47.1	1.8	47.7	40.5	30.8	9.7	34.0
25	41.3	50.8	–9.5	47.9	37.3	41.0	–3.8	39.9	32.7	26.8	5.8	28.6
26	14.3	25.6	–11.4	21.9	12.5	20.7	–8.1	18.0	10.8	13.6	–2.9	12.7
Total	66.2	74.3	–8.1	71.1	60.4	63.8	–3.4	62.5	52.9	51.0	1.9	51.7

* Data as at Dec 2010. Experimental ABS population estimates used as the denominator

Figure 3.2. National 3-dose HPV vaccination coverage for females turning 15 years of age, 2007 to 2012, by jurisdiction of residence*

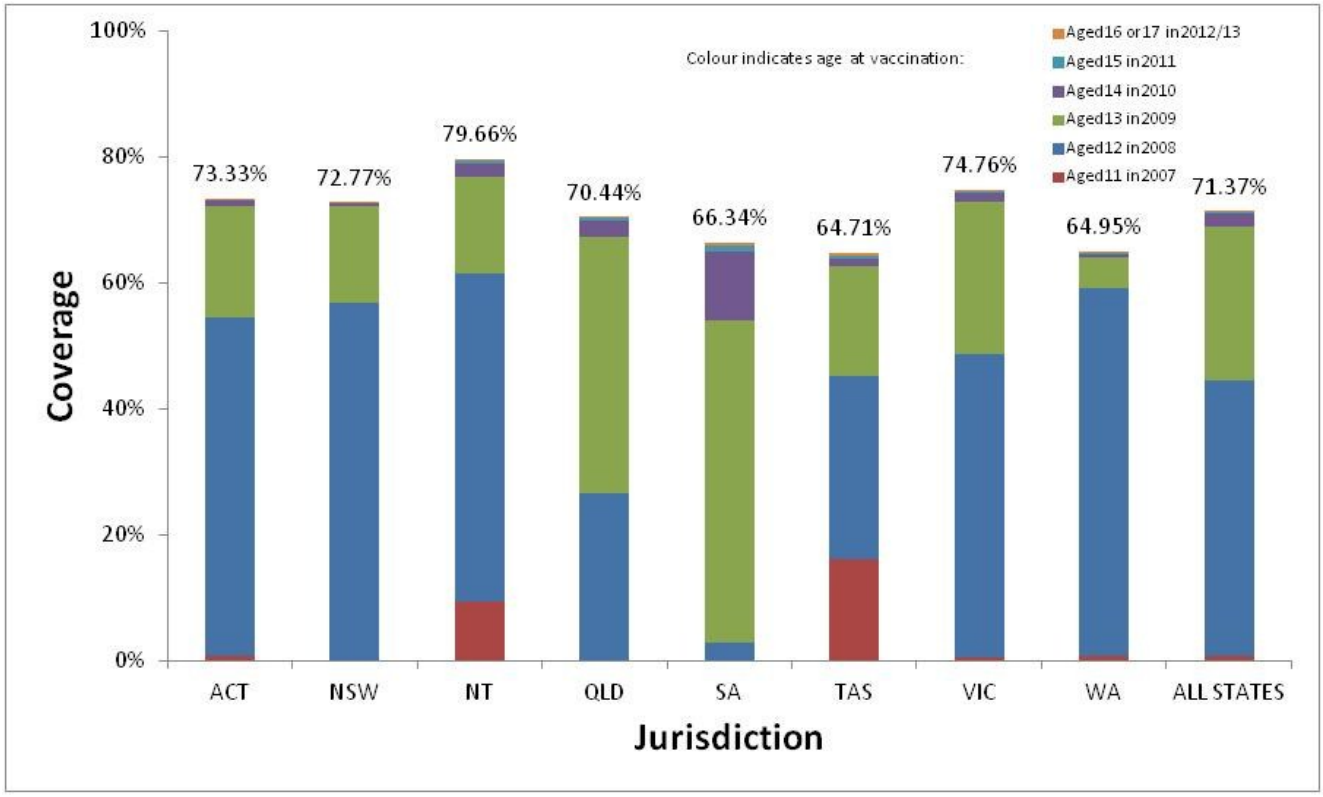
* Data extracted from the HPV Register as at 15 October 2013.

Table 3.7. National 3-dose HPV vaccination coverage for females turning 15 years of age, 2007 to 2012, by jurisdiction of residence*

	ACT	NSW	NT	QLD	SA	TAS	VIC	WA	NAT
2007	75.6%	75.2%	74.3%	73.0%	67.3%	65.3%	75.6%	61.1%	72.5%
2008	76.7%	71.4%	69.9%	71.5%	70.0%	63.9%	73.8%	63.3%	71.0%
2009	79.0%	72.4%	77.5%	69.5%	71.8%	64.1%	75.0%	63.3%	71.4%
2010	77.4%	72.2%	82.8%	70.2%	69.3%	68.5%	76.8%	62.9%	71.8%
2011	73.4%	72.8%	79.7%	70.5%	66.4%	64.8%	74.8%	65.0%	71.4%
2012	74.1%	70.8%	84.3%	68.8%	70.2%	62.8%	73.7%	69.9%	70.9%

* Data extracted from the HPV Register as at 15 October 2013.

Figure 3.3. National 3-dose HPV vaccination coverage estimates for females aged 15 in mid 2011*



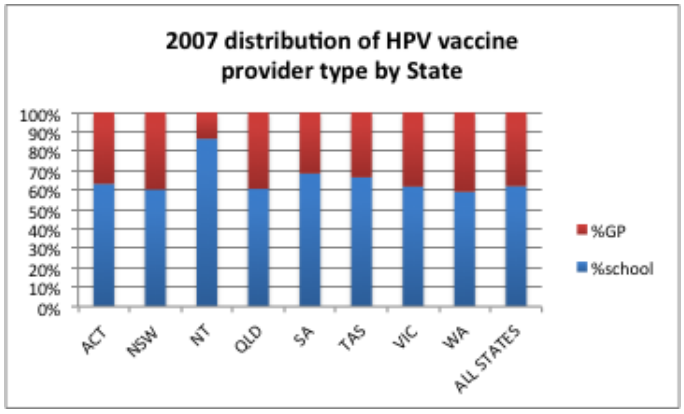
Note: Colour indicates age at vaccination.

* From the National HPV Vaccination Program Register, as at 16 July 2013.

Proportion of doses administered by general practice and non-general practice providers

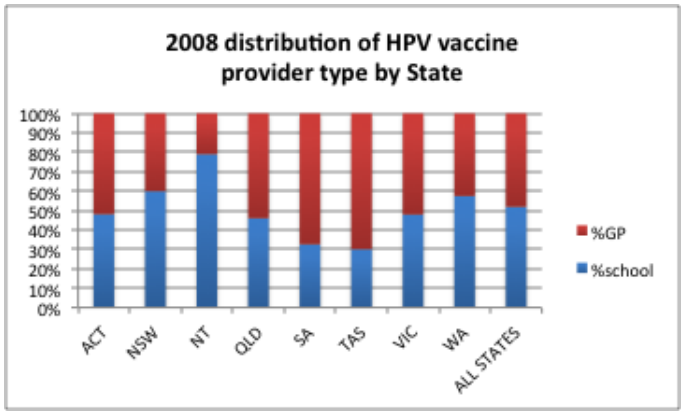
Figures 3.4a–f show the proportion of doses notified to the Register as given by school and community providers or by general practice providers, by year of administration and state. The largest percentage of notified doses given by GPs occurred in 2009 (57.2% nationally), the final year of the female catch-up program. (In 2008, it was 48.1% and in 2007, 38.0%.) Since the female catch-up program, the vast majority of doses are given by school providers (only 6.5% of doses were notified by GPs in 2010, falling to 4.5% in 2011 and 2012). Tasmania is the only state in which the percentage of notifications from GPs has remained above 10% since the catch-up program. (Tasmania had the highest proportion of GP notifications of any state in any year in 2008 at 69.9% of doses. In 2010, 2011 and 2012 the percentages of GP doses for Tasmania were 12.1%, 10.4% and 10.9%, respectively.) The percentage of doses notified by GPs will be influenced by both the actual percentage of doses given in general practice, which varies according to the method for catch-up of missed school doses by jurisdiction, and by the diligence of GPs in notifying administered doses to the Register, which may also vary by jurisdiction.

Figure 3.4a. Distribution of notified HPV vaccine doses by provider type and state, 2007*



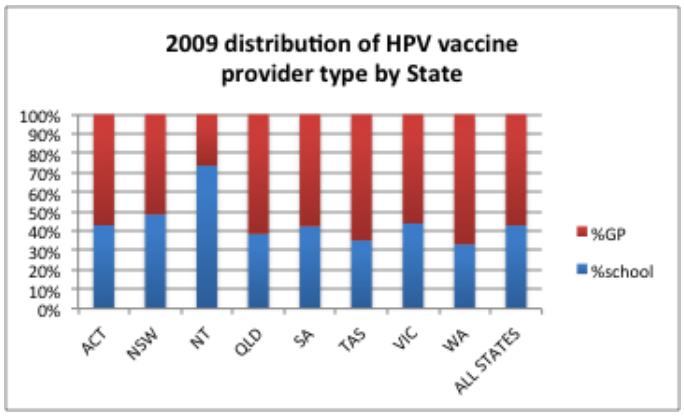
Note: Data as at 9 July 2013. Only includes valid doses given in the reporting period.

Figure 3.4b. Distribution of notified HPV vaccine doses by provider type and state, 2008*



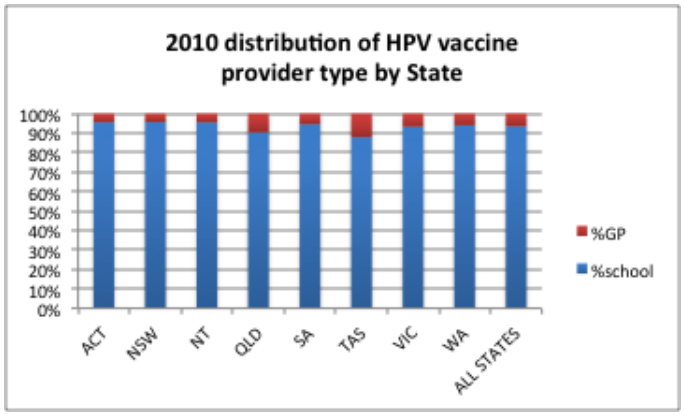
Note: Data as at 9 July 2013. Only includes valid doses given in the reporting period.

Figure 3.4c. Distribution of notified HPV vaccine doses by provider type and state, 2009*



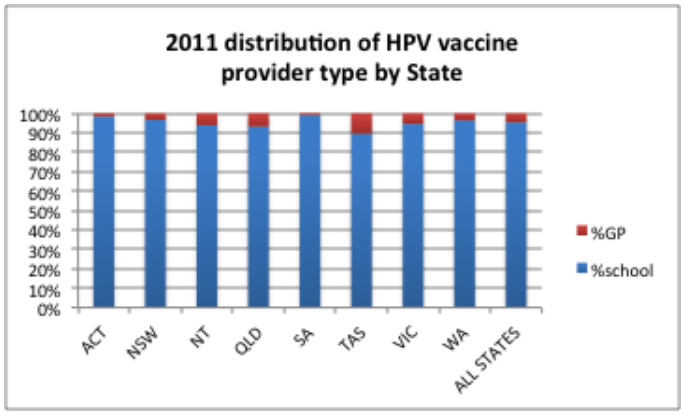
Note: Data as at 9 July 2013. Only includes valid doses given in the reporting period.

Figure 3.4d. Distribution of notified HPV vaccine doses by provider type and state, 2010*



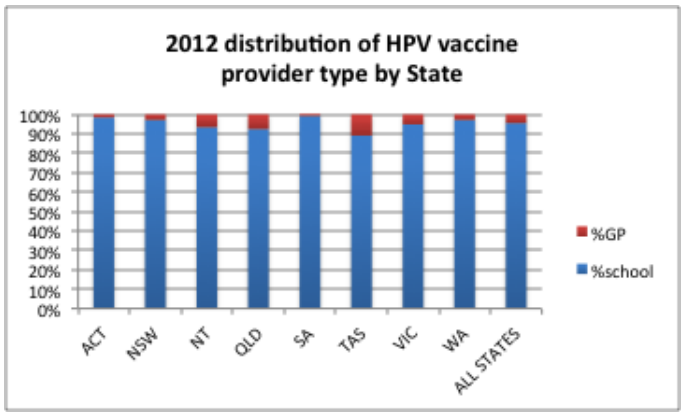
Note: Data as at 9 July 2013. Only includes valid doses given in the reporting period.

Figure 3.4e. Distribution of notified HPV vaccine doses by provider type and state, 2011*



Note: Data as at 9 July 2013. Only includes valid doses given in the reporting period.

Figure 3.4f. Distribution of notified HPV vaccine doses by provider type and state, 2012*



Note: Data as at 9 July 2013. Only includes valid doses given in the reporting period.

Timeliness of course completion

Tables 3.8a–f indicate the proportion of vaccine recipients with course completion within 6 months, 12 months or over 12 months, by calendar year of third dose receipt. The largest proportion of third doses received after 12 months was in 2009, the final year of the female catch-up program. In 2010, this fell to 4.8% and in 2011 and 2012 only about 2.5% of all completely vaccinated females completed their courses more than 12 months after the first dose, with the majority completing between 6 and 12 months after the first dose was received. The Northern Territory consistently has the largest percentage of consumers taking more than 12 months to complete the course.

Tables 3.8a–f. Timeliness of course completion by calendar year of third dose receipt and jurisdiction

Table 3.8a. 2007 calendar year (as held March 2012)

State	Number of consumers (completed course)	Within 6 Months		6–12 Months		More than 12 Months	
		n	%	n	%	n	%
ACT	5,767	5,315	92.2	452	7.8	0	0.0
NSW	87,574	83,967	95.9	3,587	4.1	20	0.0
NT	3,167	2,895	91.4	272	8.6	0	0.0
QLD	50,607	47,283	93.4	3,323	6.6	1	0.0
SA	29,042	28,041	96.6	999	3.4	2	0.0
TAS	8,967	6,934	77.3	2,033	22.7	0	0.0
VIC	91,667	85,521	93.3	6,135	6.7	11	0.0
WA	22,994	22,234	96.7	756	3.3	4	0.0
ALL STATES	**299,785**	**282,190**	**94.1**	**17,557**	**5.9**	**38**	**0.0**

Table 3.8b. 2008 calendar year (as held March 2012)

State	Number of consumers (completed course)	Within 6 Months		6–12 Months		More than 12 Months	
		n	%	n	%	n	%
ACT	11,020	1,610	14.6	9,129	82.8	281	2.5
NSW	210,558	52,461	24.9	154,041	73.2	4,056	1.9
NT	7,503	957	12.8	5,938	79.1	608	8.1
QLD	120,516	24,790	20.6	92,467	76.7	3,259	2.7
SA	31,283	9,604	30.7	20,262	64.8	1,417	4.5
TAS	11,264	3,821	33.9	6,951	61.7	492	4.4
VIC	162,972	53,136	32.6	105,212	64.6	4,624	2.8
WA	63,053	14,973	23.7	46,257	73.4	1,823	2.9
ALL STATES	**618,169**	**161,352**	**26.1**	**440,257**	**71.2**	**16,560**	**2.7**

Table 3.8c. 2009 calendar year (as held September 2012)

State	Number of consumers (completed course)	Within 6 Months		6–12 Months		More than 12 Months	
		n	%	n	%	n	%
ACT	3,951	437	11.1	2,837	71.8	677	17.1
NSW	65,165	12,595	19.3	42,837	65.7	9,733	14.9
NT	3,788	388	10.2	2,294	60.6	1,106	29.2
QLD	63,577	10,473	16.5	42,079	66.2	11,025	17.3
SA	17,576	5,221	29.7	9,228	52.5	3,127	17.8
TAS	5,426	1,448	26.7	2,992	55.1	986	18.2
VIC	59,763	14,355	24.0	35,097	58.7	10,311	17.3
WA	23,400	4,329	18.5	15,016	64.2	4,055	17.3
ALL STATES	**242,646**	**49,246**	**20.3**	**152,380**	**62.8**	**41,020**	**16.9**

Table 3.8d. 2010 calendar year (as held March 2013)

State	Number of consumers (completed course)	Within 6 Months		6–12 Months		More than 12 Months	
		n	%	n	%	n	%
ACT	1,614	11	0.7	1,561	96.7	42	2.6
NSW	31,008	9,439	30.4	20,932	67.5	637	2.1
NT	1,162	86	7.4	841	72.4	235	20.2
QLD	22,214	2,238	10.1	18,127	81.6	1,849	8.3
SA	7,493	2,732	36.5	4,258	56.8	503	6.7
TAS	2,076	603	29.0	1,333	64.2	140	6.7
VIC	25,284	7,125	28.2	17,198	68.0	961	3.8
WA	11,592	467	4.0	10,561	91.1	564	4.9
ALL STATES	**102,443**	**22,701**	**22.2**	**74,811**	**73.0**	**4,931**	**4.8**

Table 3.8e. 2011 calendar year (as held July 2013)

State	Number of consumers (completed course)	Within 6 Months		6–12 Months		More than 12 Months	
		n	%	n	%	n	%
ACT	1,446	9	0.6	1,415	97.9	22	1.5
NSW	29,559	5,665	19.2	23,741	80.3	153	0.5
NT	970	388	40.0	443	45.7	139	14.3
QLD	20,285	1,403	6.9	18,149	89.5	733	3.6
SA	6,931	2,336	33.7	4,372	63.1	223	3.2
TAS	1,989	762	38.3	1,175	59.1	52	2.6
VIC	24,938	7,554	30.3	16,715	67.0	669	2.7
WA	11,870	507	4.3	10,895	91.8	468	3.9
ALL STATES	**97,988**	**18,624**	**19.0**	**76,905**	**78.5**	**2,459**	**2.5**

Table 3.8f. 2012 calendar year (as held July 2013)

State	Number of consumers (completed course)	Within 6 Months		6–12 Months		More than 12 Months	
		n	%	n	%	n	%
ACT	1,518	7	0.5	1,494	98.4	17	1.1
NSW	32,191	3,161	9.8	28,852	89.6	178	0.6
NT	1,183	573	48.4	454	38.4	156	13.2
QLD	21,338	1,468	6.9	19,183	89.9	687	3.2
SA	6,962	2,129	30.6	4,576	65.7	257	3.7
TAS	1,994	913	45.8	1,015	50.9	66	3.3
VIC	26,093	6,769	25.9	18,663	71.5	661	2.5
WA	11,480	431	3.8	10,748	93.6	301	2.6
ALL STATES	**102,759**	**15,451**	**15.0**	**84,985**	**82.7**	**2,323**	**2.3**

Impact of using Medicare enrolments as denominator instead of ABS ERP data

For 2007, ABS population estimates enumerate 58,245 more females across Australia than Medicare enrolments. By single year of age, the ABS population estimate was higher than the number of Medicare enrolments nationally at every age except in females aged 12, 13 and 14 years, in whom only a small variation of less than 250 females nationally was evident (**Figure 3.5**). The impact of using Medicare enrolments as denominator data compared to ABS ERP estimates is shown by dose number and age group (12–17-year-old school cohorts and 18–26-year-old young adults) in **Table 3.9**. Use of Medicare enrolment data improves coverage estimates slightly.

Figure 3.5. ABS and Medicare population estimates, females aged 12–26 years, 2007

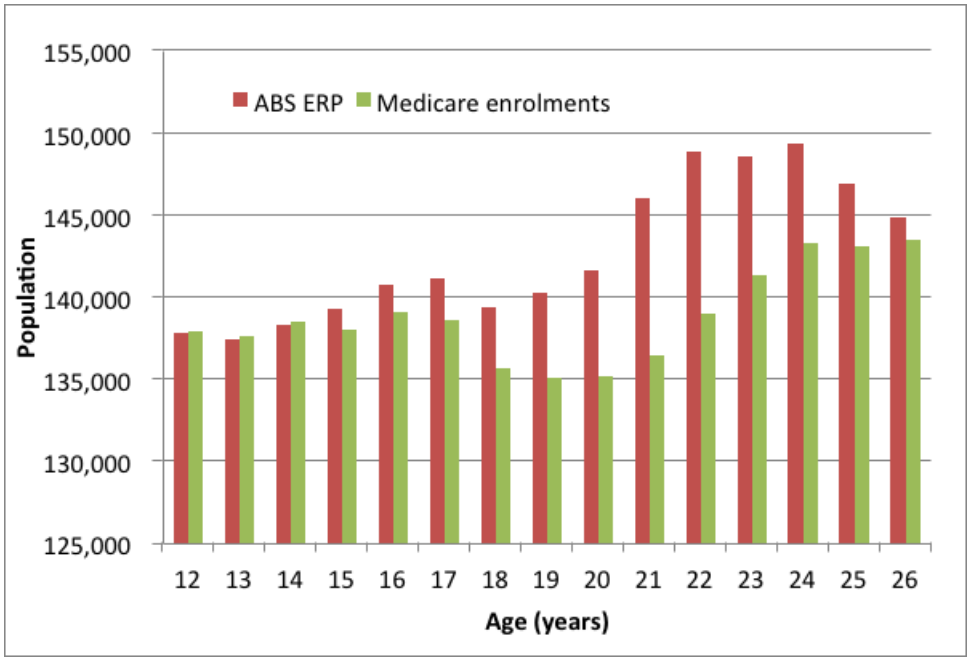


Table 3.9. Comparative vaccination coverage estimates, by dose number and age group in 2007, Australia*

	12–17 years		18–26 years	
	ABS	**Medicare**	**ABS**	**Medicare**
Dose 1	82.9%	*83.3%*	55.2%	*57.5%*
Dose 2	78.2%	*78.7%*	45.0%	*46.9%*
Dose 3	70.4%	*70.8%*	31.9%	*33.3%*

* Data as held at November 2011. Higher estimate in italics. All differences are statistically significant.

For the 12–17-year-old school-age cohort, ABS population estimates were higher than Medicare enrolments for all states except the Australian Capital Territory and the Northern

Territory, the jurisdictions with the lowest populations. For females aged 18–26 years, ABS estimates were higher in all jurisdictions except Tasmania. When results of using the ABS population estimates and Medicare enrolment data were compared by area according to remoteness classification, differences in coverage estimates varied by classification and age group (**Table 3.10**). The biggest difference was in estimates for the 12–17 years age group in remote Australia, where Medicare has higher numbers and therefore lower coverage, resulting in a 10 percentage point difference in the coverage estimate. The biggest difference in the 18–26 years age group was in very remote Australia, where Medicare has lower numbers and therefore higher relative coverage, resulting in a 9 percentage point difference. In both age groups, Medicare has lower numbers resulting in higher coverage in major cities. Conversely, in outer regional and remote Australia, Medicare enrolment data for both age groups has higher numbers than ERP data resulting in lower relative coverage.

Table 3.10. Comparative vaccination coverage estimates, by remoteness classification and age group in 2007, Australia*

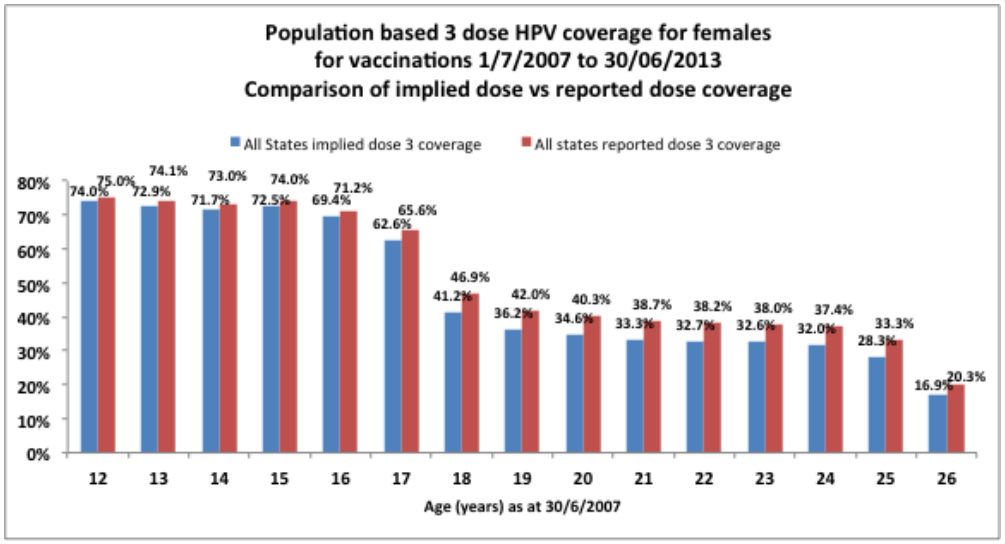
	12–17 years		18–26 years	
	ABS	**Medicare**	**ABS**	**Medicare**
Major city	70.8%	*71.4%*	31.5%	*34.2%*
Inner regional	69.1%	*70.5%*	*33.8%*	31.6%
Outer regional	*68.3%*	67.9%	*31.1%*	28.3%
Remote	*70.2%*	60.4%	*29.4%*	27.3%
Very remote	*72.9%*	70.8%	34.0%	*42.7%*

* Data as held at November 2011. Higher estimate in italics.

Effect of making a 'third dose assumption' on HPV vaccination coverage

Figure 3.6 summarises the difference between coverage calculated using confirmed doses held by the Register and coverage calculated using provider-reported third doses (third dose assumption), by single year of age for the catch-up cohorts.[43] At every age, coverage is higher using the third dose assumption. At ages 12–16 years the difference is only 1–2%, rising to 3% in 17-year olds and around 5% for adult females. Overall, however, accepting provider dose numbering for the 12–26-year-old cohort, and not reassigning duplicate doses to other dose numbers, results in a fall in dose 1 and 2 coverage from 66% to 58% and 58% to 55%, respectively. Dose 3 coverage rises from 47% to 51%.

Figure 3.6. Implied versus reported dose 3 coverage, females aged 12–26 years in 2007, Australia*



* Data as held at July 2013.

Discussion

As recorded on the NHVPR, coverage achieved in the female HPV vaccination catch-up program was substantial, with national coverage of 66/58/47% for doses 1/2/3, respectively, in the 12–26-year-old cohort. Actual coverage is undoubtedly higher, given the need for patient consent to record doses on the NHVPR and apparent under-notification of doses from general practice and community providers outside of the school program.[38,44-46] A population-based mobile phone survey of eligible women (aged 18–26 years in 2007) found self-reported coverage to be 10/15/20% higher for doses 1/2/3, respectively, than that reported on the Register, with a validation substudy able to verify 86% of self-reported doses.[45]

Within the school cohorts, coverage for 12–17-year olds (2007) was 83/78/70% for doses 1/2/3, respectively. Monitoring of coverage in the 15-year-old cohorts over time suggests relatively stable coverage since the female catch-up program. There was and is some variation in coverage achieved by jurisdiction suggesting more effective delivery in some states/territories than others. Also notable is the difference between dose 1 and dose 3 coverage, suggesting that there are barriers to completing the course. Available research suggests that these barriers are largely logistical rather than due to perceived side effects or withdrawal of consent.[41,47] Similarly, an important reason for failure to commence the vaccine course when it is offered through the school-based program may relate to difficulties with effective contact and communication with parents. Generally consent forms and

information are provided to parents via the child bringing them home from school. Significant efforts to review and streamline such processes, and in so doing to optimise school-based vaccination programs, are occurring in every state/territory. The experience in Scotland suggests that higher HPV vaccination coverage can be achieved and maintained in school-based programs through a systematic project management approach to implementation and with strong supporting information systems.[48] There are significant issues around information sharing between the education and health sectors to be resolved in Australia before school-based vaccination can operate most effectively and achieve the highest possible coverage.

The school-based delivery of HPV vaccination appears to be achieving more equal uptake by socioeconomic status than cervical screening in adult women does. There is only a 4.1% difference between 3-dose coverage in areas of lowest and highest SES (and a <1% difference for 1-dose coverage). While the national analysis presented here only focuses on 12–13-year olds, an analysis across the age groups of the catch-up program for females resident in Victoria demonstrated similarly quite equal uptake across the socioeconomic strata in both 18–26-year olds and 12–17-year olds.[49] Similarly, coverage is relatively equal by area of residence, although interestingly 1-dose coverage is highest in very remote areas, probably reflecting the active and dedicated efforts to provide vaccine in these communities. Although data interpretation is somewhat limited due to uncertainty surrounding denominator estimates particularly, Indigenous coverage in the Northern Territory and in Queensland suggests a lower coverage rate in the school-age catch-up cohorts (widening per dose in Queensland by around 5/10/15% for dose 1/2/3, respectively, but relatively steady in the Northern Territory at around 15%). Interestingly, in the Northern Territory, coverage in Indigenous women appears higher than in non-Indigenous women. It is disappointing that data quality was not adequate enough to allow estimates of Indigenous coverage from the catch-up program in other jurisdictions. Work is ongoing to improve the reporting of Indigenous status on consent forms in the school-based programs with updated ABS denominator estimates awaited from the 2011 census.

These analyses also suggest that timeliness may be an issue for Indigenous and/or remote area populations for completing HPV vaccine courses. The Northern Territory, with the highest proportion of the population being Indigenous or residing in remote areas, consistently has the highest proportion of completed courses taking over 12 months to complete. In the school-based program the majority of vaccine courses (83% in 2012) are completed within the recommended timeframe of 6 to 12 months from the first dose. In 2007 only, the overwhelming majority of courses (94%) were completed in under 6 months, reflecting the successful use of the accelerated 0, 1, 4 month schedule in that year to enable the course to be completed by the end of the year given the April program launch date. A

similar pattern of change since the catch-up program was seen in the proportion of general practice providers over time. This proportion peaked in 2009 at 57.2%, in the final year of the catch-up program. Currently only 4.5% of notified doses (2012) are administered in general practice nationally and only in Tasmania does this proportion exceed 10%.

Assessment of the impact on coverage estimates from the catch-up program of using Medicare enrolment data instead of ABS ERP estimates found that, overall, a small increase in 3-dose coverage would result (about 0.4% in school-age cohorts and 1.5% in adult females). Enrolment data is likely to more closely reflect the HPV vaccine eligible population although, as administrative data, its currency is dependent on individuals updating their details in a timely manner. ABS data are adjusted for migration and deaths on an annual basis. A third dose assumption applied to the catch-up program also improves 3-dose coverage estimates by a small amount (from 47% to 51% for the 12–16-year-old cohort overall.) The corresponding adverse impact on dose 1 and 2 coverage when provider allocated dose numbering is used suggests that provider assessment of dose number is not likely to be significantly more accurate than that assigned to doses in date order by the Register. Some under-reporting of first and second doses during the catch-up program will have occurred but currently there is no validation data, akin to previous ACIR reporting assessment,[50] assessing the overall validity of provider reporting of third doses.

Coverage measured at age 15 between 2007 and 2012 indicates that stable coverage is being achieved over time. Routinely measuring and comparing coverage as an indicator of program performance across jurisdictions at age 15 is problematic, however, given the lag time between routine vaccination and this age. However, at present there is no practical alternative, given the varying ages of administration across the country as indicated clearly in **Figure 3.3**. The solution would be to compare coverage achieved in the school cohort vaccinated in each jurisdiction annually by using school enrolment data for the appropriate population in each state or territory. This could be done in the following calendar year or sooner if jurisdictions provide timely data. However, this is not possible at present due to an inability to obtain timely school enrolment information from education departments or schools for the purpose of implementing school vaccination programs and assessing vaccination coverage.

In summary, as measured on the NHVPR, HPV vaccination coverage in Australia has reached a substantial level in a short period of time such that more than half of Australia's young adult women (aged under 30 years) are currently fully vaccinated. The NHVPR is providing an effective way to improve coverage over and above jurisdictional systems, as evidenced by responses to overdue dose reports and vaccination history statements.[51] Key challenges remaining include better measurement of Indigenous coverage, an ability to

accurately monitor ongoing coverage by school populations rather than age, closing the gap between dose 1 and dose 3 coverage, ensuring the doses delivered in general practice are notified to the Register and lifting 3-dose coverage.

CHAPTER 4. Adverse events following immunisation

Introduction

An adverse event following immunisation (AEFI) is defined as “any untoward medical occurrence that follows immunisation and does not necessarily have a causal relationship with the usage of the vaccine”. The adverse event may be any unfavourable or unintended sign, abnormal laboratory finding, symptom or disease.[52] Such an event may be caused by the vaccine(s) or may occur by chance regardless of vaccination.

Globally, HPV vaccination programs have been implemented in over 40 countries.[53] Australia was one of the first countries to license the quadrivalent HPV vaccine Gardasil® (CSL Biotherapies/Merck & Co. Inc.) in 2006.[20] After introduction of the National HPV Vaccination Program in 2007, an Australian government funded program of universal vaccination of adolescent females and a catch-up program for young adult females was implemented, first through a school-based program and then in primary care for women up to the age of 26 years.[22] As expected with any new vaccine, a substantial number of AEFIs were reported nationally to the TGA who coordinate and evaluate the safety of drugs and vaccines. Depending on the reporter and location, AEFIs are notified either directly to the TGA or are notified first to state/territory health departments and then sent on to the TGA.[54]

The safety profile of HPV vaccination reported from clinical trials was acceptable, with serious AEFIs reported in fewer than 0.1% of vaccine recipients.[55] Passive surveillance has been the only formal mechanism used for eliciting AEFI reports for the quadrivalent HPV vaccine in Australia. There was no active or prospective monitoring system in place during the female HPV program that could identify persons experiencing AEFI in a systematic or population-based way. However, case series of certain AEFIs, including anaphylaxis, multiple sclerosis, mass psychogenic illness and pancreatitis, were reported and published by various clinical groups in Australia.[56-61] The reporting of these adverse events and the responses to them are discussed in more detail below.

To support the extension of the National HPV Vaccination Program to include males, the Australian Government Department of Health, in consultation with jurisdictions, implemented a range of enhanced surveillance activities prior to the rollout of the male program, described in more detail below. The TGA has closely monitored the adverse events reported following HPV vaccination since the program was extended to males in February 2013, particularly noting reports from the enhanced surveillance using rapid reporting from school-based programs.

Aims

a. To summarise the key events in HPV vaccine safety in Australia from 1 April 2007 to 30 June 2013

b. To describe Australian passive surveillance AEFI data reported to the TGA following the administration of HPV vaccine to females and more recently to males including:

- Australian passive surveillance AEFI data reported to the TGA for HPV vaccine administered to females for the period 1 April 2007 to 30 June 2013, including reporting rates for the period 1 April 2007 to 31 December 2011, for which register-based vaccine coverage data are available for use as a denominator.
- Australian passive surveillance data for AEFI reported to the TGA for HPV vaccine administered to males for the period 1 February 2013 to 30 June 2013.

Methods

A literature review was undertaken to assess all available published safety data on the HPV vaccine (Gardasil®), including randomised clinical trials, meta-analyses and data from post-licensure studies. Medline was searched using the keyword terms 'adverse event' or 'adverse effect', combined with 'HPV vaccine' or 'quadrivalent HPV vaccine', and with 'surveillance or post marketing studies'. The search identified 1,697 potential references (after removal of duplicates), of which 75 were selected as relevant based on their titles and abstracts. The safety profile of the vaccine was assessed extensively in randomised controlled clinical trials conducted prior to licensure and has been further elucidated following licensure from surveillance data and specific studies in large populations.

De-identified information on all AEFIs reported to the TGA and stored in the Adverse Drug Reaction System (ADRS) database are released to NCIRS twice a year. AEFI records contained in the ADRS database were eligible for inclusion in the analysis if a vaccine was recorded as 'suspected' of involvement in the reported adverse event. Vaccines are classified as 'suspected' if the report contains sufficient information to be valid and the relationship between reported reactions and the vaccine is deemed to be biologically plausible. The causality ratings of 'certain', 'probable' and 'possible' are assigned to individual AEFI records by the TGA. They describe the likelihood that a suspected vaccine or vaccines was/were causally associated with the reported reaction. Factors that are considered in assigning causality ratings include the timing (minutes, hours, etc.) and the spatial correlation of symptoms and signs in relation to vaccination, and whether one or more vaccines were simultaneously administered. However, in many instances a causal

association between vaccines administered to an individual and events that subsequently occurred cannot be clearly ruled in or out. In addition, children in particular often receive several vaccines at the same time. Therefore, all co-administered vaccines are usually listed as 'suspected' of involvement in a systemic adverse event as it is usually not possible to attribute the AEFI to a single vaccine.

AEFI are defined as 'serious' or 'non-serious' by the TGA, based on information recorded in the database using criteria similar to those used by the WHO[17] and the US Vaccine Adverse Events Reporting System (VAERS).[62] Each AEFI report lists one or more symptoms, signs and/or diagnoses, which are coded by TGA staff from the reporter's description into standardised terms using the Medical Dictionary for Regulatory Activities (MedDRA®).[63] Previously, in order to analyse the data, MedDRA coding terms were grouped to create a set of reaction categories that were analogous to the reactions listed and defined in *The Australian Immunisation Handbook*. However, the methodological framework of reporting of adverse events has been recently reviewed by NCIRS in collaboration with the TGA and a revised format for AEFI analyses using MedDRA preferred terms (PTs) has been developed. For this report, the new format using MedDRA PTs was used for data analysis.

All data analyses were performed using SAS software version 9.3 (SAS Institute Inc., Cary, NC, USA). The distribution of AEFI records was analysed by age, gender and jurisdiction. AEFI reporting rates per 100,000 administered doses were estimated using the dose data from the NHVPR, extracted in December 2012 by age, jurisdiction, provider type (general practice and non-general practice), dose numbers (dose 1 – dose 3) and year of vaccination.

Results

Key events in HPV vaccine safety in Australia

In the pre-licensure clinical trials of the quadrivalent vaccine, the frequencies of most AEFI following HPV vaccination were not greater than those in the comparator groups (i.e. non-HPV vaccine or placebo control).[64] The most common systemic adverse experiences reported were headache and fever. There was no significant difference between vaccination and placebo groups.

Early in the implementation of the National HPV Vaccination Program in Australia, on 7 May 2007, a vaccine safety concern arose at a girls' school in metropolitan Melbourne where 26 females aged 12–17 years presented to the school's sick bay within 2 hours of the first dose of HPV vaccine with symptoms including dizziness, syncope and neurological complaints. Four girls were transported by ambulance to a nearby paediatric hospital with a range of symptoms, including palpitations, dizziness, syncope or collapse, weakness and aphasia.[57]

The event triggered widespread national and international media coverage, but was thoroughly investigated by the Victorian SAEFVIC (Surveillance of Adverse Events Following Vaccination in the Community) and it was concluded that no serious vaccine attributable events had occurred. The episode was characterised in a subsequent publication as fulfilling criteria for a mass psychogenic illness.[57] This event highlighted the importance of a rapid response to AEFI that includes individual case evaluation and risk communication.

Another potential vaccine safety signal (defined as "reported information about a previously unknown or incompletely documented but possible causal adverse event following vaccination"[65]) was identified in late June 2007 in New South Wales (NSW) where seven cases of anaphylaxis following quadrivalent HPV vaccination were reported.[56] NSW Health convened a panel of 13 people with a range of expertise (program delivery, paediatric allergy, surveillance of adverse events after vaccination and public health) to identify and review reports of adverse events following HPV vaccination. Following detailed analysis and review, the rate of anaphylaxis in the 2007 school-based HPV vaccination program was reported to be higher than published rates for other vaccines[56] and was comparable only to the rate following administration of vaccines containing bovine gelatin in Japan.[66] However, the estimated rate was still an order of magnitude less common than the WHO categorisation of 'very rare' adverse events after immunisation (<1 in 10,000).[65] Subsequent to this, the TGA estimated the rate of anaphylaxis based on doses distributed throughout Australia to be lower, at 2.6 episodes per million.[67] The rates for other vaccines given to children and adolescents range from 0 to 3.5 per million doses in international studies.[68]

The following year, in 2008, there was a case report from NSW of acute pancreatitis in a 26-year-old woman who developed symptoms 4 days after the first dose of the quadrivalent HPV vaccine.[58] Around the same period, from the USA, 10 cases of pancreatitis were reported to VAERS. However, all these cases had other risk factors and, because of the low numbers of reports, no statistical comparisons were possible.[69] The likelihood of HPV vaccination being causally related was considered unlikely.

In September 2008 in NSW, Sutton et al. published a report of five patients presenting with multifocal or atypical demyelinating syndromes described as multiple sclerosis (MS) within 21 days of receiving the quadrivalent HPV vaccine.[61] Following these reports the TGA established a Gardasil Expert Panel (GEP), chaired by Nobel Laureate Professor Peter Doherty, to evaluate the safety of HPV vaccine. The Panel found the incidence of demyelinating disorders, including MS, following Gardasil® to be no higher than would be expected by chance. The GEP also concluded that the rate of anaphylaxis was similar to that associated with other vaccines.[67]

In 2009, two cases of lipoatrophy of the injection site following the quadrivalent HPV vaccine were reported from Victoria.[60] Lipoatrophy has been previously reported following injections with various medications and vaccines (diphtheria, pertussis and tetanus). In the USA there have been no reports of lipoatrophy secondary to HPV vaccination found in the VAERS database. In a retrospective case series, SAEFVIC identified four cases of complex regional pain syndrome type 1 (CRPS-1) temporally associated with HPV vaccination, reflecting a known complex pain response to a painful stimulus.[71] This condition has been implicated as of sufficient public and media concern following HPV vaccination in Japan that the HPV vaccine is currently not actively recommended in that country.[72]

In the USA, vasovagal syncope was reported to VAERS at a rate of 8.2 per 100,000 distributed vaccine doses.[69] This is very similar to the findings of an analysis of Victorian AEFI data which found a reporting rate of syncope after quadrivalent HPV vaccine of 7.8 per 100,000 doses distributed.[73] Nationally the rate was lower at 2.5 per 100,000 doses distributed,[74] which may reflect the differing state-based AEFI reporting and clinical review systems within Australia.

In February 2013, the National HPV Vaccination Program was extended to males aged 12–13 years through the school-based program, including a 2-year catch-up program for males aged 14–15 years until the end of 2014. To support the extension of the National HPV Vaccination Program to males, in October 2012 the Australian Government Department of Health established the HPV Implementation Working Group as a time-limited Working Group of ATAGI, to consider the need for enhanced monitoring of AEFI following HPV vaccination of males and females. The Working Group proposed a number of enhancements to the existing AEFI surveillance system which were subsequently implemented by the Australian Government Department of Health. These include:

- Communication activities targeted at immunisation providers, the public and media on the safety of the HPV vaccine and the importance of timely reporting of AEFI.
- Rapid school-based reporting of four acute significant AEFI following HPV vaccination to the TGA in all jurisdictions (applicable to first dose only). The four conditions were: anaphylaxis; generalised allergic reaction; loss of consciousness (simple faints, faints with injury, faints with convulsion); and any condition requiring emergency department attendance or hospitalisation.
- A regular teleconference between members of the TGA, the Office of Health Protection (OHP) and Jurisdictional Immunisation Coordinators (JIC) to discuss HPV AEFI reports during administration of dose 1.

- Active surveillance of presentations to emergency departments following HPV vaccination (in NSW only).
- Development of a Protocol for National HPV Vaccination Program Action and Communication to ensure a nationally consistent program response to a potential or confirmed safety signal after HPV vaccination.
- The Adverse Events Following Immunisation – Clinical Assessment Network (AEFI–CAN) HPV Pilot, a pilot project aimed at increasing collaboration and linkage between vaccine safety clinics across Australia to facilitate provision of more standardised information on significant/unexpected AEFI following the expansion of the National HPV Vaccination Program to males.

As discussed in more detail below, no new or serious safety concerns have been identified in males or females.

Table 4.1. Chronology of significant safety concerns associated with HPV vaccination in Australia, April 2007 to June 2013

Year	Month	Vaccine safety event	Response
2007	May	Episode of mass psychogenic illness at girls' school in Melbourne Victoria.[57]	
2007	June	A potential vaccine safety signal was identified in NSW with 7 cases of anaphylaxis following quadrivalent HPV vaccination. In addition, 13 cases of possible allergic reactions were also notified.	An expert panel was convened by NSW Health and an investigation was initiated. The rate of anaphylaxis in the 2007 school-based HPV Vaccination Program was found to be higher than reported rates for other vaccines[56] but still lower than the WHO categorisation of adverse events after immunisation that are 'very rare' (<1 in 10,000).[65] Communication to schools/providers to raise awareness of and promote correct management of AEFI, including anaphylaxis. The estimated rate of anaphylaxis based on doses distributed in Australia is 2.6 per million.[67] The rates for other vaccines given to children and adolescents range from 0 to 3.5 per million doses in international studies.[68]
2009	January	Sutton et al. reported five NSW patients presenting with multifocal or atypical demyelinating syndromes within 21 days of receiving the quadrivalent HPV vaccine.	Following these reports the TGA established a Gardasil Expert Panel, chaired by Nobel Laureate Professor Peter Doherty, to evaluate the safety of Gardasil® vaccine. The panel found the incidence of demyelinating disorders, including MS, following Gardasil® to be no higher than would be expected by chance. The GEP also concluded that the rate of anaphylaxis was similar to that associated with other vaccines.
2009	June	Two cases of lipoatrophy following the quadrivalent HPV vaccine have been reported from Victoria by Ojaimi et al.[60] There were 4 cases of complex regional pain syndrome type 1 (CRPS-1) temporally associated with HPV vaccination.	CRPS-1 reflects a known complex pain response to a painful stimulus which is one of the reasons Japan has reduced the HPV program.[71] Enhanced awareness of this syndrome and its potential to occur following immunisation in the paediatric population is vital to the prompt and effective management of this condition in children and adolescents.
2013	June 2012 to February	Announcement of/planning for extension of the National HPV Vaccination Program to males as a school-based program for males aged 12–13 years as well as catch-up cohorts for all males aged 14 and 15 years delivered over 2 years until the end of 2014.	To support the extension of the National HPV Vaccination Program to include males, in October 2012 the Australian Government Department of Health established the HPV Implementation Working Group as a time-limited Working Group of ATAGI, to consider the need for enhanced monitoring of AEFI following HPV vaccination of males.
2013	February to June	Enhanced surveillance in males for anaphylaxis, generalised allergic reaction, loss of consciousness (simple faints, faints with injury, faints with convulsion) and any condition requiring emergency department attendance or hospitalisation.	No new or serious safety concerns have been identified in males or females. No indication that HPV vaccination is associated with any increase in autoimmune, neurological or vascular diseases.

2013	July	Since July 2013, enhanced surveillance is also occurring through the introduction of monthly AEFI teleconferences between the TGA, OHP and JIC.	

Analysis of AEFI reports for HPV vaccine in the TGA ADRS database

The ADRS database included a total of 2,460 AEFIs following vaccination with HPV vaccine during the period 1 April 2007 to 30 June 2013. The highest annual number of cases (n=765; 31%) was reported in 2007 with the commencement of the school-based National HPV Vaccination Program and catch-up program for young adult females in April 2007. The number of reported AEFIs substantially reduced in the following years (765 in 2007; 542 in 2008; 159 in 2009; 80 in 2010; 139 in 2011; and 160 in 2012). However, as anticipated, the numbers of reported AEFIs increased in 2013 (n=615) following commencement of HPV vaccination for males in February 2013, which included enhanced surveillance for AEFI for both females and males. Of the 615 reports in the first 6 months of 2013, 341 were reported for males and 273 for females.

Denominator data for doses of HPV vaccine administered is available from April 2007 to December 2011 for calculation of reporting rates. Results are presented for two time periods: 1) 1 April 2007 to 31 December 2012 (with reporting rates available to December 2011); and 2) 1 January 2013 to 30 June 2013.

Adverse events reports following HPV vaccination in females, April 2007 to December 2012

There were a total of 1,845 reports of adverse events following receipt of HPV vaccine during the period 1 April 2007 to 31 December 2012. All of these reports were for females except for 2 reports for infant males whose mothers were vaccinated in pregnancy. Of the reports in females, 34% (n=635) were aged 12–13 years, 32% (n=590) were aged 14–17 years, 27% (n=506) were aged 18–26 years, and 3% (n=47) were aged >26 years; only 2% (n=39) were aged <12 years (**Table 4.2**). A total of 7% (n=129) of records listed outcomes defined as 'serious'. These included 119 hospital admissions, 6 reports of life-threatening events and 4 cases reported as 'recovered with sequelae'. All the reports of life-threatening events following vaccination were in females vaccinated with HPV vaccine only and were in the 16–26 years age group. Of the 129 serious records, 86% had a causality rating of 'possible' while 14% were coded as either 'certain' or 'probable'. HPV vaccine was the only suspected vaccine in 1,505 (82%) AEFI records. Twenty per cent of all records had causality ratings of either 'certain' (15%) or 'probable' (5%), while 80% were coded as 'possible'. Of all the reports coded as 'certain', 55% were injection site reactions.

Figures 4.1 and **4.2** show trends over time in the number of AEFI reported following HPV vaccine (**Figure 4.1**) and reporting rates per 100,000 doses (**Figure 4.2**). Rates peaked in the year of the vaccine's introduction in 2007 for all age groups and declined substantially in the following years except for a slight increase in the 12–13 years age group in 2011 (**Figure 4.2**). The overall reporting rate was 34.8 per 100,000 doses administered, and the rate of reports classified as serious was 2.5 per 100,000 doses. Rates fluctuated over time with peaks in 2007 and 2011. The peak in 2007 was expected as it was the first year of inclusion of the HPV vaccine on the NIP. Although an increase was observed in 2011, it was not statistically significant (**Figure 4.2**).

Table 4.2. Adverse event reports following HPV vaccination, TGA Adverse Drug Reaction System database, 1 April 2007 to 31 December 2012

Age group (years)	AEFI records* (n)		Vaccine doses* (n)	Reporting rate per 100,000 doses (95% CI)†	
	Total	Serious		Total	Serious
<12 years	39	1	79,732	44.1 (28.5–58.1)	1.3 (0.0–7.0)
12–13 years (School-based program)	635	29	1,425,115	34.4 (31.4–37.6)	1.4 (0.9–2.2)
14–17 years (Total school catch-up)	590	54	1,496,342	39.1 (36.0–42.4)	3.6 (2.7–4.7)
18–26 years (Total general practice/ community catch-up)	506	41	1,775,874	28.4 (26.0–31.0)	2.3 (1.6–3.1)
>26 years	47	4	68,542	64.2 (46.5–86.2)	2.9 (0.3–10.5)
Total	1,845	129	4,845,605	34.8 (33.1–36.5)	2.5 (2.0–2.9)

* An AEFI record may list more than one vaccine. AEFI records are not shown if both age and date of birth were not reported

† Reporting rate per 100,000 doses are calculated from 1 April 2007 to 31 December 2011.

Figure 4.1. Number of reports of adverse events following HPV vaccination for females aged 12–13 years, 14–17 years and 18–26 years, TGA Adverse Drug Reaction System database, 1 April 2007 to 30 June 2013, by year of vaccination

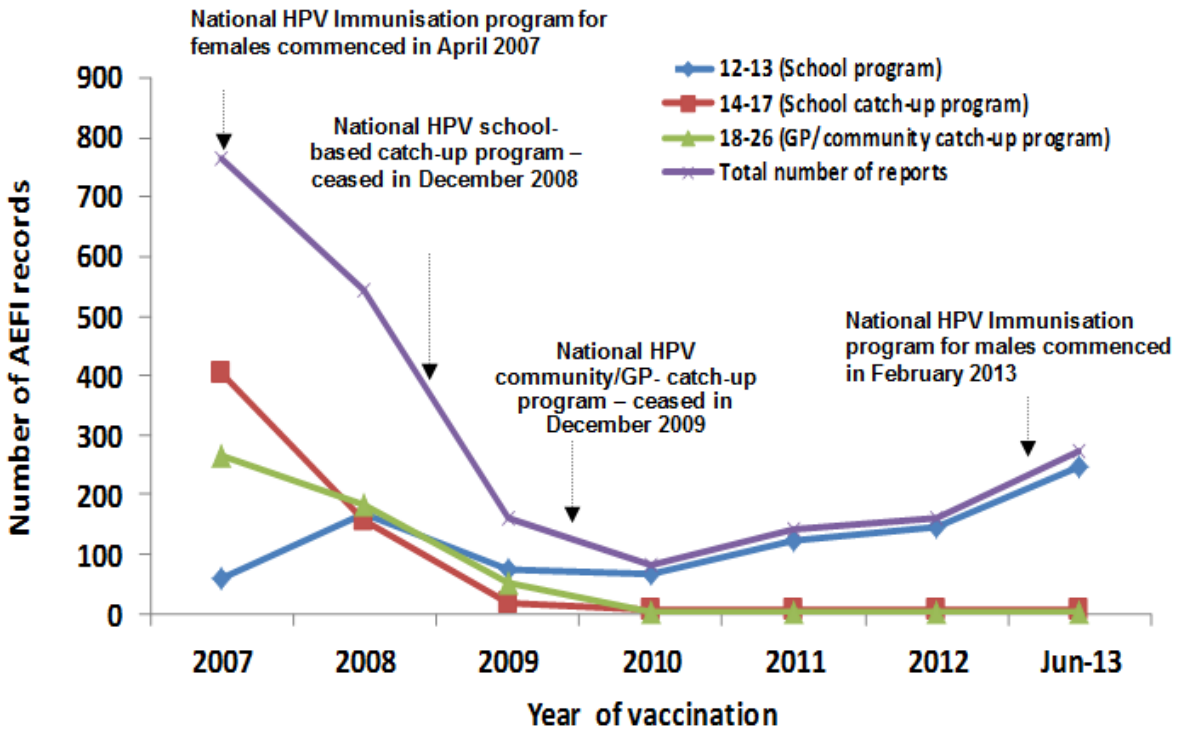
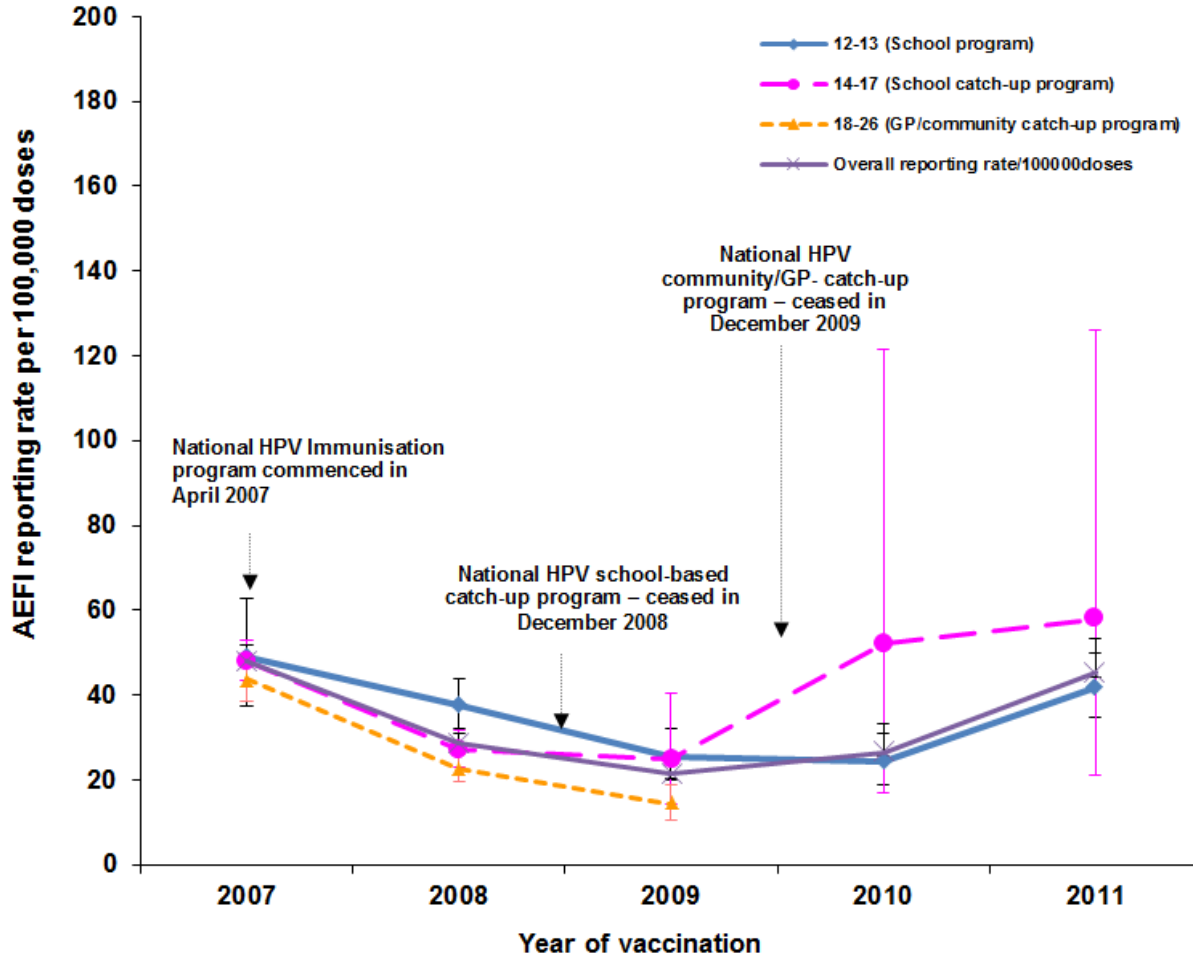


Figure 4.2. Reporting rates of adverse events per 100,000 doses following HPV vaccination in females aged 12–13 years, 14–17 years and 18–26 years, TGA Adverse Drug Reaction System database, 1 April 2007 to 31 December 2011*, by year of vaccination



* AEFI reporting rates could not be calculated for 18–26-year olds for the years 2010 and 2011 because there was no dosage data after the National HPV community/general practice catch-up program ceased in December 2009. Reporting rates could not be calculated for January 2012 to June 2013 because of the non-availability of the denominator doses data for this period.

Table 4.3 shows the total number of adverse events as well as reporting rates per 100,000 doses following HPV vaccination in females by jurisdiction, for 1 April 2007 to 31 December 2011. Overall, the majority of the cases (29%; n=485) were reported from New South Wales, followed by Victoria (22%; n=367), Queensland (17%; n=292) and South Australia (14%; n=235). In terms of reporting rates, the Australian Capital Territory and South Australia have shown higher reporting rates per 100,000 doses than the national average, while Tasmania has the lowest rate, given direct reporting from Tasmania to the TGA.

Table 4.3. Number of reports and reporting rates of adverse events following HPV vaccination in females, by jurisdiction, TGA Adverse Drug Reaction System database, 1 April 2007 to 31 December 2011

Jurisdiction	Number of reported AEFIs and reporting rates per 100,000 doses (95% CI)											
	2007		2008		2009		2010		2011		Total	
	n	Rate (CI)	n	Rate (CI)	n	Rate (CI)	n	Rate (CI)	n	Rate (CI)	n	Rate (CI)
Australian Capital Territory	37	110 (78–152)	23	67 (42–100)	4	31 (8–80)	2	34 (4–124)	1	17 (1–97)	67	73 (56–92)
New South Wales	196	44 (38–50)	194	30 (26–35)	36	18 (12–24)	16	17 (10–28)	43	46 (33–62)	485	33 (30–36)
Northern Territory	10	53 (25–97)	14	58 (32–98)	5	46 (15–108)	4	129 (35–330)	1	30 (1–168)	34	56 (40–79)
Queensland	142	50 (42–58)	81	19 (15–24)	24	13 (8–19)	14	22 (12–37)	31	47 (32–67)	292	29 (25–32)
South Australia	143	97 (82–114)	53	59 (44–77)	21	37 (23–57)	9	41 (19–77)	9	41 (19–77)	235	70 (61–79)
Tasmania	14	31 (17–53)	5	15 (5–35)	1	6 (0–33)	0	–	0	–	20	19 (11–29)
Victoria	135	29 (24–34)	122	27 (22–32)	45	25 (18–33)	29	38 (26–55)	36	46 (32–63)	367	29 (26–32)
Western Australia	49	36 (26–47)	29	15 (10–21)	9	13 (6–24)	5	15 (5–35)	14	38 (21–63)	106	22 (18–27)
Other*	39	na	21	na	14	na	1	na	4	na	79	na
National	765	48 (45–52)	542	29 (26–31)	159	22 (18–25)	80	26 (21–33)	139	44 (37–52)	1,685	35 (33–36)

Na = not applicable

* Records where the jurisdiction in which the AEFI occurred was not reported or was unclear.

Table 4.4 shows the types of AEFI reported by age group. The majority of AEFI reported for the HPV vaccine were mild transient events. The most commonly reported AEFI were headache (21%; n=381) followed by nausea (16%; n=293), dizziness (15%; n=273), fever (13%; n=231), syncope (11%; n=201) and injection site reactions (10%; n=191). Other reactions reported included pruritus (9%; n=163), urticaria (8%; n=155), myalgia (8%; n=140), rash (8%; n=146), and convulsions (4%; n=70). There were 16 reported cases (1%) of anaphylactic reaction and 8 cases of pancreatitis.

Table 4.4. Most common and other selected adverse events following HPV vaccination in females, TGA Adverse Drug Reaction System database, 1 April 2007 to 31 December 2012

MedDRA Preferred Terms	AEFI records* n Total (Serious)	Only HPV vaccine received n	≤13 years	14–17 years	≥18 years	Reporting rate per 100,000 doses† Total (Serious)
Headache	381 (19)	304	161	132	82	7.22 (0.35)
Nausea	293 (23)	232	106	111	71	5.53 (0.41)
Dizziness	273 (17)	204	126	93	51	4.85 (0.31)
Fever	231 (12)	175	100	75	54	4.40 (0.25)
Syncope	201 (10)	134	89	59	49	3.84 (0.14)
Injection site reaction	191 (3)	160	68	52	70	3.55 (0.04)
Pruritus‡	163 (7)	140	58	50	50	3.28 (0.14)
Urticaria	155 (5)	128	54	62	38	3.10 (0.10)
Myalgia	140 (12)	113	46	42	52	2.87 (0.25)
Reduced sensation	138 (10)	118	45	43	48	2.85 (0.21)
Rash	146 (7)	118	57	58	29	2.72 (0.12)
Pain	122 (9)	108	35	48	39	2.50 (0.19)
Neurological/ psychological	98 (11)	85	21	42	33	2.02 (0.23)
Injection site pain	98 (1)	89	26	28	44	1.90 90.02)
Abdominal pain	96 (14)	83	42	38	16	1.84 (0.27)
Convulsion	70 (12)	56	28	20	21	1.36 (0.21)
Vision impaired	56 (6)	47	18	22	15	1.11 (0.12)
Lymphadenopathy/itis§	47 (1)	43	19	10	18	0.95 (0.02)
Anaphylaxis	16 (4)	12	3	10	3	0.31 (0.06)
Pancreatitis	8 (7)	8	2	0	6	0.19 (0.17)
Thrombocytopenia	4 (4)	3	1	1	2	0.08 (0.08)
Encephalitis	2 (1)	2	0	1	1	0.04 (0.02)
Guillain-Barré syndrome	2 (2)	2	0	2	0	0.04 (0.04)

* One AEFI record may have multiple MedDRA Preferred Terms included.

† Reporting rates per 100,000 doses are calculated from 1 April 2007 to 31 December 2011.
‡ Includes Pruritus, Pruritus generalised and Rash pruritic.
§ Includes lymphadenitis and the more general term of 'lymphadenopathy'.

Adverse events reports following HPV vaccination, 1 February 2013 to 30 June 2013

There were a total of 615 AEFI reports received between February and June 2013 where HPV vaccine was listed as a suspected vaccine (**Table 4.5**). Of the 615 cases, 55% (n=341) were in males and 44% (n=273) were in females. HPV vaccine was the only suspected vaccine in 287 (47%) reports. Eighteen reports (3%) had causality classified as 'certain' or 'probable' while the other 597 cases (97%) were classified as 'possible'. Fourteen cases (2%) were defined as 'serious'.

Males

Since the implementation of the National HPV Vaccination Program in males in February 2013, the TGA received 341 reports for males until 30 June 2013. Sixty-seven per cent (n=229) were aged 12–13 years, 28% (n=97) were aged 14–17 years 1% (n=2) were aged 18–26 years; only 3% (n=11) were aged <12 years. HPV vaccine was the only suspected vaccine in 181 (53%) AEFI records. Five per cent of all records had causality ratings of either 'certain' or 'probable', while 95% were coded as 'possible'. Three per cent (n=10) had outcomes defined as 'serious' (i.e. recovery with sequelae, hospitalisation, life-threatening event or death). There were no reports of life-threatening events; all the serious cases were admitted to hospital. All the serious cases had multiple AEFIs including syncope (5), headache (3), lip swelling and injection site reaction (2 each), and one each of upper abdominal pain, anxiety, arthralgia, disorientation, dyspnoea, dysgeusia, epistaxis, gait disturbance, hypersensitivity, malaise, memory impairment, nausea, pyrexia, throat irritation, visual impairment and vomiting.

Ninety-seven per cent (n=330) of reports were from states and territories to the TGA; 3% were reported directly to the TGA by healthcare providers, hospitals and members of the public. Thirty-three per cent of reports (n=112) came from New South Wales, 23% (n=77) from Victoria, 22% (n=75) from Queensland, 13% (n=45) from the Australian Capital Territory, 5% (n=16) from Western Australia, 2% each from South Australia (n=7) and Tasmania (n=6), and 1% (n=3) from the Northern Territory.

The most frequently reported reactions associated with HPV administration in males are shown in **Table 4.5**. They included syncope (51%; n=173), presyncope, dizziness and nausea (8% each), headache (7%), pyrexia (6%) and vomiting (5%).

Females

There were 273 reports of adverse events following HPV vaccine for females during the period 1 February 2013 to 30 June 2013 in the ADRS database. Ninety per cent (n=247) were aged 12–13 years, 2% (n=5) were aged 14–17 years, 0.4% (n=1) were aged 18–26 years and 7% (n=19) were aged <12 years. HPV vaccine was the only suspected vaccine in 105 (38%) AEFI records. One per cent of all records had causality ratings of either 'certain' or 'probable', while 99% were coded as 'possible'.

One per cent (n=4) had outcomes defined as 'serious' (i.e. recovery with sequelae, hospitalisation, life-threatening event or death). There were 2 reports of life-threatening events and 2 cases were admitted to hospital. All the serious cases had multiple AEFIs including syncope (1), headache and blurred vision (2 each), and one each of upper abdominal pain, dyspnoea, dizziness, eye pain, muscular weakness and oligomenorrhoea. The causality rating for all the serious cases was 'possible'.

Ninety-seven per cent (n=266) of reports were reported by various states and territories to the TGA; 3% were reported directly to the TGA by healthcare providers, hospitals and members of the public. Thirty-eight per cent of reports (n=104) came from New South Wales, 21% (n=56) from Queensland, 20% (n=55) from Victoria, 14% (n=38) from the Australian Capital Territory, 6% (n=16) from South Australia, 1% (n=3) from the Northern Territory and 0.4 % (n=1) from Tasmania.

The most frequently reported reactions associated with HPV administration in females are shown in **Table 4.5**. They included syncope (45%; n=123), presyncope (14%), dizziness (9%) and nausea (8%).

Table 4.5. Most frequently reported adverse events following HPV vaccination in males and females, TGA Adverse Drug Reaction System database, 1 February 2013 to 30 June 2013*

MedDRA Preferred Terms*	Males					Females				
	AEFI records n Total (Serious)	Only HPV vaccine received n	≤13 years	14–17 years	≥18 years	AEFI records n Total (Serious)	Only HPV vaccine received n	≤13 years	14–17 years	≥18 years
Syncope	173 (6)	77	121	40	1	123 (1)	33	121	2	0
Presyncope	28 (0)	17	16	11	1	39 (0)	17	38	0	0
Nausea	28 (1)	19	20	7	–	23 (0)	11	23	0	0
Dizziness	26 (1)	12	21	5	–	24 (1)	12	24	0	0
Headache	23 (5)	13	12	11	–	15 (2)	8	15	0	0
Vomiting	16 (1)	8	11	5	–	17(0)	10	16	1	0
Pyrexia	20 (1)	11	13	7	–	9 (0)	5	9	0	0
Urticaria	15 (0)	11	8	7	–	9 (0)	6	9	0	0
Malaise	15 (1)	6	10	5	–	7 (0)	3	7	0	0
Injection site reaction	11 (2)	64	7	4	–	8 (0)	2	8	0	0
Rash†	16 (0)	11	8	8	–	12 (0)	5	12	0	0
Pallor	5 (0)	5	5	–	–	6 (0)	4	6	0	0
Pruritus	4 (0)	3	1	2	–	6 (0)	1	6	0	0
Diarrhoea	5 (0)	2	4	1	–	4 (0)	2	4	0	0
Lethargy	5 (0)	3	1	4	–	4 (0)	2	4	0	0
Paraesthesia	6 (0)	4	3	3	–	3 (0)	1	3	0	0
Anxiety	4 (1)	3	3	1	–	4 (0)	1	4	0	0
Hypersensitivity	6 (1)	3	4	1	–	2 (0)	0	2	0	0
Injection site pain	6 (0)	6	3	3	–	2 (0)	1	1	1	0
Rash pruritic	4 (0)	1	4	–	–	4 (0)	2	4	0	0
Cold sweat	4 (0)	2	4	–	–	3 (0)	2	3	0	0
Vision blurred	3 (2)	3	1	2	–	4 (2)	2	4	0	0

* Please see **Appendix 4.1** for the complete list of reported AEFIs (MedDRA preferred terms).

† Includes Rash and Rash generalised.

Discussion

When HPV vaccine was added to the NIP Schedule in April 2007, Australia became the first country to introduce a government funded National HPV Vaccination Program. The ongoing school-based HPV vaccination program is currently delivered to 12–13-year-old males and females. In 2007–2009, a 2-year catch-up program was delivered for 14–17-year-old females in schools and for 18–26-year-old females through general practice and community-based programs. During 2007–2009, an estimated 83% of females aged 12–17 years received at least 1 dose of HPV vaccine and 70% completed the 3-dose HPV vaccination course.

The AEFI reporting rate for HPV vaccine was very high in 2007 (48.2 per 100,000 doses) as expected when introducing a new vaccine. In addition, the implementation of a new AEFI reporting and evaluation system in Victoria in April 2007 may have led to more reporting.[54] Historical data show that initial high levels of AEFI reporting occur each time a new vaccine is introduced (meningococcal C conjugate vaccine in 2003 and rotavirus vaccine in 2007) as immunisation providers are more likely to report milder, less serious AEFIs for vaccines they are not familiar with, followed by a reduction and stabilisation of reporting over time (Weber effect).[75] This enhanced propensity to report events following newer vaccines increases the sensitivity of the system to detect signals of serious, rare or previously unknown events.

Current data held by the TGA indicate that the annual number of reports has decreased over the past 5 years with the highest annual number of reports in 2007 (765). The main reason for the drop was because the largest cohort was reduced once the catch-up program stopped. The number of reports declined to 80 in 2010 but slightly increased in 2011 (139), which was not statistically significant. This appears to be due to multiple factors including a sustained overall increase in AEFI reporting following the stimulated reporting related to Panvax® and Fluvax® in 2009–2010; release of the Review of the management of adverse events associated with Panvax® and Fluvax® (the Horvath review[76]); and changes in reporting whereby multiple state health departments were sending all reports, not just a selection, to the TGA.

During the first year of the program, reporting showed some clustering of AEFIs. In June 2007, a vaccine safety signal concerning anaphylaxis following HPV vaccination was observed and by early July 2007 there were 165 cases of AEFIs following receipt of Gardasil®. An expert panel was convened and an investigation was initiated.[52] There were some AEFIs that came to the attention of the media and resulted in considerable media interest both locally and internationally.[56-61]

Besides Australia, published national passive surveillance data for HPV vaccination is also available from the Netherlands, the USA and the UK.[69,77,78] However, reporting rates are different in all the countries due to differences in reporting mechanisms, case definitions and how rates are derived. For example, by the end of 2008, the US VAERS received 12,424 reports of adverse events following more than 23 million doses of quadrivalent HPV vaccine distributed, giving an overall reporting rate of 53.9 reports per 100,000 doses distributed.[69] In comparison, the reporting rate for adverse events following quadrivalent HPV vaccine in Australia was lower at 24.9 per 100,000 doses distributed, but was higher (~40.0 per 100,000) if limited to school girls only.[56,59] With the bivalent vaccine, higher reporting rates for adverse events were seen in the UK (104.5 per 100,000 doses administered) and in the Netherlands following a catch-up vaccination campaign for females 12–16 years of age (116.0 per 100,000 doses administered).[77,79,80] This is consistent with the finding that the bivalent HPV vaccine was more reactogenic than the quadrivalent vaccine in a head-to-head comparison trial.[81] Reporting rates cannot be calculated for data from multiple countries using WHO's Vigibase, due to the lack of data on doses distributed or administered.[80]

The majority of the AEFI reports for HPV vaccine were mild vaccine side effects that had been identified in pre-registration clinical trials.[55,82] These included injection site reactions, milder allergic reactions, and a range of mild non-specific symptoms including headache, nausea, dizziness, malaise and weakness. These symptoms have previously been reported to the TGA for secondary school students following receipt of meningococcal C conjugate vaccine as part of the national catch-up program in 2003 and 2004.[83,84] The above-mentioned reactions are more commonly reported in settings such as schools where many people are being vaccinated at the same time which can lead to a mass response.[57,85] Immunisation providers of mass campaigns in this age group need to be aware of this response and attempt to put measures in place to prevent these events from occurring.[57]

There was a higher than expected number of anaphylactic reactions following HPV vaccine detected in New South Wales in 2007.[56] An expert multidisciplinary panel was convened by NSW Health to investigate all reports of anaphylaxis and severe allergic reaction following HPV vaccine. The panel found that the rate of anaphylaxis in New South Wales was significantly higher for the school-based HPV vaccination program than for the 2003 school-based meningococcal C conjugate vaccine program.[56] However, the overall rate was low, and all cases were managed appropriately without serious sequelae.[56] The results of the study were shared nationally and internationally and the number of reported anaphylactic reactions following HPV vaccination dropped in the later years. However, it is recommended that vaccine recipients be observed for 15 minutes following administration of any vaccine[56] and that any symptoms and/or signs that may suggest anaphylaxis are clearly documented

to allow an accurate assessment of the AEFI report using Brighton Collaboration case definitions.[86]

A Gardasil Expert Panel was established by the TGA 1 year after the introduction of the HPV vaccination program in Australia to review the safety of the vaccine following a small number of reports of demyelination related illness following receipt of Gardasil®.[87] This was prompted in part because of a report, published in the journal *Multiple Sclerosis*, of six cases of multiple sclerosis in which HPV vaccination was implicated as a causal factor.[61] The Expert Panel reviewed a number of data sources, including passive reports made to the TGA and international passive surveillance data, and conferred with Australian specialist neurologists. The findings of this group were consistent with previous clinical trials and international post-marketing surveillance that Gardasil® was generally well tolerated with the majority of reports considered non-serious. There were no more reported cases of new demyelinating events in young women in Australia than would be expected by chance. The group recommended that all reports of such conditions following Gardasil® vaccination continue to be monitored by the TGA. It also recommended that enhanced active surveillance would be required to identify all cases of demyelinating disorders and overcome limitations of passive surveillance. The group also supported the introduction of active surveillance mechanisms for AEFI for any future large-scale vaccination programs, before the program is commenced.

Taking on board the recommendations of the Expert Panel, enhanced surveillance activities were put in place prior to the introduction of the HPV vaccination program for males in February 2013. To date there have been no significant reports of new adverse event signals following HPV vaccination in males. The most frequently reported reactions associated with HPV administration in males included syncope, presyncope, dizziness and nausea, headache, pyrexia and vomiting.

To date, with over 7 million doses of the HPV vaccine distributed in Australia, the overall safety profile of the quadrivalent HPV vaccine in females has been shown to be very good. Population-based data analyses, where vaccination status and health outcome data are available for whole populations, have confirmed that there is no indication that HPV vaccination is associated with any increase in autoimmune, neurological or vascular diseases.[88,89] Following the extension of the vaccination program to males and enhanced surveillance since February 2013, preliminary results show the safety profile of Gardasil® in males to be similar to the profile among females.[90]

Conclusion

The majority of AEFIs reported following implementation of the National HPV Vaccination Program for females and males were mild and transient. However, passive surveillance system data need to be interpreted with caution due to factors such as under-reporting, incomplete reporting and events which are reported irrespective of causality being established. Overall, the national surveillance data provide evidence supporting the good safety profile of the HPV vaccine and are consistent with data from international spontaneous reporting systems.

CHAPTER 5. Disease impact: High-grade cervical abnormalities

Aims

To assess patterns of uptake of cervical screening and trends in rates of high-grade cervical abnormalities by age group in Australian females eligible and not eligible for the funded HPV vaccination program at a national level and by jurisdiction.

Specific objectives include:

a. To determine age-specific trends in high-grade cervical abnormalities, 2004 to 2011

b. To quantify any reduction in prevalence of high-grade abnormalities (HGA) by time period ('pre-vaccine' and 'post-vaccine') in different age groups based on eligibility for the vaccine program.

Methods

This report provides a summary of cancer statistics across all states and territories in Australia. Information was taken from the Australian Institute of Health and Welfare (AIHW) reports *Cervical Screening in Australia* published during 2011–2013.[10,91,92] All data, including data presented in graphs, are from these reports unless otherwise specified.

These reports are compiled using data on the number of females screened and results of screening tests obtained from the eight jurisdictionally based cervical cytology registries ('Pap Test Registers'), all of which report standardised data on a regular basis to AIHW for monitoring of the National Cervical Screening Program (NCSP). The data need to be considered as accurate for a specific point in time. Subsequent results or clinical information received by the registries is not updated to AIHW.[92] Data collected from cytology registries aims to monitor the effectiveness of the NCSP using performance indicators for participation, rescreening, cytology, histology, and the cytology–histology correlation.[92]

The analysis was an ecologic design with comparisons between 2004–2007 and 2008–2011. The years 2008–2011 were considered as the post-vaccine period as the National HPV Vaccination Program commenced in April 2007. The 3-dose schedule over a 6-month period and the time required for an HPV incident infection to progress to a clinically detected high-grade cervical abnormality would render it extremely unlikely that the vaccine would have any impact on HGAs during 2007.

The annual rate of females attending screening was assessed according to age using ABS census data as the denominator. The population was adjusted to include only females with an intact uterus (and cervix) using age-specific hysterectomy fractions derived from the National Hospital Morbidity Database (NHMD).[92] The NHMD is a comprehensive dataset of all separations of patients admitted to public and private hospitals in Australia, compiled from

data supplied by state and territory health authorities. It includes data from virtually all public and private hospitals in Australia.[93] Females who have had a hysterectomy are not at risk of cervical cancer. It is important to note that the NCSP recommends screening biannually and hence reports screening participation over 2 years. In this report, we have calculated annual screening rates to determine if there were any changes in screening patterns on a yearly basis.

Histopathologically defined HGAs include lesions coded as cervical intraepithelial neoplasia of grade 2 (CIN 2) or 3 (CIN 3), adenocarcinoma in situ or endocervical dysplasia. HGAs detected only by cytology were excluded, as a referral for biopsy, with subsequent histologic examination, is routine following detection of HGA by cytology.[94]

Data on numbers of females screened and numbers of HGAs detected from 2004 to 2011 (2004–2007, 2008–2011 and individual years) were tabulated by age groups (<20, 20–24, 25–29, 30–34 and 35–69 years) and by jurisdiction. Trends in the rate of HGAs detected were examined. Absolute rates, rate ratios and 95% confidence intervals were used to quantify changes.

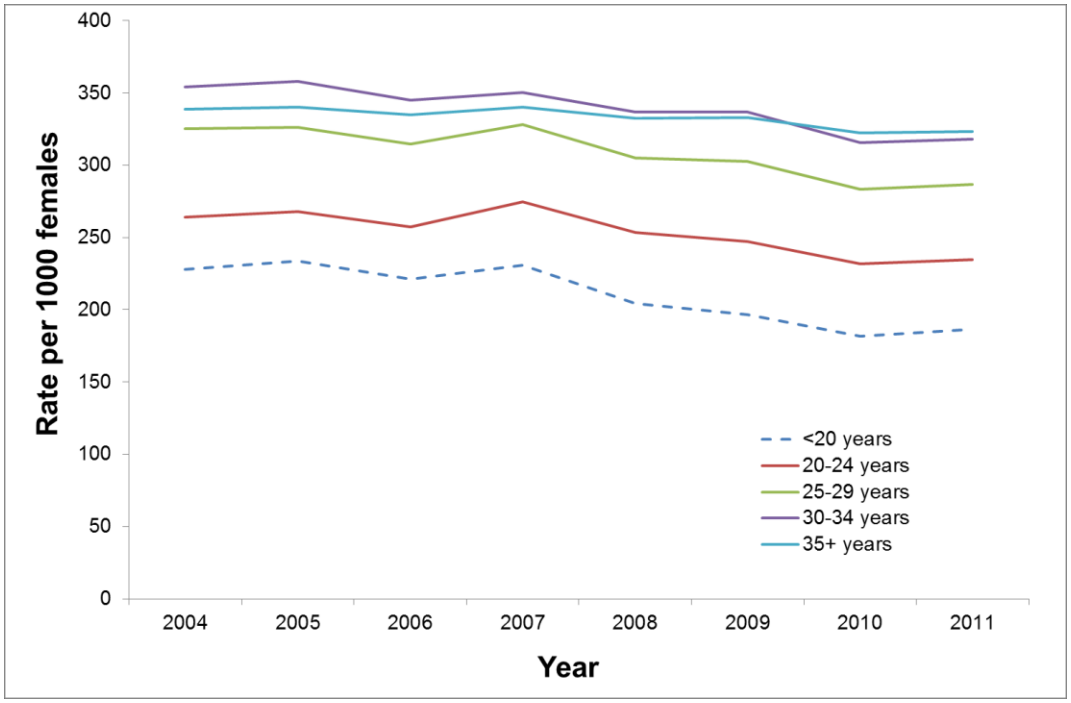
A sensitivity analysis in females aged <20 years was conducted to determine whether screening behaviour affected HGA rates observed in this population. Unscreened females were included in the analysis using pre-vaccine rates of detected HGA and examined by each post-vaccine year (2008–2011). Expected rates of HGA detected for all females in this age group had they all been screened were calculated.

Results

Annual screening rates

Trends in the AIHW data show that annual screening rates among the female population progressively declined, particularly among females <35 years of age. In particular, screening rates among females aged <20 years, 20–24 years and 25–29 years appear to have reached their maximum level in 2007 (the year the National HPV Vaccination Program commenced) and to have decreased since then, whereas screening rates among females aged 35–69 years have remained constant (**Figure 5.1**).

Figure 5.1. Screening rates by age group, per 1,000 females, 2004 to 2011*



Source: *Cervical screening in Australia 2010–2011*, AIHW and ABS census data

* Screening rate per 1,000 female population, adjusted for hysterectomy fraction.

Overall, screening rates appeared to decrease significantly across all age groups when comparing the post-vaccine period with the pre-vaccine period (**Table 5.1**). The greatest reduction in screening was observed in females <20 years of age. There was a 15% reduction in screening during the post-vaccine period compared to the pre-vaccine period. Screening rates in females aged 20–24 years and 25–29 years decreased by 9% when comparing the post-vaccine period to the pre-vaccine period. It is important not to interpret annual screening rates as screening participation given the recommended 2-year screening interval.

Table 5.1. Screening rates and rate ratios, by age group, 2004 to 2011*

Pre-vaccine period 2004–2007			Post-vaccine period 2008–2011		Post/Pre-vaccine period
Age group (years)	Screened (n)	Rate†	Screened (n)	Rate†	Rate ratio (95% CI)
<20	252,953	22.8‡	226,331	19.4‡	0.85 (0.84–0.85)
20–24	758,264	26.6	746,681	24.2	0.91 (0.91–0.91)
25–29	894,450	32.4	923,625	29.4	0.91 (0.91–0.91)
30–34	1,049,064	35.2	967,951	32.7	0.93 (0.93–0.93)
35–69	3,757,229	25.1	5,261,552	32.8	1.31 (1.30–1.31)

Source: *Cervical screening in Australia 2010–2011*, AIHW

* Comparing 2008–2011 period with 2004–2007 period, by age group, adjusted for hysterectomy fraction.

† Screening rate per 100 female population per 4-year period

‡ ABS population estimates of 18–19 years used as denominator for the <20 years age group.

HGAs detected

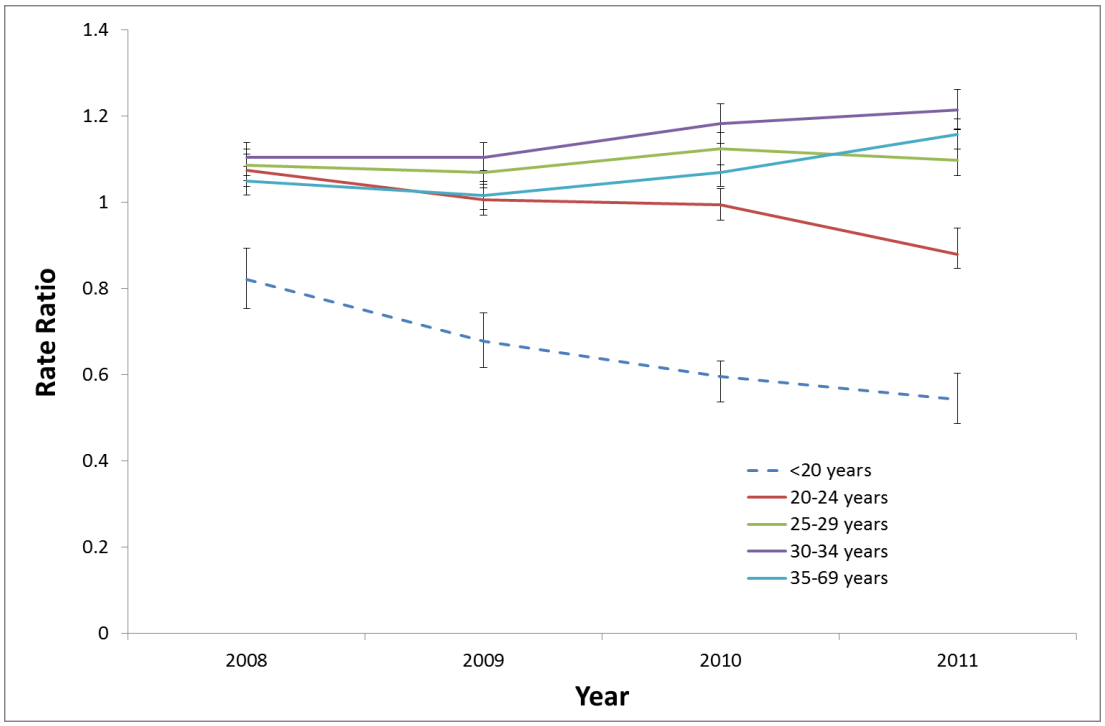
Following the implementation of the National HPV Vaccination Program, the number and rates of HGAs detected in females aged <20 years and 20–24 years of age decreased (**Table 5.2**, **Figure 5.2, Appendix 5.1**). Although the number of HGAs detected in females aged 25–29 years appeared to increase, no similar pattern in HGA rates was observed. In the older age groups (30–34 years and 35–69 years), the number of HGAs detected and the HGA rate increased over time.

Table 5.2. Number of females with high-grade abnormalities detected by histology, by age, 2004 to 2011

Age group (years)	Year							
	2004	2005	2006	2007	2008	2009	2010	2011
<20	915	851	803	750	653	518	416	385
20–24	3,673	3,826	3,707	3,823	4,044	3,799	3,566	3,220
25–29	3,879	3,931	3,861	4,186	4,379	4,464	4,524	4,543
30–34	3,111	3,127	2,945	2,933	3,126	3,155	3,201	3,378
35–69	4,418	4,434	4,602	4,729	4,908	4,839	5,000	5,500

Source: *Cervical screening in Australia 2010–2011*, AIHW

Figure 5.2. Rate ratio*† of females with a detected high-grade abnormality, per 1,000 females screened, by age group, 2008 to 2011



Source: *Cervical screening in Australia 2010–2011*, AIHW and ABS census data

* 95% confidence intervals displayed.

† Reference group: 2004–2007 pre-vaccine/baseline period.

HGA rates in females aged <20 years

The most striking reduction in the rate of HGAs detected in the post-vaccine period compared with the pre-vaccine period was observed in females aged <20 years (**Figure 5.2**). Following the introduction of the HPV vaccination program, the rate of HGAs detected in this age group in 2008 was 10.8 (95% CI: 10.0–11.6) per 1,000 females screened, an 18% (95% CI: 11–25%) reduction from the rate during the pre-vaccine period (2004–2007) of 13.1 (95% CI: 12.7–13.6) per 1,000 females screened. The rates further declined in 2009 by 33% (95% CI: 26–39%) and in 2010 by 41% (95% CI: 34%–47%) compared with the pre-vaccine period. The most pronounced decline occurred in the most recent post-vaccine year (2011): the rate was 46% (95% CI: 40–51%) lower than the rate during the pre-vaccine period.

Given limited numbers at the jurisdictional level, successive 2-year periods (2008–2009 and 2010–2011) were compared with data for 2004–2007 (**Table 5.3**). At the national level, a significant decline was observed in 2008–2009 from 2004–2007, with a further significant decline from 2008–2009 in 2010–2011. When stratifying by jurisdiction, the rates of HGA

detected per 1,000 females aged <20 years screened decreased in all jurisdictions by 2010–2011, 3 years after program introduction (**Table 5.3**). Of note, because of the high proportion of the population who are Indigenous, during the pre-vaccine period the Northern Territory reported the highest rates of HGA of all the jurisdictions. This remained the case in the post-vaccine periods, but between 2010 and 2011, a statistically significant 41% reduction (95% CI: 1–69%) in the rate of HGA detected, compared to the pre-vaccine period, was documented in the Northern Territory.

Table 5.3. Rate of high-grade abnormalities detected, per 1,000 females aged <20 years screened, and 95% confidence intervals, by jurisdiction, 2004 to 2011

Jurisdiction	Pre-vaccine period 2004–2007	Post-vaccine period 2008–2009		Post-vaccine period 2010–2011		Combined post-vaccine period 2008–2011	
	Rate (CI)*	Rate (CI)*	Rate ratio (CI)†	Rate (CI)*	Rate ratio (CI)†	Rate (CI)*	Rate ratio (CI)†
NSW	16.2 (15.3–17.2)	10.8 (9.7–11.9)	0.66 (0.59–0.75)	8.2 (7.2–9.2)	0.50 (0.44–0.58)	9.5 (8.8–10.3)	0.59 (0.53–0.65)
VIC	10.8 (9.9–11.7)	9.7 (8.5–11.1)	0.90 (0.77–1.06)	5.9 (4.9–7.0)	0.55 (0.44–0.66)	7.9 (7.0–8.8)	0.73 (0.64–0.84)
QLD	13.6 (12.7–14.6)	8.8 (7.8–9.9)	0.65 (0.56–0.74)	7.9 (6.9–9.1)	0.58 (0.50–0.68)	8.4 (7.6–9.2)	0.62 (0.55–0.69)
WA	10.0 (9.0–11.2)	8.0 (6.7–9.5)	0.80 (0.65–0.98)	7.2 (5.8–8.7)	0.71 (0.57–0.89)	7.6 (6.7–8.7)	0.76 (0.64–0.90)
SA	9.1 (7.8–10.6)	9.7 (7.7–12.1)	1.07 (0.81–1.40)	8.7 (6.8–11.0)	0.96 (0.71–1.27)	9.2 (7.8–10.8)	1.01 (0.81–1.27)
NT	18.5 (12.8–26.1)	17.8 (13.9–22.5)	1.04 (0.67–1.60)	10.1 (5.8–16.5)	0.57 (0.31–0.99)	14.6 (10.8–19.3)	0.82 (0.56–1.02)
TAS	18.1 (15.4–21.2)	16.8 (12.8–21.5)	0.93 (0.68–1.25)	6.0 (3.6–9.3)	0.33 (0.19–0.53)	11.7 (9.3–14.6)	0.65 (0.49–0.85)
ACT	11.7 (8.9–15.0)	6.2 (3.4–10.4)	0.53 (0.27–0.96)	4.1 (1.8–8.1)	0.35 (0.15–0.74)	5.2 (3.3–7.9)	0.45 (0.26–0.74)
National	13.1 (12.7–13.6)	9.8 (9.3–10.4)	0.75 (0.70–0.80)	7.5 (6.9–8.0)	0.57 (0.53–0.61)	8.7 (8.3–9.1)	0.66 (0.63–0.70)

Source: *Cervical screening in Australia 2010–2011*, AIHW

* Crude rates are the number of females with high-grade abnormalities detected by histology as a proportion of all females screened.

† Reference group: 2004–2007 pre-vaccine period.

HGA rates in females aged 20–24 years

At the national level, a progressive reduction in HGA rates in females aged 20–24 years was observed each year since 2008 (**Figure 5.2, Appendix 5.2**), although 2011 was the first year in which a statistically significant reduction was documented: a 12% decline (95% CI: 9–15%) to a rate of 17.4 (95% CI: 16.8–18.0) HGAs detected per 1,000 females screened. Women who were 20–24 years of age in 2011 would have been 16–20 years of age in 2008 and so 2011 may represent the first year in which a significant proportion of this age cohort had received HPV vaccine within a short time of becoming sexually active.[95]

Sensitivity analysis

To determine whether the decline in detection of HGAs per 1,000 females screened in females aged <20 years could be explained by a decline in screening participation alone, a sensitivity analysis was conducted. Nationally, females aged <20 years who were not screened in 2008, 2009, 2010 and 2011 were included in our analysis to estimate the expected rates of HGAs detected for all females in this age group had they all been screened (**Table 5.4**). Expected rate ratios (HGA rate if unscreened females had been screened compared to HGA rate in 2004–2007) were significantly below 1 from 2009 onwards for all scenarios, demonstrating that the patterns observed were robust to even very large (and implausible) changes in screening practices.

Table 5.4. Sensitivity analysis of rate ratios of females aged <20 years screened, 2009 to 2011

A. Year	B. No. of females with HGA screened	C. Expected no. of HGA by pre-vaccine (2004–2007) rates*	D. No. of females screened	E. No. of females not screened†	F. (B+C)/(D+E)x1000 Expected rates	G. Expected rate ratio (rate ratio for HGA compared to 2004–2007)	H. 95% CI
2008	653	3,006	60,612	229,142	12.63	0.96	0.92–1.01
2009	518	3,113	58,307	238,020	12.29	0.94	0.89–0.98
2010	416	3,151	53,297	240,163	12.15	0.93	0.88–0.97
2011	385	3,095	54,115	235,895	12.00	0.91	0.87–0.96

Source: *Cervical screening in Australia 2010–2011*, AIHW and ABS census data

* Expected number of HGAs was estimated by multiplying 2004–2007 HGA rates by the number of females not screened.

† Number of females not screened was calculated by subtracting the number of females screened from ABS population estimates for females aged 18–19 years.

Discussion

Use of national data on detection of high-grade cervical abnormalities by histologic examination of biopsy specimens provides a well-standardised measure by which to monitor the occurrence of cervical cancer precursors in the screened female population.

Our analysis indicated that, overall, screening rates declined in all age groups when comparing the post-vaccine period to the pre-vaccine period. This result was unsurprising as participation in cervical screening nationally has been gradually declining over time, with participation at 59% in 2004–2005 reducing to 57% in 2010–2011.[92] This is in line with international experience, with declines in cervical screening participation noted over the past decade, particularly among younger cohorts.[96] The most marked decline in screening rate appeared to occur in females aged <20 years.

This is in spite of recommendations during vaccination that regular Pap tests are still required and campaigns to emphasise the need for Pap tests during the implementation of the vaccination program.[97,98] Concern has previously been raised that a decline in screening participation may occur among females vaccinated with HPV due to the perception that the vaccine will negate the need for regular Pap tests.[99]

A more recent Victorian study conducted after the implementation of the National HPV Vaccination Program found that 8% of females aged 18–28 years who had never had a Pap test before indicated that the receipt of the HPV vaccine made them less likely to have a Pap test in the future.[44] However, 96% of the study population believed that Pap tests were still required following vaccination.[44] Barriers to cervical screening include embarrassment, fear of the test result, limited understanding and lack of information.[100] Falling screening rates in very young females (<20 years) are probably not of immediate policy concern, given that Australia screens far younger and more frequently than current International Agency for Research on Cancer (IARC) recommendations.[101] Current international guidelines recommend females aged <25 years not be targeted for screening based on the potential harm with minimal benefits that may occur.[101]

In Australia, the screening age and interval are currently under review. However, failure to commence regular cervical screening by a woman's mid to late 20s has the potential to result in significant risk, particularly given that many young adult females vaccinated in the catch-up program were already sexually active.[95] Obtaining HPV vaccination status for women attending screening may assist in determining whether there is a significant difference in the proportion of women who do not get screened based on vaccination status. This could ideally occur through data linkage between the NHVPR and the jurisdictional Pap

test registers. Further qualitative and quantitative studies should also be conducted to make inferences between vaccination and screening uptake on a national level.

Overall, there was a decline in the rate of detection of HGA abnormalities by histology among females aged <20 years following the implementation of the National HPV Vaccination Program, and in 2011 among females aged 20–24 years, but not among older females (≥25 years). A significant decline in HGA incidence was observed in females aged <18 years in a Victorian population-based study, though no significant change in HGA incidence among females 18–20 years of age (p=0.7) between pre-vaccine and post-vaccine periods was observed at the time.[98] This early study only utilised data until the end of 2009, during which the catch-up program was still being delivered, and was only 2 years after the implementation of the National HPV Vaccination Program.

Our analysis included two additional post-vaccine years that captured the 14 and 15 years age cohort targeted for HPV vaccine. The decline we have observed is consistent with the large decline in vaccine-type HPV prevalence observed among young Australian women in a pre- to post-program comparison of 18–24-year olds attending for cervical screening at family planning clinics.[102] Monitoring of HPV DNA prevalence can provide timely evidence of the impact of HPV vaccine among women who recently have become sexually active;[103] however, the high costs of this method[101] need to be considered.

The results of our analysis are also consistent with the high vaccine coverage obtained in the school-based HPV vaccination program[39] in females under 18 years of age and the lower expected vaccine effectiveness in women vaccinated post sexual debut.[104,105]

A number of limitations have been discussed previously in using cervical cancer screening program data as a method of assessing the impact of HPV vaccines.[98] Our results may have been affected by screening participation, particularly as there was a reduction in participation among our age group of interest (<20 years). We attempted to control for this by including non-screened women and assuming the same rates of HGA detection as observed in 2004–2007 in our analysis. This inclusion is likely to be the most extreme situation, overestimating the rate of HGA detected, as not all females aged <20 years are sexually active. A 2008 survey of secondary students in Year 10 and Year 12 in Australia found that approximately 40% of students had experienced sexual intercourse.[95] Despite this likely overestimation, a reduction in rate of HGA detected was still observed.

Changes in screening rates, access to screening and screening behaviour have been described previously as factors affecting the number of lesions detected.[103] These factors may be influenced by health promotion campaigns targeting under-screened women, which have been demonstrated to increase participation in the Australian setting.[106] This may

subsequently raise detection rates as under-screened women are more likely to have prevalent disease. This may be why a peak in screening rates was observed in 2007, coinciding with the commencement of the National HPV Vaccination Program.

We are not aware of which jurisdictions ran particular media/health promotion campaigns during the time periods under review; such campaigns could have influenced participation and detection rates. Other factors such as prominent media coverage of celebrities with cancer can also affect screening rates in a dramatic fashion. This was observed with the diagnosis and subsequent death of a young British reality television star from cervical cancer in 2008 and 2009.[107]

Our analysis included 2007 in the pre-vaccine/baseline years, although the National HPV Vaccination Program commenced in April of that year. Given the vaccine schedule and time between exposure and detection of HGA, we concluded that including 2007 in the pre-vaccine/baseline period was appropriate. Previous cohort studies have estimated the time between development of high-grade lesions following exposure to HPV infection. A cohort study in the UK among females aged 15–19 years found the risk of high-grade cervical intraepithelial neoplasia was 18 times greater in females exposed to HPV (type 16) 6–12 months ago (relative hazards ratio 18.02 [95% CI: 5.50–59.0]) compared to unexposed females.[108] Furthermore, a cohort study in the USA of 241 women identified all HPV associated CIN 2 and 3 detected occurred within the first 24 months of initial detection of HPV infection.[109] More recently, a median time of 4 months for detection of cervical squamous intraepithelial lesions following first incident HPV infection was reported in a cohort study of female university students in the USA.[110]

HGA detection may vary between jurisdictions due to random variation with small populations; underlying differences in HPV exposure or persistence (due to different sexual behaviours or mixing patterns due to age structures or geography or cofactors such as smoking); differences in the completeness of histology reporting from laboratories to the registers; or differences in the quality of specimen collection, processing and interpretation. The NCSP has standards for laboratories to maintain in relation to the detection rates of HGAs. Monitoring and feedback can result in changes in detection rates from particular laboratories over time, which may have the potential to influence average detection rates.

The Northern Territory appeared to experience one of the highest rates of HGAs in females aged <20 years and 20–24 years of all the jurisdictions. One explanation for this is that the Northern Territory has the highest proportion of Indigenous residents of all the states and territories[111] and it has also been well documented that the incidence of cervical cancer is twice as high among Indigenous women as it is in non-Indigenous women.[10] A study of pre-

vaccination HPV prevalence did not find any significant difference in HPV prevalence or prevalence of vaccine-preventable HPV types between young Indigenous and non-Indigenous Australian women.[112] Cofactors such as smoking, other sexually transmissible infections and early age of first pregnancy/high parity may be important in explaining different rates of abnormalities and the development of cancer. Indigenous status is not currently able to be collected in the national cervical screening data. If it could be captured in the future, that would enable research on Indigenous status and cervical screening participation to occur.

It must be noted that other factors[103,106] may have played a role in the observed declines in rates of HGAs which limits inferences from reductions observed in our ecological analysis. A more definitive analysis, to causally establish the role of HPV vaccination in the reduction of HGAs, requires data linkage between the NHVPR and the state Pap test registers to classify women according to their vaccination status and directly compare rates of abnormalities by vaccination status.

Conclusion

Our analysis is the first to explicitly examine national and jurisdictional screening data on changes in rates of HGA detected in women following the introduction of the National HPV Vaccination Program. The rate of HGAs detected in females eligible for HPV vaccination through the national program, particularly females aged <20 years, was significantly lower following the implementation of the vaccination program than during the pre-vaccine era, even after adjusting for screening participation. The ecological nature of the study prevents definitive conclusions from being made; however, our results identify the need for future analytical studies to be conducted. Ideally, data linkage studies hold the key in providing substantiated evidence of the impact of HPV vaccination on pre-cancerous cervical lesions. Supplemented by HPV typing studies, which can monitor the types causing HGA in Australia over time, such studies will contribute greatly to the assessment of the impact of HPV vaccination in Australia.

CHAPTER 6: Disease impact: Anogenital warts

Aims

To compare trends in hospitalisations coded as involving a diagnosis of genital warts before and after implementation of the National HPV Vaccination Program.

Methods

Data source

Data from the National Hospital Morbidity Database was obtained from AIHW. The NHMD includes public and private hospital separations.[93] Each record includes the admission and separation date, information about procedures performed, the principal diagnosis responsible for the admission, and up to fifty diagnoses in total which contributed to the admission, coded using ICD-10-AM.

All admissions for genital warts (including those where genital warts was not the principal diagnosis, but was included in other diagnosis categories) between 1 July 1999 and 30 June 2011 were included. It should be noted though that admissions which were *primarily* for genital warts were not coded consistently as the principal diagnosis over this time period. The ICD-10-AM code for genital warts is A63.0. Between July 1998 and June 2002, Australian Coding Standards (ICD-10-AM First (1998) and Second (2000) Editions) advised that anogenital warts should be coded using codes for other specified diseases/disorders relating to the relevant site as the principal diagnosis (K62.8 [perianal], N48.8 [penile], N88.8 [cervical], N89.8 [vaginal], N90.8 [vulval]), and A63.0 as an additional diagnosis. From 1 July 2002 (ICD-10-AM Third to Sixth Editions) an additional code for “other specified disorders of urethra” (N36.8) was added to the Australian Coding Standards to be used in an equivalent way for urethral warts. From 1 July 2010 (ICD-10-AM Seventh Edition), however, a fifth character was added to the existing four characters for anogenital warts (A63.0) in order to indicate the site of the warts (A63.01–A63.07; A63.00 and A63.09 indicated other or unspecified sites, respectively), and the additional chapter codes for site were no longer required by the Australian Coding Standards. Furthermore, admissions prior to July 2010 were not always coded consistently with the Australian Coding Standards current at that time. As a result, this analysis considers all admissions involving a diagnosis of genital warts, without stratification by whether or not a genital wart code was listed as the principal diagnosis. The anatomical site of warts was ascertained based on diagnosis and procedure codes involved (**Table A6.1.1** in **Appendix 6.1**).

Admission rates were derived per 100,000 individuals in the population, based on total admissions over a year period (July–June, consistent with the time period for the data

provided) and estimates of the Australian resident population by single year of age at the end of each calendar year (i.e. mid-period).[113]

Analyses by age

Subjects were categorised into four age groups, based on their likely exposure to HPV vaccination during this time period, to investigate the potential impact of HPV vaccination on admissions for genital warts (**Table 6.1**). Age was defined as the age at the time of the hospital admission. Age is associated with HPV prevalence, and therefore birth cohorts would have variations in their risk of genital warts as they age, even in the absence of vaccination. Estimated vaccine uptake by females in these age groups as at mid-2011 is also presented in **Table 6.1** based on published coverage data and population estimates for mid-2011.[38,41,113,114] Estimates are presented both for uptake of the full schedule of 3 doses and also for uptake of at least 2 doses, as recent data suggest the possibility that 2-dose efficacy may be comparable to 3-dose efficacy,[115,116] at least in the short term. The estimated proportion of females in each of these age groups ever vaccinated in the intervening years since the commencement of the National HPV Vaccination Program in 2007 appear in supplementary data (**Appendix 6.2**).

Table 6.1. Age groups used in the analysis (based on age at admission)

Age group (years)	Likely exposure to vaccination by 30 June 2011	Estimated* 3-dose (*2-dose*) vaccination coverage in this age group as at 30 June 2011
12–17	From 2007 onwards, this age group will include females who were offered HPV vaccination through the school-based program. Coverage is higher and exposure to HPV prior to vaccination is likely to be less than in older age groups. In females, approximately half of this age category would have been offered vaccination in 2007, mostly at school, and the remainder in 2008 or subsequent years (also at school).	71% (*77%*)
18–26	Catch-up vaccination was offered to females in this age group between 2007 and 2009, although coverage is lower and exposure to HPV prior to vaccination is more likely than in the younger age group. Over time, females vaccinated in school will start to move into this age group. By 30 June 2011 the females in this age group would have been offered vaccination between the ages of approximately 15 and 24 years.	45% (*56%*)
27–30	This represents an age group which will progressively include some vaccinated cohorts over the period 2008–2011, but the proportion who have been effectively vaccinated is likely to be smaller than in the younger age groups, due to low coverage and higher prior exposure. By 30 June 2011, the females in this age group would have been offered vaccination between the ages of approximately 23 and 26 years.	25% (*35%*)
31–69	This represents an age group who have never been offered HPV vaccination through the public program (by 30 June 2011, the oldest females offered vaccination would be aged 30 years). Some elective uptake is possible in this group, but is likely to be small.	Minimal†

* Estimated from published coverage data and population estimates for mid-2011.[38,41,113,114] Coverage data for females aged 12–13 years in 2011 is not yet available so estimates are based on similar coverage to those aged 14–15 years.

† Elective uptake only; cost of vaccine would have been entirely out-of-pocket.

Sensitivity analysis

Previous analyses of trends in genital warts in the post-vaccine period have reported reductions in heterosexual males, but not males with a recent male sex partner.[117] Data on sexual behaviour is not available from the NHMD and so this could not be examined directly in this analysis. However, in a sensitivity analysis we examined trends in admissions in males, stratified based on the genital warts site. Admissions were analysed separately based on whether they involved a diagnosis or procedure code associated with anal warts or whether only non-anal sites were recorded. An admission was classified as related to anal warts if it included either one of the procedure codes for treatment of anal warts (32177, 32180) or a diagnosis code related to anal warts (including perianal and perineal warts: A63.01, A63.09 or K62.8).

Analyses by Indigenous status

Additional analyses were conducted to examine whether there was also variation in rates by Indigenous status and, in particular, if any changes in admissions in the post-vaccine period in age groups exposed to HPV vaccination differed in Indigenous Australians compared to other Australians. AIHW reports note that the quality and completeness of fields capturing Indigenous status has varied over time and between states and territories.[118-120] Based on recommendations from these reports, analyses by Indigenous status were restricted to data from hospitals in New South Wales, Victoria, Queensland, South Australia, Western Australia and the Northern Territory for the period from 1 July 2004. Data prior to July 2004 were excluded because AIHW recommended that data from New South Wales and Victoria not be analysed by Indigenous status prior to this time.[118,119] Data from hospitals in Tasmania and the Australian Capital Territory were excluded based on the AIHW report recommendations; data from hospitals in these states and territories represented a comparatively small number of admissions (3.7% and 5.9% of all admissions, respectively, in Indigenous Australians since 1 July 2004). Admissions where Indigenous status was not reported (not accommodated in the data systems of certain jurisdictions) were amalgamated with admissions for non-Indigenous Australians.[119]

Estimates of the Australian population by Indigenous status, state/territory, sex and age were sourced from the ABS (consistent with ABS and AIHW recommendations, series B was used for Indigenous population estimates).[120,121]

For analyses by Indigenous status wider age groups were used in the analyses (15–24, 25–34 and 35–69 years). This was due to comparatively small numbers of admissions in Indigenous Australians and the lack of availability of population estimates by state/territory and single year of age. However, the age groups selected will still broadly represent (in females) a group offered vaccination from mid-2007 onwards, often at school and with moderate uptake (15–24 years); a group with lower uptake of vaccination and where those vaccinated were more likely to have been previously exposed to HPV than the younger age group (25–34 years); and a group never offered HPV vaccination through the public program and where uptake, if any, is likely to be extremely low (35–69 years). For context, based on available uptake data, 3-dose (2-dose) population uptake rates as at mid-2011 in females aged 15–24 years, 25–34 years and 35–69 years are estimated as 56% (65%), 16% (23%) and 0%, respectively.[38,41,113,114]

Statistical analysis

Poisson and negative binomial regression were used to assess trends in admission rates since the commencement of the vaccination program by year of admission, age group and

sex. This was done in order to examine an *a priori* hypothesis that admission rates could have been changed in some age groups by the introduction of the National HPV Vaccination Program. Specifically, the fitted models were used to estimate the overall reduction between the last pre-vaccine year (July 2006 to June 2007) and the most recent data available (July 2010 to June 2011).

Rate ratios were also calculated for post-vaccine admission rates relative to pre-vaccine admission rates. Pre-vaccine admission rates were calculated as the average in the 3-year period 1 July 2004 to 30 June 2007. Post-vaccine rate ratios were calculated for each successive 12-month period from 1 July 2007, and also to compare the 3-year post-vaccine average (1 July 2008 to 30 June 2011) with the 3-year pre-vaccine average.

Additionally, Jointpoint Poisson analysis was performed to determine whether there was a significant change in admission rates at any point in time in the period July 1999 to June 2011 and, if so, when this was estimated to have occurred and the annual percentage change in the rate of admissions from that time. It was also used to examine any pre-vaccine trends and whether any observed post-vaccine declines may represent the continuation of pre-existing trends.

Analyses were performed using SAS 9.3 (SAS Institute Inc., Cary, NC, USA), and Jointpoint 4.0.1 (Surveillance Research, National Cancer Institute, USA).

Results

Admissions for genital warts

In total over the period 1 July 1999 to 30 June 2011, there were 39,350 admissions for genital warts (24,811 in females and 14,539 in males). The most common warts sites were vulval/vaginal in females (15,194 admissions) and anal/perianal/perineal in males (6,959 admissions) (**Table 6.2**). Approximately 57% of admissions in females and 75% of admissions in males appeared to include a principal diagnosis of warts, based on either a primary diagnosis of A63.0 or another primary diagnosis consistent with the Australian Coding Standards for ICD-10-AM. However, only a minority of these apparent principal diagnoses of warts involved a warts-related procedure (33% in females; 17% in males). A very large proportion of these apparent principal diagnoses of warts involved only non-warts procedures (58% in females; 73% in males). As a result, we considered that the data did not appear to accord well with the coding standard in ascertaining whether or not warts was the principal diagnosis, and this analysis did not perform any stratification by whether or not warts was the principal diagnosis.

The median age at admission was 26 years in females (interquartile range [IQR]: 21–37 years) and 35 years in males (IQR: 26–46 years). The distribution of age at admission over the period July 1999 to June 2011 is shown, by sex, in **Figure 6.1**.

Age-standardised admission rates in females were lower in 2010/2011 (11.4 per 100,000) than in 1999/2000 (25.4 per 100,000), while admission rates in males were relatively unchanged over the same period (11.5 per 100,000 in 1999/2000; 10.9 per 100,000 in 2010/2011) (**Figure 6.2**).

Table 6.2. Hospital admissions involving a diagnosis of genital warts by sex and anatomical site, July 1999 to June 2011*

Warts site	Females	Males
Vulval/vaginal	15,194	–
Anal/perianal/perineal	4,785	6,959
Cervical	3,397	–
Urethral	279	–
Urethral/penile/scrotal	–	4,093
Unspecified	*4,762*	*3,895*

* Multiple sites were involved in some admissions so counts in this table sum to more than total number of admissions. Diagnosis and procedure codes used to assign site appear in **Table A6.1.1** in **Appendix 6.1**.

Figure 6.1. Age distribution of admissions involving anogenital warts by sex, all admissions, July 1999 to June 2011

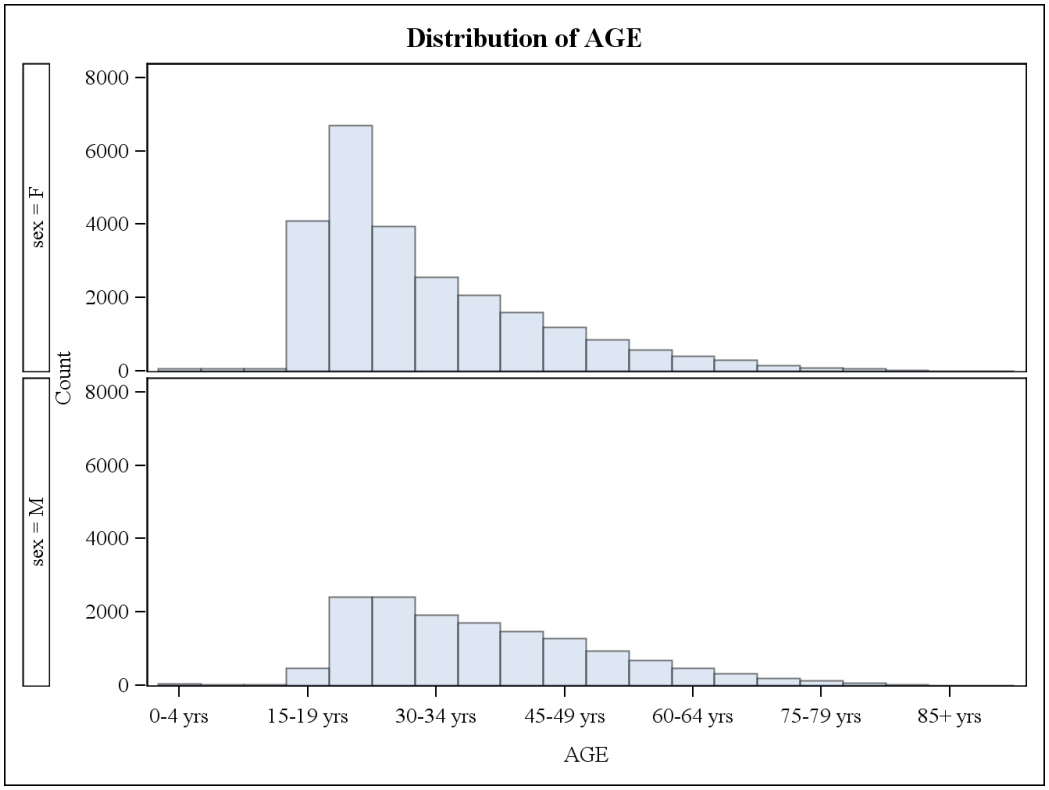
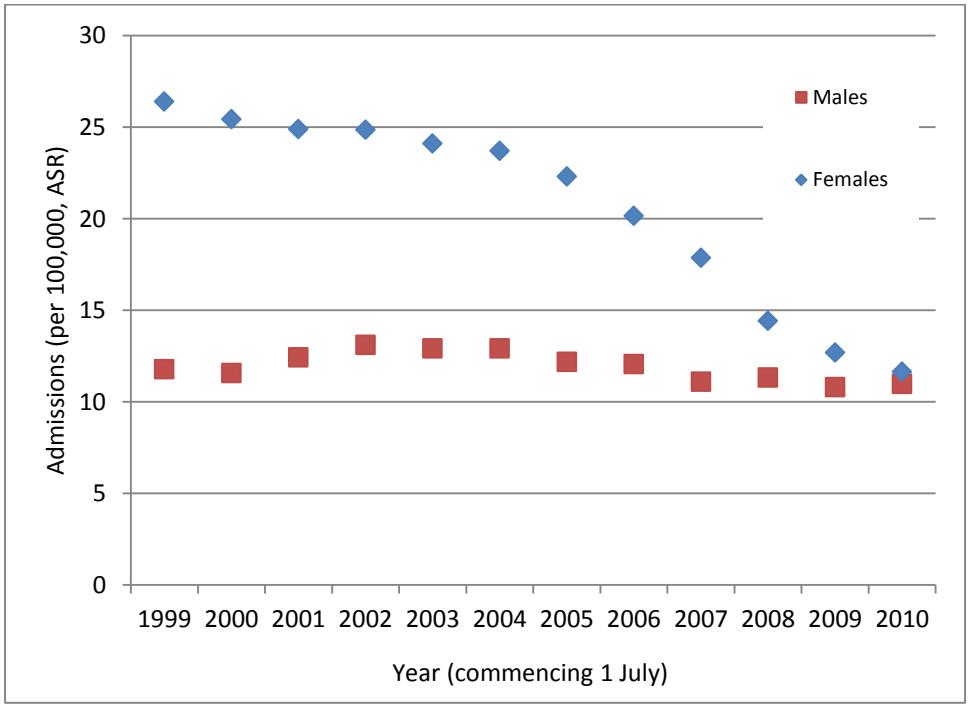


Figure 6.2. Rates* of admissions involving genital warts, July 1999 to June 2011, by sex



* Rates age-standardised, per 100,000 population, using the Australia 2001 standard population.

Concurrent diagnoses

Most admissions involved multiple diagnosis codes (91% of admissions in females; 86% in males). The median number of additional diagnoses (i.e. those other than diagnoses relating to genital warts) was 2 for both females and males. **Table 6.3** shows the most common other diagnoses which were associated with admissions involving a diagnosis of genital warts. Many of these refer to general diagnoses relating to sites commonly associated with genital warts (N90.8 vulva, N89.8 vagina, N88.8 cervix, K62.8 anus, N48.8 penis and N36.8 urethra). Prior to July 2010, the Australian Coding Standards advised that these general diagnoses be used in order to capture the site of the genital warts. From July 2010, the more detailed A63 codes allowed the site to be captured directly, and thus these 'other diagnoses' codes were no longer used for this purpose (these diagnoses virtually disappeared from this dataset in July 2010, whereas they had been very common prior to then).

Table 6.3. Most common concurrent diagnoses among patients admitted with a diagnosis involving genital warts

Females		Males	
Diagnosis	**Count**	**Diagnosis**	**Count**
N90.8 Other specified noninflammatory disorders of vulva and perineum*	11,049	K62.8 Other specified diseases of the anus and rectum*	6,022
Z72.0 Tobacco use	8,341	Z72.0 Tobacco use	4,812
N89.8 Other specified noninflammatory disorders of vagina*	4,069	N48.8 Other specified disorders of the penis*	3,079
K62.8 Other specified diseases of anus and rectum*	3,921	Z86.43 Personal history of tobacco use disorder	958
N88.8 Other specified noninflammatory disorders of cervix uteri*	3,517	N36.8 Other specified disorders of urethra*	790
B97.7 Papillomavirus as the cause of diseases classified to other chapters	2,778	B20 HIV resulting in infectious and parasitic diseases	527
N87.0 Mild cervical dysplasia (CIN1)	2,243	Z21 Asymptomatic HIV positive	513
N87.1 Moderate cervical dysplasia (CIN2)	1,602	I84.6 Residual haemorrhoidal skin tags of anus or rectum	359
D06.9 Carcinoma in situ of cervix uteri (CIN3)	1,078	I84.9 Unspecified haemorrhoids without complication	344
Z86.43 Personal history of tobacco use disorder	1,040	I10 Primary hypertension	302
N72 Inflammatory disease of cervix uteri (incl. cervicitis)	1,016	I84(.2) Haemorrhoids	299
Z37.0 Single live birth	941	Z30.2 Sterilisation (vasectomy)	285
O98.3 Other infections with a predominantly sexual mode of transmission complicating pregnancy, childbirth and the puerperium	662	B07 Viral warts (excl. anogenital/papilloma)	279
O09.1 Duration of pregnancy 5–13 completed weeks	543	K92.2 Gastrointestinal haemorrhage, unspecified	277
N92.0 Excessive and frequent menstruation with regular cycle	373	K60.2, .3 Anal fissure/fistula	414
J45.9 Asthma, unspecified	319	D01.3 Anal carcinoma in situ (AIN3)	205

* Australian Coding Standards recommended that these codes be used as principal diagnoses in admissions primarily related to genital warts from July 1998 to June 2010 (July 2002 to June 2010 for N36.8 urethra), to identify the site.

Procedures

The most common procedures performed during admissions involving a diagnosis of genital warts are shown in **Table 6.4**, by sex. Many admissions involved multiple procedures (60% of admissions in females; 43% in males), so the counts in **Table 6.4** total more than the number of admissions. However, a proportion of admissions did not have any procedures recorded (2,185 in females, 1,358 in males; approximately 9% in both sexes).

Table 6.4. Most common procedures* performed among patients admitted with a diagnosis involving genital warts

Females		**Males**	
Procedure	**Count**	**Procedure**	**Count**
Destruction of vulval wart	5,969	Removal of anal wart	1,663
Cautery/laser destruction/diathermy/ biopsy of cervix/LLETZ	3,482	Removal of other wart (incl. plantar, palmar, molluscum contagiosum)	1,513
Colposcopy	3,315	Other procedures relating to anus or rectum	1,269
Destruction of vaginal wart	2,696	Colonoscopy/sigmoidoscopy	1,020
Dilation & curettage/dilation & evacuation/dilation of cervix/curettage of uterus/suction curettage of the uterus	2,483	Other procedures relating to the urethra	571
Removal of anal wart	2,286	Procedures relating to haemorrhoids	405
Laser destruction/excision/biopsy of vulva or vagina	1,448	Other procedures relating to the penis	400
Procedures relating to childbirth/ delivery/pregnancy	1,149	Endoscopic destruction of penile wart	177
Diagnostic hysteroscopy	1,139	Endoscopic destruction of urethral wart	150
Removal of other wart	653	Procedures relating to circumcision	107
Papanicolaou smear study†	652		
Other procedures relating to anus or rectum	581		
Fertility-related (IUD insertion/removal, subdermal hormone implantation/ removal, oocyte retrieval, sterilisation)	654		

* There were also a very substantial number of procedures relating to anaesthesia, sedation and neuraxial blocks (excluding those performed in labour) – 19,702 procedures in females; 12,128 procedures in males.

† This 'Papanicolaou smear study' procedure did not appear to be related to cervical screening or management procedures; rather it predominantly occurred in the absence of any procedure relating to cervical abnormalities. It most commonly occurred concurrent with procedures for removing warts or procedures relating to dilation and/or curettage/evacuation.

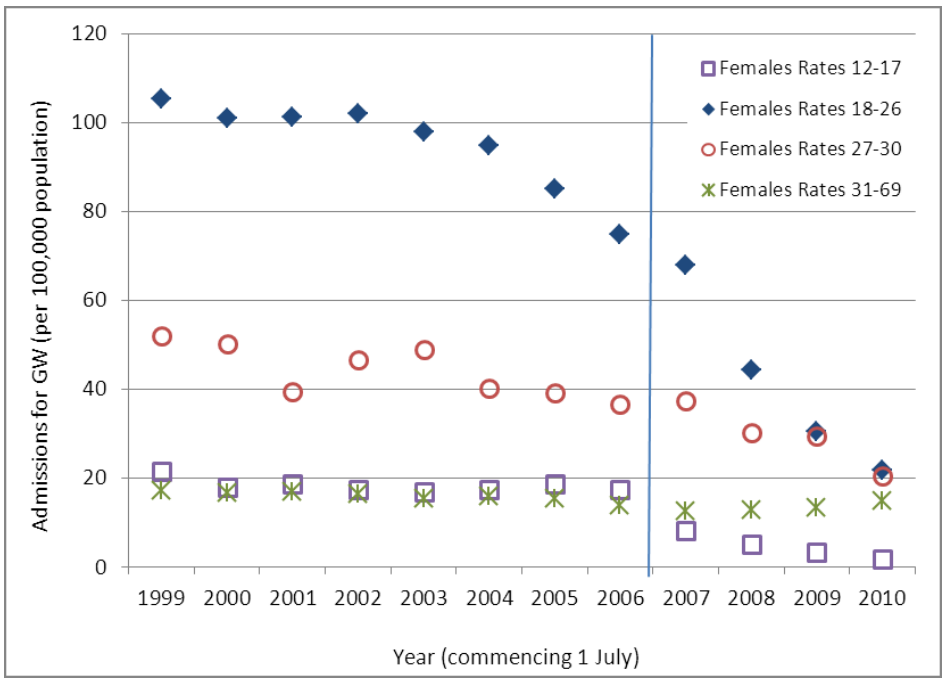
Age-related trends in admissions

Trends in admissions for genital warts by age are shown below for females (**Figure 6.3**) and males (**Figure 6.4**). Reductions in admission rates were observed after the implementation of the National HPV Vaccination Program in 2007 in younger females (all age groups ≤30 years) and also in males aged 18–26 years.

In females, the overall reductions in 2010/2011, relative to 2006/2007, were 89.9% (95% CI: 84.6–93.4%) for females aged 12–17 years, 72.7% (95% CI: 67.0–77.5%) for females aged 18–26 years and 42.1% (95% CI: 26.1–54.6%) for females aged 27–30 years. Similar results were obtained for the rate ratios that compared the period July 2010 to June 2011 with the 3-year pre-vaccine period (July 2004 to June 2007; **Table 6.5**). The rate ratios comparing each successive post-vaccine year with the pre-vaccine average also became progressively smaller in each of these groups (**Table 6.5**). This is consistent with a progressive increase in the proportion of these groups being vaccinated over time, as more cohorts offered vaccination enter these age groups and as cohorts vaccinated at school (where uptake was higher and prior exposure less likely) age over time into older age groups (**Appendix 6.3**). Based on the Jointpoint analysis, the annual percentage change (APC) in the rate of admissions was significant for females aged 12–17 years from mid-2007 (APC 44.1% decline; 95% CI: 35.4–51.6%) and for females aged 18–26 years from mid-2008 (APC 31.8% decline, 95% CI: 28.4–35.2%). However, the reduction in admissions in females aged 27–30 years appeared to be a continuation of a decline which pre-dated the vaccination program.

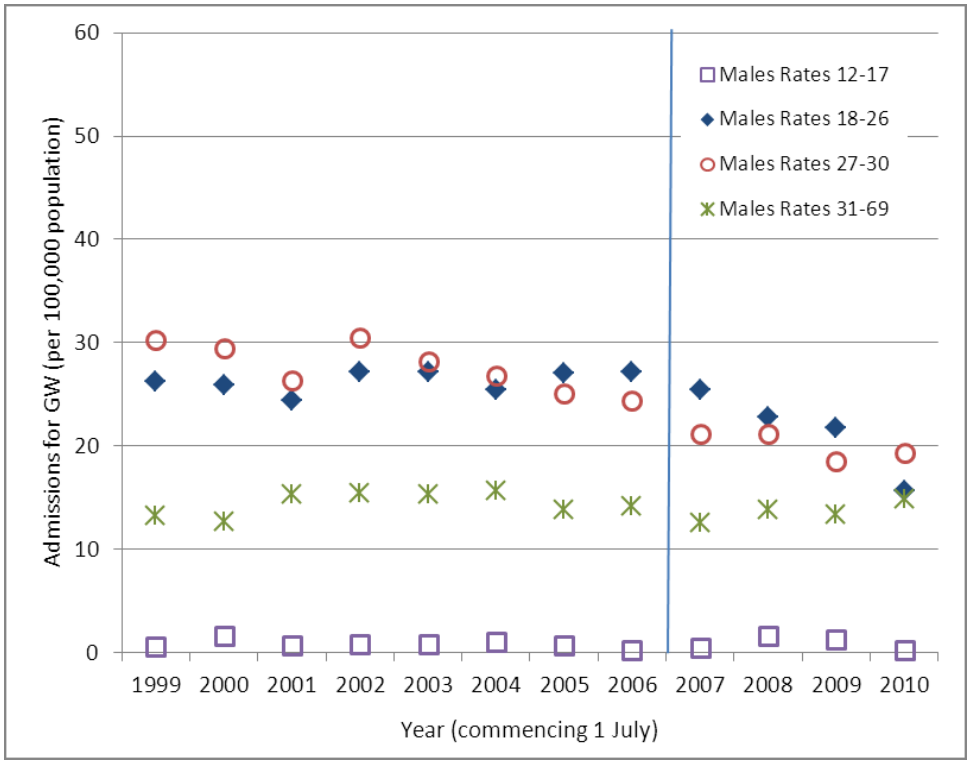
In males, the overall reduction in 2010/2011, relative to 2006/2007, was 38.3% (95% CI: 27.7–47.2%) for males aged 18–26 years. Similar results were obtained for the rate ratios that compared the period July 2010 to June 2011 with the 3-year pre-vaccination period (July 2004 to June 2007;**Table 6.5**), although in this analysis there was also an observed reduction in admission rates in males aged 27–30 years (RR=0.76; 95% CI: 0.63–0.93). The APC in the rate of admissions was significant for males aged 18–26 years from mid-2008 (APC 14.0% decline; 95% CI: 5.1–22.1%) but not for any other age group. The post-vaccine decline in the rate ratio observed in males aged 27–30 years appeared to be a continuation of a pre-existing downward trend.

Figure 6.3. Age-specific rates of admissions involving genital warts in females, per 100,000 population, July 1999 to June 2011



Line indicates commencement of National HPV Vaccination Program

Figure 6.4. Age-specific rates of admissions involving genital warts in males, per 100,000 population, July 1999 to June 2011



Line indicates commencement of National HPV Vaccination Program

Table 6.5. Admission rates for genital warts, per 100,000 population, and rate ratios, by age and sex

	Age (years)	Average admission rates (per 100,000)		Rate ratio relative to pre-vaccine period (95% CI)				
		Pre-vaccine period (Jul 2004–Jun 2007)	Post-vaccine period (Jul 2008–Jun 2011)	Overall post-vaccine period (Jul 2008–Jun 2011)	2007/08	2008/09	2009/10	2010/11
Females	12–17	17.9	3.4	0.19 *(0.15–0.24)*	0.46 *(0.35–0.59)*	0.28 *(0.21–0.39)*	0.18 *(0.12–0.26)*	0.10 *(0.06–0.17)*
	18–26	84.8	32.1	0.38 *(0.36–0.40)*	0.80 *(0.74–0.86)*	0.52 *(0.48–0.57)*	0.36 *(0.33–0.40)*	0.26 *(0.23–0.29)*
	27–30	38.7	26.6	0.69 *(0.61–0.77)*	0.97 *(0.83–1.13)*	0.78 *(0.66–0.92)*	0.76 *(0.64–0.90)*	0.53 *(0.44–0.64)*
	31–69	15.0	13.6	0.91 *(0.85–0.96)*	0.82 *(0.76–0.90)*	0.86 *(0.79–0.93)*	0.88 *(0.81–0.96)*	0.98 *(0.90–1.06)*
Males	12–17	0.7	1.1	1.53 *(0.85–2.76)*	0.66 *(0.22–1.94)*	2.29 *(1.14–4.61)*	1.80 *(0.85–3.81)*	0.49 *(0.14–1.67)*
	18–26	26.6	20.1	0.75 *(0.69–0.82)*	0.95 *(0.84–1.08)*	0.86 *(0.76–0.97)*	0.82 *(0.72–0.93)*	0.59 *(0.51–0.68)*
	27–30	25.4	19.7	0.77 *(0.67–0.89)*	0.83 *(0.68–1.02)*	0.83 *(0.68–1.02)*	0.73 *(0.59–0.89)*	0.76 *(0.63–0.93)*
	31–69	14.5	14.0	0.96 *(0.91–1.02)*	0.87 *(0.80–0.95)*	0.95 *(0.87–1.03)*	0.92 *(0.85–1.00)*	1.02 *(0.94–1.11)*

See also **Table A6.3.1** in **Appendix 6.3** for details of admission numbers by age and year.

Sensitivity analysis

A sensitivity analysis was performed which looked at age-related trends in admissions in males stratified by whether the admission involved a diagnosis or procedure relating to anal warts or whether only non-anal sites were involved (**Table A6.1.1** in **Appendix 6.1**). The reductions in warts admissions observed in younger males aged 18–26 years appeared to be confined to admissions involving only non-anal sites; there was no evidence of a reduction in admissions involving anal warts in this age group. Admissions for non-anal warts in males in 2010/2011 were estimated to have decreased by 57% (95% CI: 44–68%) compared to 2006/2007, and by 63% (95% CI: 53–71%) compared to the average for the pre-vaccine period. There was no evidence of a reduction in admissions involving anal warts among males aged 18–26 years (P=0.46).

Table 6.6. Results of analysis in males aged 18–26 years stratified by warts site (sensitivity analysis)

Parameter estimates	All sites	Anal warts	Non-anal sites only*
Average admission rates			
Pre-vaccine period (Jul 2004–Jun 2007)	26.6 per 100,000	11.4 per 100,000	15.2 per 100,000
Post-vaccine period (Jul 2008–Jun 2011)	20.1 per 100,000	10.1 per 100,000	9.9 per 100,000
Rate ratios			
Post-vaccine average relative to pre-vaccine average	0.75 *(95% CI: 0.69–0.82)*	0.89 *(95% CI: 0.78–1.02)*	0.65 *(95% CI: 0.57–0.74)*
2010/2011 admission rate relative to pre-vaccine average	0.59 *(95% CI: 0.51–0.68)*	0.88 *(95% CI: 0.73–1.06)*	0.37 *(95% CI: 0.29–0.47)*
Percentage reduction in 2010 relative to 2006 (Poisson analysis)	38% *(95% CI: 28–47%)*	10% *(95% CI: 31% to 19% increase)*	57% *(95% CI: 44–68%)*

* Excludes admissions which also included ICD-10-AM codes K62.8, A63.01, A63.09 (includes perianal and perineal warts) or procedure codes for treatment of anal warts (32177, 32180).

A number of admissions involved a concurrent HIV-related diagnosis (**Table 6.7**). These predominantly occurred in males (8.4% of all admissions in males), but were rare in females (less than 0.1% of all admissions in females). It is likely that HIV status in males is associated with men who have sex with men, as approximately two-thirds of new HIV diagnoses in Australia occur in men who have sex with men.[122] Other studies had indicated little change in new cases of genital warts in men with recent same-sex sexual contact (within the previous 12 months) since the implementation of the female-only HPV vaccination program in 2007.[117] As a sensitivity analysis, we re-analysed the data after

excluding individuals with a concurrent HIV-related diagnosis, in order to assess if this affected the estimated reductions, particularly in males aged 18–26 years. As shown in **Table 6.7**, excluding these individuals had very little impact on the estimates for the effect of vaccination in males aged 18–26 years, or in other age groups (data not shown).

Table 6.7. Results of excluding males with a concurrent HIV-related diagnosis on parameter estimates (sensitivity analysis)

Parameter estimates	Analysis including all males	Analysis excluding males with a concurrent HIV-related diagnosis*
Average admission rates		
Pre-vaccine period (Jul 2004–Jun 2007)	26.6 per 100,000	26.1 per 100,000
Post-vaccine period (Jul 2008–Jun 2011)	20.1 per 100,000	19.8 per 100,000
Rate ratios		
Post-vaccine average relative to pre-vaccination average	0.75 *(95% CI: 0.69–0.82)*	0.76 *(95% CI: 0.69–0.83)*
2010/2011 admission rate relative to pre-vaccine average	0.59 *(95% CI: 0.51–0.68)*	0.59 *(95% CI: 0.51–0.68)*
Percentage reduction in 2010 relative to 2006 (Poisson analysis)	38% *(95% CI: 28–47%)*	39% *(95% CI: 28–48%)*

* Excludes admissions which also included ICD-10 AM codes B20, B21, B22, B23, B24, Z21, O98.7, F02.4.

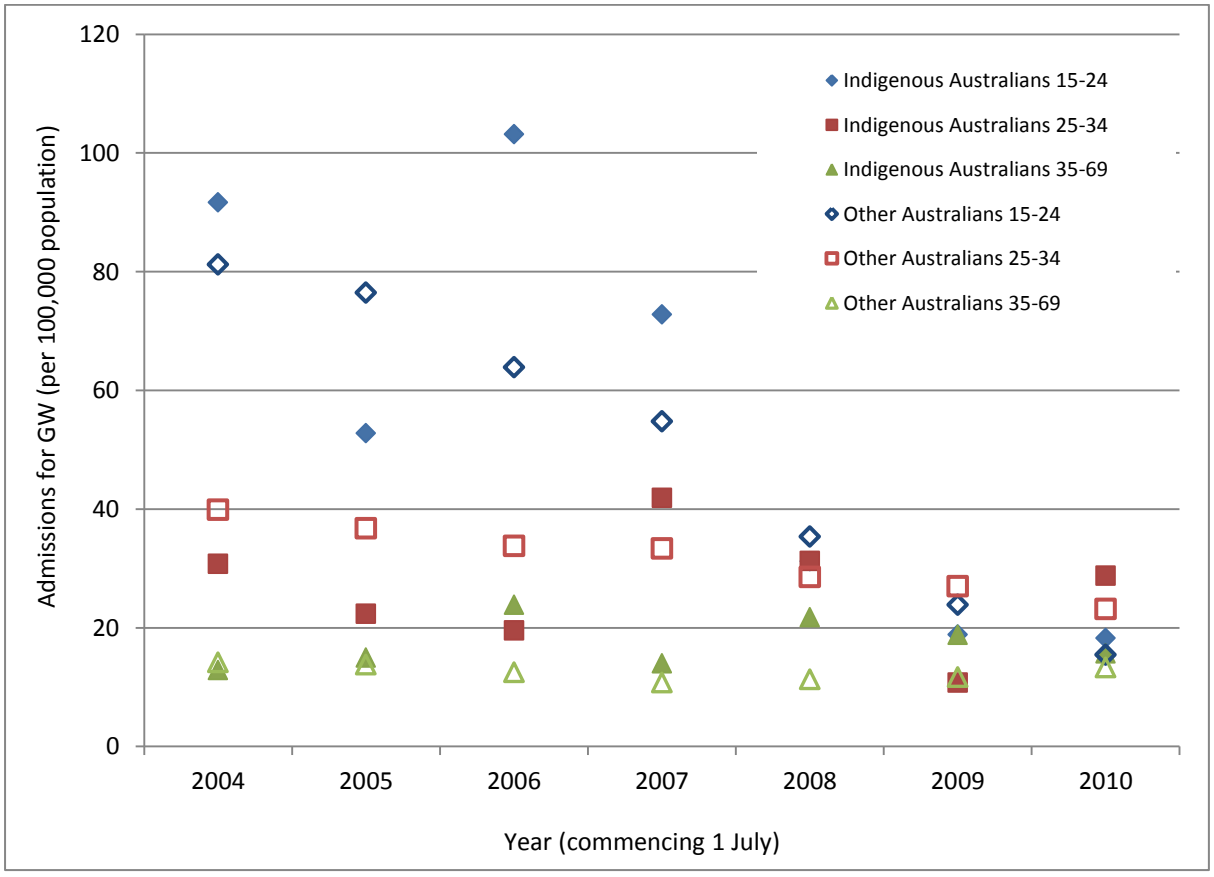
Age-related trends in admissions by Indigenous status

Admissions and rates of admissions involving a diagnosis of genital warts in females by Indigenous status are shown in **Figure 6.5** and **Table 6.8**. There were very few admissions in Indigenous males (cell sizes less than five for most age groups and years), and so these are not reported here or analysed further.

Negative binomial models were fitted, including interaction terms for Indigenous status. Substantial reductions in admission rates were observed for females aged 15–24 years since the introduction of the National HPV Vaccination Program. The declines were comparable in Indigenous females and other Australian females, and there was no evidence of variation by Indigenous status (P=0.08). Compared to admissions rates in 2006/2007, admission rates in 2010/2011 were estimated to have declined by 86.7% (95% CI: 76.0–92.7%) in Indigenous females aged 15–24 years, and by 76.1% (95% CI: 71.6–79.9%) in other females aged 15–24 years. A smaller but significant post-vaccine reduction was observed in 2010/2011 relative to 2006/2007 for other females aged 25–34 years (32.0%; 95% CI: 19.3–42.6%), but not in Indigenous females (17.7%; 95% CI: –85.4% to 73.5%). No changes in admission rates were observed for older females.

The findings were broadly similar for rate ratio estimates. The ratio of post-vaccine to pre-vaccine admission rates by age group and Indigenous status are shown in **Table 6.9**. Post-vaccine admission rates were substantially lower than pre-vaccine rates in both Indigenous females and other Australian females aged 15–24 years, and rate ratios were very similar for Indigenous and other females. The overall rate ratios comparing the average pre- and post-vaccine admission rates in females aged 15–24 years were 0.27 (95% CI: 0.19–0.40) for Indigenous females and 0.34 (95% CI: 0.31–0.36) for other females. Individual rate ratios for the intervening years followed a similar pattern in both Indigenous and other females, and the ratios of admission rates in 2010/2011 to pre-vaccine rates were 0.22 (95% CI: 0.12–0.42) for Indigenous females and 0.21 (95% CI: 0.18–0.24) for other females. Comparing post-vaccine admission rates to pre-vaccine rates, there was no significant decline in admission rates for Indigenous females aged 25–34 years nor those aged 35–69 years. A significant post-vaccine reduction was observed in other Australian females aged 25–34 years (2010/2011 RR=0.63; 95% CI: 0.56–0.71) but not in older other Australian females (**Table 6.9**).

Figure 6.5. Age-specific rates of admissions* involving genital warts in females, per 100,000 population, July 2004 to June 2011



* Includes data from hospitals in NSW, VIC, QLD, SA, WA and NT only.

Table 6.8. Admissions* and rates of admissions (per 100,000 population) involving a diagnosis of genital warts in females, July 2004 to June 2011, by Indigenous status, age and year of admission

Year (starting 1 July)	Indigenous females						Other Australian females					
	15–24 years		25–34 years		35–69 years		15–24 years		25–34 years		35–69 years	
	Admissions n	Rate	Admissions n	Rate	Admissions n	Rate	Admissions n	Rate	Admissions n	Rate	Admissions n	Rate
2004	40	91.7	11	30.8	<5	12.9	1,036	81.2	540	39.9	584	14.2
2005	24	52.8	8	22.4	8	15.0	992	76.5	498	36.8	582	13.8
2006	49	103.2	7	19.6	15	23.9	844	63.9	460	33.8	537	12.5
2007	36	72.8	15	41.9	8	14.0	739	54.8	463	33.4	472	10.8
2008	16	31.2	6	31.3	14	21.8	489	35.4	408	28.6	506	11.3
2009	10	18.9	<5	10.8	14	18.8	337	23.9	396	27.0	532	11.7
2010	10	18.3	11	28.8	12	15.7	217	15.5	345	23.2	613	13.3
July 2004–June 2011	**185**		**62**		**75**		**4,654**		**3,110**		**3,826**	

* Includes admissions from hospitals in NSW, VIC, QLD, SA, WA and NT only.

Table 6.9. Admission rates* for genital warts in females, per 100,000 population, and rate ratios, by age and Indigenous status

		Average admission rates (per 100,000)		Rate ratio relative to pre-vaccine period (95% CI)				
	Age (years)	Pre-vaccine period (Jul 2004–Jun 2007)	Post-vaccine period (Jul 2008–Jun 2011)	Overall post-vaccine period (Jul 2008–Jun 2011)	2007/08	2008/09	2009/10	2010/11
Indigenous females	15–24	82.7	22.7	0.27 *(0.19–0.40)*	0.88 *(0.60–1.28)*	0.38 *(0.22–0.64)*	0.23 *(0.12–0.44)*	0.22 *(0.12–0.42)*
	25–34	24.3	22.2	0.91 *(0.51–1.63)*	1.72 *(0.91–3.25)*	1.29 *(0.53–3.13)*	0.44 *(0.15–1.27)*	1.19 *(0.59–2.40)*
	35–69	18.3	18.6	1.01 *(0.62–1.65)*	0.77 *(0.35–1.68)*	1.19 *(0.62–2.26)*	1.02 *(0.54–1.95)*	0.85 *(0.43–1.69)*
Other females	15–24	73.8	24.9	0.34 *(0.31–0.36)*	0.74 *(0.68–0.81)*	0.48 *(0.44–0.53)*	0.32 *(0.29–0.36)*	0.21 *(0.18–0.24)*
	25–34	36.8	26.2	0.71 *(0.66–0.77)*	0.91 *(0.82–1.01)*	0.78 *(0.70–0.87)*	0.73 *(0.65–0.82)*	0.63 *(0.56–0.71)*
	35–69	13.5	12.1	0.90 *(0.84–0.96)*	0.80 *(0.72–0.88)*	0.84 *(0.76–0.93)*	0.87 *(0.78–0.95)*	0.99 *(0.90–1.08)*

* Includes data from hospitals in NSW, VIC, QLD, SA, WA and NT only.

Age-related trends in admissions prior to introduction of the National HPV Vaccination Program

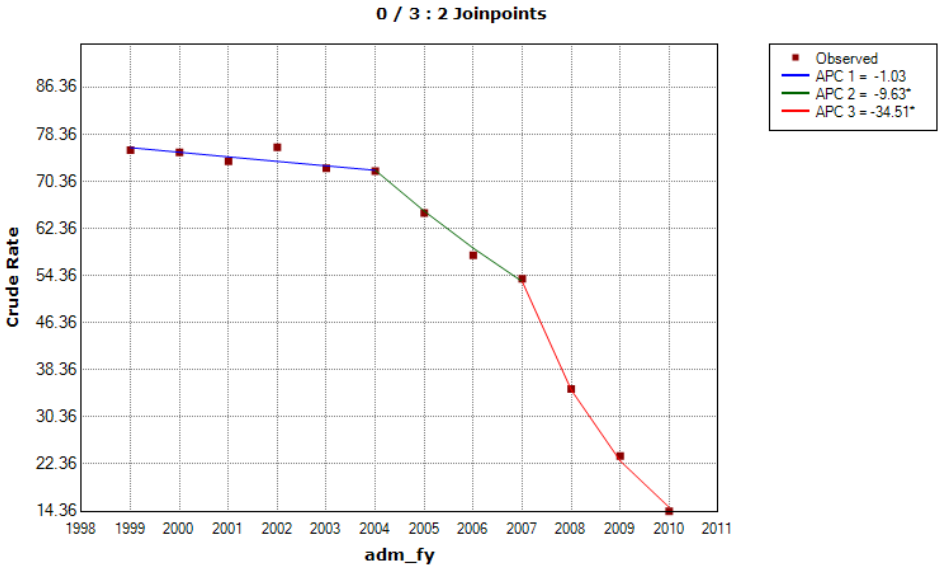
Trends in admissions prior to the introduction of the National HPV Vaccination Program were also examined. There was no evidence of a change in admissions in females aged 12–17 years (APC 2% decline; 95% CI: 5.0% decline to 0.5% increase) nor in males 18–26 years (APC 0.4% increase; 95% CI: 1.5% decline to 2.4% increase). In females aged 27–30 years, a significant decline was observed over the entire period July 1999 to June 2011 (APC 5.9% decline; 95% CI: 3.8–8.0% decline), and this was found to be a better fit to the data than models with either one or two Jointpoints. In females aged 18–26 years, the best-fitting model estimated a small decline in admissions for genital warts between July 1999 and June 2004 (APC 1.7% decline; 95% CI: 0.4–3.0% decline), a larger decline between July 2004 and June 2008 (APC 11.4% decline; 95% CI: 5.5–16.9% decline), and finally a very substantial decline between July 2008 and June 2011 (APC 31.8% decline; 95% CI: 28.4–35.2% decline). The decline in July 2008 to June 2011 was significantly greater than that in the previous period (P <0.001).

We hypothesised that the trends in warts admissions in females may be affected by changes in cervical screening practices that occurred in the time period examined here, including since the introduction of the National HPV Vaccination Program, as a substantial proportion of warts admissions in females had a procedure code or an additional diagnosis code related to investigation of cervical abnormalities; it is possible that warts may have been an incidental diagnosis for these admissions. Changes in screening practices included changes in screening participation, management guidelines and laboratories' use of recommendation codes[92,123] (personal communication, A/Prof Dorota Gertig, Medical Director, Victorian Cervical Cytology Register). To further explore this, admissions in females were divided into two groups based on whether or not the admission involved a procedure relating to investigation or treatment of a screen-detected cervical abnormality: 'potentially screening-related' or was 'unrelated to cervical screening' (see **Table A6.1.2** in **Appendix 6.1**).

Procedures relating to follow-up or treatment of screen-detected cervical abnormalities ('potentially screening related') were recorded in 25% of admissions in females aged 18–26 years. In the stratified analyses, in females aged 18–26 years, for admissions 'unrelated to cervical screening' no significant decline was observed between 1999 and 2004, followed by a decline of 9.6% per annum from mid-2005, then a more substantial decline from mid-2008 of 34.5% per annum. The decline from mid-2008 onwards (APC 34.5% decline; 95% CI: 29.7–39.0% decline) was substantially and significantly greater (P=0.001) than the trend in the preceding years (APC 9.6% decline; 95% CI: 1.2–17.3% decline). Thus, admissions

involving a diagnosis of genital warts which were unrelated to cervical screening declined at a rate which was marginally higher than our original estimate, although the difference was not significant.

Figure 6.6. Admission rates for genital warts with no cervical procedure recorded (unrelated to screening), per 100,000 population, females aged 18–26 years



Discussion

These population-based hospital admissions data suggest a substantial drop in admissions involving a diagnosis of genital warts since the introduction of the National HPV Vaccination Program. These have been most pronounced in younger females, with a 90% reduction in admissions of females aged 12–17 years and a 73% reduction in admissions of females aged 18–26 years. There has also been a substantial (38%) reduction in admissions of males aged 18–26 years, potentially representing indirect (herd) protection from the female-only program, since there was no change in this age group prior to mid-2008. There was also an observed reduction in admissions in females aged 27–30 years at admission in the post-vaccine period relative to the pre-vaccine period; however, this may have been a continuation of a decline prior to the vaccination program, and there was no evidence that the decline in the post-vaccine period was greater than that prior to mid-2007.

These results are consistent with findings from previous studies. For example, Ali et al.[124] found a 73% reduction between 2011 and 2007 in new diagnoses of genital warts among 21–30-year-old females presenting to a sentinel group of sexual health clinic sites, and estimated an average annual summary rate ratio of 0.74 (corresponding to an average 26% annual decline; 95% CI: 21–30%) over this period. We found comparable reductions in

admissions for females aged 18–26 years over a similar time period (overall reduction 73% [95% CI: 67–77%]; annual decline 32% [95% CI: 28–35%]). Similarly, our findings for the estimated reductions in admissions in females aged 12–17 years (overall reduction 90% [95% CI: 84–93%]; average annual decline 44% [95% CI: 35–52%]) and in males aged 18–26 years (overall reduction 38% [95% CI: 28–47%]; average annual decline 14% [95% CI: 5–22%]) are comparable to those observed in the study by Ali et al. for females aged <21 years (overall reduction 93%; annual decline 50% [95% CI: 45–55%]) and heterosexual males aged 21–30 years (overall reduction 51%; annual decline 16% [95% CI: 13–19%]).[124] Our results for females and males aged 18–26 years are also broadly consistent with those for females and males aged 15–24 years from a previous analysis of Medicare data relating to in-patient treatments in private hospitals for vulval or vaginal warts in females and penile and anal warts in males.[125]

Our findings are also comparable with the reduction in vaccine-included HPV type prevalence observed in a repeat cross-sectional survey of females aged 18–24 years.[126] Tabrizi et al.[126] reported a 79% reduction in vaccine-included HPV type prevalence (HPV 6,11,16,18) in 18–24-year-old females in 2010–2011 compared to the prevalence in 2005–2007 (adjusted odds ratio 0.16; 95% CI: 0.09–0.26). Our findings that admission rates for females aged 18–26 years dropped by 73% (95% CI: 67–77%), and a rate ratio estimated as 0.26 (95% CI: 0.23–0.29), correspond reasonably closely to these, although they would only be comparable to HPV6 and 11, the types associated with genital warts.

To our knowledge, this is the first analysis in Australia which has been able to examine potential impacts of the National HPV Vaccination Program by Indigenous status. We found reductions in admissions related to genital warts in the post-vaccine period for Indigenous females aged 15–24 years to be comparable to other Australian females aged 15–24 years (87%; 95% CI: 76–93% vs 76%; 95% CI: 72–80% respectively; P-value heterogeneity 0.08). This evidence of a substantial decline in admissions with a diagnosis of genital warts in the post-vaccine period in Indigenous females is encouraging, because of the higher rate of other HPV-related disease, notably cervical cancer, in Indigenous females which the vaccine may prevent in future.[92,127]

To date, there has been limited data on HPV vaccine uptake by Indigenous status, because Indigenous status is not a mandatory field for reporting to the NHVPR and completeness of reporting varies by jurisdiction.[41] Based on data from Queensland and the Northern Territory, 3-dose uptake in females aged 12–17 years in 2007 was lower for Indigenous females than for females overall in each of these jurisdictions.[41] In Queensland, this appeared to be predominantly due to lower rates of course completion in Indigenous females, whereas in the Northern Territory course completion was the same, but Indigenous females were less

likely to start the vaccine course.[41] These two jurisdictions represent approximately 40% of the female Indigenous population aged 10–14 years, with most of the remainder residing in New South Wales (approximately 30%) and Western Australia (approximately 13%).[121] It is possible that uptake in Indigenous females in other jurisdictions may be higher than reported in Queensland and the Northern Territory.

There are some caveats around the findings in this study by Indigenous status. These include the possible contribution of changes in ascertainment of Indigenous status for Indigenous patients to changes in admission rates for Indigenous people – although this would likely work in the opposite direction to the declines observed here. Also, the findings of this analysis may not be representative of the jurisdictions (Tasmania and the Australian Capital Territory) which were excluded from the analysis by Indigenous status.

A strength of this study is that it uses national, routinely collected data, which include admissions from virtually all public and private hospitals in Australia over the period examined. To our knowledge, this represents the largest dataset analysed for post-vaccine trends in genital warts in Australia, and is likely the largest data collection for genital warts available at the current time in Australia.

One of the limitations of this study is that hospital admissions data only capture a subset of genital warts, as these are mostly managed in general practice and sexual health clinics.[128] Based on published estimates for average incidence rates in Australia over the period 2000–2006, the admission rates observed in our hospital data in the same period represent approximately 8–11% of new cases in females and 3–5% of new cases in males aged under 30 years.[129] However, we would expect that these represent the majority of severe cases.

Another limitation of this study is that it is an ecological study and information about the vaccination status of the individuals is not available in this data collection. In future, an analysis of linked data from the NHVPR and NHMD would be valuable in providing stronger evidence. Nevertheless, the declines in admissions here are both substantial and specific in terms of both the age groups affected and the timing in relation to the implementation of the National HPV Vaccination Program. Furthermore, these declines are in contrast with observed increases in some other sexually transmitted infections, including chlamydia and gonorrhoea, in younger people over a similar period,[122] suggesting that a reduction in sexual risk behaviour is unlikely to explain the observed declines in genital warts.

Other possible explanations for the observed declining trend include that treatments for warts may have been increasingly performed outside of hospital settings over the post-vaccine period, for example, due to wider usage of topical treatments or other non-surgical methods. We feel this is unlikely to fully explain the substantial declines seen here, for a

number of reasons. Firstly, it is likely that such changes would affect all age groups and not just the younger age groups in whom declines were both very strong and different from those in other age groups. Secondly, the availability and price of topical treatments did not change substantially over this period.[125] Thirdly, similar declines to those we have described here have been observed in a national network of sentinel sexual health clinics in Australia, suggesting that treatments have not shifted to these sites.[124] It is possible that treatments may have moved from both hospitals and sexual health clinics towards general practice; however, this seems unlikely to fully explain the observed declines, as they are both substantial and specific to certain age groups. An analysis of trends in warts in general practice would provide further information on this point, for example, via the Bettering the Evaluation of Care and Health (BEACH) database.[130]

Another possible explanation is that there were changes in the rates of admissions for the principal diagnoses included here, when warts was not the primary reason for the admission. The most common procedures performed in males were related to warts treatment, and then procedures such as colonoscopy/sigmoidoscopy or relating to haemorrhoids. These procedures are more likely to be performed in older males, and so any changes in these are unlikely to have affected our findings for 18–26-year-old males, but rather are more likely to have affected admissions in older males, for example, those in the 31–69 years age group, where no changes were observed. In females, the most common procedures apart from those relating to warts treatments were related to follow-up or treatment of cervical abnormalities. Changes in patterns of admissions for these procedures is plausible, but are unlikely to explain the very strong declines in genital warts in younger females aged 12–17 years, as screening is not recommended for this age group.

When we excluded admissions in females aged 18–26 years which also involved a procedure plausibly for follow-up of a screen-detected cervical abnormality, a strong decline from mid-2008 was still evident, and was significantly greater than the trend in the pre-vaccine period. Thus screening changes do not appear to explain the decline from mid-2008 onwards, because this decline also occurred in women who were admitted for reasons unrelated to cervical screening. It is also unlikely to be a continuation of an earlier secular trend because the post-vaccine decline was much stronger than the earlier decline in females in age groups eligible for HPV vaccination. It is possible that a secular trend in declining referrals was occurring prior to the vaccination program; however, the underlying mechanism cannot be determined from these data. It is unlikely to have been related to cervical screening, however, because it also occurred in women who were admitted for reasons unrelated to cervical screening.

Conclusions

There has been a marked decline in admissions involving a diagnosis of genital warts in young females (aged 12–26 years) and also in young males (aged 18–26 years) in Australia since the implementation of the National HPV Vaccination Program. These declines are consistent with other evidence from Australia which suggests that the program has had a rapid and substantial impact on genital warts in young people. They also contribute to evidence of herd immunity benefits in males from the female vaccination program. This study also provides the first indication that the impact of vaccination in Indigenous females appears to be similar to that in other Australian females.

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Appendices

Appendix 2.1

Sampling matrix of stakeholders for interview in the process evaluation

Stakeholder	National	NSW	ACT	QLD	VIC	TAS	SA	NT	WA
Department of Health and Ageing	2 reps								
Key immunisation expert	2 reps								
National HPV Vaccination Register	X								
Jurisdictional Immunisation Coordinator		X	X	X	X	X	X	X	X
State/territory Cervical Screening Program managers		X	X	X	X	X	X	X	X
Division of General Practice/Medicare Locals		X	X	X	X	X	X	X	X
Regional state/territory government immunisation coordinators		X		X					X
School-based vaccination program coordinators (regional/local)		X	X	X	X	X	X	X	X
General practitioner		X			X		X		
Practice nurse		X		X				X	
Remote area immunisation provider								X	X
Health professional(s) from Aboriginal Medical Services		X						X	

Appendix 2.2

Interview questionnaire

Evaluation of the National Human Papillomavirus Vaccination Program

Immunisation Coordinators

- The National Centre for Immunisation Research and Surveillance (NCIRS) is currently undertaking an evaluation of the National Human Papillomavirus (HPV) Vaccination Program.
- The results will be provided to the Australian Government and the National Immunisation Committee (NIC) to inform future national vaccination programs.
- This questionnaire is divided into two parts:
    - **Part A** – has been designed to be completed online. It consists or a series of short answer questions on your knowledge and experience of the program. We will email you the link to the online survey. If you would prefer to complete an email version then please contact Stephanie Knox at stephanie.knox@health.nsw.gov.au for a printable copy of Part A.
    - **Part B** – these questions will be the basis for a telephone interview. They are being provided now to allow you time to reflect on them and collect any supporting information to inform your responses.
- All information you provide will be confidential and the final report to the Department of Health and Ageing will contain de-identified, summarised information.

This will cover the following

- ✓ Your role during the program
- ✓ Program planning and implementation
- ✓ Communication strategies & resources
- ✓ Data
- ✓ Program strengths and challenges

Internal Use Only

Participant	Participant Affiliation	Interviewer	Interview Date	Recorded	Transcription complete

PART B: Telephone interview

These questions will be the basis for your telephone interview, written responses are not required.

We would like to record this interview. Is this alright with you?

1. Participant details

1.1. Job title:

1.2. Organisation

1.3. Professional background

1.4. What is/was your role and its responsibilities in the implementation of the National HPV Vaccination Program:

1.4.i. School-based program for adolescent boys?

1.4.ii. School-based program for adolescent girls

1.5. Were you in your current position during the planning/roll-out of the National HPV school-based Vaccination Program for adolescent boys (From July 2012).

1.6. Were you involved in the planning/roll-out of the FEMALE National HPV Vaccination Program for adolescent girls and young women (From November 2006)?

1.6.i. In what role?

1.7. How long were/have you been involved in the female HPV program?

1.8. Is there another person from your organisation who could provide additional information regarding the implementation of either the female or the male program?

1.8.i. Name:

1.8.ii. Job title during program:

1.8.iii. Contact details:

2. Communication and Resources

MALE PROGRAM

Let's begin with the recent extension of the National Human Papillomavirus (HPV) Vaccination Program to include adolescent boys commencing February 2013.

1.1. How and when were you advised about the extension of the National HPV Vaccination Program to adolescent boys (Male program)?

1.2. Who were your target stakeholder groups/organisations to inform about the Male program?

1.3. How did you advise them about the program?

1.4. Has your organisation developed any program-specific resources for the male program?

If yes, please describe

1.4.i. What was developed?

1.4.ii. Why?

1.4.iii. When? (ie: pre/post program commencement)

1.4.iv. Who was the target audience/s?

1.4.v. How were they distributed?

1.4.vi. Key messages in these materials?

1.4.vii. Evaluations/feedback obtained?

1.5. Have you (or anyone for your organisation) attended any education specific to the male program?

If yes, please describe

1.5.i. How delivered? (ie teleconference?)

1.5.ii. Where?

1.5.iii. When?

1.5.iv. Who provided?

FEMALE PROGRAM

1.6. Can you recall what program specific information/communication resources were available for the female HPV program prior to 2013?

1.6.i. Who were the main providers of this information (ie govt, vaccine providers, professional bodies)?

1.6.ii. What was your experience of the quality and availability these information resources?

1.7. Did your organisation develop any program specific resources for the female HPV program?

1.7.i. What was developed?

1.7.ii. When?

1.7.iii. Key messages in these materials?

1.8. Have you (or anyone for your organisation) attended any education specific to the Female HPV program?

1.1.i. When?

1.1.ii. Who provided?

3. Service Delivery

1.2. Please comment on the initial rollout of the National HPV Vaccination Program for adolescent males (February 2013) in your jurisdiction. :

1.2.i. The lead time between the program announcement (July 2012) and commencement (February 2013)

1.2.ii. Obtaining vaccines

1.2.iii. Initial availability of information and resources

1.2.iv. Timetable for school-based catch-up program

1.3. Did your organisation receive any funding for the MALE program?

If yes, please describe;

1.3.i. who from?

1.3.ii. what was this used for?

1.3.iii. when was this received?

1.3.iv. Did the funding arrangements for the MALE program differ from the previous funding arrangements for the Female program?

1.4. Please describe any collaborations/partnerships which have occurred between your organisation and other health services in the delivery of the National MALE HPV Vaccination Program. (eg Medicare Locals, Cancer Council)

1.4.i. Were these collaborations different to any existing collaborations for the National FEMALE HPV Vaccination Program (eg: in 2012)?

1.5. Who do you use as immunisation providers in the male HPV program in your region?

1.6. Do you deliver the male and female HPV vaccination programs as separate or integrated programs in terms of:

1.6.i. Providers

1.6.ii. Vaccine supply?

1.6.iii. Vaccination day schedules?

1.6.iv. Information and other resources?

1.7. Were there any aspects of service delivery National HPV Vaccination Program which were different to other school-based vaccination programs? If yes, please describe.

1.8. Did any media attention affect the implementation of the MALE program (either positively or negatively)

If yes, please describe.

1.8.i. Was the impact of the media on the MALE program any different to that experienced for the FEMALE program?

1.9. Do you have a tailored program particularly for the following groups:

1.9.i. Aboriginal or Torres Strait Islander boys/girls/young people or their parents?

If yes please describe

What was developed?

Who developed?

When?

Key messages/actions?

How was it implemented?

1.9.ii. Boys/girls/young people or parents from Culturally and Linguistically Diverse backgrounds

If yes please describe

What was developed?

Who developed?

When?

Key messages/actions?

1.10. Was/is there any location/group/population who were/are not well served by the HPV vaccination program in your organisation's catchment? (Due to access/information/consent issues?)

4. School engagement

1.11. Please describe how you and your organisation communicate with schools and the education sector in your region in the delivery of the National HPV Vaccination Program? Eg:

1.11.i. Informing Schools of the program

1.11.ii. Informing students and parents

1.11.iii. Organising consent

1.11.iv. Organising vaccination days

4.1. Have there been any issues of parental consent in your jurisdiction?

4.1.i. For the vaccination of adolescent males?

4.1.ii. For the vaccination of adolescent females?

4.1.iii. Do you have any program specific strategies for obtaining parental consent?

Please describe

5. The vaccine

1.12. Please describe any issues with vaccine supply (i.e. vaccine shortage) and/or vaccine management which you have encountered with the human papillomavirus vaccine?

1.12.i. For the male HPV program

1.12.ii. For the female HPV program

1.13. Are you aware of any reports of administration issues with the human papillomavirus vaccine?

1.13.i. If yes, please describe (What and who reporting).

6. Data

1.14. Can you please describe your reporting requirements and processes to the National HPV Vaccination Program Register?

1.15. With the start of the male program, the Department of Health and Ageing, in conjunction with the TGA and states and territories, introduced rapid school-based reporting of four acute significant adverse events following immunisation (AEFI) with HPV to the TGA. How do you record and report adverse events following immunisation?

1.16. How well is information on the Indigenous Status of vaccination recipients collected and recorded in your program? (eg consent forms, providers' reporting).

1.17. Do you have access to coverage data for:

1.17.i. The school-based program for adolescent girls?

1.17.ii. The school-based program for adolescent boys?

1.17.iii. The community catch-up program for young women?

1.18. Do you have any other comments or concerns about data requirements or availability?

7. Strengths and challenges

1.19. From your perspective and compared with other national vaccination programs;

1.19.i. What, if any, are the strengths of the implementation of the extended National HPV Vaccination Program for males?

1.19.ii. What, if any, are the challenges of the implementation of the extended National HPV Vaccination Program for males?

1.19.iii. What, if any are the issues/problems which you have encountered with implementing the extended National HPV Vaccination Program for males?

1.19.iii.a. Have they been resolved? If so, how? (e.g. vaccine supply, systems/processes, consent)

1.20. From your experience with the original female National HPV Vaccination Program;

1.20.i. Have there been any particular strengths that were specific to the original female HPV program?

1.20.ii. Have there been any particular challenges that were specific to the original female HPV program?

1.21. Based on your experiences with the National HPV Vaccination Program, do you have any recommendations for planning/implementing future national immunisation programs?

1.21.i. If yes, please describe.

1.22. Any further comments?

THANK YOU FOR YOUR PARTICIPATION

Appendix 2.3

Themes in the Australian news media on the National HPV Vaccination Program

Year	Positive themes	Negative themes
2006	Ian Frazer as Australian of the Year Federal Government support for possible national immunisation program Cancer survivors advocate for vaccine Safe effective vaccine TGA approval Vaccine will be available in September 2006 First vaccines given Vaccine uptake on private market Advocating for vaccine for males Federal government will fund the vaccine on the NIP at the right price Female program announced	Vaccine may promote teenage promiscuity Expensive vaccine Commercial pressure for vaccine on NIP Risk of reduced Pap testing Vaccine refused subsidy in first round Cost to females being vaccinated privately Government should reconsider and fund the vaccine Mr Abbott will not vaccinate his daughters Pharmaceutical company will make millions from the national vaccination program Lives more important than cost of the vaccine Causal factors between HPV and cervical cancer not established Councils will not be subsidised to deliver vaccine on NIP
2007	The start of the school-based program announced in states and local regions Vaccine is an important medical breakthrough Federal funding support for delivery Successful program and good uptake Promiscuity claims adversely affecting important health intervention Few Australian parents have concerns around the vaccine and promiscuity Catholic parents will make an informed choice. Cervarix® licensed for older women Protection against genital warts Ian Frazer advocates for vaccines for males Advocating for free vaccines of males	Limited value of vaccine if already sexually active Commercial pressure to list vaccine on PBS Politicisation of vaccine program Opposition to vaccine due to fear of sexual promiscuity Schools refuse vaccine Vaccine may not be most appropriate treatment for HPV Lack of funding for delivery delays start of program Adverse events “Experimenting on Australian girls” Cost to males being vaccinated privately Gaps/inconsistencies in age eligibility

Year	Positive themes	Negative themes
2008	Safe vaccine Advocating for male program Awards to Ian Frazer HPV a normal part of the vaccination schedule and preventative health measures Reminder of deadline for end of female community catch-up program Encourage women to have cervical screening Review of interval for cervical screening Effective vaccine Eradication of cervical cancer Millions of doses have been administered	Adverse events Promiscuity concerns HPV register is a burden on GPs Limited effectiveness of vaccine for older women Vaccine should not have been licensed Cost to older women to vaccinate privately
2009	Advocating for male program Reduction in incidence of genital warts Female catch-up extended Need to be cautious about linking British school-girl death to vaccine HPV vaccine will change Pap test schedule Reminder of end of community catch-up	Adverse events following immunisation Vaccine released too soon Poor uptake in young women Immunisation causes spike in health spending
2010	Reduction in incidence of genital warts World first program for boys	
2011	Effective vaccine reducing high-grade cervical lesions Advocating for male program	Class action against manufacturer Inconclusive evidence of effectiveness
2012	World first program for boys	Cervical cancer message may discourage males
2013	Start of the male program	

Appendix 2.4

Summary table of strengths and challenges of the National HPV Vaccination Program raised by stakeholders at interview

STRENGTHS	CHALLENGES
Successful program • It is an effective and safe vaccine. • The female program has been going long enough to provide evidence that HPV vaccination is a success. • Australia is world first in introducing a national HPV program for adolescent males. • Program managers reported that the program to extend HPV vaccination to males rolled out smoothly in most jurisdictions. • The program has progressed well. • Vaccine supply worked well.	**Lead-time from the announcement** • Six months lead-time is adequate for childhood but not school-based vaccination programs as school-based programs need to accommodate school holidays. • Some jurisdictions had already allocated their budgets for 2013 by the time of the announcement in July 2012 of the extension of the program to males. • Some jurisdictions had to scramble to negotiate with schools over fitting three visits into the next school calendar year. • The lead-time for the female program was even shorter than for the male program.
Funding • Australian government funding of the vaccine for adolescent males was welcomed by stakeholders. • Australia is a world leader in funding the HPV vaccine on a population level.	**Funding** • Funding and resources were among the biggest challenges. • There was a lack of Australian government funding for service delivery for the male program. • There was an opportunity cost for jurisdictions in delivering the HPV program for males. • Funding for the delivery of school-based programs has not increased while wages and costs have increased. • Funding of service delivery is important for the long-term sustainability of the program. • Councils or other providers cannot be expected to keep supporting programs without funding. • Due to funding uncertainties some jurisdictions made a late decision to implement the program and this further shortened the lead-time for the rollout. • A better model for funding of service delivery is needed.
Jurisdiction know-how and capacity • The program happened because of the dedication of the jurisdiction. • Jurisdictions have a wealth of knowledge and experience on how to deliver a quality program. • Jurisdictions were very responsive in delivering the female and male programs in such a short timeframe due to jurisdictional expertise. • A lot of work went into resources, contracts, procurement of vaccines. • Knowledgeable spokespersons were able to address community concerns about adverse events at the start of the female program. • Jurisdictions invest time, money and effort	**Capacity** • Jurisdiction resources are finite and stretched everywhere. • The girls program in the first 2 years was all of high school with a big catch-up program. There were difficulties in finding enough staff to run the program. • One respondent thought that the rollout of the female program had needed a national coordinator. • The male program is a big program of 3 doses and a catch-up program for Year 9, all of which demands considerable resources. • Increased cohort required finding extra vaccination days in school calendars. • There are too few funded staff to run the program in some regions. • Some jurisdictions had difficulty in finding staff for

in building staff capacity. • Training immunisers maintains capacity for future pandemics. • Jurisdictions place faith in collaboration with local government. • Councils managed the challenge of the extended program well.	delivering the extended HPV school-based program. • Data collection and recording places a further burden on staff. • There is a high rate of staff turnover in remote communities which affects continuity. • The program in remote communities uses community volunteers who perhaps should be paid. • There is a question of sustainability of the program in remote communities. • There was a risk that the program may not have been successfully implemented due to jurisdiction capacity constraints. • There needs to be more flexibility allowed to jurisdictions in their delivery of the program. • There was a limit to the collaborations that could be expected between the jurisdictions and schools and jurisdictions and local government. • There was a limit to how many more vaccines could be added to the school-based program.
School-based program • School-based programs are a good way to reach adolescent age groups and more effective than through general practice. • Australia has a good international reputation for delivering school-based immunisation programs. • The female program helped to establish the schools immunisation team in the ACT. • The female program brought the Queensland government into the school-based program which was formerly run by local councils. • Parents accept school-based vaccination programs. • Teachers accept and support the school-based program.	**School-based program** • Collaborations with the school sector depended on goodwill. Therefore it was important not to stretch the friendship. • Scheduling 3 doses at the right intervals into a busy school calendar year is a challenge. • There were issues around managing vaccination day logistics and risks to staff. • School absenteeism, return of consent forms and completing 3 doses were all mentioned as challenges to the program. • General practice was not actively involved in the catch-up of missed doses for the male program.
Communication and resources • The Australian Government Department of Health had a thorough information strategy for the extended program. • There had been good consultation with other stakeholders in the development of information resources for the male program. • The information resources for the extended program were exceptionally good. • The Australian Government Department of Health HPV website was a good resource. • Information resources produced for the male program are eye-catching. • The Australian Government Department of Health had developed better communication with schools with the male program.	**Communication and resources** • Australian Government Department of Health information resources came out late for female program. • Australian Government Department of Health information resources had been prepared too late for distribution for the extended program in most jurisdictions. • Some respondents thought that the Australian Government Department of Health resources were not very useful. • Promotional material did not meet states' needs. • The market research approach to developing materials was not useful. • It was impractical for providers to carry all the information resources as well as the vaccine materials to schools, so the information materials were not distributed to schools. Incentives to distribute materials are needed. • Promoting the vaccine for STIs in males was not as

• The Australian Government Department of Health was more proactive in anticipating and countering negative messages with the extended program for males. • It was a positive initiative developing Indigenous resources for the extended program. • Information resources produced by the pharmaceutical company, cervical screening and the Cancer Council were important resources during the initial rollout of the female program. • With the initial female program there was more active engagement of general practice.	straightforward a message as the cervical cancer message for females. • There was a lack of communication with general practice around the male program. **Indigenous resources** • Indigenous resources were too wordy for people from remote communities. • Some Indigenous resources were not clear that HPV was a STI. • Materials need a message that is succinct and clear. • There is an ongoing challenge of bringing message to Indigenous people in a culturally sensitive way. • There is an ongoing need for consultation around Indigenous information and materials. • Protecting children before they are sexually active can be controversial and sensitive.
STI message • The initial message of a vaccine against cervical cancer was an easier message to promote as it was targeting a specific disease. • The extended program for males allowed more emphasis on HPV as a sexually transmitted infection.	**STI message** • Rather than a cervical cancer vaccine message it should have been an HPV vaccine message from the start of the female program.
Community acceptance • Parents have now accepted HPV vaccination for females. • The HPV program has become established as a normal part of the immunisation schedule. • Through the female program parents and the community are now better informed about HPV, cancer, genital warts, sexual transmission and the benefits of the vaccine. • Increased knowledge will encourage parents to continue with the program. • There is now less controversy over the vaccine and sex in the female program. • The success of the girls' program created a positive message for implementing the boys' program. • The evidence for the clinical effectiveness of the HPV vaccine from the female program was one of the best reasons for extending the vaccine to males. • A program for both sexes is a consistent approach and increases the acceptability of the program. • It is easier to communicate with the community and schools that the vaccination is for all adolescents. • Parents were expecting and wanting the program for their boys. • There was no community backlash for the male program.	**Community acceptance** • Initially the school-based program for young adolescent females faced major challenges to acceptance by parents and the community. • Parents and community were apprehensive about a new vaccine. • There was an initial lack of knowledge by women about HPV and the link to cancer. • There were initial concerns about adverse events in the female program. • There was a negative message from anti-vaccine groups which were quite active at the start of the girls' program. • The initial female program attracted negative media attention around vaccine safety and adverse events, in particular the media focus on the episode of mass psychogenic effects in Victoria. • It was the first vaccine that was overtly to do with sexual health. • Targeting young females during the period of sexual development in adolescence complicated the messages around the vaccine. • Parents were concerned the vaccine may encourage early sexual activity in their daughters. • The initial female specific program placed the burden of disease prevention on women and girls. • The program should have included both sexes from the start.

• There was less controversy and fewer misconceptions around the HPV vaccine for the male program. • Early apprehension in the female program around a new vaccine and adverse events were not seen with the extension of the program to adolescent males. • The male program didn't attract so much attention from the anti-immunisation lobby as the female program had. • There has not been a big issue with the vaccine and sexual activity for the male program. • As a sexually transmitted disease it makes sense to vaccinate both males and females against HPV. • The program provides equity for males and females. • A universal program protects vulnerable individuals without targeting and stigmatising them. • Including adolescent males in the HPV vaccination program is likely to improve male uptake of other school-based vaccines and help improve males' general health education. • The good uptake of the vaccine by adolescent males was an indication of community acceptance of the program. **Female program paved the way for the male program** • Extending the program to include adolescent males was a logical progression from the female program. • It was good that the value in giving adolescent males the vaccine had been acknowledged by the Australian government. • The Australian government and jurisdictions could apply the lessons learnt from the female program when implementing the male program. • Rolling out the program in two stages allowed learning for the delivery of the program to remote communities. • Adding males to the ongoing school-based program for females was not much of a problem for implementation.	
Coverage • Millions of doses of vaccine have been delivered in the girls' program. • The whole-of-high-school catch-up program for females provided good coverage for the target group. • Including both males and females increases herd immunity. • Including both males and females is a more cost-effective way to reduce disease	**Coverage and eligibility** • It was important to provide the best coverage possible. • Improving coverage for both males and females remains a challenge. • Older age groups in the female catch-up program and the male catch-up programs were harder to reach. • Male uptake is reasonable but could be better. • In spite of high uptake an appreciable percentage

burden for all related cancers. • Access to remote communities and mobile populations potentially affects coverage. However, stakeholders working in remote communities reported that they were successfully reaching eligible young males and achieving good uptake of the vaccine. • Staff have strategies to obtain optimal levels of consent. • Staff put in the effort to reach people from CALD backgrounds.	of males don't get dose 1 at school. There is a need to understand more about the reasons for that coverage gap. • Are the adolescent males who miss out at school being vaccinated in general practice? • We need to know more about how parents attitudes affect uptake. • Changes to the eligibility criteria for the free vaccine over the course of the program created confusion for providers and the potential for eligible adolescents to miss out on the vaccine. • The male catch-up was too restrictive in terms of age eligibility and the 2-year timeframe. This restricted availability of the free vaccine and disadvantaged individuals who did not vaccinate due to difficult circumstances. • There is a need to improve outreach and strategies for vaccinating disadvantaged groups. • GPs find it hard to obtain reliable information on HPV doses received by patients through the school program. • Lack of reliable information on patient vaccination status and limited access to the vaccine creates barriers to providing opportunistic HPV vaccination in general practice. • There is a lack of incentives for general practice to be proactive in providing HPV vaccinations.
	Sustainability • Sustaining coverage rates over the long term is a challenge. • There is a need to avoid complacency about the program. • There is an ongoing need to educate the public about the value of the vaccine.
Data • The NHVPR is a good resource. • Systems were put in place for any anticipated AEFI with the male program.	**Data** • The NHVPR was not up and running smoothly for most of the period of the community catch-up program for young women. • It is an ongoing challenge to encourage general practice to report consistently to the NHVPR. • GPs report difficulty finding patient dosage records on the NHVPR.
	Commonwealth/state partnership • In reflecting on both the female and male phases of the program many respondents commented that the collaboration between the jurisdictions and the Australian government could be improved. • Delivery of the program is a jurisdiction/Australian government partnership. • Jurisdictions need a directive from the Australian government about allocating sufficient jurisdictional funding for programs. • Jurisdictions and the Australian government need agreement on goals and targets for each vaccine. • The current partnership model of school-based programs provide very cost-effective coverage for the Australian government.

	• The Australian government supports service delivery of childhood immunisation in general practice through Medicare. However, there are very few service delivery costs to the Australian government for the HPV school-based vaccination program for adolescent males. • Partnership with Australian government around funding is not really 50/50. • Jurisdictions will be demanding funding in the future.

Appendix 4.1

Reported adverse events following HPV vaccination, TGA Adverse Drug Reaction System database, 1 February 2013 to 30 June 2013

MedDRA Preferred Terms*	Male				Female				Total			
	AEFI records		Serious	Only HPV vaccine	AEFI records		Serious	Only HPV vaccine	AEFI records		Serious	Only HPV vaccine
	Total	%			Total	%			Total	%		
Syncope	173	28.1	5	77	123	20.0	1	33	296	48.1	6	110
Presyncope	28	4.6		17	39	6.3		17	67	10.9	0	34
Nausea	28	4.6	1	19	23	3.7		11	51	8.3	1	30
Dizziness	26	4.2		12	24	3.9	1	12	50	8.1	1	24
Headache	23	3.7	3	13	15	2.4	2	8	38	6.2	5	21
Vomiting	16	2.6	1	8	17	2.8		10	33	5.4	1	18
Pyrexia	20	3.3	1	11	9	1.5		5	29	4.7	1	16
Urticaria	15	2.4		11	9	1.5		6	24	3.9	0	17
Malaise	15	2.4	1	6	7	1.1		3	22	3.6	1	9
Injection site reaction	11	1.8	2	4	8	1.3		2	19	3.1	2	6
Rash	9	1.5		6	9	1.5		3	18	2.9	0	9
Pallor	5	0.8		5	6	1.0		4	11	1.8	0	9
Pruritus	4	0.7		3	6	1.0		1	10	1.6	0	4
Rash generalised	7	1.1		5	3	0.5		2	10	1.6	0	7
Diarrhoea	5	0.8		2	4	0.7		2	9	1.5	0	4
Lethargy	5	0.8		3	4	0.7		2	9	1.5	0	5
Paraesthesia	6	1.0		4	3	0.5		1	9	1.5	0	5
Anxiety	4	0.7	1	3	4	0.7		1	8	1.3	1	4
Hypersensitivity	6	1.0	1	3	2	0.3			8	1.3	1	3
Injection site pain	6	1.0		6	2	0.3		1	8	1.3	0	7
Rash pruritic	4	0.7		1	4	0.7		2	8	1.3	0	3
Cold sweat	4	0.7		2	3	0.5		2	7	1.1	0	4
Vision blurred	3	0.5		3	4	0.7	2	2	7	1.1	2	5
Abdominal pain	2	0.3		1	4	0.7		2	6	1.0	0	3
Abdominal pain upper	2	0.3	1	1	4	0.7	1	2	6	1.0	2	3
Dyspnoea	4	0.7	1	2	2	0.3	1	1	6	1.0	2	3
Rash erythematous	3	0.5		1	3	0.5		2	6	1.0	0	3
Arthralgia	5	0.8	1	3	0	0.0			5	0.8	1	3
Chest discomfort	4	0.7		3	1	0.2			5	0.8	0	3
Fatigue	2	0.3		1	3	0.5		2	5	0.8	0	3
Injection site swelling	2	0.3			3	0.5		3	5	0.8	0	3
Swelling face	1	0.2		1	4	0.7		2	5	0.8	0	3
Tremor	3	0.5		2	2	0.3		2	5	0.8	0	4
Chills	3	0.5		1	1	0.2		1	4	0.7	0	2
Decreased appetite	0	0.0			4	0.7		2	4	0.7	0	2
Feeling hot	3	0.5		2	1	0.2		1	4	0.7	0	3
Injection site rash	1	0.2			3	0.5		3	4	0.7	0	3
Lymphadenopathy	3	0.5		3	1	0.2		1	4	0.7	0	4
Visual impairment	4	0.7	1	4	0	0.0			4	0.7	1	4
Feeling abnormal	3	0.5		3	0	0.0			3	0.5	0	3
Flushing	2	0.3		1	1	0.2			3	0.5	0	1
Gait disturbance	2	0.3	1	2	1	0.2		1	3	0.5	1	3
Hyperhidrosis	2	0.3		1	1	0.2			3	0.5	0	1
Injection site mass	1	0.2			2	0.3		1	3	0.5	0	1
Lip swelling	2	0.3	2	1	1	0.2		1	3	0.5	2	2
Myalgia	1	0.2		1	2	0.3		2	3	0.5	0	3

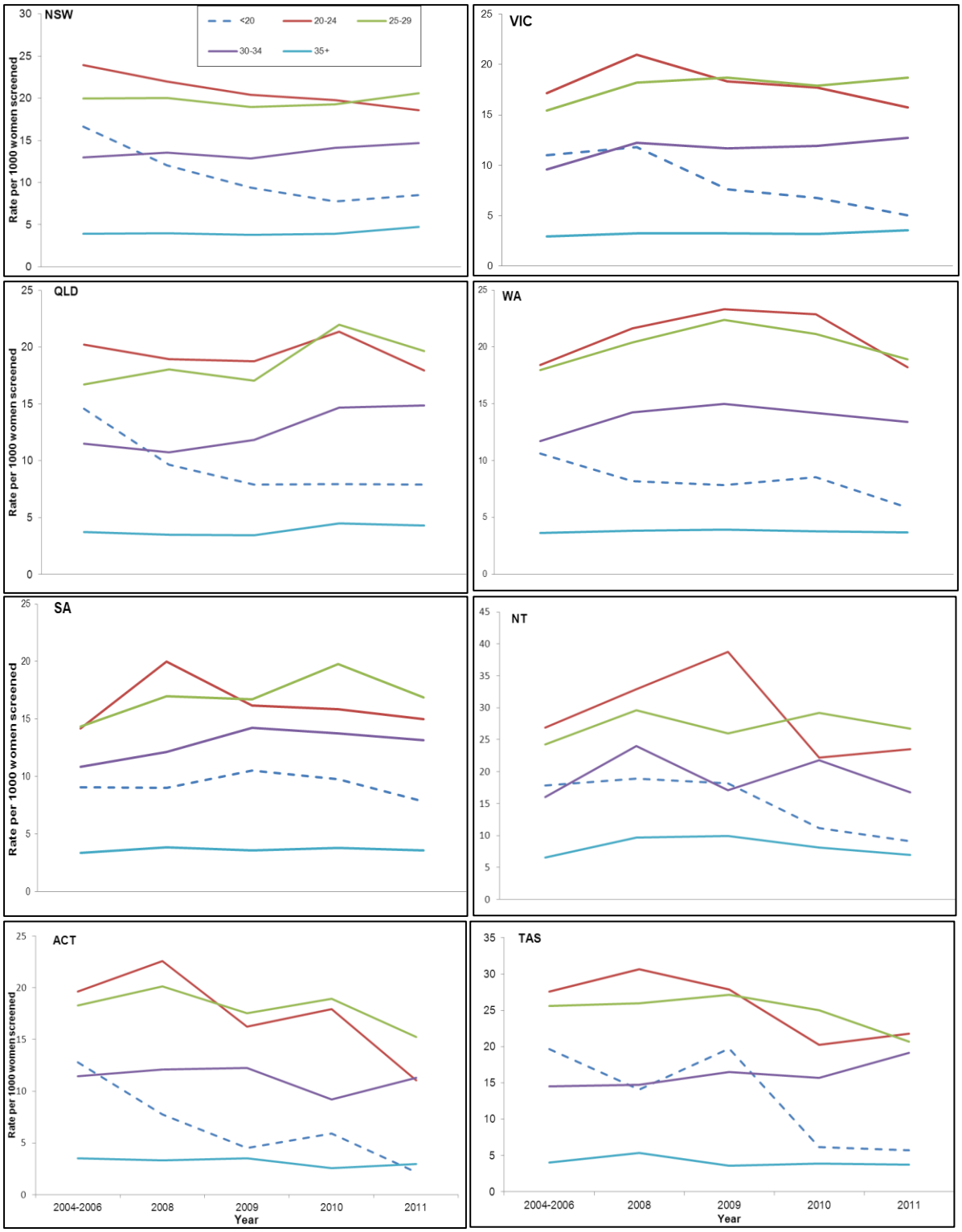
Pain	1	0.2		1	2	0.3		1	3	0.5	0	2
Asthenia	1	0.2			1	0.2			2	0.3	0	0
Blister	1	0.2		1	1	0.2			2	0.3	0	1
Concomitant disease aggravated	2	0.3		2	0	0.0			2	0.3	0	2
Convulsion	0	0.0			2	0.3			2	0.3	0	0
Cough	2	0.3		2	0	0.0			2	0.3	0	2
Dysphagia	0	0.0			2	0.3		1	2	0.3	0	1
Epistaxis	1	0.2	1	1	1	0.2		1	2	0.3	1	2
Extensive swelling of vaccinated limb	1	0.2			1	0.2		1	2	0.3	0	1
Eye pain	0	0.0			2	0.3	1		2	0.3	1	0
Eye swelling	1	0.2		1	1	0.2			2	0.3	0	1
Hyperventilation	1	0.2			1	0.2			2	0.3	0	0
Hypoaesthesia	0	0.0			2	0.3		2	2	0.3	0	2
Loss of consciousness	2	0.3			0	0.0			2	0.3	0	0
Migraine	1	0.2		1	1	0.2		1	2	0.3	0	2
Pain in extremity	2	0.3		2	0	0.0			2	0.3	0	2
Paraesthesia oral	1	0.2			1	0.2			2	0.3	0	0
Pharyngeal oedema	0	0.0			2	0.3			2	0.3	0	0
Rash vesicular	1	0.2		1	1	0.2			2	0.3	0	1
Rhinitis	1	0.2		1	1	0.2		1	2	0.3	0	2
Skin discolouration	1	0.2		1	1	0.2			2	0.3	0	1
Swollen tongue	1	0.2		1	1	0.2		1	2	0.3	0	2
Tachycardia	2	0.3			0	0.0			2	0.3	0	0
Tearfulness	2	0.3		2	0	0.0			2	0.3	0	2
Throat irritation	2	0.3	1	1	0	0.0			2	0.3	1	1
Urinary incontinence	1	0.2			1	0.2		1	2	0.3	0	1
Abnormal behaviour	0	0.0			1	0.2			1	0.2	0	0
Amnesia	0	0.0			1	0.2		1	1	0.2	0	1
Ataxia	1	0.2		1	0	0.0			1	0.2	0	1
Balance disorder	1	0.2			0	0.0			1	0.2	0	0
Cluster headache	1	0.2		1	0	0.0			1	0.2	0	1
Corneal reflex decreased	1	0.2		1	0	0.0			1	0.2	0	1
Dermatitis allergic	1	0.2		1	0	0.0			1	0.2	0	1
Disorientation	1	0.2	1		0	0.0			1	0.2	1	0
Drug administration error	1	0.2		1	0	0.0			1	0.2	0	1
Dysarthria	1	0.2			0	0.0			1	0.2	0	0
Dysgeusia	1	0.2	1	1	0	0.0			1	0.2	1	1
Dystonia	0	0.0			1	0.2			1	0.2	0	0
Emotional distress	1	0.2		1	0	0.0			1	0.2	0	1
Erythema	0	0.0			1	0.2		1	1	0.2	0	1
Exfoliative rash	1	0.2		1	0	0.0			1	0.2	0	1
Eyelid oedema	0	0.0			1	0.2		1	1	0.2	0	1
Hearing impaired	0	0.0			1	0.2		1	1	0.2	0	1
Hypopnoea	1	0.2			0	0.0			1	0.2	0	0
Influenza like illness	0	0.0			1	0.2		1	1	0.2	0	1
Incontinence	0	0.0			1	0.2			1	0.2	0	0
Injected limb mobility decreased	1	0.2		1	0	0.0			1	0.2	0	1
Injection site coldness	1	0.2		1	0	0.0			1	0.2	0	1
Injection site erythema	0	0.0			1	0.2		1	1	0.2	0	1
Injection site induration	1	0.2			0	0.0			1	0.2	0	0
Injection site pruritus	0	0.0			1	0.2			1	0.2	0	0
Injection site urticaria	0	0.0			1	0.2			1	0.2	0	0

Irritability	0	0.0			1	0.2		1	1	0.2	0	1
Labia enlarged	0	0.0			1	0.2			1	0.2	0	0
Lacrimation increased	1	0.2		1	0	0.0			1	0.2	0	1
Limb discomfort	1	0.2		1	0	0.0			1	0.2	0	1
Lymphadenitis	1	0.2			0	0.0			1	0.2	0	0
Memory impairment	1	0.2	1	1	0	0.0			1	0.2	1	1
Muscle spasms	0	0.0			1	0.2			1	0.2	0	0
Muscular weakness	0	0.0			1	0.2	1		1	0.2	1	0
Musculoskeletal chest pain	1	0.2			0	0.0			1	0.2	0	0
Musculoskeletal stiffness	1	0.2		1	0	0.0			1	0.2	0	1
Nasopharyngitis	1	0.2		1	0	0.0			1	0.2	0	1
Oligomenorrhoea	0	0.0			1	0.2	1	1	1	0.2	1	1
Oropharyngeal pain	1	0.2		1	0	0.0			1	0.2	0	1
Papulae	0	0.0			1	0.2			1	0.2	0	0
Photophobia	1	0.2		1	0	0.0			1	0.2	0	1
Rash maculopapular	1	0.2		1	0	0.0			1	0.2	0	1
Reflux gastritis	1	0.2		1	0	0.0			1	0.2	0	1
Restlessness	1	0.2		1	0	0.0			1	0.2	0	1
Skin mass	0	0.0			1	0.2			1	0.2	0	0
Sneezing	1	0.2		1	0	0.0			1	0.2	0	1
Somnolence	1	0.2		1	0	0.0			1	0.2	0	1
Swelling	1	0.2		1	0	0.0			1	0.2	0	1
Tachypnoea	1	0.2			0	0.0			1	0.2	0	0
Throat tightness	1	0.2			0	0.0			1	0.2	0	0
Vaccination error	0	0.0			1	0.2		1	1	0.2	0	1
VIIth nerve paralysis	1	0.2		1	0	0.0			1	0.2	0	1
Vulvovaginal pruritus	0	0.0			1	0.2			1	0.2	0	0
Weight decreased	1	0.2	1	1	0	0.0			1	0.2	1	1
Wheezing	1	0.2		1	0	0.0				0.0	0	1

***** One AEFI record may have multiple MedDRA Preferred Terms included.

Appendix 5.1

Rates of HGA per 1,000 women screened, by jurisdiction and age group, 2004 to 2011*



Source: *Cervical screening in Australia 2010–2011*, AIHW

* Crude rates are the number of women with abnormalities detected by histology as a proportion of all women screened.

Appendix 5.2

Rate of HGA detected per 1,000 females aged 20–24 years screened and 95% confidence intervals, by jurisdiction, 2004 to 2011

Jurisdiction	Pre-vaccine 2004–2007	Post-vaccine 2008–2009		Post-vaccine 2010–2011		Combined post-vaccine period 2008–2011	
	Rate (CI)*	Rate (CI)*	Rate ratio (CI)†	Rate (CI)*	Rate ratio (CI)†	Rate (CI)*	Rate ratio (CI)†
NSW	23.1 (22.4–23.7)	21.2 (20.4–22.1)	0.92 (0.88–0.97)	19.2 (18.4–20.0)	0.83 (0.79–0.88)	20.2 (19.6–20.8)	0.88 (0.84–0.91)
VIC	17.4 (16.8–18.0)	19.6 (18.8–20.6)	1.13 (1.07–1.20)	16.7 (15.9–17.6)	0.96 (0.91–1.02)	18.2 (17.6–18.8)	1.05 (1.00–1.10)
QLD	19.4 (18.7–20.1)	18.8 (17.9–19.8)	0.97 (0.91–1.03)	19.6 (18.7–20.6)	1.01 (0.95–1.08)	19.2 (18.5–19.9)	0.99 (0.94–1.04)
WA	18.2 (17.3-19.2)	22.5 (21.1–23.9)	1.23 (1.14–1.34)	20.5 (19.2–21.9)	1.12 (1.03–1.22)	21.5 (20.5–22.5)	1.18 (1.10–1.26)
SA	15.1 (14.1–16.1)	18.1 (16.5–19.7)	1.20 (1.07–1.34)	15.4 (14.0–17.0)	1.02 (0.91–1.15)	16.8 (15.7–17.9)	1.11 (1.01–1.22)
NT	25.6 (22.4–29.0)	35.8 (30.7–41.5)	1.40 (1.15–1.71)	22.9 (18.7–27.6)	0.89 (0.70–1.13)	29.5 (26.2–33.2)	1.15 (0.97–1.38)
TAS	28.6 (26.2–31.1)	29.3 (25.8–33.0)	1.02 (0.88–1.19)	21.0 (18.1–24.3)	0.73 (0.62–0.87)	25.2 (22.9–27.7)	0.88 (0.78–1.00)
ACT	19.7 (17.6–22.1)	19.5 (16.5–22.9)	0.99 (0.81–1.20)	14.5 (11.9–17.6)	0.74 (0.58–0.92)	17.1 (15.1–19.3)	0.87 (0.73–1.03)
National	19.8 (19.5–20.1)	20.6 (20.1–21.1)	1.04 (1.01–1.07)	18.5 (18.1–19.0)	0.94 (0.91–0.96)	19.6 (19.3–19.9)	0.99 (0.97–1.01)

Source: *Cervical screening in Australia 2010–2011*, AIHW

* Crude rates are the number of females with abnormalities detected by histology as a proportion of all females screened.

† Reference group: 2004–2007 pre-vaccine period.

Appendix 6.1

Definitions

Table A6.1.1. Definition of diagnoses and procedures related to anogenital warts

Warts-related diagnoses		Warts-related procedures	
A63.0	Anogenital warts	32177	Removal of anal wart
A63.00	Anogenital warts, unspecified site	32180	Removal of anal wart
A63.01	Perianal warts	35507	Removal of vulval/vaginal wart
A63.02	Cervical warts	35508	Removal of vulval/vaginal wart
A63.03	Urethral warts	36815	Destruction of penile/urethral wart
A63.04	Vaginal warts	30189	Removal of other wart
A63.05	Vulval warts		
A63.06	Penile warts		
A63.07	Scrotal warts		
A63.09	Perineal warts NEC		
K62.8	Anal/perianal warts		
N36.8	Urethral warts		
N48.8	Penile warts		
N88.8	Cervical warts		
N89.8	Vaginal warts		
N90.8	Vulval warts		

Table A6.1.2. Definition of diagnoses and procedures influenced by cervical screening

Diagnoses influenced by cervical screening		Procedures influenced by cervical screening	
D06	Carcinoma in situ of cervix	35539-02	Laser destruction of lesion of cervix
N87	Cervical dysplasia	35608	Biopsy/cautery/other destruction of cervical lesion
R87.6	Abnormal cytology from cervix, vagina, vulva*	35614	Colposcopy
		35618	Cervical cone biopsy/others procedures/amputation
R87.7	Abnormal histology from cervix, vagina, vulva*	35646	Radical diathermy of cervix
		35647	Large loop excision of transformation zone (LLETZ)
R87.9	Unspecified abnormal finding from cervix, vagina, vulva*	35648	LLETZ in conjunction with ablative treatment of additional areas

* It is not possible to determine which of cervix, vagina or vulva these related to via diagnosis codes; procedure codes were used to better define admissions potentially influenced by changes to cervical screening management.

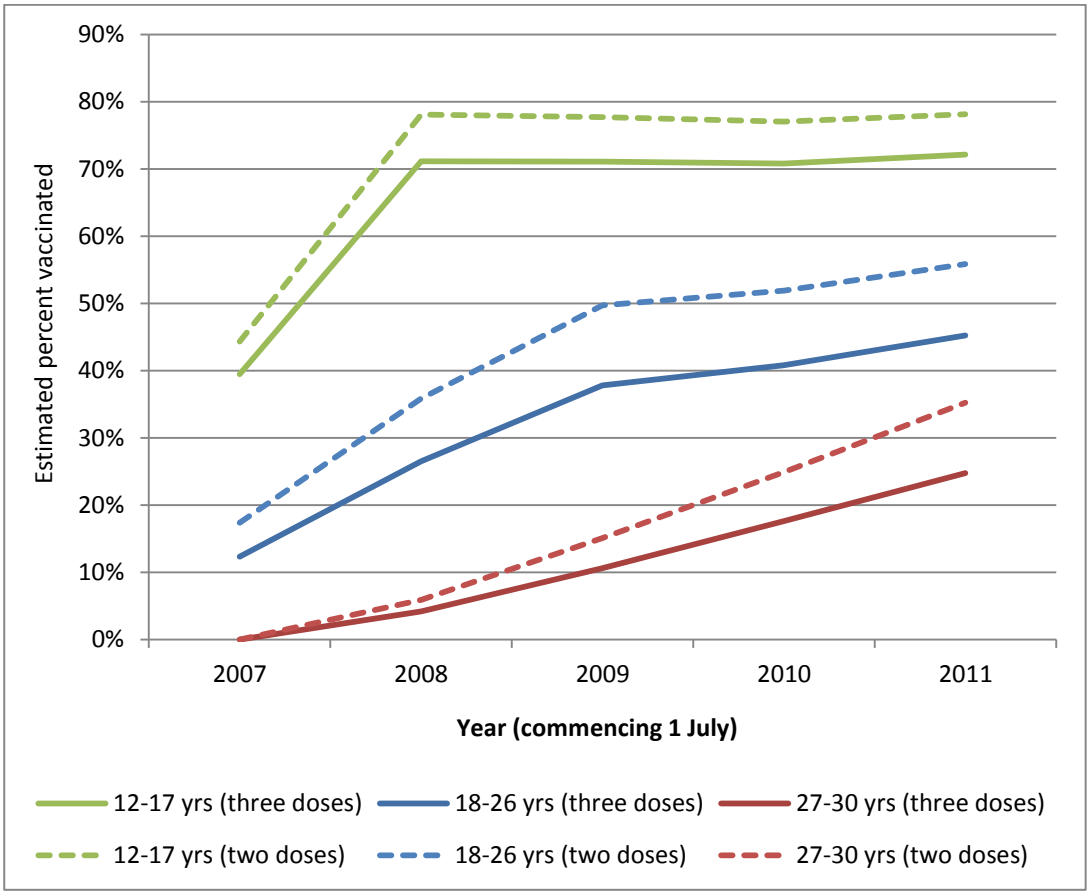
In order to best define admissions which may have been influenced by changes to the National Cervical Screening Program Guidelines (and thus decreased admissions associated with managing women with cervical abnormalities with a concomitant diagnosis of warts), this was investigated using procedures and/or diagnoses. A large proportion of admissions with potentially screening-related diagnoses and at least one procedure recorded did not have any screening-related procedures (40%). Among these admissions, the majority had warts procedures, other non-cervical procedures or both. Using diagnoses to define admissions potentially influenced by changes in screening management or participation is limited by the fact that three diagnosis codes do not distinguish between whether the abnormalities (cytology, histology or unspecified abnormal finding) relate specifically to the cervix, or whether they relate to the vulva or vagina.

Appendix 6.2

The following chart shows the estimated percentage of females in each age group who have ever been vaccinated, in each year since the introduction of the National HPV Vaccination Program. The estimates take into account the aging of cohorts offered vaccination into older age groups over time. Estimates are based on published coverage data and population estimates.[38,41,113,114] Coverage data for females aged 12–13 years in 2011 is not yet available so estimates in the chart are based on similar coverage to those aged 14–15 years in 2011. The percentage effectively immunised may be lower, however, due to some prior exposure to vaccine-included HPV types, especially in females in the catch-up program.

The estimates are uncertain for 2007 and 2008 in particular, because of uncertainties around the precise timing of uptake within the catch-up program, particularly the general practice/community-based component for females aged 18–26 years. Additionally, the specific ages and grades offered vaccination through schools in 2007 and 2008 varied by jurisdiction. The estimated uptake in females aged 12–17 years in 2007 attempts to take into account the different age groups offered vaccination in each state and territory during 2007 and 2008, but is uncertain.

Figure A6.2.1. Estimated* percentage of females in each age group ever vaccinated, by year



* Estimated from published coverage data and population estimates.[38,41,113,114] Coverage data for females aged 12–13 years in 2011 is not yet available so estimates are based on similar coverage to those aged 14–15 years in 2011. Percentage effectively immunised may be lower due to some prior exposure.

Appendix 6.3

Table A6.3.1. Admissions by sex, age and year, all admissions

Year (starting 1 July)	Females					Males				
	12–17 years	18–26 years	27–29 years	≥30 years	Total	12–17 years	18–26 years	27–29 years	≥30 years	Total
1999	166	1,221	248	853	2,506	5	312	137	662	1,121
2000	139	1,171	247	853	2,430	13	308	135	644	1,109
2001	147	1,182	166	883	2,394	6	293	106	787	1,197
2002	139	1,205	208	846	2,412	7	332	132	804	1,277
2003	135	1,176	206	839	2,363	7	338	117	804	1,273
2004	141	1,160	166	865	2,349	9	323	114	829	1,283
2005	151	1,061	174	838	2,238	6	350	113	753	1,228
2006	143	955	162	786	2,059	3	361	101	776	1,245
2007	67	891	164	730	1,861	4	349	90	721	1,167
2008	42	602	136	751	1,539	14	326	106	775	1,223
2009	26	424	136	788	1,381	11	318	102	763	1,198
2010	15	305	103	851	1,279	3	230	102	876	1,218
Total	**1,434**	**12,212**	**2,272**	**10,498**	**26,579**	**92**	**4,085**	**1,458**	**9,651**	**15,356**