NCIRS
National Centre for Immunisation Research and Surveillance

Impact evaluation of Australian national human papillomavirus vaccination program

Final report

February 2021

Authors

The impact evaluation of the national human papillomavirus vaccination program was coordinated and managed by the National Centre for Immunisation Research and Surveillance.

Literature review

Caitlin Swift, Aditi Dey, Sanjay Jayasinghe and Julia Brotherton

Stakeholder perspectives

Caitlin Swift, Aditi Dey, Harunor Rashid, Katrina Clark, Ramesh Manocha, Julia Brotherton and Frank Beard

Vaccination coverage

Alexandra Hendry, Julia Brotherton, Aditi Dey, Brynley Hull and Frank Beard

Vaccine safety

- Adverse Events Management System (AEMS) data: This part of the chapter was based on a publication submitted to the journal, Vaccine. The authors are Anastasia Phillips, Megan Hickie, James Totterdell, Julia Brotherton, Aditi Dey, Richard Hill, Tom Snelling and Kristine Macartney.
- AusVaxSafety data: Catherine Glover and Alexis Pillsbury on behalf of the AusVaxSafety team

Impact on disease burden

High-grade cervical abnormalities and cancers: Julia Maguire, Aditi Dey, Han Wang, Sanjay Jayasinghe, Julia Brotherton and Frank Beard

Genital warts: Harunor Rashid, Aditi Dey, Sanjay Jayasinghe, Julia Brotherton and Frank Beard

Contents

List of tables

List of figures

Acknowledgements

The project team would like to acknowledge the contribution of the advisory committee, which was formed to oversee the overall evaluation activities and provide guidance to the National Centre for Immunisation Research and Surveillance on the conduct of the evaluation and the development of the report. The committee members and their organisations are listed below:

- Alison Marcus, Consumers Health Forum of Australia
- Christine Selvey, NSW Health
- Cristyn Davies, Discipline of Child & Adolescent Health, University of Sydney
- Hope Peisley, Ingrid Mayer, Megan Downie, Phillipa Lowrey, Australian Government Department of Health
- Julia Brotherton, VCS Population Health
- Karen Canfell, Megan Smith, Cancer Council NSW
- Lisa Whop, Menzies School of Health Research
- Megan Hickie, Therapeutic Goods Administration
- Michelle Giles, Australian Technical Advisory Group on Immunisation
- Paul Effler, Communicable Disease Control Directorate, Department of Health, WA
- Rebecca Guy, The Kirby Institute
- Sonya Bennett, Communicable Diseases Network Australia
- Suzanne Garland, Dorothy Machalek, The Royal Women's Hospital, Melbourne

In addition, a cultural advisory committee was formed to provide cultural input on the conduct of the evaluation. The role of this committee was to provide advice and cultural guidance at key project stages to ensure that NCIRS placed First Nations people's voices at the forefront in the evaluation. The committee included six Aboriginal experts from various states and territories.

We would like to thank all the stakeholders, general practitioners and other immunisation providers who participated in the evaluation.

We would like to also thank Karen Winch and Karen Peasley from the National HPV Vaccination Program Register (HPV Register) for assistance with provision of data. The HPV Register NHVPR was fully funded by the Australian Department of Health and operated by VCS Foundation.

The National Centre for Immunisation Research and Surveillance is supported by the Australian Government Department of Health, the NSW Ministry of Health and the Sydney Children's Hospitals Network. The opinions expressed in this report are those of the authors, and do not necessarily represent the views of these agencies.

Glossary

ACCHS	Aboriginal Community Controlled Health Services
ACIR	Australian Childhood Immunisation Register
ACT	Australian Capital Territory
AEFI	adverse events following immunisation
AEFI-CAN	Adverse Events Following Immunisation: Clinical Assessment Network
AEMS	Adverse Events Management System
AESI	adverse event of special interest
AIHW	Australian Institute of Health and Welfare
AIR	Australian Immunisation Register
AMS	Aboriginal Medical Service
CALD	culturally and linguistically diverse
HGA	high-grade abnormalities
GP	general practitioner
HPV	human papillomavirus
LGBTQ	lesbian, gay, bisexual, transgender and queer
MA	medical attendance
MSHC	Melbourne Sexual Health Centre
MSM	men who have sex with men
NCIRS	National Centre for Immunisation Research and Surveillance
NSW	New South Wales
NHPVR	HPV Register
NIP	National Immunisation Program
NT	Northern Territory
QLD	Queensland
RCT	randomised controlled trial
SA	South Australia
SAEFVIC	Surveillance of Adverse Events Following Vaccination in the Community
SBIP	school-based immunisation program

SES	socioeconomic status
SASFTP	Services Australia Secure File Transfer Protocol
STI	sexually transmitted disease
TAS	Tasmania
TGA	Therapeutic Goods Administration
US VAERS	United States Vaccine Adverse Events Reporting System
VIC	Victoria
WA	Western Australia
WHO	World Health Organization

Executive summary

Background

Human papillomavirus (HPV) is responsible for malignant and non-malignant lesions, mostly affecting the anogenital region but also other parts of the body, notably the head and neck region. Australia was the first country to implement a fully funded national HPV vaccination program for girls (aged 12–13 years) via schools in 2007 using three doses of the quadrivalent HPV (4vHPV) vaccine, Gardasil®. There was also a community-based catch-up program for girls and women up to the age of 26 years that concluded in 2009. The program was extended in 2013 to include boys aged 12–13 years (ongoing school-year based cohort along with girls), with catch-up for boys aged 14–15 years till end-2014.

The National HPV Vaccination Program Register (HPV Register) was established in 2008 to capture the HPV vaccinations administered as part of the National HPV Vaccination Program. The 9-valent HPV (9vHPV) vaccine, Gardasil®9, replaced the 4vHPV vaccine in the National Immunisation Program (NIP) from February 2018. Gardasil®9 provides protection against the four HPV types (6, 11, 16 and 18) in the 4vHPV vaccine and an additional five oncogenic HPV types (31, 33, 45, 52 and 58), which are the next most frequently detected in cervical cancers globally after HPV types 16 and 18. The bivalent HPV vaccine (2vHPV) has never been funded under the NIP.

9vHPV vaccine has been offered via school-based programs for children aged 12–13 years in a 2-dose schedule, with the second dose given 6–12 months after the first dose since 2018 in all states and territories, except New South Wales (NSW), which introduced the 2-dose schedule in 2017. Catch-up vaccination is available under the NIP, mostly via primary healthcare settings, up to the age of 19 years. With the expansion of the Australian Childhood Immunisation Register to the whole-of-life Australian Immunisation Register (AIR), all HPV vaccination records held in the HPV Register were transferred into AIR in late 2018. All HPV vaccinations given through the school-based programs as well as doses given by other immunisation providers are now reported directly to AIR.

Aims

- To assess the overall uptake and impact of the National HPV Vaccination Program since the last evaluation in 2014
- To identify any key knowledge gaps related to the impact/outcomes of the program
- To make recommendations regarding ongoing monitoring and program enhancements

Methods

Guided by a conceptual framework based on the logic model of program outcomes, we reviewed relevant published and unpublished data and interviewed key stakeholders to monitor and assess

outcomes/impact of the HPV vaccination program to date, particularly those observed since the previous evaluation, in terms of vaccination coverage, vaccine safety and disease burden.

Literature review

Literature searches were conducted in OVID Medline and OVID EMBASE databases for publications on HPV vaccine coverage, safety and disease impact for the period 1 January 2013 to 25 October 2019. The Australian-focussed Informit Health databases were also searched for both published and grey literature. Searches were limited to studies in humans, written in English and from Australia. All publications listed in the previous evaluation report were excluded. Content experts were consulted and reference lists of key papers were reviewed, along with websites of key Australian organisations, to identify additional relevant literature.

Stakeholder assessment

A mixed methods approach was used to collect both qualitative and quantitative data from semi-structured interviews and an online survey. Purposive sampling was used to recruit a broad range of key stakeholders for interview. Stakeholders were approached directly or referred by other participants. Interviews were conducted from October 2019 to March 2020.

An anonymous online survey was distributed to other stakeholders, predominantly immunisation providers, general practitioners (GPs), practice nurses, school-based nurse immunisers, Aboriginal health workers, sexual health physicians, cervical cancer screening managers) with a mix of open- and closed-ended questions using either Likert-type scales or check-box options. The survey was open for completion from November 2019 to February 2020.

Vaccination coverage

AIR data, as at 29 February 2020, were obtained and vaccine encounters up to 31 December 2019 were analysed by gender, state/territory, remoteness/socioeconomic status of area of residence, and Aboriginal and Torres Strait Islander status. Eligible year-wide birth cohorts for female and male adolescents aged 12 to <20 years as at 31 December 2019 were used to assess cumulative HPV vaccination coverage (1, 2 or 3 doses), calculated using the number of individuals with a record of relevant HPV vaccine doses between 1 January 2007 and 31 December 2019 as the numerator and the overall number of adolescents in the relevant AIR cohort as the denominator. We also assessed trends in HPV vaccination coverage (1, 2 or 3 doses) between 2016 and 2019 for females and males aged 15 years, calculated using the number of 15-year-olds recorded on AIR to have received the relevant number of doses as numerator, and the total number of 15-year-olds in the relevant AIR cohort as denominator. Historical coverage data from the HPV Register was sourced from the VCS Foundation. AIR and HPV Register coverage estimates were compared by calculating coverage for female and male adolescents by year of age using the number with a record of HPV vaccination received by 30 June 2018 on each register as the numerator, and the relevant Australian Bureau of Statistics Estimated Resident Population (HPV Register) or AIR cohort population, as at 30 June 2017, as the denominator.

Vaccine safety

Information on all adverse events following immunisation (AEFI) associated with HPV vaccines reported via passive surveillance to the Therapeutic Goods Administration (TGA) from April 2007 to December 2017 and stored in its Adverse Events Management System database were obtained and analysed. We calculated age and sex-specific AEFI reporting rates.

AusVaxSafety national enhanced active surveillance system data (obtained using two participant-based SMS-based survey surveillance tools, SmartVax and Vaxtracker installed at sentinel sites across Australia) were also analysed.

Disease impact

Impact of HPV vaccination on high-grade cervical abnormalities, cervical cancer, anogenital cancers, oropharyngeal cancers and genital warts was assessed using an ecological design and 'before and after' comparisons with analysis of incidence data from the Australian Cancer Database, 2002–2016 and hospitalisation data from the National Hospital Morbidity Database, 2002–2017.

Results

Stakeholder assessment

Key stakeholder interviews (n=42) and online survey responses (n=1,513) provided valuable perspectives on the National HPV Vaccination Program. Key stakeholders who participated in the interviews included staff from the state/territory health departments, Australian Government Department of Health, TGA, local councils, Aboriginal Community Controlled Health Services, remote areas, sexual health physicians, cervical screening program managers, Seqirus and HPV researchers. The online survey participants included GPs, practice nurses, school-based nurse immunisers, Aboriginal health workers, sexual health physicians and cervical screening managers.

The change to a 2-dose schedule of 9vHPV vaccine was reported to have many benefits for jurisdictions, immunisation providers and the public. However, reduced opportunities for school-based catch-up vaccination, because of the 6- to 12-month dosing interval leading to dose-2 often being given late in the school year when absenteeism is higher, have led to perceptions that impact on coverage has not been as positive as anticipated.

Major barriers to achieving higher coverage in the school-based vaccination program were reported to be absenteeism and the reliance on return of paper consent forms. Reported enablers to improving consent form return included:

- school immunisation teams having access to parent contact details and resources/capacity to conduct follow up of unreturned forms
- appropriate consent forms and information available for population subgroups with different languages and levels of literacy

- education for students to increase their understanding of and encourage participation in the consent form process
- supportive school staff who engage with students and assist with ensuring consent form return.

While almost all key stakeholders believed that electronic consent forms would assist with consent form return, only two of eight state/territories have been able to progress developing these to date.

Catch-up vaccination remains essential, given the challenge of school absenteeism. Stakeholders reported that school-based catch-up is more convenient for families and leads to measurable increases in HPV vaccination coverage, but is conducted inconsistently across school-based providers and not at all in some jurisdictions. Increased emphasis on and resources to improve capacity to provide school-based catch-up vaccination across the country was considered likely to be beneficial. Free council immunisation clinics, where available, were generally considered a more effective alternative method of catch-up vaccination than reliance on GPs.

Various enablers of and challenges to HPV vaccination in culturally and linguistically diverse (CALD) and Aboriginal and Torres Strait Islander people were identified. Participants outlined several initiatives currently in development or implemented in the last 5 years to increase HPV vaccination coverage in these populations and improve equity within the program. However, many stakeholders reported that identification of CALD and Aboriginal and Torres Strait Islander people can be difficult, which means that assessing the effectiveness of these initiatives may also be challenging.

Most key stakeholders perceived vaccine hesitancy to have had little negative impact on HPV vaccination coverage in Australia. However, stakeholders highlighted the potential for vaccine-hesitant views to spread rapidly on social media and the need to be vigilant and monitor public attitudes towards HPV vaccination.

Almost all stakeholders believed that Australia could achieve the World Health Organization (WHO) cervical cancer elimination target of 90% course completion for females aged 15 years by 2030, but that an increase in effort, support for the program and development of additional strategies were required to achieve this. Stakeholders made many recommendations to increase HPV vaccination coverage, including:

- improving processes for consent form return
- increasing education of adolescents and parents
- strengthening messaging for parents around the benefits of vaccination
- improving vaccination reporting by immunisation providers
- improving vaccination coverage in CALD and Aboriginal and Torres Strait Islander people

Some stakeholders also suggested that the potential to reduce the schedule to a single dose, currently being investigated, would assist Australia in achieving the WHO coverage target.

The opportunity for enhanced integration between the national HPV vaccination program and the cervical screening program was also highlighted by many stakeholders, particularly given the transition to HPV-based cervical screening, which presents an opportunity to enhance cervical

cancer prevention in Australia. This enhanced integration would allow ascertainment of HPV vaccination status of women attending cervical cancer screening services.

Limitations of the stakeholder interview approach include that opinions are likely based, to a variable degree, on data or research findings and/or practical experience. In addition, given variations within Australia in the HPV vaccination program delivery, national or jurisdictional perspectives may not accurately reflect processes and factors influencing the program in all regions.

Vaccination coverage

Trends in HPV vaccine coverage at 15 years of age show increase in dose 1 and dose 3 coverage from 2016 to 2018. In 2019, most adolescents in NSW, South Australia and Western Australia had transitioned to the 2-dose schedule. Dose 2 coverage in 15-year-olds declined in 2019 in Aboriginal and Torres Strait Islander female and male adolescents compared with that in 2018. 9vHPV vaccine doses in adolescents aged 15 to <20 years between 1 July 2017 and 31 December 2019 were predominantly administered in GP settings in all jurisdictions except the Northern Territory where community health services and Aboriginal health services provided the majority of HPV vaccines.

Cumulative HPV vaccine coverage derived from AIR (based on age at 31 December 2019) is broadly consistent with historical data trends from previous coverage estimates derived from the HPV Register. For adolescents turning 15 years in 2019, the 2-dose coverage was 82.6% in females and 79.9% in males. Consistent with the previous HPV Registerestimates, dose 1 coverage is roughly equivalent for Aboriginal and Torres Strait Islander and non-Indigenous adolescents, except in 13–14-year-old Aboriginal and Torres Strait Islander males who have 4–5% lower coverage of dose 1 than their non-Indigenous peers.

Comparison of coverage estimates from the HPV Register and AIR showed that the HPV Register estimates were universally higher than the AIR estimates for females aged 13–18 years and males aged 13–17 years. However, for 19-year-old females and 18–19-year-old males, AIR coverage estimates for each dose were higher. The differences in coverage estimates are due to the different denominators used for estimating coverage in the HPV Register and AIR.

Vaccine safety

For the 11-year period 2007–2017, the overall rate of adverse events reported following HPV vaccination from the national TGA AEMS database was 48.5 per 100,000 doses administered. Excluding an enhanced surveillance period (2013–2014), it was 39.8 per 100,000 doses. These reporting rates of adverse events following HPV vaccine administration in Australia were consistent with data from similar surveillance systems internationally and did not reveal any new or concerning safety issues over the 11-year period.

During the period 1 February 2018 – 31 December 2019, AusVaxSafety sentinel active surveillance captured 73,627 HPV vaccination encounters in adolescents aged 11–14 years. The majority of encounters (91.1%) were captured by the SmartVax tool at 269 national sentinel sites. All Vaxtracker encounters were captured via the NSW school-based immunisation program.

Of the 73,627 adolescent HPV vaccination encounters captured in AusVaxSafety, 42,067 (57.1%) of caregivers participated by responding to the day 3–5 post vaccination survey. Of these, 3,690 (8.8%) reported any AEFI and 235 (0.6%) reported seeking medical attention for an AEFI. The caregivers for 114 adolescents provided details about their child's reported medical attendance; of these, 106 (88.6%) presented to a GP and 13 (11.4%) to an emergency department.

These national surveillance data provide evidence supporting the good safety profile of the HPV vaccine and that AEFI rates are low and consistent with data from reporting systems in other countries.

Disease impact

High-grade cervical abnormalities

The overall cervical high-grade abnormalities (HGA) incidence rate in cervical screening data decreased from the pre-vaccine period (2004–2006) to the post-vaccine period (2007–2016) in vaccine-eligible age groups by 48% and 20% in females aged <20 and 20–24 years, respectively. In contrast, cervical HGA incidence rate increased by 13% in the non–vaccine-eligible cohort of females aged ≥30 years. There was a progressive decline in the proportion of cervical HGA that was diagnosed in individuals aged <30 years from 53% in 2004–2006 to 50% in 2007–2012 and then to 41% in 2013 – June 2017. The overall age-standardised cervical HGA rate declined from 8.4 per 1,000 females screened in 2007 to 5.8 per 1,000 females screened in the first half of 2017.

The hospitalisation rates for cervical HGA (as principal diagnosis) in non-Indigenous females aged <30 years decreased from pre-vaccine period (2002–2007) to post-vaccine period (2008–2017) by 69%, 36% and 9% in the age groups of <20, 20–24 and 25–29 years, respectively. In Aboriginal and Torres Strait Islander females, cervical HGA hospitalisation rates declined over the same period in the age groups of <20 and 20–24 years, by 58% and 14%, respectively.

Cervical cancer

Overall the cervical cancer incidence rate was not significantly different between the pre-vaccine period (2000–2007) and post-vaccine period (2008–2015), but the mortality rate was 12% lower in the post-vaccine period. The age-standardised mortality rate of cervical cancer decreased from 5.2 to 1.8 per 100,000 females between 1982 and 2019.

The hospitalisation rate for cervical cancer (as principal diagnosis) in the post-vaccine period was lower than in the pre-vaccine period. The cervical cancer hospitalisation rate decreased in women aged ≥30 years (both Aboriginal and Torres Strait Islander and non-Indigenous), who were not vaccine-eligible, and in Aboriginal and Torres Strait Islander females aged 25–29 years.

These reductions in cervical cancer hospitalisations and mortality, without a similar decline in overall cervical cancer incidence, likely reflect earlier detection through the cervical screening program along with better treatments. Vaccination was not anticipated to have yet had an impact on cancer rates as at the time of this assessment.

Juvenile-onset recurrent respiratory papillomatosis

An impact of the National HPV Vaccination Program is the significant reduction in juvenile-onset recurrent respiratory papillomatosis (JoRRP), a condition associated with vertical transmission of HPV infection before or during birth, particularly type 6 or 11. This decline is evidence of reduced mother-to-child HPV transmission around the time of birth. Estimated hospitalisation rates (noting there is no unique International Statistical Classification of Diseases and Related Health Problems [ICD] code for RRP) followed the expected pattern, with JoRRP predominantly affecting children aged <12 years and adult-onset RRP (AoRRP) adults aged 20–30 years and ≥60 years.

Anogenital warts

There has been a remarkable decline in hospitalisations for anogenital warts in Australia. A decline of 74.4%, 54.1% and 22.1% from the pre-vaccine period (2002–2007) to the post-vaccine period (2008–2017) was observed in individuals aged 10–19 years, 20–29 years and 30–39 years, respectively. This is consistent with evidence of decreases in the incidence of anogenital lesions seen in outpatient settings, such as sexual health clinics.

Strengths and limitations of data sources in the evaluation

Data sources used in this evaluation of the National HPV Vaccination Program have inherent strengths and limitations in determining the impact of the program on the burden of disease. One of the strengths is the availability of national hospitalisation data for HPV-related cancers and genital warts coded using ICD-10-AM (International Statistical Classification of Diseases and Related Health Problems, 10th edition, Australian modification) codes both before and after the program. However, there is considerable lag in hospitalisation data availability; data on immunisation status are not available; and genital warts admissions represent only a small proportion of the disease burden, as genital warts are mostly managed in general practice and sexual health clinics, with hospitalisations representing only severe cases. Vaccine coverage estimates are likely to underestimate actual levels of coverage by a small but uncertain proportion because of under-reporting.

Limitations of vaccine safety data from the spontaneous/passive surveillance system include differences in data quality, accuracy and timeliness of reports of AEFI between jurisdictions. However, enhanced active sentinel surveillance data complement the passive surveillance data and are more timely and complete.

A specific surveillance plan that included analysis of linked data (from the various data sources above) would increase the ability to extend the impact evaluation presented here and generate new knowledge, for example around equity of the program and areas of unmet need.

Conclusion

HPV vaccine has been successfully incorporated into Australia's NIP, with relatively high coverage achieved since the implementation of the program. The change to a 2-dose schedule of 9vHPV vaccine has been well received by stakeholders, although challenges including reduced

opportunities for school-based catch-up vaccination and the 6–12-month dosing interval leading to dose 2 being given late in the school year persist.

Available data show the HPV vaccination program has substantially reduced the burden in vaccine-eligible age groups of cervical HGA in females and genital warts in both sexes, and has also led to substantial indirect disease reduction, particularly HGA, in other age groups. Reported HPV vaccine–related AEFI were predominantly mild and transient in nature and the vaccine has a safety record similar to that of other vaccines on the NIP. Continued monitoring of HPV vaccine coverage, AEFI and disease epidemiology is needed to ensure successes achieved to date are maintained and anticipated declines in cancer incidence realised. Using new approaches to both evaluate program impacts and increase vaccination coverage should allow further health benefits to be obtained.

Recommendations

Consent forms

- Develop and use electronic consent forms in school-based immunisation programs, for all vaccines, including HPV vaccine.
- Consider development of a nationally standardised consent form with minimum core data fields.
- Consider strategies to increase consent form return, for example, combination of hard copy and electronic consent reminders.

Information and education for parents and adolescents

- Consider a dedicated national website linked to the current Australian Government Department of Health website for students and parents to obtain information online about HPV vaccination in an appealing and accessible way.
- Enhance information for parents and adolescents around the benefits of HPV vaccine, why it is given to both females and males and why in early adolescence.
- Include HPV education in school curriculum, collaborating with young people and teachers to develop appropriate educational materials.
- Enhance HPV education at school just before vaccination days, which could include showing HPV videos. Emphasise the importance of completing the HPV vaccine schedule.
- Continue to conduct media campaigns about the benefits of the HPV vaccine and its availability, including at general practice. Promote good news stories about vaccine impact, particularly in social media.
- Develop online education for students to access outside of school time to improve their self-efficacy, co-designed with parents and students and in addition to education in schools.
- Develop/improve HPV vaccination resources in Aboriginal and Torres Strait Islander languages and for CALD people.

Catch-up opportunities

- Consider expanded healthcare clinics in schools with training and funding of school nurses to vaccinate.
- Provide more catch-up opportunities at schools, for example, additional visits.
- Increase opportunities for school-based catch-up, or community outreach visits, for schools with high Aboriginal and Torres Strait Islander student enrolment, where there are higher rates of absenteeism and students may not want to go to an Aboriginal Medical Service.
- Include HPV vaccination in the regular health program and pathways that adolescents in out-of-home care receive.

- Increase community partnerships between schools and GPs to streamline catch-up vaccination.
- Consider targeted HPV catch-up vaccination outside of normal school hours at schools, and in general practice settings, in low coverage areas.

Education of immunisation providers

- Provide information to immunisation providers (e.g. GPs and practice nurses) on how to use AIR to generate overdue lists to recall adolescents due for HPV vaccination, particularly before they turn 15 years old.
- Provide ongoing information and guidance to immunisation providers about the importance and methods of reporting HPV vaccination to AIR.
- Campaign to increase GP awareness and encourage checking adolescents' HPV vaccination history.
- Educate immunisation providers on how to counsel HPV vaccine–hesitant parents/guardians (e.g. using Sharing Knowledge About Immunisation [SKAI] resources).
- Provide additional information to immunisation providers regarding the safety and efficacy of HPV vaccines.

Data quality and reporting

- Consider training for data entry staff to improve HPV immunisation data quality and reporting to AIR.
- Consider financial incentives for GPs to record HPV vaccine doses in AIR.
- Link vaccination (all vaccines including HPV) reporting to AIR with accreditation of immunisation providers (e.g. GPs).
- Enhance provision of timely vaccination coverage rates by schools to allow school-based immunisation providers to identify gaps before the end of the school year.

Research to inform interventions

- Conduct research into why coverage rates are low in certain areas, for example, using the WHO's Tailoring Immunization Programmes approach to understand barriers to vaccination and inform interventions to address them.
- Monitor scientific literature on 1-dose HPV vaccine effectiveness to inform consideration of reducing the HPV vaccination schedule to one dose.
- Consider regular community surveys of attitudes towards HPV vaccination in Australia.
- Evaluate the effectiveness of strategies such as reminders to parents/carers from AIR to encourage completion of HPV vaccination courses.

- Conduct analyses of de-identified data from large linked databases, for example, AIR, cervical screening database, hospitalisations and others to identify where gaps in program delivery and equity of impact can be addressed.

Funding and support

- Increase funding to support delivery of HPV vaccinations in remote areas.
- Provide funded HPV vaccine for high-risk occupational groups who are not currently eligible, for example, migrant sex workers.
- Increase resources and funding for evaluation of the school-based program and research into factors affecting coverage.
- Consider funding for HPV vaccination for high-risk groups who are recommended to receive the vaccine, as per the Australian Immunisation Handbook, but are not currently funded, notably men who have sex with men and immunocompromised individuals.

Programmatic and policy issues

- Target marginalised students at higher risk of HPV infection and absenteeism in low coverage areas with tailored strategies.
- Implement measures to enhance uptake of HPV vaccination in special school students, for example, additional personnel to help or facilitate access to specialist immunisation services.
- Share initiatives/strategies used by local government areas/schools with high HPV vaccination coverage with lower coverage areas/schools.
- Ensure the program is well accepted by adolescents, for example, install privacy screens, vaccinate anxious students first.
- Enhance processes for schools to provide timely class lists with parent contact details to school-based immunisers, considering relevant privacy issues and any need for legislative changes.
- Promote HPV vaccination and cervical screening as a wellness program to improve reproductive health to remove the stigma around sexual health.
- Consider inclusion of HPV vaccine in immunisation requirements under ‘No Jab No Pay’ policy, with due consideration of assessment age and number of doses.
- Develop plan to assess and address areas where improved coverage and equity could be better achieved in order to meet the WHO target of 90% coverage by 2030.

Introduction

Human papillomavirus (HPV) is responsible for malignant and non-malignant lesions in both sexes, mostly affecting the anogenital region, but also other parts of the body notably the head and neck region.[1] Some HPV types, including types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 and 68, are designated as oncogenic types because 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.[2] Other HPV types, including types 6, 11, 40, 42, 43, 44, 54, 61, 70, 72, 81 and 89, are classified as 'low-risk' and are predominantly associated with non-malignant lesions, such as genital warts.[3]

Globally, each year, more than half a million women are diagnosed with cervical cancer.[4-6]

To eliminate cervical cancer as a public health problem (incidence rate <4 per 100,000), the World Health Organization (WHO) has recommended the '90-70-90' targets to be reached by 2030: 90% of girls fully vaccinated with the HPV vaccine by 15 years of age; 70% of women screened with a high-precision test at 35 and 45 years of age; and 90% of women identified with cervical disease receive treatment and care (90% of women with pre-cancer treated and 90% of women with invasive cancer managed).[7] Australia is on track to eliminate cervical cancer as a public health problem by 2028.[8]

Australia has been a world leader in HPV vaccination and was the first country to implement a fully funded national HPV vaccination program for girls (aged 12–13 years) via schools in 2007 using three doses of the quadrivalent HPV (4vHPV) vaccine, Gardasil®, which provides protection against four HPV types (6, 11, 16 and 18).9, 10 There was also a community-based catch-up program for women up to the age of 26 years that concluded in 2009. The HPV vaccination program for girls was extended in 2013 to boys aged 12–13 years, with catch-up for those aged 14–15 years old till end of 2014.[9,10]

The 9-valent HPV (9vHPV) vaccine, Gardasil®9, replaced the 4vHPV vaccine in the National Immunisation Program (NIP) from February 2018.[11] Gardasil®9 provides protection against the four HPV types contained in the 4vHPV vaccine and an additional five oncogenic HPV types (31, 33, 45, 52 and 58), which are the next most frequently detected types in cervical cancers globally after types 16 and 18.

Since 2018, 9vHPV vaccine is provided routinely via school-based programs for girls and boys at ages 12–13 years in a 2-dose schedule. The second dose is given 6–12 months after the first dose.[12] Catch-up is available under the NIP from primary care up to the age of 19 years.

Evaluation of the National HPV Vaccination Program

The National Centre for Immunisation Research and Surveillance (NCIRS), under a funding agreement with the Australian Government Department of Health (Health), evaluated the national 4vHPV vaccination program for the period 2007 to 2012/2013 and submitted a final report to Health in 2014.[9] This evaluation included a process evaluation and short- to medium-term outcome/impact evaluation (vaccine coverage, adverse events following immunisation [AEFI], cervical high-grade abnormalities [HGA] and anogenital warts).[9] The implementation process was viewed as successful overall by stakeholders.[9] The recommendations included continued

monitoring and evaluation of vaccine coverage, AEFI and disease epidemiology to determine if program impacts are sustained or improved subsequently, particularly in light of the extension of the program to male adolescents in early 2013.[9]

For the present NCIRS-led evaluation undertaken during 2019–2020, the focus was on evaluating the impact of the program, particularly on outcomes/impacts observed since the previous evaluation in terms of vaccination coverage, AEFI and disease burden. This evaluation is funded by Health. Guided by a conceptual framework based on the logic model[13] of program outcomes (refer to Figure 1), we reviewed relevant published and unpublished data and interviewed key stakeholders to monitor and assess outcomes/impact of the HPV vaccination program to date.

HPV vaccination coverage monitoring is a core component of Australia's HPV surveillance plan,[14] and serves several important public health purposes. Immunisation providers need short-term estimates of coverage being achieved during delivery to assess whether coverage is improving or declining; to ensure that vaccine supplies are sufficient; and to identify areas that may benefit from further visits or intensive follow-up to improve coverage. For this, as close to real time data as possible are needed, including current numbers of eligible students, and usually local records are used. Coverage estimates over larger geographic areas (up to state and national levels) are best provided by a comprehensive vaccination registry. They are used to monitor trends over time, ensure that coverage achieved is adequate to control disease and are useful to inform research and evaluation of program impacts and delivery methods, including input into modelling studies.

The evaluation of HPV vaccination coverage in this report is notable for two main reasons. First, at the time of transition between registers in 2018, Australia implemented a 2-dose 9vHPV vaccine program. Before this, the program used a 3-dose 4vHPV vaccine program. From 2018 those aged ≤14 years at first dose were eligible for the 2-dose course, with three doses still required for those aged ≥15 years at first dose or those with significant immunocompromise. No estimates of coverage achieved with 9vHPV vaccine or the 2-dose course have yet been published. There is some complexity in the interpretation of per-dose coverage over time, as New South Wales (NSW) initiated the 2-dose course early and age at vaccination determines eligibility for two rather than three doses. Also, not all children in a single school year level are the same age at vaccination.

Second, it is of interest to compare the historical estimates of coverage from the National HPV Vaccination Program Register (the HPV Register) with the same estimates calculated using the Australian Immunisation Register (AIR) data. AIR uses the Medicare population as the denominator, and a previous study found some minor differences in HPV vaccine coverage estimates when using Medicare versus ABS populations.[15] In addition, when data from the HPV Register were transferred into AIR, some data cleaning and merging using Medicare details occurred. As a result, dose rules may differ somewhat, meaning that numerator data may not be identical. Understanding any differences in historical coverage between the two methods is important for interpreting coverage and coverage trends into the future. The inclusion of HPV vaccines in AIR is expected to improve completeness of reporting of doses administered in general practice, which were incompletely notified to the HPV Register. Since 2017 all people aged up to 19 years are eligible for catch-up HPV vaccination through their primary care provider if they missed vaccination at school but no systematic assessment of the level of catch-up vaccination occurring in 15–19-year olds has yet been made.

We have collated all relevant information into a comprehensive report documenting the successes of what has been described as a world-leading program,[10,16] and provided recommendations to further enhance the program.

Aims

The aims of this evaluation were to:

- assess the overall uptake and impact of the National HPV Vaccination Program since the last evaluation in 2014
- identify any key gaps in knowledge
- make recommendations regarding ongoing monitoring and program enhancements.

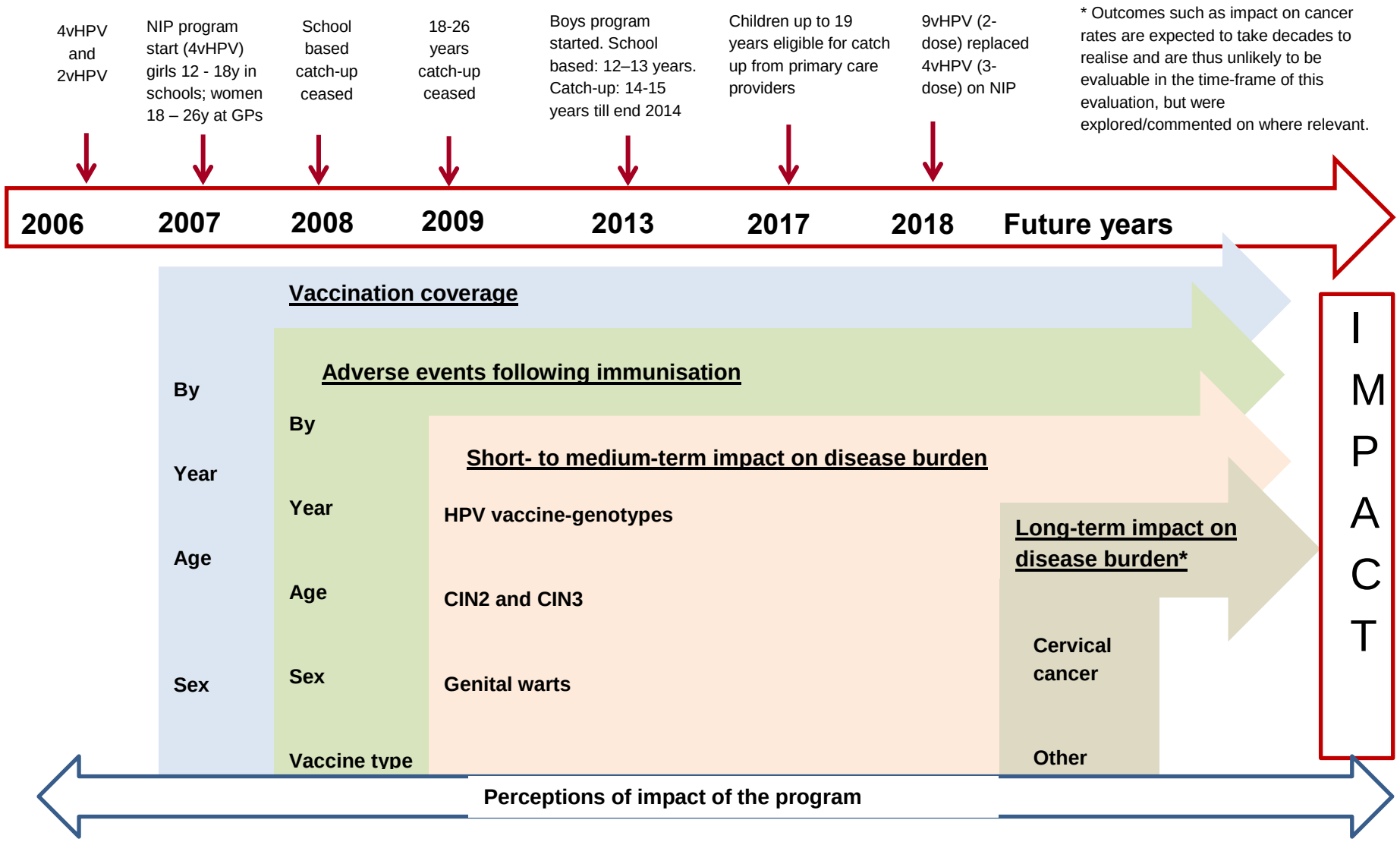
This evaluation included assessment of:

- vaccination coverage by age group, sex, Aboriginal and Torres Strait Islander status, state/territory of residence, school versus primary care, timeliness of vaccination and trends in vaccine doses administered and coverage
- vaccine safety, including reports of adverse events following immunisation (AEFI) using both passive and active surveillance data
- vaccine impact on disease burden, including genital warts, recurrent respiratory papillomatosis, CIN 2, CIN 3, cervical cancer, anogenital cancers and other related cancers, with analysis stratified by age group, sex and Aboriginal and Torres Strait Islander status
- stakeholder perspectives on the impact of the HPV vaccination program, including any influences of the 2018 change to a 2-dose vaccine schedule and perceptions of vaccine safety/vaccine hesitancy on coverage. A particular focus was on factors that could influence program outcomes/impacts, either positively or negatively, in the future.

The objectives of this evaluation were to:

- provide evidence supporting the safety of HPV vaccines
- provide evidence of the impact of the program on genital warts and high-grade cervical abnormalities, and determine if any impact on cervical or other HPV-related cancers is evident in Australia to date
- identify any inequities in HPV vaccination coverage and disease impact within Australia and make recommendations to address these
- contribute to the global evidence supporting the use of HPV vaccination and cervical screening to progress towards elimination of cervical cancer as a public health problem.

Figure 1: Conceptual framework for assessing impact of the HPV vaccination program



Ethical considerations

Ethical approval for this study was granted by the Sydney Children's Hospitals Network Human Research Ethics Committee, protocol 2019/ETH12453

Literature review

Aims

To conduct a comprehensive literature review (including grey literature) to assess:

- vaccination coverage
- vaccine safety
- vaccine impact on prevalence of HPV infection and on HPV-associated disease (genital warts, juvenile-onset recurrent respiratory papillomatosis [JoRRP], pre-cancerous cervical lesions, cervical cancer, other anogenital cancers and related cancers).

Methods

The scope of this literature review includes publications in peer-reviewed journals and grey literature from Australia since the previous evaluation of the National HPV Vaccination Program.[9] Literature searches were conducted in OVID Medline and OVID EMBASE databases for HPV vaccine coverage, safety and disease impact for the period 1 January 2013 to 25 October 2019 (final search conducted on 25 October 2019). The searches used database thesaurus and text word terms. Thesaurus terms used in OVID Medline included 'papillomaviridae', 'papillomavirus infections', 'immunization', 'vaccines' and 'papillomavirus vaccines' as well as terms specific to coverage, vaccine safety and disease burden. Text word terms included those that represent HPV vaccine (2-valent, 4-valent or 9-valent vaccine). The Australian-focussed Informit Health databases were also searched for both published and grey literature. The searches were limited to studies in humans, written in English and from 'Australia'. The search strategy was adapted to account for differences of syntax and controlled vocabulary terms for subsequent searches. All citations in the previous evaluation report were excluded. Content experts were also consulted and reference lists of key papers and websites of selected peak Australian organisations were reviewed to identify additional relevant literature.

Results

Sexual health strategies and cancer control plans

An updated plan for monitoring the impact of HPV vaccination in Australia was published by the Communicable Diseases Network Australia in 2013 following the introduction of the male HPV vaccination program.[14] This plan, which included surveillance of HPV vaccine coverage and safety, HPV infections, non-cancer disease endpoints and cancer endpoints,[14] informed the structure of this literature review.

Control of HPV-associated diseases and other sexually transmissible infections (STIs) in Australia is currently guided by the Fourth National STI Strategy 2018–2022[17] and Fifth National Aboriginal and Torres Strait Islander Blood Borne Viruses and STI Strategy 2018–2022.[18] Under the Third National STI Strategy 2014–2017 the target for national adolescent HPV vaccination coverage was

70%, which was reached in both females and males in 2016.[19] Under the Fourth National STI Strategy this coverage target was increased to 80%.[17,18] Australia's current National Framework for Gynaecological Cancer Control also emphasises the role of the National HPV Vaccination Program in primary prevention of cervical cancer, highlighting both the higher risk of gynaecological cancer and lower HPV vaccination coverage in Aboriginal and Torres Strait Islander females.[20] However, this national framework does not include any targets/goals for the National HPV Vaccination Program.

Most states and territories also publish their own sexual health strategies that include HPV vaccination. Although there is no published sexual health strategy referring to HPV vaccination in Victoria or Tasmania, the Victorian Cancer Plan 2016–2020[21] includes focus areas for HPV vaccination. Tasmania included reference to improving HPV vaccination coverage in their Cancer Framework and Strategic Cancer Plan 2010–2013,[22] but this has not been publicly updated since then. South Australia has also published an Aboriginal Cancer Control Plan 2016–2021,[23] along with a state-wide STI strategy, that includes priorities and actions for improving HPV vaccination coverage in Aboriginal people. All other jurisdictions do not have current published cancer control plans that refer specifically to HPV vaccination.

The targets/goals and actions or activities relevant to HPV vaccination that are included in the current national and jurisdictional sexual health strategies and cancer control plans are summarised in Table 1. Of note, many of these strategies and plans cover different time periods to the current Fourth National STI Strategy and several jurisdictional strategies are shortly due for update and do not yet reflect the updated 80% national HPV vaccination coverage target.

Table 1. National and jurisdictional sexual health strategies and cancer control plans relating to HPV vaccination, 2011–2022

Jurisdiction	Strategy	Target/Goal	Actions/Activities
National	Fourth National Sexually Transmissible Infections Strategy 2018–2022[1]	Achieve and maintain HPV adolescent vaccination coverage of 80% by the end of 2022. Note: The strategy mentioned, "Sustained efforts are needed to continue to improve adolescent vaccination, particularly in males, to meet the target of 80 per cent coverage by 2022."	Priority area: • Support further increases in HPV vaccination coverage in adolescents in line with the National Immunisation Strategy Key area for action: • Increase access to HPV vaccination of eligible individuals under the National Immunisation Program and support the actions to expand vaccination coverage outlined in the National Immunisation Strategy
National	Third National Sexually Transmissible Infections Strategy 2014-2017	Achieve HPV adolescent vaccination coverage of 70%	Note: This strategy (Third National Sexually Transmissible Infections Strategy 2014-2017) is no longer publicly available on the website. This has been superseded by the Fourth National Sexually Transmissible Infections Strategy 2018-2022.
National	Fifth National Aboriginal and Torres Strait Islander Blood Borne Viruses and Sexually Transmissible Infections Strategy 2018-2022[2]	Achieve and maintain HPV adolescent vaccination coverage of 80% by the end of 2022	Key area for action: • Develop initiatives to support further increases in vaccination coverage for HPV in adolescents, in and outside of school settings, in support of the actions of the National Immunisation Strategy
National	Fourth National Aboriginal and Torres Strait Islander Blood Borne Viruses and Sexually Transmissible Infections Strategy 2014-2017		Note: This strategy (Fourth National Aboriginal and Torres Strait Islander Blood Borne Viruses and Sexually Transmissible Infections Strategy 2014-2017) is no longer publically available on the website. This has been superseded by the Fifth National Aboriginal and Torres Strait Islander Blood Borne Viruses and Sexually Transmissible Infections Strategy 2018-2022.

ACT	Hepatitis B, Hepatitis C, HIV and Sexually Transmissible Infections. ACT Statement of Priorities 2016-2020[3]*	Achieve HPV adolescent vaccination coverage of 70% (Achieved in 2016[4])	None specified
QLD	Queensland Sexual Health Strategy 2016-2021[5]	None specified	Strategic directions and priority actions: • Continue to provide HPV vaccination to Aboriginal and Torres Strait Islander young people, migrant and refugee populations and young people who are disengaged from school through innovative outreach models
NSW	NSW Sexually Transmissible Infections Strategy 2016-2020[6]	Maintain high coverage of HPV vaccination	Priority areas of action: • Maintain high coverage of HPV vaccination for year 7 school students in accordance with the Australian Immunisation Handbook
NT	Northern Territory Sexually Transmissible Infections and Blood Borne Viruses Strategic and Operational Plan 2019-2023[7]	Increase the uptake of HPV vaccine	Activities: • Continue to provide the HPV vaccine to year-seven girls and boys through the School Vaccination Program, and strengthen the process by which consent is obtained from parents and guardians • Enable access to the HPV vaccine for high-risk populations, including gay men
SA	South Australian Sexually Transmissible Infection Implementation Plan 2016-2018[8]	Increase uptake of HPV vaccine	Response and activities: • Continue to advocate for free HPV vaccination for MSM with few lifetime partners who are not able to access school-based vaccination • Continue to provide HPV vaccinations as part of the catch-up schedule for eligible newly arrived refugee and asylum seeker clients • Continue to provide prescription of HPV vaccine for at-risk individuals, with few lifetime partners who are not eligible for school-based HPV vaccination • Continue to provide counselling and obtain informed consent where off label use is indicated, such as outside the labelled age limits

			• Collaborate with research focussed on HPV to contribute to the expansion of evidence based knowledge of HPV transmission and vaccination • Continue to promote the importance of HPV vaccination in teacher training
SA	South Australian Aboriginal Cancer Control Plan 2016-2021[9]		Priority: • Increase Aboriginal peoples' participation rates in HPV and hepatitis B immunisation. Actions: • Monitor and report on HPV and hepatitis B immunisation rates in the Aboriginal population with an emphasis on data quality and currency to ensure accuracy and timeliness of reporting
VIC	Victoria Cancer Plan 2016-2020[10]	Enhance HPV vaccination coverage	Focus: • Increase uptake of HPV vaccination for at-risk individuals. • Provide catch-up vaccination for young people who missed scheduled immunisation during school immunisation program and for at risk populations • Provide HPV vaccination for immunosuppressed women and girls
WA	Western Australian Sexually Transmissible Infections Strategy 2019-2023[11]	Achieve and maintain HPV adolescent vaccination coverage of 80% or more	Action areas: • Support further increases in the number of adolescents including Aboriginal adolescents completing the HPV vaccination series as per the National Immunisation Strategy and the Western Australian Immunisation Strategy 2016–2020
WA	Western Australian Aboriginal Sexual Health and Blood-borne Virus Strategy 2019-2023[12]	Achieve and maintain HPV adolescent vaccination coverage of 80% or more	Action areas: • Increase hepatitis B and HPV vaccine schedule adherence by providing diverse delivery methods and sites so as to ensure a range of options are available to meet the needs of Aboriginal people

ACT – Australian Capital Territory, NSW – New South Wales, NT – Northern Territory, QLD – Queensland, SA - South Australia; TAS – Tasmania, VIC – Victoria, WA – Western Australia

HPV vaccination coverage

Estimates from immunisation coverage reports

National immunisation coverage annual reports for the years 2010–2018 were published in the time period of this review, but the 2018 report did not include HPV vaccine data as transition of data from the HPV Register to AIR was not yet complete.[32] HPV vaccination coverage estimates in the 2010–2017 reports were ascertained from the HPV Register and reported as the proportion of adolescents aged 15 years with recorded 3-dose course completion, with coverage in males available from 2014. Aligning with the data in these annual reports, historical coverage data from the HPV Register have also been made available online by the Australian Government Department of Health following the transition of HPV vaccination reporting to AIR.[33] The HPV Register data showed that coverage increased over time, varying by jurisdiction, and was higher in younger age groups than in older, and was the highest for dose 1, with coverage decreasing for doses 2 and 3.[34-41]

Annual vaccination coverage estimates showed 3-dose HPV vaccination coverage for females increased from 71.9% in 2012 to 80.2% in 2017 and for males from 62.4% in 2014 to 75.9% in 2017.[34] In 2017, 3-dose coverage for females ranged from 74.6% in Tasmania (TAS) to 92.5% in the Northern Territory (NT) and for males from 64.0% in TAS to 84.8% in the NT.[34] National vaccine coverage for females aged 15 years reached 86%, 83%, 78% for dose 1, 2, 3, respectively, in 2015.[42]

Despite the increases in adolescent HPV vaccine coverage nationally over time, there is evidence of a disparity in course completion between Aboriginal and Torres Strait Islander and other Australians. Vaccine coverage for Aboriginal and Torres Strait Islander adolescents aged 12 years in 2015 (data available for New South Wales [NSW], Queensland [QLD], NT and ACT only) highlighted that course completion was a challenge.[43] The coverage for HPV vaccine dose 1 was higher in Aboriginal and Torres Strait Islander adolescents than in other Australian adolescents (87.3%–95.9% versus 87.0%–97.7% in females and 82.4%–94% versus 83.3–96.3% in males). However, the coverage for dose 3 was lower in Aboriginal and Torres Strait Islander adolescents than in other Australian adolescents across all jurisdictions, except for females in NSW.[43] The dose 3 coverage by jurisdiction ranged from 66.5%–82.6% for Aboriginal and Torres Strait Islander females to 78.4%–87.7% for other females and from 61.2%–72.6% for Aboriginal and Torres Strait Islander males versus 73.7%–83.7% for other males.[43]

The 2017 immunisation coverage annual report included data on HPV vaccine course completion by Aboriginal and Torres Strait Islander status nationally.[34] The 2017 data showed that Aboriginal and Torres Strait Islander adolescents were less likely to complete their HPV vaccine course.[34] The proportion of adolescents aged 15 years in 2017 who received dose 1 and completed the 3-dose course was 91% and 90% for non-Indigenous females and males, respectively, but lower at 79% and 77% for Aboriginal and Torres Strait Islander females and males, respectively.[34]

Studies have assessed the effectiveness of a reduced dose schedule in young adolescents, as was implemented in Australia in 2018 concurrently with the change to 9vHPV vaccine.[44] This change to 9vHPV vaccine will provide broader protection against additional HPV genotypes and is

predicted to enhance the expected declines in cervical and other HPV-related cancers in Australia. Recent literature[45-49] also indicates potential effectiveness of a single-dose HPV vaccine strategy (non-inferiority of immune responses and disease reduction), which would assist in overcoming the barriers to course completion both in Australia and globally and reduce cost and resources required for vaccine program delivery. This evidence is under ongoing review by the Strategic Advisory Group of Experts on Immunization of the World Health Organization (WHO). Results from ongoing randomised controlled trials of single dose vaccination are awaited. Single dose HPV vaccination is not currently recommended in Australia.

Factors associated with HPV vaccine uptake

We identified several studies that assessed factors associated with the uptake of HPV vaccination in Australia (refer to Table 2). We also identified additional studies that primarily assessed vaccine impact on HPV disease but also reported on demographic factors associated with HPV vaccination in Australian females.[50-54]

Factors shown to be associated with higher likelihood of being vaccinated with HPV vaccine as an adolescent or a young woman included being born in Australia,[50-52,55-58] younger age,[50,51-53] current contraceptive use (hormonal[50,55] or unspecified[57]), unmarried,[55,58] speaking English at home,[51,58] high knowledge of HPV and HPV vaccine,[56] never having had a child,[55] current consumer of alcohol,[55] history of other STIs,[55] private health insurance holder[57] and completion of vaccinations due in childhood.[57] Vaccinated women were more likely to reside in outer regional, remote or very remote areas,[55] while unvaccinated women were more likely to reside in major cities.[53,54]

No significant difference was seen between vaccinated and unvaccinated females for age of sexual debut,[50,57] the number of previous Pap smears or history of abnormal cytology[55] or of undergoing a Pap smear in the preceding 2 years.[57]

For certain other factors such as lifetime number of sexual partners,[50,55,57] socioeconomic status,[50,52-55] educational attainment[50,55] and smoking status,[50,57] the association with likelihood of HPV vaccination was uncertain in published studies. However, national HPV vaccination data show a small but consistent relationship between HPV vaccination and socioeconomic status.[59]

Reasons identified for HPV vaccination courses not completed in females eligible for the catch-up program 2007–2009 included not being aware of doses missed, forgetting to have all recommended doses, the vaccine no longer being free and pregnancy.[58,60] The reasons for not receiving any HPV vaccine doses among eligible females included concerns about vaccine safety or side effects,[56,60] uncertainty of their eligibility,[56] perception that HPV vaccination was not needed if in a monogamous relationship[56] and needle phobia.[57]

Parents and students concerns about HPV vaccine safety and side effects have been identified as key barriers to vaccination in adolescents in international literature and two recent Australian studies.[57,61] However, these concerns were less prevalent among Australian parents (15.4%) than among parents in the United States of America (USA; 60.5%) and the United Kingdom (UK; 36.4%).[62] Other barriers to HPV vaccination in adolescents identified in Australian studies included student anxiety or needle phobia,[57,61,63] low parental literacy or health literacy[61] and parental perception of their daughter as low risk.[57] The reasons reported for non-completion of HPV vaccine

course included not being aware of the need for a third dose, availability of vaccine from general practitioners and adolescents not wanting further doses.[64] Similarly reasons reported for failure to vaccinate adolescents in school-based programs included logistical barriers such as non-return of consent forms,[57, 61] school absenteeism[57,61] and difficulty contacting parents.[61] Anxiety or distress were other reasons, with about a fifth of school students from specialist schools who had the vaccine described by school immunisation coordinators as 'very challenging', 'required extra support' or 'became very distressed'.[65]

Coverage estimates of the first dose of HPV vaccine in 374 students from specialist schools in Victoria were 66% for females and 67% for males. These estimates were similar to those for school-based diphtheria-tetanus-pertussis (dTpa) vaccine uptake in the same schools.[65]

Vaccine uptake appears to be associated with parental knowledge. Although higher parental knowledge of HPV vaccine was associated overall with increased likelihood of their daughters' receipt of HPV vaccine, one study showed that parents in the USA, the UK and Australia who had either very high or very low HPV vaccine knowledge were less likely to have their daughters vaccinated.[62] However, parents with high HPV vaccine knowledge scores expressed attitudes in favour of their daughter receiving the vaccine in future.[62]

One study found high levels of community acceptance for school-based immunisation programs (SBIP) in Australia, with 76% of 1,926 adults aged 18–95 years surveyed by telephone in 2011 in South Australia (SA) indicating that schools were the best place for adolescent immunisation.[63] Males, younger people and parents with high school children were significantly more likely to support SBIP.[63] Convenience, public funding of the immunisation program and compliance were key reasons for willingness to participate (support having children vaccinated) in SBIP.[63] On the other hand, a preference for family physician or council clinic, child immunisation anxiety, past history of adverse vaccine reaction and anti-vaccination beliefs were reasons for non-participation in SBIP.[63]

Of note, a study in Western Australia (WA) showed that the proportion of students that received HPV vaccine through SBIP declined as the school year progressed. Only 0.9% of consented HPV vaccines scheduled in term 1 were not delivered compared with 3.4% in term 2 and 11.5% in term 4.[66]

Strategies to improve HPV vaccination coverage in adolescents

A recent mixed methods study in WA suggested some key enablers to improve school-based HPV vaccination uptake: educating parents and students on HPV vaccination, promoting and providing relevant information online, sending reminders to return consent forms and providing education about immunisation and HPV vaccination to students in class.[61,67] This was explored in a randomised-controlled trial (RCT) of a complex educational intervention in 40 schools across SA and WA in 2012–2014.[68] In this RCT, educational materials provided around the time of consent form distribution and again when dose 1 was given resulted in significantly improved knowledge and understanding of HPV and HPV vaccination, leading to favourable attitudes towards vaccination.[68]

Another intervention to improve school-based HPV vaccination tested in an RCT in 31 schools in Victoria (VIC) in 2016 was sending SMS reminders to parents who had already consented to HPV vaccination (3 doses of 4vHPV vaccine) for their children, ahead of the third school visit of the immunisation providers.[69] The SMS reminders sent 2 working days before immunisation providers visited school were either 'self-regulatory' (a regular SMS reminder) or 'motivating' in tone. Vaccination rates for this school visit (for any dose of the vaccine) were significantly higher in the groups that received the self-regulatory (89.0%) and motivational (88.4%) SMS texts than in the group that received none (85.7%). The SMS reminder effectiveness between the two intervention groups was maintained during catch-up vaccinations.[69] Another study showed that letters (history statements) from the HPV Register to immunisation providers and individuals overdue for vaccination improved coverage.[70]

HPV vaccination coverage in men who have sex with men

HPV vaccination uptake was assessed in a cohort of men who have sex with men (MSM) who were offered the vaccine at their first presentation to the Melbourne Sexual Health Centre (MSHC) in 2017, when a state-funded 4vHPV catch-up campaign was undertaken targeting MSM aged ≤26 years.[71] The study excluded those who would have been age-eligible for HPV vaccination through the school-based program, of whom only 26.7% self-reported receiving the vaccine.[71] Of the remaining cohort, 73.2% who were offered HPV vaccine at first presentation received it on that day.[71] The reasons stated by study participants for declining HPV vaccine were 'wanting time to think', 'being uncertain of past history of HPV vaccination' , 'travelling', 'time constraints' and 'issues with needles'. However, 15.1% of those who initially declined did receive the vaccine within 3 months.[71] Factors significantly associated with receiving the vaccine in this cohort included age 20–26 years compared with 16–19 years, a history of genital warts and >4 male partners in the last 12 months.[71]

Perceptions of HPV vaccination assessed using social media postings

Two studies have used Twitter to assess perceptions around HPV vaccine in Australia.[72, 73] In one study, tweets from Australia, the UK and Canada showed that the proportions that expressed HPV vaccine concerns were 19.3%, 22.6% and 14.9%, respectively.[72] The most common concern across all three countries was related to perceived barriers to vaccination, which included both logistical and psychological barriers, such as perceived harms of the vaccine.[72] This study also showed that Twitter users who expressed concerns disproportionately connected with Twitter users in other countries who also posted similar tweets on HPV vaccines.[72] The second study found an association between HPV-related tweets and HPV vaccine coverage in different regions in Australia.[73] This study showed that a higher proportion of Twitter users in low HPV coverage regions had exposure to information critical of vaccination.[73]

Table 2. Summary of studies that assessed factors associated with HPV vaccine uptake in Australia (published since 2013)

Author	Source and year	Location	Study design	Participants	Key results
Brotherton JML et al.[13]	*Vaccine*, 2014	Australia	Random sampling mobile phone survey	1,379 females eligible for catch-up vaccination	HPV vaccination was significantly associated with: • born in Australia • permanent resident/living in Australia since 2007 • speaking English at home • unmarried Reasons for incomplete vaccination in those who had planned to complete the course: • lack of time • pregnancy • forgetting • away/moving Reasons for not planning on receiving more vaccine doses: • unsure of the benefit of additional doses • unaware three doses were needed • the vaccine no longer being free/ costing too much • advised by their doctor against further doses
Brotherton JML, et al.[14]	*Sexual Health*, 2016	VIC	Random sampling household telephone survey	956 females eligible for catch-up vaccination	Reasons for incomplete vaccination included forgetting, not knowing three doses were needed, running out of time while the vaccine was free and becoming pregnant. Reasons for not being vaccinated included not knowing about it, being too old, not an Australian resident, forgetting and safety or side effect concerns.
Burns, S et al.[15]	Data published on the WA website in	WA	Mixed methods-online survey, student focus	184 total participants	Reasons for parents not consenting or delaying vaccination included fear of side effects, consent form not given to parent or returned by student, lack of information about the vaccine, religious beliefs, parent not understanding due to low literacy and parents believing their child is too young.

	2019 and in Vaccine, 2020 [16]		groups, parent interviews		Barriers to students being vaccinated at school included student anxiety, absenteeism, parental perceptions about vaccine safety, low parental health literacy, difficulty contacting parents and student beliefs about pain or side effects of the vaccine.
Canfell, K et al.[17]	*Vaccine*, 2015	NSW	Postal questionnaire sent to controls in Cervical Health Study following recent normal Pap smear	1,139 females who had been eligible for catch-up vaccination	Factors significantly associated with having received ≥1 HPV vaccine dose were being never married, nulliparous, Australian-born, residing in outer regional, remote or very remote areas, having history of sexually transmitted infection, current hormonal contraception use and being a current alcohol drinker. Factors significantly associated with decreased likelihood of receiving HPV vaccine were decreasing socioeconomic status of place of residence and higher number of sexual partners. No significant associations were found between HPV vaccine uptake and educational attainment, number of previous Pap smears or abnormal cytology tests.
Gunasekaran B, et al.[18]	*Vaccine*, 2015	VIC	Recruitment for web-based questionnaire via *Facebook* advertising	278 females aged 16-25 years	Predictors of self-reported 3-dose coverage were being Australian-born and having high HPV and HPV vaccine knowledge. Predictors of high HPV vaccine knowledge were being Australian-born and having awareness of Chlamydia. The most common reasons for receiving HPV vaccine were protection against HPV infection and cervical cancer, because it was free, and 'join the fight against cervical cancer'. The most common reasons for not receiving HPV vaccine were uncertainty of eligibility, concern about a bad reaction and perceiving it was not needed as in a monogamous relationship.
McGrath L, et al.[19]	*Sexually transmitted Infections*, 2019	Melbourne Sexual Health Centre	Retrospective chart review of HPV vaccine uptake among eligible MSM in 2017	2108 MSM aged 16-26 years	58.2% of all eligible MSM were offered HPV vaccine by clinicians at first consult, increasing from 25% in April 2017 to 79% in December 2017. 73.2% of those offered HPV vaccine received it on the same day. The most commonly documented reasons for declining HPV vaccine included wanting time to think, being unsure of immunisation records, travelling, time constraints and issues with needles. 15.1% of MSM who initially declined received the vaccine within 3 months.

					Factors significantly associated with HPV vaccine uptake were age 20-26 years compared to age 16-19 years, history of genital warts and >4 male partners in last 12 months Overall coverage was 42.6% during first consult and 50.4% after 3 months follow-up.
Nickel B, et al.[20]	*Preventive Medicine Reports*, 2017	Australia, UK, USA	Online survey of female and male parents with daughters aged 9-17 years	Total=179 parents Australia n=53, UK n=59, USA n=67	Parents' HPV knowledge had the strongest association with daughter's vaccination status, followed by HPV vaccine specific knowledge. Parents with both low and high HPV and HPV vaccine specific knowledge scores were less likely to have vaccinated their daughters. Parents from the USA and male parents in all three countries were less likely to vaccinate their daughters. Australian parents were significantly less likely to worry about vaccine side effects (15.4%) compared to parents in the USA (60.5%) and UK (36.4%)
Staples, et al.[21]	*Sexual Health*, 2016	Hunter New England Local Health District	Postal survey sent to parents of adolescent females incompletely vaccinated in 2010	207 responses from parents or carers	The most common reasons for non-completion of HPV vaccination were being unaware catch-up doses were available from GP, unaware of the need for a third dose and their daughter not wanting further doses.
Tung IL, et al.[22]	*PLoS One*, 2016	VIC	Supplementary postal survey sent to participants in VACCINE study[23]	417 females who had been eligible for catch-up vaccination	HPV vaccination was significantly associated with being Australian-born, having completed childhood vaccinations and parents being the main decision-makers for participants' HPV vaccination. Vaccinated women were significantly more likely to be non-smokers, have private health-insurance and use contraception. There was no significant difference between vaccinated and unvaccinated women for age at first sex, lifetime sexual partners or having had a pap smear in the last 2 years. The most common reasons for non-vaccination included parental concern about vaccine safety, perception of daughter as low HPV risk, needle phobia and practical barriers e.g. absenteeism, lack of consent form. 61% of unvaccinated participants reported a GP recommendation would encourage them to receive HPV vaccine.

Vaccine safety

Annual national vaccine safety reports for the years 2012–2017 were within the time period of this review. The number of HPV vaccine–related adverse events notified to the Therapeutic Good Administration (TGA) increased from 155 in 2012 75 to 786 in 2013.[76] The large increase in 2013 was due to the extension of the HPV vaccination program to males and the introduction of enhanced school-based surveillance of adverse events of special interest. The total number of HPV vaccine–related adverse events reported annually declined in each subsequent year: 571 in 2014,[77] 374 in 2015,[78] 396 in 2016[79] and 299 in 2017.[80]

In 2015 the TGA published results of the enhanced surveillance that occurred in 2013 during the implementation of the male HPV vaccination program.[81] This enhanced surveillance, undertaken in addition to the routine monitoring, focussed on anaphylaxis, generalised allergic reaction, loss of consciousness and emergency department presentation or hospitalisation. The enhanced surveillance did not identify any particular safety signals. Overall the types and rates of AEFI reported were consistent with the information in the 4vHPV vaccine product information.[81]

The rate of AEFI captured in enhanced surveillance was higher in females (122 per 100,000 for females aged 12–13 years) than males, and among males it was higher in younger adolescents (101 per 100,000 for males aged 12–13 years and 44 per 100,000 for males aged 14–15 years).[81] Syncope was the most common adverse event in all three groups (overall rate 37 per 100,000 vaccine doses) and accounted for 25.9% of the total number of AEFI reported. However, injury due to syncope was uncommon and only one case required hospital attendance.[81] There was one episode of anaphylaxis (rate of 0.12 per 100,000 vaccine doses). The rate of generalised allergic reaction was 7.1 per 100,000 vaccine doses.[81]

Before the expansion of the HPV vaccination program to include males, background annual incidence rates of neurological and allergic events in adolescent boys in VIC, based on hospital emergency department and discharge data, were 252.9 and 175.2 per 100,000 person-years, respectively.[82] On the basis of the background rate of these events, it was estimated that there would be 2.4 cases of Guillain-Barre syndrome expected within 6 weeks of HPV vaccination in boys, and an expected 3.9 seizures and 0.3 cases of anaphylaxis and 6.5 of acute allergy within 1 day of vaccination.[82] This highlights the possibility of coincidental events erroneously being attributed to vaccination and the need for thorough causality assessment.

In VIC, SAEFVIC (Surveillance of Adverse Events Following Vaccination in the Community), an enhanced state-based passive surveillance system, is integrated with clinical services to monitor AEFI and has been operating since 2007. From 2007 to 2013, three cases (0.32 per 100,000 doses) of anaphylaxis following 4vHPV vaccine were reported to SAEFVIC.[83] Two cases involved an urticarial skin reaction after dose 1 followed by anaphylaxis after dose 2, and no information was provided

about the third case.[84] SAEFVIC became a founding member of AEFI-CAN (Adverse Events Following Immunisation: Clinical Assessment Network), a national network linking all state/territory vaccine safety clinics, in 2013. From January 2013 to June 2014, AEFI-CAN assessed 118 HPV vaccine–related AEFI reports.[85] Most of these AEFI occurred after HPV vaccine dose 1 (59%), followed by dose 2 (34%) and dose 3 (7%). All of these adverse events were following 4vHPV vaccine except for one that occurred after 2vHPV vaccine.85 The reported AEFI included rash (24%), allergy (urticaria/angioedema) (23%), serious neurological events other than syncope (19%), syncope (10%), anxiety (4%), anaphylaxis (3%) and somatic complaints (2%).[85] Of these 114 vaccinees, 76 underwent clinical review and 31 (41%) received further doses of HPV vaccine after which three experienced a rash.[85]

In a multi-centre trial in Australia that assessed the safety and immunogenicity of 4vHPV vaccine in immunocompromised children (n=59, mean age 12.3 years, range 5–18 years), local adverse events were more common than systemic adverse events and both declined in frequency following subsequent doses.[86] The proportion of vaccinees who reported adverse events following doses 1, 2 and 3, respectively, were 28.0%, 18.2% and 15.4% for local reactions and 15.8%, 12.7% and 5.8% for systemic reactions.[86] Although no clinically significant adverse events related to HPV vaccine were reported, disease flared in two trial participants (3.5%) after dose 1.[86] HPV antibody titres after three doses were significantly higher than baseline titres and considered satisfactory in participants, but were lower, particularly in females, than in healthy controls in other studies.[86] Among 37 of the participants followed up for 5 years after vaccination, antibody titres remained well above those associated with natural infection, with no serious adverse events reported.[87]

The effect of prior exercise on HPV vaccine–related adverse events such as pain, anxiety and fear was assessed in an RCT among 116 female and male students who received three doses of 4vHPV vaccine in a SBIP in Sydney. The intervention (exercise) group underwent 15 minutes of upper body exercise before vaccination and the control group received the vaccine as per usual procedures.[88,89] In the control group, the number of students who reported pain and anxiety associated with HPV vaccination was significantly higher in females than in males. However, this difference was not seen in the intervention group, suggesting that exercise before vaccination reduced the negative experience for females more than for males.[89] After vaccination, females in both control and exercise groups reported significantly more days of pain, tenderness, swelling and feeling ill than males in respective groups. However, among females those in the exercise group reported significantly fewer days of pain, tenderness, feeling ill and appetite loss than those in the control group. This suggests that exercise may mitigate the experience of minor adverse events following HPV vaccination in adolescent females.[88]

AusVaxSafety began actively monitoring adverse events following HPV vaccination in adolescents in 2018 concurrent with the changeover from 4vHPV to 9vHPV on the NIP. AusVaxSafety surveillance data to date, from over 41,000 parent or carer

responses, show that in 91.2% of the cases the child did not experience any adverse events following 9vHPV vaccination.[90] Among those who did report adverse events, the most common experiences were injection site reactions (pain, swelling or redness), tiredness, headache and fever, all of which were self-limiting.[90] Only 0.6% reported taking their child to a doctor or emergency department in the days after vaccination.[90]

There are two systematic reviews of HPV vaccine safety by Australian authors: the first in 2013 on 2vHPV and 4vHPV vaccines[91] and the other in 2017 that included 9vHPV vaccine as well as safety in special populations.[92] These comprehensive reviews covered relevant international evidence extensively and reinforced the excellent safety profile of all HPV vaccines.

Vaccine impact on HPV-associated diseases

HPV causes the third highest burden of all vaccine-preventable diseases in Australia, with the highest burden in people aged 15–39 years and 77% of the burden attributed to mortality due to cervical cancer.[93] The significant decline in HPV-associated disease burden from 48.2 Disability Adjusted Life Years (DALY) per 100,000 population in 2005 to 15.8 DALY per 100,000 population in 2015[93] likely reflects the combined impact of the cervical cancer screening program and the National HPV Vaccination Program. In Aboriginal and Torres Strait Islander people, the decline in HPV-associated disease during the same time period was from 263 DALY per 100,000 population to 81 DALY per 100,000 population. Despite these gains, HPV still causes the largest burden of all vaccine-preventable diseases in Aboriginal and Torres Strait Islander people.[93]

Numerous studies show the significant declines in HPV prevalence and several specific HPV-associated disease outcomes in Australia following the introduction of the National HPV Vaccination Program.[10] Table 3 summarises the studies that have been published since 2013 (i.e. excluding those referenced in the previous evaluation report[9]). Because of a long lead time from HPV infection to the development of cancer, the true magnitude of the impact of vaccination against HPV, including various cancer outcomes, will become more clearly visible with time.

Complementing the gains thus far, the transition from 4vHPV vaccine to 9vHPV vaccine in Australia in 2018 has been predicted to prevent a further 15% of cervical cancers and 11% of anal cancers. On the basis of genotype data from the USA, the 9vHPV vaccine could reduce HPV-associated vaginal, vulval and penile cancers by approximately a further 18%, 14% and 9%, respectively, in the USA. Overall the 9vHPV vaccine is expected to prevent almost 90% of cervical cancers and up to 96% of anal cancers in Australia.[10]

Vaccine impact on prevalence of HPV infection

HPV prevalence in females

A study found there was a significant reduction in the prevalence of HPV genotypes covered by the 4vHPV vaccine in women aged ≤25 years attending MSHC with chlamydia infection in the first 3 years of the National HPV Vaccination Program.[94] The reduction was the highest in Australian-born women aged ≤21 years, with no cases of HPV types 6/11 observed in this group from 2008–2009 to the end of the study in mid-2014.[94] A significant reduction in 4vHPV genotypes was also observed in unvaccinated Australian-born women, indicating a herd protection effect.[94]

The prevalence of 4vHPV genotypes in 1,058 females aged 18–24 years attending family planning clinics in Sydney, Perth and Melbourne for routine cervical screening in 2010–2012 was significantly lower than that in females recruited in the same way in 2005–2007 (pre-vaccine introduction) in both vaccinated females (prevalence ratio 0.07, 95% CI: 0.04–0.14) and unvaccinated females (prevalence ratio 0.65, 95% CI: 0.43–0.96), further supporting both direct and herd impacts of the vaccine.[50] The adjusted vaccine effectiveness for 4vHPV vaccine genotypes was 86% (95% CI: 71–-93%, p<0.0001) for fully vaccinated women compared with unvaccinated women in the post-vaccine period against HPV types 6, 11, 16 and 18, and 58% (95% CI: 26–76; p=0.003) against HPV types 31, 33 and 45.[50]

Similarly HPV prevalence was assessed in females attending family planning clinics in urban VIC and NSW for routine cervical screening in 2015 compared with that in the pre-vaccine period (2005–2007).[95] This study found a 92% decline in the prevalence of 4vHPV vaccine genotypes in females aged 18–35 years (from 15.3% to 1.3%).[95] In the subset of women aged 25–35 years, in whom the verified uptake of 4vHPV vaccine was only 40%, prevalence declined from 11.8% to 1.1%.[95] The prevalence of 4vHPV genotypes was also significantly lower in partially vaccinated and unvaccinated females in 2015 than in the pre-vaccine period, suggesting herd protection as well as the effectiveness of even partially completed vaccination courses.[95]

The Vaccine Against Cervical Cancer Impact and Effectiveness (VACCINE) study validated self-reported HPV vaccination status and assessed the prevalence of 4vHPV vaccine genotypes in Victorian females aged 18–25 years recruited using Facebook from 2011 to 2015,[52] with interim results available for 2011–2013.[51] At the study conclusion, from 737 self-collected vaginal swabs the prevalence of any HPV genotype was 25.0%, high-risk genotypes 13.8% and 4vHPV genotypes 1.8%.[52] All 13 females positive for 4vHPV genotypes were either unvaccinated or fully vaccinated but after sexual debut.[52]

As a result of the transition to HPV-based screening in December 2017, the national cervical screening program provides a new tool to monitor HPV prevalence in

Australia.[96] Before this transition, in 2005–2008 the HPV prevalence in 2,620 females aged 18–60 years participating in cervical screening was 26.4% for all high-risk HPV genotypes and 10.8% for HPV genotypes 16/18.[97]

In addition, in 2006–2010 the seroprevalence of HPV genotypes 16/18 in 3,729 women aged 30–64 years was 23.5% in women with normal cervical cytology and 43.8% in women with confirmed cervical HGA.[98]

A retrospective cross-sectional review of 195,606 specimens submitted for HPV testing from 1 December 2017 to 31 May 2018 found that oncogenic HPV genotypes were detected in 8.1% of screening tests (95% CI: 7.9–8.2) and 20.9% of non-screening tests (95% CI: 20.5–21.3).[99] In addition, 35.5% (95% CI: 34.7–36.4) of women of recommended screening age with positive oncogenic HPV screening test results also had a cytological abnormality.[99] Also the proportion of HPV types 16/18 – positive samples with HGA – was 15.3% (95% CI: 14.2–16.6); the proportion of samples positive for other oncogenic HPV types was 6.3% (95% CI: 5.8–6.8).[99]

Consistent with the above estimates, in 116,052 samples in VIC during the first 7 months of the renewed national cervical screening program the prevalence of any oncogenic HPV types was 9.3%, and for HPV types 16/18 2.1%.[96] The prevalence of non–HPV 16/18 oncogenic types in females peaked at age 25–29 years and then declined rapidly across older age groups. The prevalence of HPV types 16/18 was highest in females aged 35–44 years but low and stable across all ages.[96]

HPV prevalence in Aboriginal and Torres Strait Islander females

A significant decline in HPV prevalence has also been demonstrated separately in Aboriginal and Torres Strait Islander females in the Vaccine Impact in the Population-Indigenous (VIP-I) study.[100] The post–vaccine period sample in this study included 142 Aboriginal and Torres Strait Islander females aged 18–26 years attending health services in Central Australia, North QLD and rural NSW for routine cervical screening in 2014–2015.[100] Compared with the pre–vaccine period cohort recruited at the same sites in 2007, prevalence of all HPV genotypes in 2014–2015 declined from 58.1% to 36.2% and that of 4vHPV vaccine genotypes from 23.9% to 1.4% (two cases of HPV type 16, no case of HPV types 6/11/18).[100]

HPV prevalence in males

Significant declines in HPV prevalence have also been demonstrated in Australian males, initially due to herd protection from the female-only program and later from direct protection following the extension of the program to include males. In national serosurveillance studies, the seroprevalence of 4vHPV vaccine genotypes in males aged 15–39 years in 2012–2013 was substantially lower than that in 2005, indicating herd impact from the female program.[101] However, in 2012–2013 over 9% of males

were still seropositive for at least one 4vHPV vaccine genotype by age 20 years, suggesting a potential additional role of male vaccination in direct protection.[101]

The prevalence of penile infection with 4vHPV vaccine genotypes in sexually active heterosexual males aged 17–19 years in Australia was relatively low even before the commencement of male HPV vaccination, likely due to herd protection from the female-only program. This prevalence, which was 2.6% in 152 males sampled in 2014–2015, declined to 0.7% among 142 males sampled in 2016–2017, suggesting incremental direct benefit from the male vaccination program. In the 2016–2017 cohort, of whom 55.5% had received ≥1 dose of HPV vaccine, only one case of infection with a 4vHPV genotype was detected (HPV type 6 in an unvaccinated male).[102]

There was a decline in 4vHPV genotype prevalence in urine and urethral samples from unvaccinated heterosexual men aged ≤25 years attending MSHC with chlamydia infection over the period 2004–2015, suggesting ongoing herd protection impact of the female program.[103] From 2004–2005 to 2014–2015, the prevalence of 4vHPV genotypes significantly declined from 22.4% to 5.7%, while non-vaccine genotypes significantly increased.[103] In Australian-born males aged ≤21 years, the reduction in 4vHPV genotypes was particularly impressive, from 30.8% in 2004–2005 to 0% in 2014–2015 with no HPV type 16/18 detected after 2011–2012.[103]

As a further indication of herd protection effects in males, penile swabs collected in 2014–2016 from unvaccinated sexually active heterosexual males across Australia showed the prevalence of 4vHPV genotypes was significantly lower in males aged 16–25 years than in those aged 25–35 years, whose female partners were less likely to have been vaccinated.[104] The prevalence of oncogenic non-vaccine HPV genotypes was not significantly different between the two groups.[104]

Unlike in heterosexual men, no statistically significant herd protection effect from the female HPV vaccination program has been documented in MSM. MSM aged ≤26 years who presented for the state-funded catch-up 4vHPV vaccine in Victoria in 2017 had a prevalence of high-risk anal HPV infection of 56.5%,[105] consistent with the knowledge that MSM are at higher risk of HPV infection and related diseases. In addition, 43.1% of these unvaccinated MSM had at least one anal 4vHPV genotype detected and 53.4% had at least one 9vHPV vaccine genotype detected.[105] In an older MSM population in Sydney (aged ≥35 years, median 49 years), the baseline prevalence (in 2010) of anal HPV genotype 16 infection was 29.4%, and 64.7% of the cohort had at least one anal 9vHPV genotype detected by study end (2018).[106]

Vaccine impact on cervical abnormalities

A steady decline in cervical HGA in females aged <20 years started soon after the National HPV Vaccination Program commenced.[107] In females aged 20–24 years, a notable decline began in 2011 which led to the peak age for detection of HGA shifting

from 20–24 years to 25–29 years.[107] With vaccinated cohorts moving up into older age groups, declines in cervical HGA have also been seen since 2014 in women aged 25–29 years and 30–34 years.[107] The overall rate of HGA in screened women of all ages has declined from >8 per 1,000 women screened in 2007 to 7.1 per 1,000 women screened in 2017, while the incidence of cervical cancer in Australia has been stable at around 7 new cases per 100,000 women of all ages since 2002.[107] The incidence of cervical cancer is expected to increase transiently following the introduction of HPV-based screening because of earlier detection of prevalent cases, as HPV testing is highly sensitive, but should significantly decline thereafter due to the combination of HPV vaccination and screening.

Significant reductions in HGA[108-111] and evidence of vaccine effectiveness against cervical abnormalities in women less likely to have been sexually active before vaccination[111] were also demonstrated in other literature published before the time period of this review. The impact of HPV vaccination was also seen in excisional treatments for cervical dysplasia, which were significantly lower in women aged <35 years across Australia in the post-vaccine period (2008–2013) than in the pre-vaccine period (2004–2007), while the rate remained unchanged in females aged ≥35 years.109

Cervical abnormalities in Aboriginal and Torres Strait Islander females

National cervical screening program outcomes cannot be reported accurately by Aboriginal and Torres Strait Islander status as that information was not captured on all pathology forms. Linkage of cervical screening and hospitalisation data enabled more complete identification of Aboriginal and Torres Strait Islander females. Linked data showed that among women screened in Queensland in 2010–2011, Aboriginal and Torres Strait Islander women had significantly higher prevalence of cytological low- and high-grade abnormalities and histologically confirmed HGA than non-Indigenous women.[112] The incidence of cervical cancer in Aboriginal and Torres Strait Islander women is more than double the rate in non-Indigenous women of the same age, with an age-standardised rate in 2011–2015 of 22.3 per 100,000 (based on data from five jurisdictions).[107]

Other data linkage studies

A key data linkage study (linking the HPV register and state and territory cervical cancer screening registers) showed that between 2007 and 2014 fully vaccinated women had a lower incidence of HGA (8.5 per 100,000) than unvaccinated women of the same age (13.2 per 100,000) regardless of jurisdiction and remoteness/socioeconomic status area–based indices.[113] Those vaccinated before the age of 14 years had the lowest rate of HGA, followed by girls vaccinated at age 14–15 years and then age ≥16 years.[113] The rate of HGA was 26.4 per 100,000 in females screened before the introduction of HPV vaccination, significantly higher

than in unvaccinated females screened in the post-vaccination period, indicating a herd protection effect.[113] In this study cervical screening participation in 2013–2014 was higher in vaccinated females than in unvaccinated (45.5% versus 33.1% for females aged 20–24 years and 56.5% versus 44.3% for females aged 25–29 years).[113] Importantly, this finding of higher rates of cervical screening participation in vaccinated women was in contrast to earlier studies.[114] This is likely due to markedly improved ascertainment of vaccination status among screened women as a result of updating of demographic details prior to data linkage.[113]

Results from a study using linked data across Victorian cervical cytology and national HPV vaccination registries support the greater benefits of HPV vaccination when administered before sexual debut. In this study of females who were eligible for HPV vaccination in 2007, and who had records of cervical screening in 2007–2011, there was significant effectiveness of HPV vaccine against high- or low-grade cervical abnormalities, even among partially vaccinated women, if all doses were received before the initial screening (which was used as a proxy for sexual debut). When the timing of vaccination in relation to initial screening was disregarded, there was significant effectiveness only for those fully vaccinated with 3 doses.[53]

The effectiveness of less than three doses of HPV vaccine on cervical abnormalities has been assessed using data linkage in QLD. In females attending their first cervical screening in QLD between 2007 and 2011, three doses were 46% effective against HGA and 34% against other abnormalities.[115] The effectiveness of two or more doses was 21% against both high-grade and other cervical abnormalities. The effectiveness of a single dose was not statistically significant. The adjusted vaccine effectiveness of one or more doses was 26% (95% CI: 15–36) against cervical HGA and 22% (95% CI: 18–25) against other cervical abnormalities.[115]

Linkage of national cervical screening and HPV vaccination data for females who were aged ≤15 years when first eligible for vaccination during 2007–2014 showed that receiving one, two or three HPV vaccine doses had similar effectiveness against histologically confirmed cervical HGA (adjusted hazard ratio for 1 dose 0.65 [0.52–0.81], 2 doses 0.61 [0.52–0.72] and 3 doses 0.59 [0.54–0.65]).[54]

Cervical cancer

From 2007 to 2012, 101 cases of cervical cancer were diagnosed in females fully vaccinated with HPV vaccine in Australia. Among these, 99 were in females who are likely to have been exposed to HPV before vaccination, based on their age, dates of vaccination and initial cervical screening. The remaining two cases were cervical cancers not associated with HPV.[113] Declines in cervical cancer following HPV vaccination programs have not yet been demonstrated because of the long natural history of HPV-related cancers.

It is also important to assess the potential impact of the program on cervical cancers by monitoring the HPV genotypes found in cervical cancers. A large study that included 847 cervical cancers diagnosed from 2005 to 2015 in NSW, VIC and QLD found that they more frequently contained HPV types 16/18 than in overseas studies.[116] Of the 847 cancers, 92.9% had HPV detected. Of the HPV-positive cancers, 607 of 787 (77.1%) contained HPV type 16 or 18, 125 (15.9%) contained HPV type 31/33/45/52 or 58, and 55 (7.0%) another HPV genotype.[116] This high preponderance of HPV type 16/18 could be due to the high levels of cervical screening in Australia, reducing the incidence of squamous cancers and resulting in a higher proportion of adenocarcinomas, in which types 18 and 16 more strongly predominate.[116] Ongoing cancer genotyping is recommended to monitor the impact of the HPV vaccination program on cervical cancers.

Several modelling studies have estimated potential time-frames until expected declines in cervical cancer are evident in Australia. It has been estimated that from 2017 to 2035 there will be a decline in the rate of cervical HGA by 40% (range 40–44%) and invasive cervical cancer by 51% (range 42–51%).[117]

Modelling further predicts that the incidence rate of invasive cervical cancer in Australia will decline to <4 new cases per 100,000 women by 2028 (range 2021–2035), which would be considered the elimination of cervical cancer as a public health problem.[8] However, this study acknowledges that this model may not be directly applicable to all population subgroups, such as Aboriginal and Torres Strait Islanders and migrants, who may have lower HPV vaccination coverage and screening participation rates, and that it will therefore take longer to achieve cervical cancer elimination in such groups unless these disparities are addressed.[8]

Modelling has also predicted large declines in the incidence of cervical adenocarcinoma in Australia as a result of HPV vaccination combined with primary HPV screening, with 55–81% decline estimated by 2040.[118] This is particularly significant, given cervical cytology–based screening has resulted in a limited decline.[119]

Genital warts

Genital Warts Surveillance Network

The Genital Warts Surveillance Network comprises 54 sentinel sexual health clinic sites across Australia that have been used to assess the proportion of genital warts diagnoses in new patients over time. Data from the network show a steady decline from 2007 to 2017 in genital warts diagnoses in young Australian-born populations in both urban and non-urban areas.[120-122] In the non-Indigenous population, the most recent surveillance data available, for 2017, showed a 96% decline in the proportion of attendees with a genital warts diagnosis in females aged <21 years since 2007 (from 11.0% to 0.5%) and an 87% decline in females aged 21–30 years (from 10.7%

to 1.4%). These declines were seen early and quickly due to the relatively short incubation period from infection to warts becoming apparent. However, the proportion of females aged >30 years with genital warts has been fluctuating.[122] There was also a concomitant decline in genital warts diagnoses in non-Indigenous heterosexual males of 88% (from 9.3% to 1.1%) in those aged <21 years and 76% (16.6% to 3.9%) in those aged 21–30 years.[122] Among heterosexual males aged >30 years, a downward trend since 2010 has led to a 53% decline in genital warts diagnoses.[122] These declines were also seen in non-Indigenous MSM between 2007 and 2017 – a 72% decline in gay males (from 11.2% to 3.1%) and 51% decline in bisexual males (from 5.5% to 2.7%), but these declines are believed to reflect changes in the population attending the clinics over time, with more asymptomatic males attending in recent years and thus inflating the denominator.[122]

Large declines in genital warts diagnoses in Aboriginal and Torres Strait Islander people aged <30 years have also been reported.[120-122] As of 2017, the declines in genital warts diagnoses in Aboriginal and Torres Strait Islander females were greater than in non-Indigenous females, with a 100% decrease from 2007 to 2017 in Aboriginal and Torres Strait Islander females aged <21 years (from 4.4% to 0%) and 21–29 years (from 5.1% to 0%), with no cases diagnosed in either age group from 2016.[123] From 2007 to 2017, there were large declines in the proportion of heterosexual Aboriginal and Torres Strait Islander males with genital warts among sexual health clinics attendees, with an 82% decline in those aged <21 years (from 6.0% to 1.1%) and a 62% decline in those aged 21–29 years (from 10.2% to 2.1%).[123] From 2007 to 2015, there was a decline in the proportion of Aboriginal and Torres Strait Islander MSM with a genital warts diagnosis, from 6.8% to 2.6%.[121]

Genital warts hospitalisations

Genital warts hospitalisations, representing more severe cases, have also declined markedly since the HPV vaccination program commenced. The proportional declines in genital warts hospitalisation rates between 2006–2007 and 2010–2011 in females aged 12–17 years, 18–26 years and 27–30 years were 89.9% (95% CI: 84.6–93.4), 72.7% (95% CI: 67.0–77.5) and 42.1% (95% CI: 26.1–54.6), respectively. There was no significant change in genital warts hospitalisation rates in females aged >30 years.[124] There were also declines in genital warts hospitalisation rates in males over the same time period: 38.3% (95% CI: 27.8–47.2) in those aged 18–26-years and 21.2% (95% CI: 0.8–37.4) in those aged 27–30 years. There was no significant change in males aged >30 years.[124] The decline in genital warts hospitalisations in males aged 18–26 years was statistically significant only for non-anal sites, which likely represents herd protection from the female HPV vaccination program.[124]

In Aboriginal and Torres Strait Islander females aged 15–24 years, there was an 86.7% (95% CI: 71.6–79.9) decline in the genital warts hospitalisation rate in the same time period. This was greater than the 76.1% decline (95% CI: 76.0–92.7) in

non-Indigenous females of the same age. However, sufficient data were not available to assess changes in genital warts hospitalisation rates in Aboriginal and Torres Strait Islander males.[124]

Additional analyses showed that the declines in genital warts hospitalisation rates in females aged 10–19 years and 20–29 years observed between 2006–2007 and 2010–2011 were equitably distributed across socio-economic groups, both within and outside major cities.[125] Similarly, the declines in genital warts hospitalisation rates in males aged 20–29 years that were limited to non-anal sites were also equitably distributed.[125]

Assessment of vaccine impact on genital warts using other data sources

Consistent with the overall findings from the National Genital Warts Surveillance Network data, to which MSHC contributes data, there were significant declines in the proportion of new patients diagnosed with genital warts at MSHC. Among Australian-born females aged <21 years who attended MSHC, the proportion with genital warts declined from 18.4% in 2004–2005 to 1.1% in 2013–2014.[126] In those aged 21–32 years, who were vaccine-eligible but possibly sexually active before vaccination, there was a smaller but significant decline, from 12.4% to 2.5%.The proportion of genital warts diagnoses in new female patients aged >32 years, who were ineligible for HPV vaccination, increased from 4.0% to 8.5% over this time period.[126]

There is also evidence of a marked impact of HPV vaccination on genital warts incidence from GP encounter data. The management rates of genital warts in a nationally representative set of general practices that formed the Bettering Evaluation and Care of Health (BEACH) program decreased by 61% in vaccine-eligible females from pre-vaccine period (2002–2006) to post-vaccine period (2008–2012) (4.33 per 1,000 encounters to 1.67 per 1,000 encounters). No change was observed in older females.[127]

A mobile telephone survey in 2011 among randomly selected Australian females aged 18–39 years also showed a 41% decrease in self-reported genital warts diagnoses in vaccine-eligible females and a 64% increase in vaccine-ineligible females compared with corresponding estimates from a similar survey in 2001.[128] This survey also found that 63.3% of females reporting a genital warts diagnosis were treated by a GP, 15.2% in hospital and 12.7% at a sexual health clinic.[128]

As additional evidence of herd protection, the proportion of Australian-born heterosexual males presenting to MSHC and diagnosed with genital warts declined from 17.3% in 2004–2005 to 7.6% in 2013–2014. The largest declines were in those aged <21 years (from 11.3% to 2.8%) and 21–32 years (from 19.1% to 5.9%), with lower decline (from 15.7% to 11.4%) in males aged >32 years.[126] A lower but significant decline (from 7.8% to 5.2%) in genital warts diagnoses was also observed

in MSM over the duration of this study period, but this is also attributed to greater attendance by asymptomatic MSM.[126]

Another study from MSHC showed that the odds ratio of having penile warts in heterosexual males was significantly lower in males with an Australian-born female partner aged ≤32 years than in males with partners aged >32 years who had not been eligible for HPV vaccination (OR 0.52, 95% CI: 0.28–0.99).[129]

Genital warts modelling studies

Modelling has shown that the strong herd protection effects of female HPV vaccination and rapid reductions in genital warts were achieved in Australia. These sustained changes are attributable to the vaccination of multiple cohorts during the national time-limited catch-up HPV vaccination program in addition to the high coverage achieved in the routine vaccination program.[130]

Modelling studies predict that the male HPV vaccination introduced in 2013 will have a substantial incremental impact on genital warts incidence, compared with female vaccination alone, and will result in near elimination of genital warts in the Australian heterosexual population.[131] This model did not account for the MSM population though, or the impacts of immigration and travel on genital warts in Australia – factors that are acknowledged as potential barriers to actually achieving genital warts elimination.[131]

Vaccine impact on juvenile-onset recurrent respiratory papillomatosis

A new finding on the impact of the National HPV Vaccination Program in Australia since the previous evaluation is a significant reduction in juvenile-onset recurrent respiratory papillomatosis (JoRRP). JoRRP is a rare, but serious, medical condition with significant morbidity and mortality, resulting from vertical transmission of HPV infection before or during birth, particularly genotypes 6 or 11 which are the most common cause of genital warts. From 2000 to 2009, 30 cases of JoRRP were identified in NSW tertiary paediatric hospitals translating/extrapolating to a national prevalence of 0.81 per 100,000 children aged <15 years from 2000 to 2013.[132]

Active sentinel surveillance established by the Australian Paediatric Surveillance Unit to monitor JoRRP in Australia (via participating paediatric otorhinolaryngologists treating JoRRP in each state and territory) captured 15 new cases in children aged <15 years from 2011 to 2016. Of these, seven were genotyped and all were positive for HPV type 6 or 11. Over this period the annual count of cases declined with a statistically significant reduction in incidence from 0.16 per 100,000 in 2012 to 0.02 per 100,000 in 2016 (refer to Table 3).[133] This decline incidence suggests a reduction in mother-to-child HPV transmission as a result of a reduced prevalence of genital infection with HPV types 6 and 11 in young women, which, in turn, is a result of HPV

vaccination. This decline in JoRRP incidence was the first such documented decline following the implementation of a 4vHPV vaccination program.[133] In 2017, there were only three notifications of JoRRP, one of which was a duplicate report.[134] Both cases were classified as probable, with a case of non-laryngeal papillomatosis.[134] There were no cases of JoRRP in 2018.[134]

Table 3. Summary of key Australian studies demonstrating impact of the National HPV Vaccination Program on HPV-related disease burden, published since 2013

Author	Source and year	Setting	Study method	Participants	Results
HPV prevalence					
Garland et al.[24]	*Vaccine*, 2018	Victoria	VACCINE study- validated self-reported HPV vaccination status and assessed HPV prevalence from self-collected vaginal swabs	Females aged 18-25 years (n=737)	Prevalence of any HPV genotype 25.0%; high-risk HPV 13.8%. Prevalence of 4vHPV-targeted genotypes 1.8% (13 cases- 11 cases of HPV 16, 2 cases of HPV 6. No cases of HPV 11/18). Of the 11 HPV 16 cases- 5 unvaccinated, 6 vaccinated after sexual debut Of the 2 HPV 6 cases- 1 unvaccinated, 1 vaccinated after sexual debut
Machalek et al. 2018[25]	*Journal of Infectious Diseases*, 2018	Urban family planning clinics in Victoria and NSW	Validated self-reported HPV vaccination status and assessed HPV prevalence in females attending routine cervical screening in 2015 or 2010-2012, compared to	Females aged 18-35 years (n=381)	In females recruited in 2015- 53.3% fully vaccinated, 32.6% partly vaccinated and 14.2% unvaccinated Prevalence of 4vHPV-targeted genotypes significantly decreased by 92% from 15.3% in 2005-2007 to 1.3% in 2015 In females aged 18-24 years the prevalence decreased from 22.7% in 2005-2007 to 7.3% in 2010-2012 to 1.5% in 2015 In females aged 25-35 years (40% verified 3-dose vaccination coverage) the prevalence decreased from 11.8% in 2005-2007 to 1.1% in 2015 5 cases of 4vHPV-targeted genotypes were detected in 2015: 4 cases of HPV 16, 1 case of HPV 18 , no cases of HPV 6/11

			pre-vaccine (2005-2007)		
High-grade cervical abnormalities					
AIHW[26]	Online report, 2019	National	Reporting of National Cervical Screening Program data		Declines in cervical high-grade abnormalities in older age groups are evident with increasing age of the vaccinated cohorts: Decline evident since 2007 in females aged <20 years: 11.6 per 1000 women screened in 2007 to 3.9 per 1000 women screened in 2017 Decline evident since 2011 in females aged 20-24yrs: 19.7 per 1000 women screened in 2010 to 10.0 per 1000 women screened in 2017 Decline evident since 2014 in females aged 25-29 years: 20.3 per 1000 women screened in 2013 to 14.4 per 1000 women screened in 2017 Decline evident since 2014 in females aged 30-34 years: 14.5 per 1000 women screened in 2013 to 12.9 per 1000 women screened in 2017
Genital warts					
The Kirby Institute[27] (reporting for the Genital Warts Surveillance Network)	Online report, 2018	National	Proportion of new patients diagnosed with genital warts	new attendees to 43 sexual health clinics	Declines from 2007-2017 in non-Indigenous Australian-born population: Females <21 years: 96% decline (11.0% to 0.5%) Females 21-30 years: 87% decline (10.7% to 1.4%) Females >30 years: Fluctuating proportion (5.8% in 2007, 3.4% in 2017 Heterosexual males <21 years: 88% decline (9.3% to 1.1%; 33% decline since male vaccination introduced) Heterosexual males 21-30 years: 76% decline (16.6% to 3.9%; 40% decline since male vaccination introduced) Heterosexual males >30 years: 53% decline from 2010-2017 (11.6% to 5.5%) Declines from 2007-2017 in Aboriginal and Torres Strait Islander population:

					Females <21 years: 100% decline (4.4% to 0%) Females 21-29 years: 100% decline (5.1% to 0%) Females ≥30 years: Fluctuating proportion (1.0% in 2007, 2.3% in 2017) Males <21 years: 82% decline (6.0% to 1.1%) Males 21-29 years: 80% decline (10.2% to 2.1%) Males ≥30years: Fluctuating proportion (6.3% in 2007, 3.9% in 2017)
Juvenile-onset recurrent respiratory papillomatosis					
Novakovic, et al.[28]	*Journal of Infectious Diseases*, 2018	National	Prospective surveillance of all JoRRP cases reported to Australian Paediatric Surveillance Unit, October 2011-December 2016	diagnosed <15 years (n=15 cases)	Annual case count: Highest in 2011 (n=7) decreased each year. (n=1 in 2016). Incidence rate: Decline from 0.16 per 100 000 in 2012 to 0.022 per 100 000 in 2016. *Characteristics of cases* 14/15 born in Australia. 13/14 Caucasian, 1 Indigenous, 1 ethnicity unknown. 3/15 history of genital warts present in mothers. 3/15 mothers received HPV vaccine, none before birth of the affected child. 13/15 delivered vaginally, 1 caesarean, 1 method unknown. No affected children were immunocompromised.
Nunez et al[29]	*Communicable Diseases Intelligence 2019*	National	JoRRP cases reported to Australian Paediatric Surveillance Unit 2017 & 2018.	diagnosed <15 years 2017 (n=3) 2018 (n=0)	Three notifications were received in 2017, one of which was a duplicate report. Both cases were classified as probable, with a case of non-laryngeal papillomatosis.

Summary/discussion

This literature review documents extensive surveillance and research in Australia on HPV vaccination and the impact of the National HPV Vaccination Program on HPV-associated disease burden.

In terms of HPV vaccination coverage, the literature shows that while vaccine coverage nationally has increased over time, disparities still exist between females and males, between jurisdictions and for course completion in Aboriginal and Torres Strait Islander adolescents compared with non-Indigenous adolescents. Although modelling predicts Australia is on track to eliminate genital warts in heterosexual individuals overall and cervical cancer, this does not necessarily extend to high-risk groups such as Aboriginal and Torres Strait Islander people and migrants. Addressing disparities in HPV vaccination coverage would help ensure the impact of the National HPV Vaccination Program in Australia is more equitable.

Reflecting this need, the current national and jurisdictional STI strategies and cancer control plans incorporate goals to continue increasing HPV vaccination coverage, particularly in higher risk individuals. Several of these strategies highlight the need for improved access to HPV vaccine for Aboriginal and Torres Strait Islander people and other high-risk populations outside of the existing school-based vaccination setting, which should be a focus of initiatives to improve coverage.

More generally, many of the barriers to HPV vaccination that were identified in the literature could likely be minimised through initiatives to increase education regarding HPV vaccine safety, dosing schedule and eligibility as well as improved processes to ensure return of consent forms and follow up of students who are absent during vaccination visits. Ongoing reminders/notifications from AIR to ensure that the second dose is received would also benefit significantly.

The HPV vaccine safety literature demonstrates a decline and stabilisation in the reporting of adverse events with time and confirms the comprehensive vaccine safety surveillance undertaken in Australia. Evidence to date regarding 9vHPV vaccine safety in Australia is consistent with pre-licensure clinical trial data that showed an increase in injection site reactions, but an otherwise reassuring safety profile of the vaccine.

Studies that assessed vaccine impact on HPV-related conditions suggest significant effectiveness of 4vHPV vaccination. The 2018 change to 9vHPV vaccine with a 2-dose schedule requires further monitoring, including of genotype-specific infection and disease, to document the additional impact of the vaccine's extended coverage. While many published studies of genotype-specific HPV infection in Australia were located in the review, there was a notable lack of studies that monitored HPV genotype-specific disease (e.g. cervical disease or cervical cancer). Such studies are now vital to monitor the component of disease burden that is vaccine-preventable and to clearly document the anticipated decline in cervical cancer. The literature also indicates potential effectiveness of a single-dose HPV vaccine strategy, which would assist in overcoming barriers to course completion and reduce the cost and resources required for vaccine program delivery. Further data and findings of randomised trials of single-dose vaccination are awaited.

WHO will seek endorsement of its current draft global strategy towards elimination of cervical cancer as a public health problem at the next World Health Assembly in 2020, with goals and targets to be confirmed for the period 2020–2030 in the setting of challenges arising from the COVID-19 pandemic.[135] The WHO approach to cervical cancer elimination is three-pronged: 90:70:90 – 90% coverage of HPV vaccination in girls by 15 years of age; 70% coverage of cervical screening; and 90% treatment of precancerous lesions and management of invasive cancer cases. The current national HPV vaccination target in Australia is 80% adolescent HPV vaccination coverage, in the context of a universal, rather than female-only, program.

Stakeholder assessment

Aim

The aim of stakeholder assessment was to assess stakeholder perspectives on the impact of the National HPV Vaccination Program, including factors that have positively or negatively influenced program outcomes and impacts to date, or that could do so in future.

Methods

Semi-structured interviews and online survey

A mixed-methods approach was used to collect both qualitative and quantitative data from semi-structured interviews and an online survey.

Key stakeholder interviews

Purposive sampling was used to recruit a broad sample of key stakeholders from across Australia for interview. Stakeholders were approached directly or referred by other participants through respondent-driven sampling. A sampling matrix (Appendix 1) was used to ensure representativeness across stakeholder groups and jurisdictions.

Interviews were conducted from October 2019 to March 2020. A structured interview questionnaire was developed by staff at NCIRS and finalised following review by and feedback from members of the Advisory Committee and the Cultural Advisory Committee. The topics explored in the interviews included vaccination coverage, vaccine safety, vaccination reporting, cervical screening disease impact, strengths and challenges of the program and recommendations, with the questionnaires tailored to be relevant for each stakeholder group (refer to Appendix 2 for an example questionnaire used for state and territory immunisation program managers).

The questionnaire was emailed to the stakeholders before their interview to allow them to collect relevant information and to prepare responses. Interviews were recorded with the consent of the participants and professionally transcribed. Draft interview transcripts were sent back to each participant for review and approval, with amendments incorporated into the final interview transcript for analysis.

Stakeholder online survey

An anonymous online survey was developed by staff at NCIRS using SurveyMonkey® for distribution to other stakeholders, predominantly immunisation providers. The survey was finalised following review and feedback from members of the Advisory Committee and the Cultural Advisory Committee. The online survey (refer to Appendix 3) included questions on the same topics as the telephone interview questionnaire.

The survey questions were a mix of open- and closed-ended, with most closed-ended questions either Likert-type scale questions or check-box options. The survey contained 'skip logic' so that participants could skip sections not relevant to them.

The survey was open for completion from November 2019 to February 2020. Different weblinks were used for distribution to different stakeholder groups to allow tracking of response numbers.

The survey was initially distributed in collaboration with Healthed, a national provider of education services for general practitioners (GPs), primary care nurses and other healthcare professionals. Healthed offered a random prize draw incentive of 5 x $100 David Jones gift vouchers for completion of the survey, with the option to supply a mobile phone number for the purpose of contacting the randomly chosen winners. The survey was emailed to the Healthed distribution list on 12 November 2019 and three reminder emails were sent by Healthed over the following 3 weeks.

The online survey was distributed to school-based immunisation providers in the Australian Capital Territory (ACT), New South Wales (NSW), the Northern Territory (NT), Queensland (QLD), South Australia (SA), Victoria (VIC) and Western Australia (WA) through either jurisdictional immunisation program managers or other suggested means, such as school program coordinators or local council representatives. The survey was not distributed in Tasmania (TAS) as qualitative research was being undertaken there concurrently under the HPV Partnership Project.

Following Aboriginal ethics approvals, the survey was distributed to Aboriginal and Torres Strait Islander healthcare providers in NT, SA and TAS.

Analysis

- Interviews: We did thematic analysis of comments from stakeholder groups who participated in the interviews, and selected quotes to illustrate key findings.
- Online survey: We did descriptive analysis of response frequencies.

Results

Key stakeholder interviews

Participants

A total of 26 semi-structured interviews involving 42 participants (some interviews had multiple participants) were completed. A summary of participants from each stakeholder group is outlined below and summarised in Table 4.

Australian Government Department of Health

Representatives from:

- Immunisation Branch (4)
- Cervical Screening Section (2)

Therapeutic Goods Administration (TGA)

- A consolidated written response was provided by the TGA.

Jurisdictional immunisation program managers and other relevant staff

A total of 17 participants from state and territory health departments contributed to the interviews, including all jurisdictional immunisation program managers, except NT, which lacked someone in this role at the time. In several jurisdictions other staff also participated (see below).

Jurisdictional representatives who participated in an interview included:

- ACT - Immunisation Program Manager
- NSW - Immunisation Program Manager, School-based Program Coordinator
- NT - Immunisation Public Health Nurse, Centre for Disease Control
- QLD - Immunisation Program Acting Manager, Clinical Nurse Consultant
- SA - Nursing Director and Nurse Consultant, Immunisation Section
- TAS - Nurse Manager and Nurse Consultant, Communicable Disease Prevention Unit
- VIC - Immunisation Program Manager, Immunisation Nurses x 3, Operations Officer, Administration Officer (vaccine forecasting and ordering)
- WA - Immunisation Program Manager

Local council immunisation staff

- Two immunisation staff members from separate Victorian local councils were interviewed.

Remote area immunisation coordinators

- Two remote area immunisation coordinators were interviewed, one from QLD and one from NT.

Sexual health physicians

- One sexual health physician from NSW was interviewed.

Seqirus

- Three Seqirus staff members participated in an interview. Seqirus distributed the HPV vaccine on behalf of Merck Sharp & Dohme Corp. (the manufacturer), a subsidiary of Merck & Co., Inc.

Jurisdictional cervical screening program managers

- One jurisdictional cervical screening manager was interviewed.

HPV researchers

- Two HPV researchers were interviewed.

Aboriginal Community Controlled Health Services

A total of six semi-structured interviews were conducted with seven participants working in services primarily for Aboriginal and Torres Strait Islander people: five from SA, one from NT and one from TAS. Two were nurse immunisers, two were chief executive offcers of health services, two were immunisation coordinators and one was a program services manager.

Table 4. Interviewed stakeholders by role in HPV vaccination program

Type of stakeholders	Interviewed n=42	Percentage (%)
Australian Government Department of Health staff	6	14.4
Therapeutic Goods Administration*	1	2.4
State/territory health department staff	17	40.5
Local council immunisation staff	2	4.8
Remote area immunisation coordinators	2	4.8
Seqirus† staff	3	7.1
Sexual health physicians	1	2.4
Cervical screening program managers	1	2.4
HPV researchers	2	4.8
Aboriginal Community Controlled Health Service staff	7	16.7

* A consolidated written response was provided by the Therapeutic Goods Administration.

† Seqirus distributed the HPV vaccine on behalf of Merck Sharp & Dohme (the manufacturer).

Change to a 2-dose schedule of 9vHPV vaccine

Stakeholders were asked their thoughts on the benefits and challenges of the change from a 3-dose schedule of 4-valent HPV (4vHPV) vaccine to 2-dose schedule of 9-valent HPV (9vHPV) vaccine for adolescents aged <15 years. Their responses are summarised below.

Australian Government Department of Health

The Immunisation Branch staff perceived the benefits of the change to a 2-dose schedule of 9vHPV vaccine as being simpler to administer within one school year and one less dose to achieve course completion, with an expectation that this change would increase completion rates.

Seqirus

The Seqirus staff perceived the benefits of the change as broader spectrum of protection offered by the 9vHPV vaccine and increased course completion rates.

They perceived challenges to be the potential for reduced uptake because of the change in dose 2 timing and a lack of information for healthcare professionals and consumers about individual-level benefits of receiving 9vHPV vaccine in those who had already received the 4vHPV vaccine, compounded by a lack of government funding for dose 3 in those aged 15–19 years, causing confusion regarding the scheduling of doses.

Jurisdictional immunisation program managers and other relevant staff

Jurisdictional immunisation program managers and other relevant staff reported that the change to a 2-dose schedule was well accepted and had operational benefits, including:

- school staff happier due to less interruptions and demand on their time
- easier to schedule school visits
- better accepted by adolescents and parents (particularly as less needles)
- reduced service delivery cost to state/territory governments
- reduced staffing requirements
- reduced vaccine storage and distribution requirements
- less data to collect.

Two jurisdictions (WA, ACT) used the space in the school immunisation program created by removal of an HPV vaccine dose to provide the meningococcal ACWY (MenACWY) vaccine to year 10 students. NSW transitioned to a 2-dose schedule of 4vHPV in 2017, a year before other jurisdictions, on the basis of international evidence regarding the effectiveness of the 2-dose schedule and to allow for implementation of the NSW state-funded MenACWY program.

The perceived impact of the change to a 2-dose schedule was mentioned by 4 out of 8 jurisdictional immunisation program managers and other relevant staff.

These perceived impacts included:

- course completion increased but less than expected (VIC)
- potentially increased coverage (TAS)
- dose 2 coverage now equal to previous dose 3 coverage (QLD, SA)

- decreased course completion (WA)
- no perceived impact on coverage (ACT, NT)

> *"We've seen benefits of reduced visits required, less demand on school time and staffing resources. It reduces service delivery costs to the State and a challenge is the course completion remains an issue."*
>
> *"We were very excited when we were moving from a three-dose to a two-dose. I thought intuitively that we would see a big increase in (uptake)……..... But the sad reality is we just haven't seen an improvement in uptake."*

Two jurisdictions (SA, NSW) were also concerned about declining coverage in their school-based program before the change in schedule (dose 1 and dose 2 coverage for SA; dose 2 coverage only for NSW).

Other reported challenges included a reduced opportunity for school catch-up due to less school visits (2 out of 6 jurisdictions that conduct school catch-up) and increased education and support required for providers during the transition period (4 out of 8). Confusion among providers during the transition was considered largely resolved by the time of interview, with Commonwealth resources and the Australian Technical Advisory Group on Immunisation advice considered helpful.

It was also acknowledged that previous challenges of the school-based vaccination program remained despite the reduction to two doses.

> *"All the particulars around the school vaccination program really don't change ……children's absence etc., it doesn't change."*

All jurisdictions reported a dosing interval of 6–7 months in their school-based HPV vaccination program, with doses usually given in term 1 and 3 or term 2 and 4 (term 1 and 4 in ACT), with dose 2 delivered variably from late August to December.

Challenges specific to the 6–12-month dosing interval included:

- difficulty fitting both doses into the school year
- increased absenteeism towards the end of the year
- reduced likelihood of missed doses at the end of the year being caught up
- end of year difficult for schools with study and exam periods
- forgetting catch-up after 6 months due to at least 6 months interval between dose 1 and dose 2.
- difficulty retaining a casual nursing workforce.

"I think one of the challenges is that six month gap, fitting it into the school calendar has been a challenge for a number of providers."

"The second dose being given so late, like November, December, there is basically little time to do any catch-up doses that are missed."

Other key stakeholders

The local council staff and remote area immunisation coordinators reported similar benefits and challenges of the schedule change to those reported by jurisdictional immunisation program managers. An additional challenge of the schedule change in remote Queensland was staff resignations due to reduced hours, with casual staff required to fill the gaps.

One HPV researcher noted additional benefits of the change: reduced cost to Medicare through a reduction in GP visits required for catch-up vaccination and decrease in adolescent anxiety as fewer needles needed. (Adolescents are known to experience significant anticipatory anxiety about vaccination because of their developmental stage.) Another perceived benefit was that the broader spectrum of HPV genotypes covered by the 9vHPV vaccine would potentially have a greater impact on reducing high-risk HPV infections and cervical cancer.

A sexual health physician and a HPV researcher reported a benefit of the change to 9vHPV vaccine was the use of leftover 4vHPV vaccine in time-limited catch-up campaigns conducted in several jurisdictions (VIC, SA, WA and NSW) for men who have sex with men (MSM) who had never received the vaccine at school.

Aboriginal Community Controlled Health Services

Six stakeholders agreed that the change from three to two doses had been beneficial: fewer needles resulting in greater acceptance. One stakeholder explained that it has not been easier, but logistics are simpler.

> *"Yeah, so I feel it's been better, particularly kids of that age, they struggle with having vaccinations. Like a lot of them don't really understand why they've got to have them done. They just say it hurts too much. I've had kids say to me even, "I'd rather get cancer than have it done," because they just don't really have the full concept of what's going on."*

Another nurse immuniser said it would be even better if there was only one needle:

> *"If you say it's just two, 'okay', and even better, if you could say it's just one that would be even better."*

However, the respondents had differing opinions on whether vaccination coverage had increased in Aboriginal and Torres Strait Islander children.

> *"No. Personally, no. I mean, it might in the long run, but we're still doing catch ups…."*

"I think, more so, the females will uptake it very well, but it's the boys. That's still relatively new and as with contraception and stuff like that, the boys seem to think it's the girls' responsibility, so it's about - the girls."

School-based HPV vaccination programs

Australian Government Department of Health

Factors reported by the Australian Government Department of Health staff that are positively impacting the school-based HPV vaccination program included collaboration between the Department of Health and states and territories and the use of evidence-based resources and vaccination delivery through schools.

Factors negatively impacting school-based HPV vaccination programs included consent form return issues, absenteeism (particularly in areas with a higher Aboriginal and Torres Strait Islander population or of lower socioeconomic status) and some parents choosing not to consent specifically for the HPV vaccine.

Jurisdictional immunisation program managers and other relevant staff

Factors reported by jurisdictional immunisation program managers and other relevant staff to be positively impacting their school-based HPV vaccination programs included:

- schools that are supportive and well engaged
- good relationships between schools and immunisation teams
- supportive school staff, for example, health-promoting school nurses (specific to NT), Aboriginal Liaison Officers
- following up unreturned consent forms
- increased education for students, for example, using Commonwealth resources

Consent form return and absenteeism were the issues most commonly perceived to be negatively influencing school-based program coverage, with consent form return mentioned as a perceived negative factor in six jurisdictions (QLD, WA, TAS, ACT, VIC and NSW). Strategies to increase consent form return were variable between providers and within jurisdictions, but include active follow up of unreturned forms through phone calls, emails, letters or SMS; posting consent forms home; and sending a 'second-chance' consent pack home. In NSW, lack of access to parent contact details until consent is returned leads to inability to follow up unreturned forms. Several jurisdictions had authorised verbal and/or faxed consent on vaccination day for students with unreturned consent forms, but this was considered time-consuming and not ideal.

Projects to develop electronic consent forms are underway in two jurisdictions (NSW, VIC), while five other jurisdictional immunisation program managers (QLD, TAS, SA, ACT, WA) also expressed interest in this as a strategy to improve consent form return.

Absenteeism, particularly later in the school year, was perceived to be negatively influencing school-based coverage in six jurisdictions (QLD, WA, SA, NT, NSW, VIC). Other negative factors perceived by jurisdictional immunisation program managers included:

- complacency by parents and students (belief that not at risk/don't need vaccine)
- language barriers
- health literacy
- preference to go to GP
- parents not consenting if child does not want the vaccine
- student anxiety and refusal
- scheduling difficulties, for example, class being away on scheduled vaccination day

The use of third party immunisation providers subcontracted by some local councils to deliver school-based vaccination programs was also perceived to be negatively influencing school-based coverage in two jurisdictions (SA, VIC).

"What our experience has been is over the last few years the councils that have been doing this have disinvested in terms of their interest and their infrastructure and their management of the program. And so the performance of these providers has fallen."

In one jurisdiction (VIC), financial pressure and budget cuts within local councils were also perceived to be negatively influencing school-based coverage, largely through reduced resources for follow up of consent forms and absent students.

Of note, TAS, WA and NSW are currently participating in a HPV Partnership Grant funded by the National Health and Medical Research Council. This project, being undertaken in collaboration with The Kirby Institute and other research partners, is aimed at assessing factors impacting school HPV immunisation coverage and evaluating strategies to improve coverage.

Other key stakeholders

One local council perceived factors that would positively influence school-based coverage included actively following up all unreturned consent forms; vaccinating anxious students first; and implementing a state-endorsed Mature Minor policy to allow students living independently to consent with school principal endorsement. Posting consent forms home had also been trialled but was unsuccessful due to postal delays. Factors reported by local council staff to be negatively influencing school-based coverage were consistent with those reported by other stakeholders, particularly absenteeism and scheduling difficulties with schools, with a perception that some schools do not value the immunisation program.

The remote area immunisation coordinators reported factors positively influencing school-based vaccination coverage similar to those raised by jurisdictional immunisation program managers. Negative factors reported that are unique to remote areas included the highly mobile population and events such as wet season, cyclones, floods and fires that can force vaccination days to be

rescheduled. The limitations of electronic consent and digital technology in remote areas were also highlighted, with an emphasis on the need for trials before implementing this and support for providers with limited technological skills.

One HPV researcher perceived that increased education for students at school before vaccination, plus strategies to mitigate anxiety (e.g. putting up privacy screens and ensuring appropriate clothing is worn) can positively influence coverage. It was also highlighted that adolescents have a right to health information under the United Nations Charter on the Rights of the Child in Adolescence.

> *"If they've been taught about it and they know it's a good thing to have, and the teachers can tell them to get the consent form back, and so, they're much more likely to play a positive role if they have the appropriate education. Because otherwise they're just fearful and they have no idea of the benefits."*

Factors the HPV researcher perceived to be negatively influencing school-based coverage were consistent with those reported by other stakeholders: absenteeism, consent form return issues and parental concerns, largely around side effects but also the risks and benefits of vaccination, particularly among parents of boys.

> *"The parents really don't know that this vaccine prevents genital warts. That just doesn't seem to be on their radar at all. It's all about cancer… there's not much more information beyond cervical cancer that's on the parents' mind, whether or not it's on the factsheet."*

Challenges reported by other stakeholders relating to the school-based immunisation program for Aboriginal and Torres Strait Islander people

Several challenges relating to the overall school-based immunisation program for Aboriginal and Torres Strait Islander people were raised:

- transient and mobile populations
- higher levels of absence on the day of vaccination at school
- lower level of return of consent forms
- time consuming to update immunisation records on the register
- change from three to two doses confusing for general practice catch-up
- vaccine supply and storage issues
- parents of boys having concerns

> *"Look, we also have challenges with vaccine supply cold chains, between cyclones, distances, and very remote locations, we're almost set up for failure."*

> *"And I guess the other challenge was the parents of boys who said how come all of a sudden you want the boys to have it when it was just for the girls to start with. So just to get rid of that stigma around it's only a girl vaccine as being one of the other challenges that I've had."*

Catch-up HPV vaccination

Australian Government Department of Health

The Immunisation Branch staff perceived the community catch-up program to be beneficial as it offered extended opportunity for catch-up up to the age of 19 years; however, they thought there is insufficient awareness about this option among parents and students.

Jurisdictional immunisation program managers and other relevant staff

All jurisdictions, except SA, ACT, conduct school-based catch-up vaccination, which was reported to increase HPV vaccination coverage by 3–4% in WA and 8–10% in NSW. Limited school-based catch-up vaccination was available in WA in 2019 as the program was being administered in two simultaneous cohorts following a change in the first year of high school (Year 7 students were moved from primary to high school in 2015, in line with other states and territories in Australia).

The general method of delivery of school-based catch-up vaccination reported by jurisdictional immunisation program managers and other relevant staff is summarised in Table 5.

Table 5. Comparison of school-based catch-up across jurisdictions

Jurisdiction	Method of school-based catch-up HPV vaccination
ACT	No school-based catch up Reminder letter send at end of year referring students with missed doses to their GP Trial of school-catch up only for Aboriginal and Torres Strait Islander students commencing in 2020
NSW	From 2020 school catch-up will be available for both dose 1 and 2 in year 8 if consent was received in year 7 (previously had to have received dose 1 in year 7)
NT	Variable between providers
QLD	Variable between providers
SA	No school-based catch up Students with missed doses followed up by phone call or letter and offered an opportunity to have the vaccine e.g. council immunisation clinic
TAS	Variable between local councils Unlikely to offer school catch-up the following year
VIC	Variable between local councils
WA	Variable between providers Generally try to do catch-up in term 1 the following year

Community-based catch-up vaccination was perceived by jurisdictional immunisation program managers and other relevant staff as necessary, both as a safety net for adolescents who miss doses at school and because some parents or adolescents prefer that vaccines be given at a general practice.

A commonly perceived barrier to community-based catch-up vaccination was cost if a general practice didn't bulk bill, reported as a particular challenge in ACT and regional NT, but also occurring sometimes at general practice discretion elsewhere. Another perceived barrier to community-based catch-up was the general practice not having the vaccine in stock, particularly in ACT where HPV vaccine must be specifically ordered for each individual.

Free council immunisation clinics, some held after hours, were a commonly perceived enabler to community catch-up vaccination, but are not available in all areas.

Other key stakeholders

One local council staff member reported that they offered school-based catch-up at the next school visit later in the year. However, they checked the Australian Immunisation Register (AIR) record first and followed up with parents of adolescents thought to be overdue to confirm consent and avoid over-vaccinating, as this had occurred previously. The council had stopped offering catch-up vaccination at school in the following year (Year 8) to avoid over-vaccination and because of logistical challenges.

> *"It just makes the session messy. We're waiting for teachers to go and get one or two children. It just increases pressure on the session… and then there are issues about do they walk back to class by themselves after the 15 minutes?"*

Local council immunisation staff reported easier accessibility of free council immunisation sessions to be an enabler for community-based catch-up vaccination, with information regarding catch-up opportunities sent to parents via an SMS or a letter. It was also reported that catch-up doses are best received soon after the missed school dose to reduce the likelihood of families forgetting and to ensure any subsequent dose required can be received at school as scheduled.

Community-based catch-up vaccination was considered adequate in remote QLD, where it is conducted by a mixture of Queensland Health staff, GPs, Aboriginal Medical Service (AMS) staff and the Royal Flying Doctor Service. In some areas of Cape Tribulation, staff members travel to remote communities once or twice a year in school holidays to follow up adolescents aged 12–19 years due for vaccination.

Community-based catch-up vaccination was also considered adequate for non-Indigenous adolescents in remote NT, enabled by free community health clinics and all remote clinics keeping the vaccine in stock.

One HPV researcher perceived that enhancing opportunities for school-based catch-up vaccination would likely be more cost-effective than relying on community-based catch-up vaccination, although the latter is still necessary in certain situations and for population groups with particularly high rates of absenteeism.

> *"Definitely the option for that parent of a child, adolescent who is needle phobic or wants to have a one-on-one with a doctor to…. address their concerns about safety, but I otherwise question whether it is a cost-effective way of catching up. I really think that going back into the school is a much better way of catching up."*

Seqirus

Seqirus staff reported that they support the provision of catch-up vaccination at GPs by supplying various promotional materials, including booklets, posters and pamphlets, in several languages. Seqirus also reported an increase in demand for HPV vaccines by Chinese university students studying in Australia and so it has developed resources in Chinese for university health clinics to use with these patients. The HPV disease awareness website (www.hpv.com.au) led by Seqirus is also available in Chinese. Seqirus has been supporting education, primarily of GPs, regarding the potential individual benefits of HPV vaccination in females aged up to 45 years.

HPV vaccination in population subgroups

In interviews with key stakeholders, the perceived enablers ('what is working well') and challenges of HPV vaccination in several population subgroups, including Aboriginal and Torres Strait Islander people, Culturally and Linguistically Diverse (CALD) people, people of low socioeconomic status (SES), people living in remote locations and any other specifically identified population subgroups, were identified.

Aboriginal and Torres Strait Islander people

Australian Government Department of Health

The Australian Government Department of Health staff viewed the school-based method of program delivery as an enabler of HPV vaccination in Aboriginal and Torres Strait Islander people, compared to the primary care setting, albeit challenged by higher school absenteeism in Aboriginal and Torres Strait Islander students. Another enabler was ensuring the program is culturally sensitive, which the staff contributed to by supporting development of a specific brochure and an animation for Aboriginal and Torres Strait Islander audiences.

Jurisdictional immunisation program managers and other relevant staff

Jurisdictional immunisation program managers and other relevant staff reported providing HPV vaccination to Aboriginal and Torres Strait Islander people was particularly challenging in WA, ACT and metropolitan SA.

Of the eight jurisdictional immunisation program managers and other relevant staff, five felt they could comment on factors influencing HPV vaccination coverage in Aboriginal and Torres Strait Islander people in their jurisdiction and identified the following enablers:

- good Aboriginal Health Services in remote regions
- close relationships between healthcare staff, families and students
- partnerships between health services, community organisations and community elders
- actively following up students without signed consent forms
- Aboriginal Liaison Officers at schools

- Aboriginal Immunisation Health Workers targeting Aboriginal students for vaccinations
- little or no vaccine hesitancy
- differentiating messages about the variety of needles Aboriginal and Torres Strait Islander children may receive, for example, vaccinations versus penicillin
- simplification of the consent form for remote communities.

All these five program managers identified high rates of absenteeism as a particular challenge, with other challenges including:

- transient/mobile population leading to students transferring schools more frequently
- lack of close relationship between healthcare staff, families and students in metropolitan areas
- difficult follow up due to changed mobile numbers and changed addresses
- separation of women's and men's health issues in Aboriginal and Torres Strait Islander culture, with a need to promote vaccination in a culturally appropriate way
- unlikely to seek catch-up vaccination in the community if missed at school
- literacy in remote regions
- language barriers and wordy English consent forms
- varying levels of support from communities.

Accurate identification of Aboriginal and Torres Strait Islander adolescents was believed to be adequate in some jurisdictions (e.g. in ACT) but inadequate in others.

Other key stakeholders

Specific enablers of HPV vaccination reported for Aboriginal and Torres Strait Islander people in remote areas included engaging with the community, consistency of staff delivering the program, doing catch-up in school holidays and recording of vaccinations provided to Aboriginal and Torres Strait Islander people in the Communicare system (electronic health and practice management system for use in community health) to allow providers at AMS facilities easy access to information and prevent over-vaccination. Particular challenges in remote areas included staff turnover, older male adolescents not accessing health services after leaving school and high population mobility.

One HPV researcher perceived that a range of strategies are required to improve health equity in Aboriginal and Torres Strait Islander people, particularly increasing opportunities for catch-up vaccination, such as at school or through community outreach, as many Aboriginal and Torres Strait Islander adolescents are unwilling to go to an AMS due to confidentiality concerns.

Although the jurisdictional cervical screening manager interviewed did not directly work in immunisation, they suggested potential enablers for improving vaccination coverage in Aboriginal and Torres Strait Islander people could be adapted from strategies used in cervical screening. These include engaging Aboriginal and Torres Strait Islander people in research, plus formal national training networks to provide workshops for providers and opportunities to share information and ideas about what works in difference places.

Aboriginal Community Controlled Health Services

When asked if their area of service conducts a HPV vaccination catch-up program, two Aboriginal Community Controlled Health Services (ACCHS) staff said no, two said yes to some extent, depending on the availability of 'fly in fly out GP service', and three did not comment. These catch-up programs were not continuous and were reliant on availability of staff, resources and time.

The ACCHS staff identified main enablers to be 'No Jab, No Pay', despite HPV vaccine not being included in the requirements, and the expansion of the AIR to 'whole of life', facilitating the catch-up of children when they came for health checks, attend sexual or female health services.

Another enabler identified was parental recommendation or encouragement.

> *"Well they're kids, and if they've missed it, they're going to say, "Woohoo. I've got out of that," so unless the parents go, "No, you're not getting out of that. You need to go to the doctor and have it done. I'm making the appointment," then they're not going to get done, are they?"*

A key barrier identified was mobile populations having insufficient health education and knowledge about immunisation.

The key strength identified was having Aboriginal health workers and local community members work for their ACCHS, as they could translate where required (e.g. where English not the first language) and help ensure cultural appropriateness. In addition, in some places they provided incentives, such as giving colourful T-shirts to those coming for health checks, including screening for STIs. During health checks, missed vaccines could be provided. Some organisations also use computer-based recall systems.

> *"And, we're always working with community to try and make sure that education and health promotion activities are done with them. So, here we have broken down a lot of the cultural barriers; everyone feels comfortable to access and they know how we operate."*

> *"We have some people come down from the traditional lands here and they don't understand English at all. So, it can be complicated. But usually, if they come in, they bring a local family member in with them and they become their interpreter. Or there's generally another health worker in the building that is related or has come from the same area and they become the interpreter."*

Stakeholders also reported that there were transport/bus services for people to come for vaccinations, including HPV and bush mobile vaccination teams.

> *"We have bush mobile teams that go out to remote areas. We have buses that go to each clinic.. ……. which is free to pick up clients or clients can come in their car, their own vehicle, their own transport."*

Knowing the community was identified as an important aspect of delivering vaccination programs.

> *"Well, probably one of the socioeconomically most disadvantaged people are the Aboriginal people, in our area. But what's working well is that our team here has been together for a*

long time and so the community feel [sic] very safe with us and that's a big advantage with rapport. ……They know me and they know they can ring me at any time."

The key challenge identified by stakeholders was having fly-in fly-out staff or frequent changeover of staff, as it takes time for communities to feel they can trust newcomers. In addition, the addresses and phone numbers of Aboriginal and Torres Strait Islander people change frequently. Also, in tight-knit communities, messages propagate quickly so if one teenager says vaccination hurts, many others may refuse.

"One of the other biggest problem is they might be homeless, so the address they gave you this week, or the phone number they gave you this week, may not be their contact details next week. That can be a real issue in following up people. That's the beauty of having Aboriginal health workers working with you, because they know the community and they know where people are or who to ask where people are."

Culturally and linguistically diverse populations

Australian Government Department of Health

The Immunisation Branch use translated resources to support HPV vaccination for CALD populations, including a brochure in 10 languages and social media animations in 4 languages.

Jurisdictional immunisation program managers and other relevant staff

Jurisdictional immunisation program managers considered CALD populations to be generally accepting of vaccinations and compliant with recommendations. However, difficulties in identifying these populations and assessing any inequities in HPV vaccination coverage were recognised as challenges.

Two jurisdictions have developed their own translated resources for school immunisation teams to use (NSW - 26 languages, WA - 15 languages). Other jurisdictions rely on translated resources from other sites, the Commonwealth or interpreter services. Lack of free access to interpreter services for school immunisation teams was a particular challenge identified in SA.

Specialist refugee immunisation clinics were identified as particularly valuable for providing HPV vaccinations to the CALD population. A project is currently also underway using PAIVng (Providing Access to Immunisation for Vulnerable Groups) software to support vaccination delivery in Victorian refugee asylum seekers and another project is underway in QLD in collaboration with TAFE to develop immunisation information resources for people of non–English-speaking background and integrate immunisation as a topic in English language classes.

A particular challenge in CALD populations identified in NSW was in regards to students at Intensive English Centre schools who are eligible to receive up to seven different vaccines at school and often have very complex vaccination histories, and there is limited access to their vaccination records which are often not in English.

Other key stakeholders

The local council immunisation staff reported using translated resources when needed and the challenge of interpreting international immunisation records.

In remote areas, disadvantaged CALD populations (e.g. refugees) were considered particularly supportive of vaccination but challenged by a lack of support services (resources and interpreter services) in their languages. In remote NT, CALD populations were considered generally well educated and had no issues with the language. Religious beliefs of these populations about the association of the vaccine with sex were a potential barrier, although most provided consent.

One HPV researcher reported finding that enablers to HPV vaccination in CALD populations include their trust in the Australian Government, working with communities to develop appropriate resources in relevant languages/dialects and provision of information face to face where possible. Barriers to HPV vaccination in CALD populations have been limited use of available translated resources, conservative beliefs among parents/families and anti-vaccination views derived from social media.

People of lower socioeconomic status

Jurisdictional immunisation program managers and other relevant staff

Enablers of HPV vaccination in adolescents from a low SES background identified by jurisdictional immunisation program managers and other relevant staff included supportive and engaged providers that follow up in relation to unreturned consent forms and students requiring catch-up, free council immunisation clinics and GPs who bulk-bill low SES clients. A project using PAIVng software to support catch-up vaccination in homeless youth in metropolitan Victoria is also currently underway.

Challenges of HPV vaccination in this group included consent form return, the often chaotic lives of students from low SES background leading to vaccination not being a priority, unstable home environments, poor parental literacy and difficulty contacting parents. This was also noted to be a difficult group to identify and assess inequities in HPV vaccination coverage.

Other key stakeholders

One local council immunisation staff member reported enablers of HPV vaccination in adolescents from a low SES background to be extra support provided by staff to get consent forms signed, a Mature Minor policy allowing students to consent and opportunistic HPV vaccination when council staff conducted home visits for overdue infant vaccinations. A challenge is that transient students were not being followed up, particularly if they moved outside the council's area.

Similar themes were also reported by remote area immunisation coordinators, with the main enabler perceived to be school staff engaging with students and parents to facilitate consent form return. Perceived challenges of vaccination in low SES populations in remote areas included parental literacy, vaccination not being a high priority and adolescents with non-permanent addresses.

One HPV researcher perceived that the school-based program works well for providing HPV vaccination to adolescents of low SES background but would be enhanced by prioritising additional opportunities for school catch-up in disadvantaged areas, instead of requiring a GP visit.

People living in remote locations

Jurisdictional immunisation program managers and other relevant staff

Jurisdictional immunisation program managers and other relevant staff identified the following enablers of HPV vaccination in people living in remote areas: close relationships with healthcare staff (e.g. remote area nurses that seek out overdue students in the community); daily vaccination recall lists; and provision of vaccination by the Royal Flying Doctor Service. Barriers and challenges include vaccination not being a priority for parents (priority given to acute or emergency presentations); capacity (services often have a single provider); absenteeism at school; gaining consent for students at boarding schools; the logistics of vaccine delivery to remote areas; and access to GPs or AMSs for catch-up vaccination, which may be located far away.

Other key stakeholders

The two remote area immunisation coordinators interviewed perceived that HPV vaccination was working well in their regions (NT and QLD). They reported enablers to be: smaller communities allowing efficient follow up and highly skilled remote area nurses who can vaccinate and have regular training so are kept up-to-date on HPV-related information. Challenges reported include inclement weather, staff turnover, staffing shortages and Sorry Business making remote communities inaccessible for ill-defined periods of time.

Other population subgroups

HPV vaccination coverage in students at special schools was reported by several stakeholders to be of concern, with one jurisdiction reporting coverage in students in these schools 10–20% lower than for students in other schools. Despite parents being keen for vaccination and good consent form return rate, challenge in safely vaccinating these children in the school environment was identified as the major barrier. School staff can assist by providing background information and helping with physically stronger students, which may require additional personnel on vaccination day. It was also reported that special school students are sometimes vaccinated during medical or surgical procedures requiring sedation.

Other diverse population groups reported by stakeholders to be at risk of missing out on HPV vaccination included home schooled children and marginalised groups, who are also at increased risk of HPV infection and include adolescents who are homeless, in out-of-home care, have dropped out of school or identify as lesbian, gay, bisexual, transgender and queer (LGBTQ).

One HPV researcher also identified older MSM (aged up to 45 years) as an additional population group who would benefit from a national HPV vaccination program.

"We know that MSM are at a high risk of getting anal HPV and also anal cancer. So it's beneficial to have a national program like the UK is doing… ……So I think it would be good if Australia can consider expanding the national program to include MSM for older cohorts."

Initiatives to increase HPV vaccination coverage

Key stakeholders were asked to identify initiatives implemented by their workplace or jurisdiction in the last 5 years (since the previous evaluation) to increase HPV vaccination coverage. A summary of these initiatives, as well as initiatives currently in development, is shown in Table 6.

Table 6. Jurisdictional or stakeholder group initiatives to increase HPV vaccination coverage since 2014

Stakeholder or jurisdiction	Initiatives
Australian Government Department of Health (Immunisation Branch)	Communication campaign to provide evidence-based information regarding vaccine benefits, importance, safety and efficacy, and to increase uptake in adolescents eligible for school-based vaccination and young adults eligible for catch-up vaccination. Included advertising online, on social media and through public relations materials (fact sheet for GPs, poster, brochure) Specific resources developed for Aboriginal and Torres Strait Islander audiences (brochure and animation), available online and promoted through social media Translated resources also available in multiple languages, available online and promoted on social media Development of a series of videos for school students about the vaccinations they receive at high school.
Seqirus	Distributed 9vHPV Clinical Update booklets to GPs in early 2018 Developed a 9vHPV FAQ booklet for patients; available in multiple languages Implemented a reminder system for individuals who have been prescribed or administered 9vHPV to register for automatic SMS reminders when next doses are due (instructions included in FAQ booklet) HPV disease awareness pamphlets for GP waiting rooms and targeting international students Maintaining HPV disease awareness website Provided funding support for the development of two CPD programs for GPs
ACT	Year 6 postcards sent home at the end of the school year to raise awareness about vaccination in year 7 and encourage parents to look out for consent forms Signing consent forms included at top of page in school ‘to-do’ packs for parents HPV vaccination promoted at parent information evenings in high schools with low consent form return Infinity cards provided to children post-vaccination (Appendix 4) Developing a new communications strategy to target the CALD population Mop-up vaccination program to be trialled in 2020 in 3-4 schools with higher Aboriginal and Torres Strait Islander populations (return to school a few weeks after the clinic) Electronic consent forms - discussed but not progressed due to privacy concerns
NSW	Electronic consent- Consent and Record Management for Immunisation (CARMI) project in development Consent forms translated into 26 languages and available online for school teams to use School catch-up program extended in 2020 to allow students with consent given in year 7 to receive both dose 1 and 2 in year 8 (previously could only catch-up in year 8 if dose 1 was received in year 7) Pilot catch-up program for Aboriginal and Torres Strait Islander students in year 8-12- commenced in term 3 and 4, 2019 and was offered in selected schools with high proportion of Aboriginal and Torres Strait Islander students and low coverage Second-chance second consent pack sent home with students with unreturned consent forms

	Template letter available for public health unit staff to send to school principals reporting the school's vaccination coverage compared to the state average Consent forms reviewed and updated annually Variety of initiatives used at discretion of public health units including reminder SMS sent to parents of students with missed doses, specific targeting of schools with low coverage, school newsletter articles, promoting the vaccination program at year 7 information days at end of year 6 Annual workshop for school immunisation staff. Introduction of pilot AusVaxSafety program in 2019 in selected metropolitan Sydney PHUs to monitor HPV vaccine safety through sentinel active SMS-based surveillance.
NT	Providers educated to routinely check vaccination history when seeing adolescent patients Simplified consent form with dual HPV/dTpa consent created particularly for boarding students from remote communities (Appendix 5) Resources translated into Indigenous languages with assistance of clinic staff Have used promotional comic books, posters and talking books at various times Meetings between NT Centre for Disease Control and school principals to inform changes to the program School nurses provide information at school sessions for year 6 parents prior to moving to year 7
QLD	The *Public Health Act* amended to allow immunisation providers access to student contact details Year 6 postcards at end of the school year to raise awareness about vaccination in year 7 (Appendix 6) Consent packs reviewed annually, to make them attractive for students to take home Financial incentives provided for school immunisation providers to catch up students with missed doses Piloting using AIR data to send reminder letters to year 8 students with incomplete or no HPV vaccinations Bi-annual school immunisation provider forum held in Brisbane focussing on HPV vaccination program Performance indicators in contracts for provision of the school vaccination program Consent forms for boarding school students sent home with report card at end of year 6 Electronic consent forms - started talks with providers Project currently in development with TAFE to produce immunisation information resources for people of non-English-speaking-background and use immunisation as a topic in English language classes
SA	Developed a Memorandum of Agreement - Ministerial arrangement with the Department for Education providing executive-level support for school program (used to encourage schools that are slow to respond) Closely monitoring the coverage data due to concerns about declining coverage State-wide mail-out reminder sent in January 2020 to students with incomplete vaccinations who turned 14 years in 2019 with a plan to review the coverage data again in several months to assess the impact Planning a larger communication strategy in 2020 in response to declining coverage Planning to review the school program service agreements with local councils, to upscale and be more prescriptive about the requirements of council to follow up students with missed doses
TAS	Developed a state-wide consent form (previously each local council had their own consent form)

	Consent form recently updated to address common concerns (Appendix 7) Annual workshop for local council immunisation providers to discuss the school-based vaccination program and share ideas and initiatives around consent forms, catch-up doses etc. Local councils offer various incentives for adolescents to receive vaccination e.g. BBQs, movie tickets
VIC	Public Health and Wellbeing Regulations amended to authorise local councils to collect contact details Continued use of the Immune Hero website (http://immunehero.health.vic.gov.au) to agree between high schools and local councils on roles and responsibilities in providing the vaccination program in schools Projects to increase vaccination coverage in homeless youths and refugees using PAIVng software Cancer Council Victoria website used by local councils to provide information to families Electronic consent- currently in development
WA	Trial of SMS reminder in mid-2018 (not considered effective based on AIR records) Transition of the school-based program from year 8 to year 7 in 2019 to reduce absenteeism Pilot program in 2020 to introduce immunisation to the year 7 and year 10 school curriculum Developing promotional materials for use by school nurses at school assemblies at start of year 7 More appropriate information and consent materials for remote Aboriginal populations Improve the relationship between school vaccination program and school nurses, to assist with promoting and running the program (ultimately aiming to have WA school nurses providing catch-up vaccinations)

Vaccine hesitancy and social media

Australian Government Department of Health

The Immunisation Branch staff at the Australian Government Department of Health acknowledged that a small group of parents are hesitant specifically about the HPV vaccine, largely due to safety concerns. Correspondence received at the department and a very active presence of this group of parents on social media, including comments on activities that the department has conducted, reinforce this view. This activity has remained at a consistent level since the program started and does not appear to have changed following the transition to 9vHPV vaccine in 2018. However, attitudes on social media towards HPV vaccination are largely positive.

> *"We do get a lot of negative comments on our social media platforms about this vaccine and other vaccines as well, but we do – it's certainly a much more positive conversation. So, the number of likes on our posts completely outweigh the negative comments. And actually, most of the comments that we get on our social media platform are the negative comments and we think that that's purely because people who are supportive of vaccination tend not to comment and just like posts."*

Seqirus

Seqirus staff reported that they receive occasional enquiries from people expressing hesitancy towards HPV vaccine or vaccines in general due to safety, philosophical or religious reasons, and perceive that social media can influence people's attitudes towards HPV vaccination either positively or negatively.

Seqirus has limited capacity to use social media for vaccine promotion due to industry regulations, but highlighted the positive work of the Australian Government Department of Health in targeting adolescents and parents on social media.

Therapeutic Goods Administration

The TGA reported that it does not receive more inquiries from external stakeholders regarding HPV vaccine safety than it did for other vaccines.

Jurisdictional immunisation program managers and other relevant staff

Jurisdictional immunisation program managers generally perceived HPV vaccine hesitancy to be present in a small proportion of the population, but did not consider it a major issue and had minimal impact on HPV vaccination coverage. Several managers believed that vaccine hesitancy is a more prominent issue in relation to childhood vaccination in Australia. This view was based on relatively few concerns expressed by parents and infrequent phone calls regarding HPV vaccine hesitancy to immunisation help lines.

> *"We don't have a major issue in our jurisdiction."*
>
> *"Most people are compliant, however, there will always be a small percentage... we try and address any concerns or demyth, debrief around any myths about the HPV vaccine and things like that. But we don't get a lot."*

Measurable hesitancy specific to HPV vaccine is demonstrated by a discrepancy in coverage between HPV and dTpa vaccines, given in the same school visit, varying from 2–3% lower for HPV vaccine in WA and SA to up to 10% lower in some parts of QLD.

> *"There's still small amounts of parents and guardians who object and who have demonstrated on the card that they do not wish their child to be immunised. So, they might consent to the child being immunised with dTpa, but on the same consent form they won't consent to HPV."*

A variety of perceived reasons for HPV vaccine hesitancy were provided by jurisdictional immunisation program managers, including the association of the vaccine with sexual activity, philosophical objection and religious objection. Of note, not all jurisdictions have a 'no' option on consent forms, meaning that it cannot be determined what proportion of forms are not returned due to objection.

Steiner schools, and some religious schools, do not allow the vaccination program to occur in their school, and stakeholders expressed uncertainty about whether the vaccination information they provided was passed on to parents.

Vaccine hesitancy was reported as more common in certain geographical areas, where people with anti-vaccination beliefs had written directly to schools to dissuade participation in the school-based vaccination program. It was reported that the schools targeted in this way remained supportive and continued to participate in the program.

The influence of social media on HPV vaccination coverage was reported to be both positive and negative. Some jurisdictions use social media to promote vaccination campaigns, which was perceived to have a positive influence. Conversely, negative social media messaging about vaccination was perceived to potentially spread very quickly and have a powerful effect on both adolescents and parents, with several jurisdictional immunisation program managers commenting on the need for awareness:

> *"I think we have to be constantly reviewing what the messages are that are out there. It doesn't mean that we respond to every single message but it is a powerful influencer and we do have to be aware of that."*

One jurisdiction (QLD) was concerned that negative messaging on social media regularly impacts consent for HPV vaccination, but other jurisdictions were less concerned about any negative influence of social media. They reported that occasional circulation of discredited studies and anecdotes leads to queries to immunisation teams but generally gains little traction.

> *"The vast majority of cases generally self-correct where somebody comes on with an anti-vaccination sentiment or what have you. The majority of people really sort of overwhelm; the sensible perspective generally tends to overrule and drown out anybody who comes on and says well HPV causes sexual promiscuity or what have you."*

Other key stakeholders

One local council staff member reported a large increase in high school vaccinations following the 'No Jab No Pay' policy, despite HPV vaccine not being included, and perceived that indifference, ignorance and non-return of consent forms were more significantly impacting HPV vaccination coverage than vaccine hesitancy. The other local council staff member also did not perceive vaccine hesitancy to be impacting HPV vaccine coverage in their area. Social media was again perceived to have both positive and negative influences by these staff members, through promotion of the vaccination program and prompting return of consent forms, but also exposure to anti-vaccination views.

The sexual health physician interviewed perceived that vaccine hesitancy in Australia is common to all vaccines and driven overwhelmingly by safety concerns. However, one HPV researcher perceived although there were some safety concerns, vaccine hesitancy was not a significant issue for HPV vaccination, and trust in the vaccine was enhanced by its delivery in the school-based vaccination program.

Social media was also perceived by one HPV researcher to negatively influence attitudes towards HPV vaccination in a small part of the population but not having a great impact. One HPV researcher commented that Australia could consider conducting regular societal surveys of vaccine acceptance, as are conducted in the United Kingdom, to monitor for any increase in the negative influence of social media.

> *"I think it does play a role…. people can get the information very easily from the internet and there is actually lots of different information which may influence the attitudes or also the perception of the HPV vaccination."*

It was also reported that social media have been used positively in the promotion of HPV vaccine knowledge and availability of catch-up vaccination to MSM, with an emphasis on HPV-related cancers occurring in this group.

Aboriginal Community Controlled Health Services

Four of six ACCHS stakeholders reported that social media (mainly Facebook) plays a role in spreading negative messages regarding HPV vaccination in their area. One stakeholder said that Facebook could also be used to promote vaccination.

A nurse immuniser reported that negative messages were often spread via social media.

> *"The anti-vaxxers are always going to troll any vaccination advertisement or information that comes onto any of the social media. That goes without saying."*

Vaccine safety

Australian Government Department of Health

The Immunisation Branch staff reported no concerns from any stakeholders specifically about the safety of 9vHPV vaccine and also highlighted the role of AusVaxSafety in monitoring the implementation of 9vHPV vaccine.

Therapeutic Goods Administration

The TGA reported that 9vHPV vaccine undergoes enhanced monitoring as a drug of special interest and that since 2018 there have been an average of 215 adverse events following immunisation (AEFI) reports per year related to this vaccine, compared with an average of 335 per year for 4vHPV vaccine for the period 2006–2019 (noting fewer doses of 9vHPV vaccine are administered because of the 2-dose schedule). The top 10 most frequently reported adverse events to date are almost identical for both 4vHPV and 9vHPV vaccines, with the three most frequently reported being syncope, headache and nausea for 4HPV vaccine and injection site reaction, headache and syncope for 9vHPV vaccine.

Jurisdictional immunisation program managers and other relevant staff

No concerns were reported by jurisdictional immunisation program managers about HPV vaccine safety, with no change in frequency or type of adverse events observed following the transition from 4vHPV vaccine to 9vHPV vaccine.

Other key stakeholders

One HPV researcher commented that the increase in injection site reactions seen in clinical trials with 9vHPV vaccine requires monitoring, as this could affect adolescents because of their anxiety about vaccination and potentially lead to students refusing or not turning up for the second dose.

Aboriginal Community Controlled Health Services

ACCHS stakeholders reported no major change in the type and frequency of adverse events following HPV vaccination.

Vaccination reporting

Australian Government Department of Health

The Immunisation Branch staff perceived the transition of HPV vaccination reporting from the HPV Register to AIR to be beneficial as AIR was a whole-of-life register and a single location for all immunisation records.

> *"The AIR is a source of truth, one stop place, immunisation history statements will all have - will have everyone's full immunisation history including HPV."*

Challenges of the transition included differences in the method of calculation and reporting of coverage rates, and the need for ongoing efforts to raise awareness among providers of the importance of HPV vaccination reporting. Several challenges associated with the transition of existing records from the HPV Register to AIR were reported, including:

- more records without Medicare numbers than known Medicare-ineligible population, suggesting some records of Medicare-eligible individuals could not be matched
- incorrect provider numbers, for example, illegible writing on paper consent forms
- no consistent method of recording schools (now Australian Curriculum Assessment and Reporting Authority Schools List)
- changes in names and addresses over time.

These challenges prevented automatic matching and required developing new matching systems in the software or laborious manual matching of individual records.

Overall, approximately 60,000 individual HPV vaccination records were manually matched but 30,000 could not be matched. As state and territory immunisation databases are integrated into

AIR, more records are expected to be matched. Records can also be matched if an individual notifies to Services Australia that a vaccine has been administered, leading to a planned promotion for people to check their vaccination records.

> *"Some work that we've been doing this year, and that we will continue to do over the next couple of years, is work on AIR data quality and asking people to check their immunisation history statement, asking them to check whether or not it's up to date, if it's not visit your vaccination provider, get the vaccination provider to update the AIR."*

The Immunisation Branch staff also reported that vaccination records entered into AIR that end up in a 'Pending file' and are not visible on a person's record are largely due to providers entering incorrect information, most frequently incorrect dose numbers. Systems have been developed to identify 'Pending records' that may impact payment of federal government family benefits (although this is not relevant to HPV vaccine) but there is a need to continue improving the quality of the data.

> *"We've been doing quite a bit of work with providers to teach them how to use their systems. We've been working with the software developers to improve how data comes into the AIR, to improve the data quality of the AIR and give the right level of access to AIR data to the right people. So that's our aim."*

A significant future change that will improve the quality of AIR data is the requirement for all software developers that have vaccination providers as customers to include AIR functionality in their software and keep it updated.

The Immunisation Branch is also exploring ways to improve bulk uploading of school-based vaccinations and systems to improve reporting of vaccinations given in hospitals. Both of these measures should assist with improving vaccination reporting and accuracy of coverage estimates.

Jurisdictional immunisation program managers and other relevant staff

Jurisdictional immunisation program managers were very supportive of the transition of HPV vaccination reporting from the HPV Register to AIR, and reported that immunisation providers were also happy with the change.

Perceived benefits of reporting to AIR included:

- simpler system to use for providers
- single place for all vaccinations to assist people accessing vaccination records
- uploading to AIR is often built into practice software and so GP reporting of HPV vaccinations may improve.

The managers also reported several concerns arising from the transition, most common of which (reported by six out of eight) was concern about missing data. This was usually flagged when a member of the public or a provider noticed a record was incomplete and led to concerns about falsely low jurisdictional coverage rates.

Another major concern reported was a decrease in the quality of data reports initially available from AIR compared with the HPV Register, particularly the inability to extract reports by school. Some were extracting reports by date of birth and others by postcode, both of which had potential to be incomplete if students were in the wrong year level for their age or not listed at the correct address on their Medicare record.

> *"The biggest loss for us is the information by schools. Our database was set up by schools, so we could look at denominators – we had a lot of information by school which we no longer have."*

The biggest barrier jurisdictional immunisation program managers perceived to HPV vaccination reporting was failure of immunisation providers to update practice software to allow automatic uploading to AIR, but this was thought to be improving with time. Other perceived barriers included providers not recognising the importance of reporting and reporting not being a priority for providers, particularly because of high staff turnover in some areas and lack of incentives for reporting adolescent vaccinations, unlike childhood vaccinations.

Other key stakeholders

The local council immunisation staff interviewed perceived similar benefits of the transition to those highlighted by other stakeholders. One of the challenges identified by these immunisation staff was not all doses given by GPs are reported to AIR, as found when following up adolescents with incomplete courses recorded on AIR. This can lead to a risk of over-vaccination. These staff also reported that they needed to rely on council software to upload vaccination records rather than being able to upload directly to AIR, which delayed reporting.

Remote area immunisation coordinators reported particular challenges of the transition to AIR, including AIR regularly dropping in and out during the day (requiring users to log in again) due to AIR data security settings, delays due to the need for manual uploading and limited access to computers in small communities. Despite these challenges, both remote area immunisation coordinators believed the completeness of HPV vaccination reporting to AIR in their areas was very high.

> *"The thing with timeliness is if you've got a lot of schools you won't get that data on quickly. It's actually going to take a month or a couple of months before you actually get that data entry in. The appropriate staff to do the data entry and…… an electronic system in a school would work really well. You know, do it straight there in school. But again, that would slow the whole process down of the vaccinations. But that would be utopia."*

Aboriginal Community Controlled Health Services

Five of six ACCHS stakeholders said migration of HPV vaccination data to AIR has made the task of reporting easier, reduced delay and facilitated access to records of HPV vaccinations given in GP surgeries.

"I think the fact that we now have access to the records of the immunisations being given, without having to go to another agency, or having AIR available to us now, it makes it very easy to check up who's had their vaccines."

All ACCHS stakeholders however noted that reporting of data to AIR was incomplete in their practices/services.

Cervical screening

Australian Government Department of Health

The Immunisation Branch staff felt the change to HPV-based cervical screening could improve HPV vaccine uptake through the change in language used, which may lead to more people associating HPV vaccination and cervical screening.

Representatives from the Cervical Screening Section noted the literature showing higher cervical screening participation in vaccinated women than unvaccinated, but pointed out that these were older females who received catch-up vaccination and so were likely to be more aware of health prevention activities. They noted that there is no evidence yet of either reduction or increase in screening participation by females vaccinated in the school-based program.

The Cervical Screening Section staff were also aware of anecdotal reports of females believing screening is not needed following HPV vaccination. An ongoing focus of all communication resources to both healthcare providers and consumers has been the need to screen irrespective of vaccination status. These national resources are available in a large range of languages, including Braille, and translator/interpreter services are also available. Many states and territories also develop their own resources and the Cervical Screening Section is looking at promoting a move to a more consistent national approach. In regards to any influence of the change to HPV-based cervical screening on HPV vaccination uptake, the Cervical Screening Section staff perceived that possibly more people may be able to make the link between HPV vaccination and cervical screening, although this may depend on the language used.

The Cervical Screening Section staff also perceived that it might be helpful to raise awareness of screening as a preventative health measure in young people through communication at the time of HPV vaccination, who could then increase awareness of cervical screening in their mothers.

"We're thinking more around increasing awareness of preventative health, that screening is a preventative health measure. So you don't want people to be fixated with screening from the age of 12, but having an awareness of it and having an opportunity to talk to their parents about it as well and to ensure that they're – because I think we had some issues with older women who stopped screening because they've had children, they don't see screening as necessarily being a priority anymore. Nothing to do with vaccination, but it's another opportunity to target a group that is potentially able to influence others."

Jurisdictional immunisation program managers and other relevant staff

Most jurisdictional immunisation program managers provided little or no comment on cervical screening as this was not their area of expertise. Of those who did, it was generally perceived that the public did not usually associate HPV vaccination and cervical screening, as there was generally a long interval between vaccination and commencement of screening. Of the three managers who commented about any potential impact of the change to HPV-based cervical screening on HPV vaccination uptake, two thought there would likely be no impact and one thought that there may be a positive impact, but in the longer term.

Jurisdictional cervical screening manager

The jurisdictional cervical screening manager interviewed reported that while females can frequently recall they had been vaccinated, they often do not have a good understanding about the HPV vaccine or the connection between vaccination and screening, and that there is still a misconception among some females that screening is not required after receiving the vaccine.

The importance of the HPV vaccination and cervical screening programs working collaboratively to provide a clear message that vaccination on its own does not protect against all types of cervical cancer was also emphasised, particularly in higher risk populations.

> *"You know, the media saying elimination of cervical cancer in Australia, we're going to be the first country and all this stuff, it is only as good as the paper you write it on if we don't bring our First Nations people into this. And they are the ones not screening. And they are also the ones with lower rates of vaccinations. So we have a real agenda ahead of us to make sure that both of these messages get really strongly articulated for that group, and our CALD populations."*

The jurisdictional cervical screening manager also perceived a potential benefit of increasing awareness about screening among adolescents at the time of HPV vaccination was that they could influence their mothers to undergo screening.

Other key stakeholders

Similar to other stakeholders, the sexual health physician interviewed also perceived that many people did not link HPV vaccination and cervical screening because of the extended interval between vaccination and screening.

Disease impact

Australian Government Department of Health

The Immunisation Branch staff reported that their promotional materials for the HPV vaccination program include information on the impact of the vaccine on disease burden, but this information is not included in the consent form process and for students being vaccinated. This is based on

research showing that disease impact was not considered an important message by parents for consent.

The Cervical Screening Section staff highlighted the evidence of reductions in cervical HGA in Australia since the National HPV Vaccination Program began, and an expectation that this will also extend to cervical cancer.

Other key stakeholders

The sexual health physician interviewed reported that the incidence of genital warts started declining within 3 months of the National HPV Vaccination Program commencing, and continues to trend down. However, genital warts are still common in the older MSM population never eligible for vaccination. It was also reported that there has been no change in cervical HGA in unvaccinated migrant women who attended sexual health clinics for cervical screening and that the relative proportion of HPV infections in migrants is expected to increase in coming years as prevalence in the overall population decreases.

Related to this, one HPV researcher also highlighted the significant declines seen in genital warts in Australia in both females and males but raised the potential challenge of sexual mixing between the Australian population likely to have been vaccinated at school and people from other countries who come to Australia, who are less likely to be vaccinated.

WHO cervical cancer elimination target

All key stakeholders were asked whether they believed Australia could achieve the HPV vaccine–related WHO global scale-up target for the elimination of cervical cancer as a public health problem. This target is to achieve 90% of females fully vaccinated by 15 years of age by 2030.

Australian Government Department of Health

The Immunisation Branch staff believed that Australia can achieve this target and that we are already achieving higher coverage than many other countries.

> *"Certainly they're targets that we'd be looking to work towards and to be able to do that, and [we] are probably in a much better position than other countries to be able to do that, given the delivery mechanisms and the resources and materials that I guess are put behind the program."*

The Cervical Screening Section staff highlighted inclusion of cervical screening targets in the WHO targets for cervical cancer elimination and believed that Australia is close to achieving these.

> *"I think we're closer than we think we are. You look at 90-70-90 and think that's hard but actually Australia is probably pretty close."*

Jurisdictional immunisation program managers and other relevant staff

Seven out of eight jurisdictional immunisation managers believed that the WHO elimination target is achievable in Australia. While all of them acknowledged that this target is aspirational and challenging, they highlighted the fact that 90% coverage was already being reached in some cohorts, particularly for dose 1, exemplified the perceived achievability of the target. All jurisdictional immunisation program managers also emphasised the need for increased support and strategies for the program, particularly around the delivery of dose 2, to be able to achieve the target.

Other key stakeholders

Both local council immunisation staff interviewed also perceived this coverage target to be achievable, with electronic consent and improved consent form return considered as prerequisites to achieving this.

Both remote area immunisation coordinators believed that improved accessibility to vaccine was required for Australia to achieve the target, with vaccine hesitancy and social media considered a barrier.

> *"I know they rely on GPs too much down South…… some kids even go for their childhood needles to the GP. So, I think having Community Health Centres that are free and health-promoting school nurses is a lot more effective."*

The sexual health physician believed that the coverage target is achievable for dose 1 but potentially not for dose 2 because of attrition, while one HPV researcher was not sure if Australia could achieve this target.

The other HPV researcher believed this target is achievable with improved consent form return, increased school-based catch-up and increased understanding of the school-based program. Increased resources and funding would be required to study and evaluate the school-based program, but this was perceived to have potential for Australia to become a world leader in school-based vaccination programs and model how to achieve a successful school-based program for other countries as well as supporting the introduction of other vaccines through school-based programs in future.

> *"We could do better, but we need to - I think we're at the point where we need to understand why. I mean, we've sort of gotten to this point where we can't seem to get any higher, so we just need to have a better understanding of what are the weaknesses, and do some testing of different strategies for addressing those weaknesses."*

> *"Because a school is like a mini community or a mini society and we really fully haven't worked it out, and we could be a leader for the rest of the world because a lot of countries don't have school-based vaccination, and they might be concerned that it may not be acceptable or they don't know how to do it and we could actually - if we're able to do a bit of research, we could sort of model… how you make a school-based vaccination program very successful."*

Aboriginal Community Controlled Health Services

Four of five ACCHS stakeholders who answered this question said the 90% vaccination target in girls by age 15 years is achievable.

Factors influencing program outcomes and impacts

Key stakeholders were asked which factors influenced the HPV vaccination program outcomes and impacts most positively and negatively. The responses are summarised by stakeholder group in Table 7.

Table 7. Stakeholder perspectives on factors most positively and negatively influencing the HPV vaccination program

Stakeholder group	Positive factors	Negative factors
Department of Health	• Collaboration between Commonwealth, states/ territories and GPs • Convenience of school-based program delivery • Partnership between the HPV vaccination and cervical screening programs to raise awareness of cervical cancer preventative strategies and work towards elimination	• Concerns from consumers that there are safety issues with the HPV vaccine, and/or vaccine hesitancy in general • Lack of perceived immediate benefit and parental perception that vaccination can be done in future • Lack of understanding around timing of the vaccine at a young age and before being sexually active
TGA	• Positive benefit-risk balance of the vaccine	
Seqirus	• School-based program for vaccine delivery well accepted in Australian culture • Gender-neutral program minimises stigma about the association with sexual activity • Highly engaged local immunisation coordinators • High quality surveillance systems to monitor population-level coverage and impact • Availability of catch-up vaccination • Emphasis on cancer prevention • Government social media campaigns	• Lack of electronic consent • Lack of publically available annual state-based data on uptake in schools • Complacency by parents and adolescents regarding HPV-related diseases, receiving the vaccine or following up missed doses • Large variety in how the program is conducted leading to lack of free flowing information between providers regarding best practice
Jurisdictional Immunisation	• Reductions in disease demonstrating effectiveness of the program (“good news stories”)	• Reliance on consent form return

Program Managers	• Potential for impact on cervical cancer • Convenience of school-based program delivery • Normalisation of the vaccine as routine through delivery to both females and males in age group cohorts • Public trust in an NIP vaccine that is recommend and funded by the Government • Excellent school immunisation teams • Commonwealth taking the lead to support the program, develop resources and supply the vaccine to states and territories • Strong communication about the vaccine benefits for both females and males and the need for two doses • Availability of coverage data • Partnerships with community organisations that interact with young people to reinforce positive messaging	• Absenteeism leading to not all students vaccinated at school • Reliance on parents to go to council clinic or GP for catch-up • Poorly engaged schools and school staff • Inequity across population groups • Stigma around HPV as an STI • Perception that the vaccine is for females • Misinformation about vaccine safety on the internet and safety rumours on social media • Misinformed opinions from prominent people • Long dosing interval leading to loss of interest or understanding of the importance of the vaccine • Complacency regarding getting the vaccine at school due to free catch-up available to age 19 years • Risk of complacency regarding vaccination through promoting the reductions in disease • Third party immunisation providers impacting the integrity and quality of the program • Lack of GP awareness about offering a free catch-up vaccine
Local Council Immunisation staff	• Ease of the consent process for families and schools and timely return of consent • Reductions in disease	• Relying on students to carry and parents to complete hard copy consent forms • Time-poor families busy with their own agendas
Remote area immunisation coordinators	• Good relationships between schools and providers • Staff who are flexible with service delivery e.g. providing vaccine after hours • Reductions in disease • The program is well received in the community • Good state level support for the program e.g. producing consent forms • Working across programs to improve health outcomes	• Vaccine hesitancy and how this is managed • Social media • Personal beliefs • Accessing parents of adolescents that have chaotic lives and are frequently absent

Sexual Health Physician	• The national catch-up vaccination program, which increased the population impact and speed of the effect • Combination of vaccine promotion by the Government and marketing skills of the pharmaceutical company	• Potential for other people eligible for vaccination outside the school program missing out if GPs are not aware of e.g. migrants • General vaccine hesitancy common to all vaccines
Jurisdictional cervical screening manager		• Limited understanding and awareness of the benefits of the vaccination program • Information provided in schools is complex and hard to understand for people with low literacy
HPV Researchers	• Convenience of the school-based program • Parental trust in school-based vaccinations • AIR provides a good record of coverage	• Consent form return • Absenteeism
Aboriginal Community Controlled Health Services	• Good, free vaccine • School-based program • Change in cervical screening strategy • 2 doses	• Confusion around why boys have been included in the program. • Facebook and other social media spread rumours •

Recommendations

Many recommendations to improve the National HPV Vaccination Program were made by key stakeholders. These are summarised in Table 8.

Table 8. Key stakeholder recommendations

Stakeholder group	Recommendations
Department of Health	• Continued efforts to increase education • Electronic consent forms by states and territories
Seqirus	• Provide information for GPs and practice nurses about how to use the AIR to recall adolescents due for vaccination before turning 15 years, to prevent the need for 3 dose, and before turning 19 years to remain eligible for funded catch-up • Increased education for immunisation providers on how to counsel parents hesitant about HPV vaccine • Increased information for providers and the public regarding the safety and efficacy of HPV vaccines and the impact on disease burden achieved to date

	• Increased promotion to GPs of importance of HPV vaccination reporting to the AIR • Education for GPs regarding potential benefits of HPV vaccination in females to 45 and males to 26 years • Emphasise the benefits of vaccination in males • Consider inclusion in 'no jab no pay' policy • Include HPV education in school curriculum • Increased collaboration to maximise educational efforts for healthcare professionals and consumers • Harmonised national approach to missed doses • Consider financial incentives for GPs to record doses to the AIR as exists for childhood immunisations • Link vaccination reporting with accreditation
Jurisdictional immunisation program managers	• Electronic consent forms • Don't use 'sex' in promotional messages, more that the vaccine is for cancer prevention • Include immunisation in school curriculums • Provide more catch-up opportunities at schools • Incorporate information on disease impacts into education and the consent process for parents • Develop new resources and initiatives for vulnerable or hard to reach populations to improve equity • Stronger messaging for parents and adolescents around the benefits of the vaccine, why it's given to females and males and why given in early adolescence • Ongoing communication to providers about the importance of HPV vaccination reporting • Research into why coverage rates low in certain areas • Reduce the HPV vaccination schedule to 1 dose • Consider reducing minimum dosing interval to 5 months • Consider including HPV vaccine in 'no jab no pay' • Increased sharing of initiatives to improve coverage • Increased funding to support delivery in remote areas • Improved resources in Indigenous languages • Increased political will to develop strategies for improved vaccination coverage in adolescents and adults, not just children • Improved quality of AIR data • AIR reports available by school and school year • Raise profile of the program with the Department of Education, to support schools in delivering the program • Media campaigns about benefits and availability at GP • Campaign to increase GP awareness and encourage checking adolescents' vaccination histories

	• Consent forms for parents with low literacy
Local Council Immunisation staff	• More encouragement for schools to provide timely class lists with parent contact details • Timely vaccination coverage rates available for council per school, to identify gaps before end of school year • Electronic consent forms • Ability to download consent forms on social media and return to council or school via email
Remote area immunisation coordinators	• Promote whole of life immunisation in general • Education for parents, nurses and midwives about the ramifications of cervical cancer treatment • AIR reports available by school per region • Working with the languages of CALD people • Providing the vaccine outside of normal hours • Emphasise importance of finishing course post dose 1 • Appropriate staff for data entry for vaccination reporting to reduce incorrect data input (may not be providers)
Sexual health physician	• Target minority population groups who may not currently be eligible e.g. migrant sex workers • Monitor the scientific literature about one dose • Continual promotion of the good news stories in coming decades about vaccine impact particularly social media • Opt-out system for parents to only indicate if they did not want their child vaccinated
Jurisdictional cervical screening manager	• Improved research and engagement with priority populations • Promote HPV vaccination and cervical screening as a wellness program to improve reproductive health, to remove the stigma around sexual health
HPV researchers	• Increased education around HPV vaccination, transmission and risk amongst males • National program for HPV vaccination in older MSM • Ensure the program is well accepted by adolescents e.g. privacy screens, appropriate clothing, vaccinate anxious students first • Provide education at school just before getting the vaccine to improve student's understanding • Work with young people and teachers to develop educational materials that align with school curriculum. • Ensure parents well informed about the benefits of vaccination, including for boys e.g. prevention of genital warts and HPV-related cancers, not cervical cancer • Develop online education for students to access outside of school time to improve their self-efficacy, co-designed with parents and students and in addition to education in schools

	• Increase opportunities for school catch-up e.g. additional visits to schools, expansion of healthcare clinics in schools, train school nurses to vaccinate • Increase opportunities for catch-up at schools with high Aboriginal and Torres Strait Islander student enrolment, where there are high rates of absenteeism and students may not want to go to an AMS e.g. increased school-based catch up or community outreach visits • Target marginalised students at high risk of HPV infection and absenteeism with tailored strategies • Include vaccination in the regular health program and pathways that adolescents in out-of-home care receive • Increase coverage in special school students who may have behavioural issues - may need to go back to the school more often or have more personnel to help • Community partnerships between schools and GPs to streamline catch-up (not just sending a letter home) • Coverage targets for the jurisdictions and health districts to promote partnerships with schools • Look at why we don't get all consent forms back and use strategies to increase consent form return e.g. combination of hard copy and electronic consent, reminders, sending the consent pack home again • If electronic consent was developed could include a site for students and parents to obtain information online in a more appealing and accessible way and triage information based on parental views • Look at what regions in Australia with high coverage do to achieve this e.g. local government areas or schools • Consider regular societal surveys of attitudes towards vaccination in Australia • Increased resources and funding for evaluation of the school-based program and factors affecting coverage
Aboriginal Community Controlled Health Services	• More education around HPV vaccination. Media campaign may need to be done afresh to deliver the same message to male and female populations since confusion following boys being included.

Online survey

A total of 1,513 responses were obtained from the online survey. Not all respondents answered all questions and hence, denominators presented vary across questions.

The majority of respondents were females (87.2%). Forty-five per cent of respondents were 55 years and older. Figure 2 shows the age groups of the respondents. The highest proportion of respondents were from NSW (31.5%), followed by VIC (26.6%) (refer to Figure 3). The majority of respondents worked in major cities (60.2%) followed by regional (33.8%) and remote areas (6.0%) (refer to Figure 4). There were respondents from all stakeholder groups, with just over half (51.4% [778/1,513]) of the respondents being GPs, 13.9% practice nurses and 11% (166/1,513) school-based nurse immunisers (refer to Table 9). Many respondents selected the ‘other’ option,

including local government immunisation team leaders and nurses, maternal and child health nurses, remote area nurses, midwives, pharmacists and gynaecologists.

Figure 2: Proportion of respondents by age group (n=1,513)

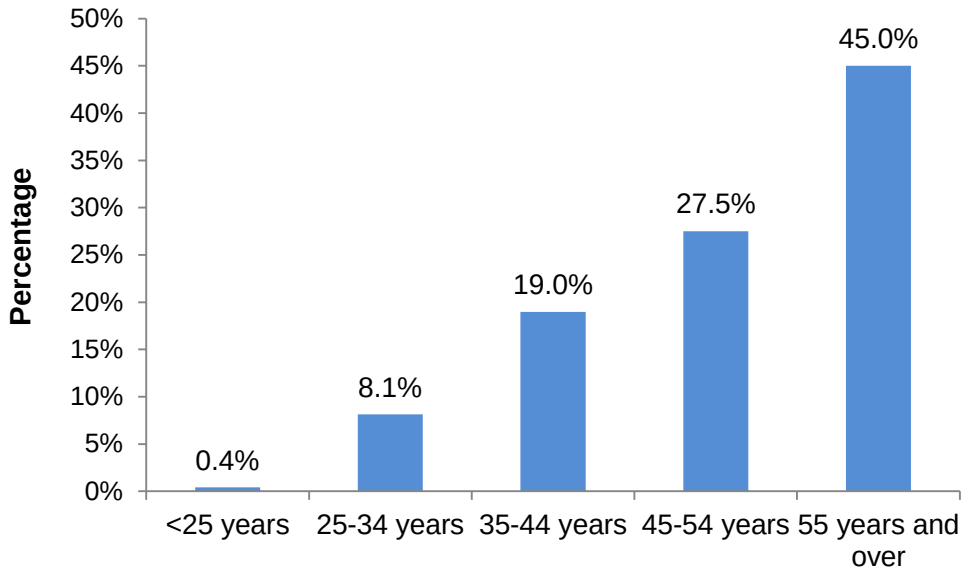


Table 9. Distribution of respondents by stakeholder group (n=1,513)

Respondent	n (%)
GP	778 (51.4)
School-based nurse immuniser	166 (11)
Practice nurse	210 (13.9)
Aboriginal Health Worker	5 (0.3)
Sexual health physician	9 (0.6)
Cervical screening manager	3 (0.2)
Other	342 (22.6)

Figure 3: Proportion of respondents by jurisdiction of employment (n=1,513)

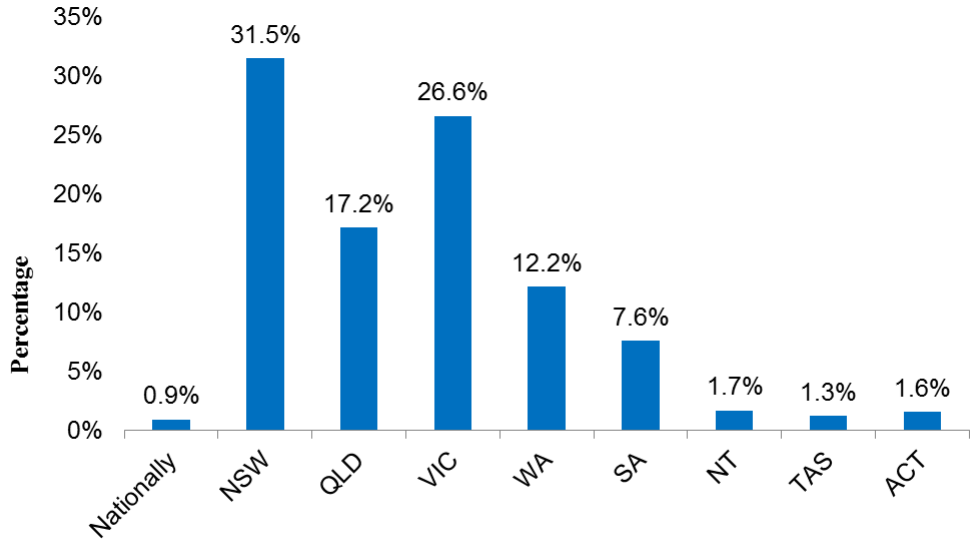
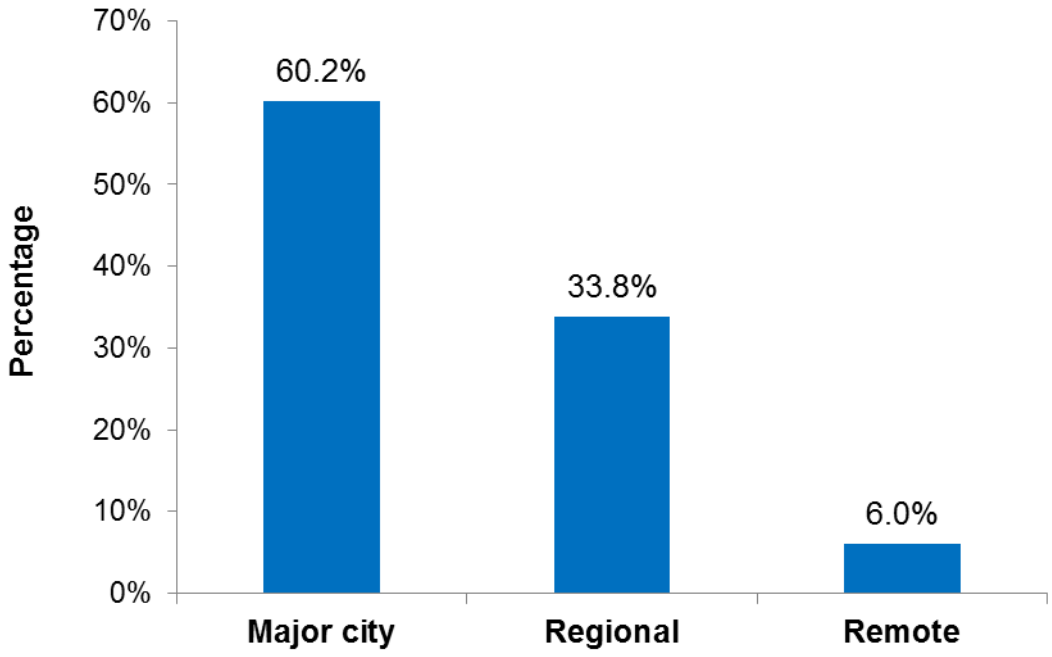


Figure 4: Proportion of respondents by location of practice/service (n=1,513)



Fifteen respondents worked in an ACCHS and five (0.3%) reported that they were Aboriginal health workers. Of these, only one Aboriginal health worker worked at an ACCHS.

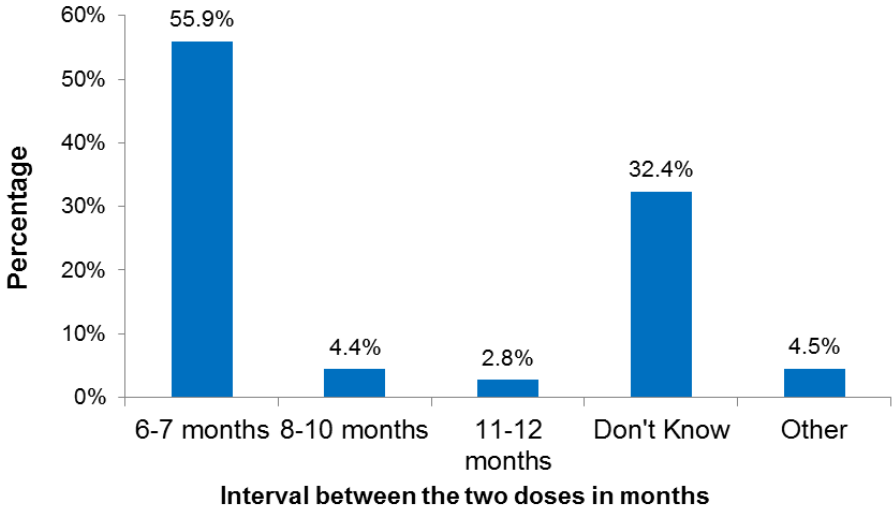
Change to a 2-dose schedule of 9vHPV vaccine

More than 47% (535/1,128) of respondents thought there were advantages of implementing the 2-dose 9vHPV vaccination program. However, a few (2.2%, 25) respondents thought that the 2-dose schedule had decreased coverage. Perceived advantages largely related to the increased convenience of delivering two doses, better acceptance by schools and students (particularly those who are needle-phobic), increased compliance with the course and being able to promote greater protection against HPV types with the increased valency.

> *"I believe that the 2 dose course is much easier to plan and implement through the schools and also better on the students' fear of getting a needle. It provided less disruption to the running of the schools and break in their lesson plans. I know the teachers are happier about this" (male school-based nurse immuniser, age group 45–54 years).*
>
> *"Health promotion about the increased valency helps to sell the program to parents" (female clinical nurse specialist age group 55–59 years).*

The majority of respondents (74.2% [837/1,128]) had experienced no issues with implementing the 9vHPV program, with 13.2% (149/1,128) reporting a few issues and 12.6% (142/1,128) responses being not applicable. Of the issues reported, the majority related to parental safety concerns, confusion about eligibility for 2- or 3-dose courses and parents requesting revaccination. In addition, 55.9% (631/1128) of respondents reported an interval of 6–7 months between the two doses of the vaccine in their school immunisation program or practice (refer to Figure 5).

Figure 5: Proportion of respondents reporting interval between the 2 doses of vaccine in their practice/program (n=1,128)



Although many respondents could not comment on any impact of the change to a 2-dose schedule on HPV vaccination coverage for adolescents aged <15 years in their area, most who did comment perceived that dose 1 coverage was unchanged (40.5%, [457/1,128]) but dose 2 coverage had

increased (39.3% [443/1,128]), while very few believed coverage for either dose 1 or 2 had decreased (refer to Table 10).

> *"It is easier with 2 doses for students to complete the full course. However due to the 6 month gap, the 2nd visit pushes into a busy time in the school year and many students are away, so still require catch ups. But it is one dose to be caught up so overall easier for families to complete course" (female school-based nurse immuniser, age group 35–44 years)*

Table 10. Perceived impact that a change from the 3-dose to 2-dose schedule has had on HPV vaccination coverage for adolescents aged <15 years (n=1,128)

	Increased coverage n (%)	No change n (%)	Decreased coverage n (%)	Don't Know or N/A n (%)
Dose 1	269 (23.9)	457 (40.5)	3 (0.3)	399 (35.4)
Dose 2	443 (39.3)	249 (22.1)	25 (2.2)	411 (36.4)

School-based vaccination program

Most respondents (n= 1,066) did not answer the question on the perceived factors impacting school-based HPV vaccination coverage in their area. The responses of those who answered this question (n=447, 70% of whom were nurses/midwives) are shown in Table 11.

Table 11. Perceived factors impacting school-based HPV vaccination coverage (n=447)

	Never n (%)	Rarely n (%)	Sometimes n (%)	Frequently n (%)	Don't Know or N/A n (%)
Absenteeism	3 (0.7)	21 (4.7)	142 (31.8)	124 (27.7)	157 (35.1)
Consent forms not returned	2 (0.5)	30 (6.7)	131 (29.3)	127 (28.4)	157 (35.1)
Inadequate education for parents	11 (2.5)	89 (19.9)	118 (26.4)	56 (12.5)	173 (38.7)
Parents not consenting	9 (2)	95 (21.3)	164 (36.7)	30 (6.7)	149 (33.3)
Student refusal	9 (2)	137 (30.7)	136 (30.4)	10 (2.2)	155 (34.7)

Staffing shortages	116 (26)	106 (23.7)	50 (11.2)	8 (1.8)	167 (37.4)

Additional comments on other factors impacting school-based HPV vaccination coverage area were as follows:

> *"Engagement of the school with the program - if they have a champion for the consent card return rate and coordination of the program as one of their single tasks, return rate is improved and sessions on the day run smoothly - if this is ad-hoc without any real ownership this is reflected in all parts of the process" (female immunisation team leader, age group 35–44 years)*

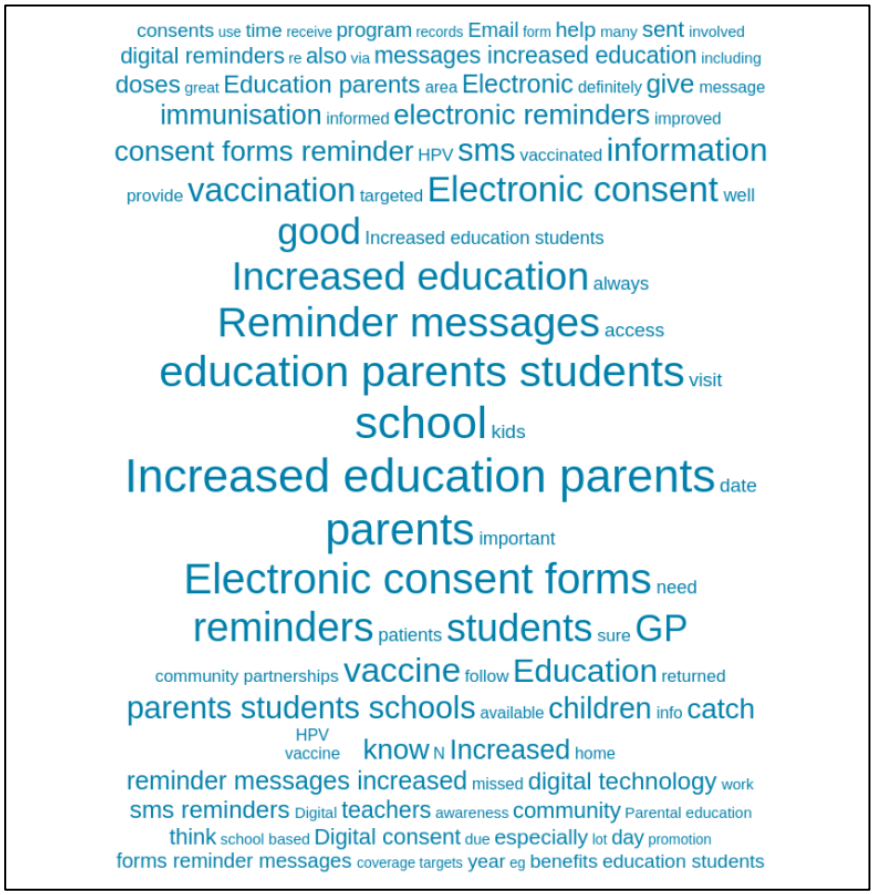
> *"There is plenty of information, brochures and links to websites given to parents. ……. Students themselves also need to be informed as so many have no idea what they are having. In most cases, they are the ones responsible for taking the forms home and bringing them to school in time. ……. Empowering students through their science or PDHE teachers I feel could be very beneficial" (female school-based nurse immuniser age group 55–59 years)*

Respondents were offered the opportunity to suggest strategies to improve school-based HPV vaccination coverage. The most commonly suggested strategies included:

- electronic consent forms
- increased education for parents.

> *"An option for electronic forms for those that prefer this but also an option for current consent cards for those that prefer this. Also all versions of consent cards should be available in other languages. The translated version should have English and other language on the same piece of paper so that there is no confusion for whoever is reading the form"* (female council nurse immuniser age group 55–59 years)

Comments provided (n = 849) regarding strategies to improve school-based HPV vaccination coverage are summarised in the word cloud below, with comments in larger text most frequently mentioned.



Community-based catch-up vaccination

There were mixed opinions from respondents about the adequacy of utilisation of community-based catch-up vaccination in their area, but it was generally perceived to be better for adolescents aged <15 years receiving 2 doses than those aged ≥15 years receiving 3 doses (refer to Table 12). Comments regarding the barriers to community catch-up vaccination included:

> *"Patients not had vaccine due to parents' refusal and then when they realise importance are too old to get free vaccination"* (female GP age group 55–59 years)

> *"The cost of the final dose in a catch up program is not covered by the scheme. If patients cannot afford it they may not be fully immunised"* (female GP, age group 45–54 years)

Table 12. Perception that community catch-up is adequately utilised (n=1,128)

	Yes n (%)	No n (%)	Don't Know n (%)
Age <15 years (2 doses)	439 (38.9)	276 (24.5)	413 (36.6)
Age ≥15 years (3 doses)	309 (27.4)	375 (33.2)	444 (39.4)

Forty-nine per cent of the respondents (548/1,128) were satisfied with the relationship between the school-based HPV vaccination program and primary care providers in their area. However, over a fifth were unsatisfied (22.0% [248/1,128]) and the rest did not answer (29.4% [332/1,128]).

Respondents commented that information sharing and communication were key factors to improving the relationship between the school-based immunisers and primary care providers.

HPV vaccination in population subgroups

Five hundred and forty one respondents reported that their work involved HPV vaccination in schools or communities with significant representation of various population subgroups at risk of lower coverage:

- Aboriginal and Torres Strait Islander people (46.4% [251/541])
- CALD people (53.2% [288/541])
- socioeconomically disadvantaged people (57.7% [312/541])
- other diverse population groups (21.3% [115/541]).

These other diverse population groups included refugees, special schools, boarding school children, Pacific Islander population, alternative schooling pathways, home school parents, young people in out of home care and the LGBTQ population.

HPV vaccine hesitancy

While 28.4% (310/1,090) of respondents had not encountered any instances of HPV vaccine hesitancy, 47.3% (515/1,090) had encountered refusal of HPV vaccination and 36.2% (395/1,090) had encountered delayed HPV vaccination.

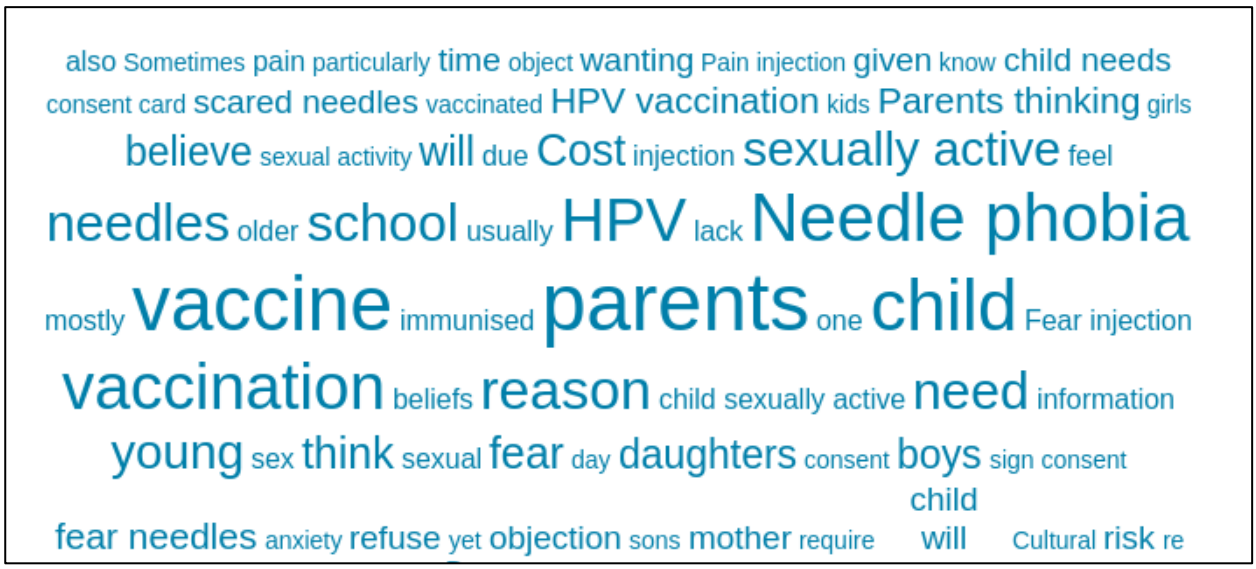
Regarding HPV vaccine hesitancy, 44.2% (351/795) had encountered this rarely; 42.9% (341/795) sometimes; 5.5% (44/795) frequently; and 1.3% (10/795) very frequently. The perceived importance of reasons encountered in relation to HPV vaccine hesitancy is shown in Table 13, with safety concerns most commonly perceived as very important (36.1% [279/773] of respondents).

Table 13. Perceived importance of reasons for HPV vaccine hesitancy

	Not important n (%)	Slightly important n (%)	Moderately important n (%)	Very important n (%)	Don't know n (%)
Safety concerns (n=773)	101 (13.1)	159 (20.6)	154 (19.9)	279 (36.1)	80 (10.4)
Religious objection (n=739)	339 (45.9)	97 (13.1)	83 (11.2)	91 (12.3)	129 (17.5)

Philosophical objection (n=746)	213 (28.6)	128 (17.2)	145 (19.4)	12 (16.1)	140 (18.8)

Reasons for vaccine hesitancy are summarised in the word cloud below.



> *"Some parents believe it is an unnecessary vaccine for this age group as they are not yet sexually active. Parents and students are not fully educated that this vaccine is most effective when given early prior to any sexual activity commencing"* (female business support worker for immunisation service, age group 45–54 years).

Influence of social media

Of 1,090 respondents who answered this question, 29.4 % (320) reported that social media has a positive impact or very positive impact on the uptake of HPV vaccination, with only 12.8% (140/1,090) respondents perceiving social media having a negative or very negative influence. Many respondents (37.2% [405/1,090]) did not know if social media played any role.

Vaccine safety

The majority of respondents perceived no change in frequency (72.3%) or type (70.6%) of AEFI with 9vHPV vaccine compared with 4vHPV vaccine (refer to Figures 6 and 7). 29 (2.7%) respondents perceived a decrease in the frequency of adverse events and only 8 (0.7%) respondents perceived an increase in these events. Several respondents commented that syncope was still relatively common with 9vHPV vaccine but more said the frequency is decreasing. No other significant adverse events of concern were reported in the comments.

Figure 6: Respondents' perception of change in frequency of adverse events following vaccination with 9vHPV compared with 4vHPV vaccine (n=1,085)

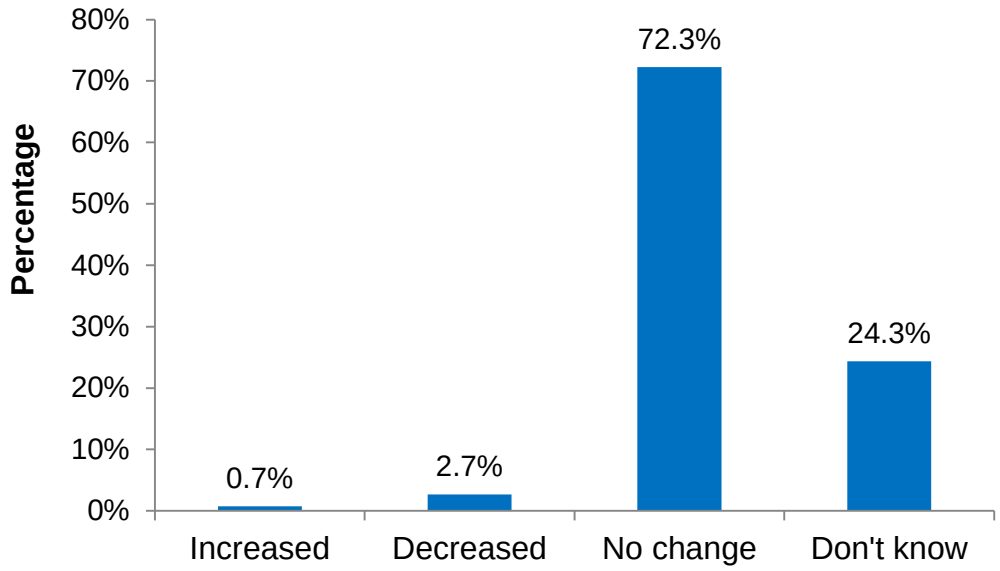
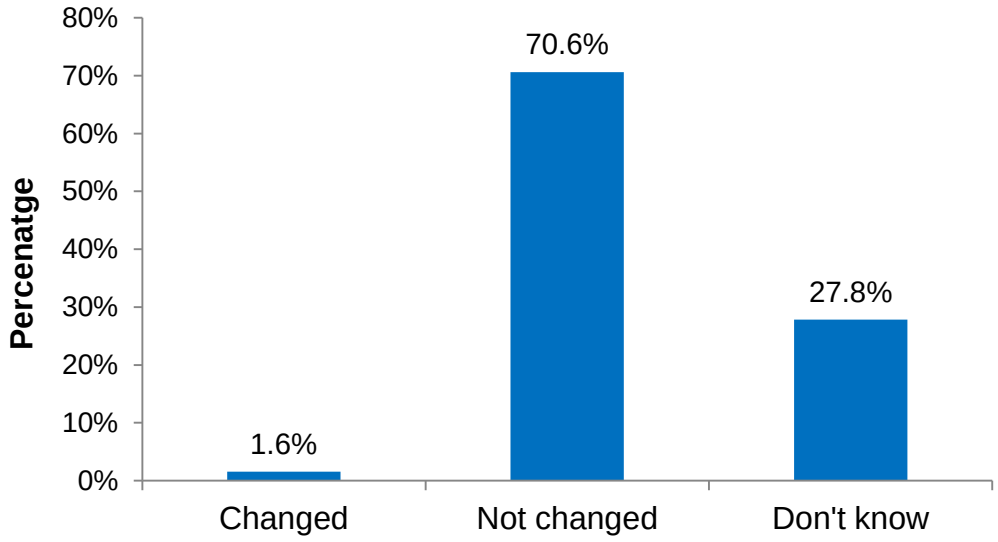


Figure 7: Respondents' perception of change in type of adverse events following vaccination with 9vHPV vaccine compared with 4vHPV vaccine (n=1,085)



HPV vaccination reporting

The majority of respondents (63.9%) were satisfied with the transition of HPV vaccination reporting from the HPV Register to AIR and agreed that all HPV vaccinations they provided get reported to AIR. Refer to Table 14 for respondents' views on the transition.

Table 14. Respondent opinions on transition of HPV vaccination reporting to AIR (n=1,072)

	Strongly disagree n (%)	Disagree n (%)	Neutral n (%)	Agree n (%)	Strongly agree n (%)	Don't know n (%)
Satisfied with the transition	22 (2.1)	28 (2.6)	166 (15.5)	400 (37.3)	400 285 (26.6)	171 (16)
All vaccinations I provide get reported to AIR	23 (2.2)	19 (1.8)	63 (5.9)	338 (31.5)	469 (43.8)	160 (14.9)

Additional comments regarding the transition are listed below.

> *"Changing to the AIR made the information more accessible to providers and the reporting is much more simplified with many medical records systems linked to AIR and not the HPV register. It was an excellent move"* (female immunisation nurse, age group 35–44 years)
>
> *"Most in the community did not know the HPV register existed or if they did, wouldn't know how to access it. Most people are very aware of the Australian Immunisation Register"* (female nurse immuniser, age group 45–54 years)
>
> *"Easier to look up what they have had at school, previously we couldn't do that from medical centres. Therefore less phone calls to the school team to ask about records."* (female school-based nurse immuniser, age group 45–54 years)
>
> *"While I am happy that the HPV gets put onto AIR - how this occurs is much, much, much more labour intensive for nurses now. Before it was a large bulk import done by admin staff - now each child needs to be done individually and it takes at least 5 minutes per child to enter onto CHIS [CHIS stands for Community Health Information System] which transfers to AIR. I hate it!"* (female school-based nurse immuniser, age group 35–44 years)

Cervical screening

Only those respondents who indicated that their work involved cervical screening were asked questions about cervical screening. Their level of agreement with statements pertaining to cervical screening and HPV vaccination is shown in Table 15. Responses to any influence of HPV vaccination on participation in cervical screening were relatively varied, but almost half of

respondents (48.6% [341/702]) agreed and 9.3% (65/702) strongly agreed that females who have received HPV vaccine have adequate knowledge that they still require cervical screening.

Table 15. Agreement with statements on cervical screening and HPV vaccination program (n=702)

	Strongly Disagree n (%)	Disagree n (%)	Neutral n (%)	Agree n (%)	Strongly Agree n (%)	Don't Know n (%)
Receiving HPV vaccine influences the uptake of cervical screening	24 (3.4)	129 (18.4)	274 (39)	148 (21.1)	26 (3.7)	101 (14.4)
Females who have received HPV vaccine are MORE likely to undergo cervical screening than unvaccinated females	21 (3)	184 (26.2)	216 (30.8)	122 (17.4)	27 (3.9)	132 (18.8)
Females who have received HPV vaccine are LESS likely to undergo cervical screening than unvaccinated females	33 (4.7)	225 (32.1)	211 (30.1)	96 (13.7)	9 (1.3)	128 (18.2)
Females who have received HPV vaccine have adequate knowledge that they still require cervical screening	8 (1.1)	117 (16.7)	120 (17.1)	341 (48.6)	65 (9.3)	51 (7.3)

Additional comments are listed below.

> *"I don't get the feeling that females really make an association between the HPV vaccine and cervical cancer screening. Also, there is a long time interval between when they are immunised as a teenager and when they start screening at 25 years"* (female GP, age group 35–44 years)
>
> *"Due to dislike of the cervical Pap smear process, some woman will use having had the HPV vaccine as an extra excuse in their mind to put off having Pap smears"* (female practice nurse, age 45–54 years)
>
> *"Many patients have been surprised that I have recommended cervical screening test ('but I've been immunised')"* (female GP, age group 35–44 years)

"The assumption by many who have received what is marketed as a 'cancer vaccine' is that the vaccination protects them from cervical cancer, so then why would they need to screen further for cancer" (female GP, age group 55–59 years)

Respondents also had mixed perceptions about whether the change to HPV-based cervical screening could have any impact on HPV vaccination uptake in Australia (Yes - 28.4% [199/702], No - 37.8% [265/702], Don't Know – 33.9% [238/702]).

Additional comments indicated that respondents largely believed that the change to HPV-based cervical screening could potentially increase HPV vaccination uptake through increased awareness about the link between HPV and cervical cancer.

"I have found more people interested in being vaccinated after they find out the new test is looking at HPV" (female GP, age group 35–44 years)

*"I'm hopeful it will spark more conversation about HPV and its role in cervical cancer and therefore the role of vaccination in preventing it" (*female GP, age group 35–44 years)

Disease burden

Respondents who indicated that they saw patients with HPV-related conditions were asked questions on disease burden. Perceptions of decline in disease burden varied: 63.4% (433/683) of respondents perceived a decrease in genital warts in females; 60.8% (415/683) perceived a decrease in cervical HGA and 37.8% (258/683) perceived a decrease in genital warts in males (refer to Table 16).

Table 16. Perceived changes in HPV-related conditions since introduction of HPV vaccination (n=683)

	No decrease n (%)	Small decrease n (%)	Moderate decrease n (%)	Large decrease n (%)	Don't know or N/A n (%)
High-grade cervical abnormalities	69 (10.1)	167 (24.5)	145 (21.1)	103 (15.1)	199 (29.1)
Genital warts in females	50 (7.3)	123 (18)	137 (20.1)	173 (25.3)	200 (29.3)
Genital warts in males	64 (9.4)	75 (11)	93 (13.6)	90 (13.2)	361 (52.9)

Factors positively influencing the program

The perceived importance of factors in positively influencing coverage and impact of the National HPV Vaccination Program are shown in Table 17. The school-based program (91.2%); funded vaccine (87.9%); cancer prevention promotion (87.2%); community catch-up option (84.7%); gender-neutral program (78.8%); and reduction to a 2-dose schedule (65.9%) were considered 'very important' by respondents.

Table 17. Perceived importance of factors in positively influencing coverage and impact of the National HPV Vaccination Program (n=1,024)

Factor	Not important n (%)	Slightly important n (%)	Moderately important n (%)	Very important n (%)	Don't know n (%)
Funded on the NIP	8 (0.8)	20 (2)	48 (4.7)	900 (87.9)	48 (4.7)
School-based program	3 (0.3)	4 (0.4)	51 (5)	934 (91.2	32 (3.1)
Community catch-up option	4 (0.3)	25 (2.4)	97 (9.5)	867 (84.7)	32 (3.1)
Gender-neutral program	34 (3.3)	28 (2.7)	80 (7.8)	807 (78.8)	75 (7.3)
Reduction to 2-dose schedule	10 (1)	61 (6)	221 (21.6)	675 (65.9)	57 (5.6)
Promotion of HPV vaccination as cancer prevention	5 (0.5)	14 (1.4)	86 (8.4)	893 (87.2)	26 (2.5)

Other factors that respondents perceived as positively influencing the program included education, promotion through social media and promotion of the vaccine as also preventing genital warts and other cancers.

The risk of inducing complacency regarding cervical screening by promoting the vaccine as preventing cervical cancer was also expressed by one respondent:

> *"Promoting a vaccine as cancer prevention when it doesn't fully do so (because of other carcinogenic strains not included in the vaccine) and likely to make many women complacent about ongoing cervical screening."* (female GP aged 55-59 years)

Factors negatively influencing the program

Respondents' perceptions of the importance of factors negatively influencing coverage and impact of the National HPV Vaccination Program are shown in Table 18. The negative factors perceived as 'very important' were unreturned consent forms (47.3%); school absenteeism (46.8%); concerns about HPV vaccine safety (38.0%); concerns about promoting promiscuity or early sexual initiation (31.8%); lack of agreed national HPV vaccine coverage target (26.6%); cultural or religious barriers (26.4%); and social stigma around HPV as an STI (24.6%).

Table 18. Perceived importance of factors negatively influencing coverage and impact of the national HPV vaccination program (n=1,024)

Factor	Not important n (%)	Slightly important n (%)	Moderately important n (%)	Very important n (%)	Don't know n (%)
School absenteeism	15 (1.5)	144 (14.1)	298 (29.1)	479 (46.8)	88 (8.6)
Return of consent forms	16 (1.5)	99 (9.7)	259 (25.3)	484 (47.3)	167 (16.3)
Lack of agreed national HPV vaccine coverage target	90 (8.8)	149 (14.6)	241 (23.5)	272 (26.6)	272 (26.6)
Social stigma around HPV as a STI	176 (17.2)	229 (22.4)	237 (23.1)	252 (24.6)	130 (12.7)
Parental concern about HPV vaccine safety	34 (3.3)	236 (23.1)	288 (28.1)	389 (38)	77 (7.5)
Parental concern about promoting promiscuity or early sexual initiation	102 (10)	255 (24.9)	241 (23.5)	326 (31.8)	100 (9.8)
Cultural or religious barriers	87 (8.5)	274 (26.8)	240 (23.4)	270 (26.4)	153 (14.9)

Other negative factors identified included anti-vaccination beliefs and misperception that the vaccine is only for females.

> *"Lack of understanding by many parents that this vaccine is as important for boys as well as girls and can prevent many cancers in both genders"* (female GP, age group 55–59 years)

WHO cervical cancer elimination target

The majority of respondents (84.4%) believed that Australia can achieve the WHO cervical cancer elimination target of 90% of girls fully vaccinated by age 15 years by 2030, with a small proportion not believing this was possible and some being unsure (refer to Table 19).

Table 19. Perceptions about the WHO cervical cancer elimination target (n=1,024)

	Respondents, n (%)
Achievable	864 (84.4)
Not achievable	47 (4.6)
Don't know	113 (11)

Additional comments largely demonstrated that increased education and focus on consent form return are required to achieve this target, and this would be pose a challenge to achieving this coverage target in all areas (e.g. remote areas and those with high levels of vaccine refusal) and population subgroups (e.g. Aboriginal and Torres Strait Islander people).

> *"Only if the [program] is tweaked. I feel there should be more responsibility on the schools / teachers to assist with the return of consent forms. This totally relies on the school to decide if they want to assist us at the moment. Some schools are great, some are terrible. The ones that have no desire to chase up consent forms have no consequences, return rates are low, vaccination rates are low and it's almost impossible for us to chase up these students"* (female school-based nurse immuniser, age group 55–59 years)

> *"90% very high - many girls at this age have needle phobias, parents not quite as vigilant about immunisation with teens as infants"* (female practice nurse, age group 45–54 years)

Achievements of the National HPV Vaccination Program

The majority of respondents were satisfied or very satisfied with the achievements to date of the National HPV Vaccination Program relating to local and national coverage and disease impacts (refer to Table 20).

Table 20. Satisfaction with achievements to date of the National HPV Vaccination Program (n=1,024)

Achievement	Very dissatisfied n (%)	Dissatisfied n (%)	Neutral n (%)	Satisfied n (%)	Very satisfied n (%)	Don't know n (%)
Local vaccine coverage	11 (1.1)	15 (1.5)	92 (9.0)	475 (46.4)	292 (28.5)	139 (13.6)
National vaccine coverage	6 (0.6)	14 (1.4)	138 (13.5)	406 (39.7)	159 (15.5)	301 (29.4)
Impact on disease burden	8 (0.8)	8 (0.8)	79 (7.7)	426 (41.6)	362 (35.4)	141 (13.8)

Successes and challenges of HPV vaccination in Aboriginal and Torres Strait Islander people

A total of 192 respondents provided a response to the question on successes and challenges of HPV vaccination in Aboriginal and Torres Strait Islander people. Successes were reported by 81 of 192 (42.2%) respondents and of these home visits were identified as a successful initiative reported by 16 (19.8%), with the rest recounting initiatives such as ensuring flexible arrangements

while engaging with Aboriginal and Torres Strait Islander people. Overall, stakeholders perceived that the 2-dose schedule has been better than the 3-dose one, reported a favourable outcome of the HPV vaccination program in Aboriginal and Torres Strait Islander people and perceived that the program was actually better than in the mainstream population.

> *"As with anything, we generally get good results from all of these areas and if we don't it is not because of the type of 'group' they are classified in, it is because of the individual family. We also utilise Aboriginal Liaison Officers for those families who are very chaotic"* (female school-based nurse immuniser, age group 45–54 years)

> *"Aboriginal people strongly support vaccination and we need to recognise and build on this strength"* (female GP, age group 45–54 years)

Building relationships with the Aboriginal and Torres Strait Islander people was reported to be a key factor leading to the success of the program.

> *"I work a lot with Indigenous populations and have found that it's all about building relationships with these populations.… I also work off overdue lists that for some reason the students have fallen through the cracks.… There is a lot of work chasing parents and students outside of the running of the program"* (male school-based nurse immuniser, age group 45–54 years)

Of the 192 respondents who provided a response to the question on challenges of HPV vaccination, 174 (90.6%) identified a challenge in Aboriginal and Torres Strait Islander populations. Returning the consent form was the most important challenge reported, by 40 of 174 (23%) respondents, followed by absenteeism (15.5% [27/174]), language barrier (10.9% [19/174]), lack of awareness (9.2% [16/174]), loss to follow up (4% [7/174]), frequent change of contact details (4% [7/174]) and fear factor, including needle phobia (2.3% [4/174]). A range of diverse reasons were reported by 31% (54/174) of respondents, including issues of weather, sorry business and the need for extensive follow-up work.

> *"It is always harder to get consent forms returned for these young people and when we do get consents returned, these are the students who are often absent on the immunisation day. It is often a challenge to follow these students up successfully."* (female school-based nurse immuniser, age group 55–59 years)

Despite these challenges, 16 of 81 (19.8%) stakeholders reported improvement in immunisation coverage.

> *"Our Indigenous girls are in boarding school- it takes some time and effort to ensure consent forms are returned (the school nurse is responsible for this) but we have achieved close to 100%"* (female school-based nurse immuniser, age group 45–54 years)

> *"Indigenous girls [sic] very accepting of vaccination…….Only one mother has said that vaccine causes many health problems and refused her daughter's vaccination."* (female GP, age group 55–59 years)

Summary/discussion

The key stakeholder interviews and online survey provided many valuable perspectives on the National HPV Vaccination Program from stakeholders involved at all levels of the program, from immunisation providers to national government representatives. The findings provide valuable insights into what is currently working well and the perceived barriers to enhancing outcomes and impacts of the program in Australia, along with recommendations to overcome these barriers.

The change to a 2-dose schedule of 9vHPV vaccine was well received and had many benefits for jurisdictions, providers and the public. However, the major challenges included reduced opportunities for school-based catch-up vaccinations and the 6–12 months dosing interval leading to dose 2 given late in the school year when absenteeism is higher, which have led to a disappointing perceived impact of the change on coverage compared to what had been broadly anticipated.

The major barriers to achieving higher coverage in the school-based vaccination program were largely identified as reliance on return of paper consent forms and absenteeism. Identified enablers to improve consent form return include school immunisation teams having access to parent contact details and resources to conduct follow up of unreturned forms; appropriate consent forms and information available for population subgroups with different languages and levels of literacy; increased education for students to increase understanding and encourage their participation in the consent form process; and supportive school staff who engage with students and assist with ensuring consent form return. While almost all key stakeholders believe that electronic consent forms would assist with consent form return, only two jurisdictions have been able to progress to developing this technology to date.

Catch-up vaccination remains essential, given the challenge of school absenteeism. School-based catch-up is generally more convenient for families and leads to measurable increases in HPV vaccination coverage, but is conducted by inconsistent methods across providers and not conducted at all in some jurisdictions. Increased resources to improve capacity to provide school-based catch-up vaccination across the country would likely be beneficial. Where available, free council immunisation clinics were generally considered a more effective alternative method of catch-up vaccination than reliance on visiting a GP.

Various enablers of and challenges to HPV vaccination were identified in population subgroups at risk of lower coverage, including Aboriginal and Torres Strait Islander and CALD populations. Participants outlined many initiatives currently in development or those that were implemented across Australia in the last 5 years to increase HPV vaccination coverage in these population subgroups. This suggests concerted efforts are underway in Australia to increase the equity of the HPV vaccination program and its impacts across different population groups. A common theme among stakeholders was that the identification of people within these subgroups can be a challenge and hence, assessing the effectiveness of these initiatives is likely to be a challenge too.

Regarding vaccine safety, in keeping with strong evidence from the literature, key stakeholders reported no concerns about HPV vaccine safety. Continued education on the proven safety and efficacy of HPV vaccines and rationale for vaccination at a young age were thought to possibly assist with improving vaccine coverage among the relatively small group of parents known to be hesitant about HPV vaccine. Most key stakeholders perceive vaccine hesitancy to be having little negative impact on HPV vaccination coverage in Australia. However, the potential for vaccine-hesitant views to spread rapidly on social media and need to maintain vigilance and monitor public attitudes towards HPV vaccination were highlighted.

Almost all stakeholders believed that Australia could achieve the WHO cervical cancer elimination target of 90% course completion for females aged 15 years by 2030, but that increase in effort, support for the program and development of strategies were required to achieve this. Many recommendations were suggested by stakeholders to increase HPV vaccination coverage, which largely related to improved processes for consent form return, increased education, stronger messaging around the benefits of vaccination, improved vaccination reporting and quality of data reports available and strategies to improve vaccination coverage in key population subgroups.

Some stakeholders also suggested reducing the schedule to a single dose, which would assist Australia in achieving the WHO coverage target. Emerging evidence indicates that a single dose schedule is effective; however, the evidence will require further monitoring to inform future decisions.

The opportunity for enhanced collaboration between the National HPV Vaccination Program and the Cervical Screening Program was also highlighted by many stakeholders in the wake of the transition to HPV-based cervical screening. This transition presents an opportunity for the relationship between the two programs to be improved to facilitate enhanced outcomes for both programs and a greater impact on cervical cancer prevention in Australia.

Limitations of the key stakeholder interview approach include that while some responses were based on the results of data or research findings known to the participant, many were anecdotal and the findings should be interpreted as such. In addition, given there is such a large degree of variation within Australia in the HPV vaccination program delivery, opinions provided from a national or jurisdictional perspective may not accurately reflect the processes and factors influencing the program in all regions.

Vaccination coverage

Aims

- To compare cumulative HPV vaccination coverage estimates in eligible birth cohorts calculated using the National HPV Vaccination Program Register (the HPV Register) numerator data and the Australian Bureau of Statistics (ABS) Estimated Resident Population (ERP) denominator data with HPV vaccination coverage estimates calculated using the Australian Immunisation Register (AIR) data.
- To assess cumulative HPV vaccination coverage as at 31 December 2019 in eligible birth cohorts, by gender, state/territory of residence, remoteness of area of residence, socioeconomic status (SES) and Aboriginal and Torres Strait Islander status.
- To assess HPV vaccination coverage by age 15 years over time (2016–2019), by gender, state/territory of residence and Aboriginal and Torres Strait Islander status.
- To calculate the number of HPV vaccine doses administered to adolescents aged <15 years during 2018 and 2019 and the proportion recorded as 9vHPV vaccine, by gender and state/territory of residence.
- To calculate the proportion of adolescents aged <15 years who commenced HPV vaccination in 2018 and completed the 2-dose 9vHPV vaccination schedule by 31 December 2019, by gender, state/territory of residence, remoteness of area of residence, SES, Aboriginal and Torres Strait Islander status
- To assess the interval between the administration of dose 1 and dose 2 of 9vHPV vaccine, by gender and state/territory of residence.
- To calculate the number/proportion of HPV vaccines administered to adolescents aged <15 years in primary care settings between 1 January 2018 and 31 December 2019, by state/territory of residence and gender.
- To calculate the number/proportion of HPV vaccines administered to adolescents aged 15 to <20 years in primary care settings between 1 July 2017 and 31 December 2019, by state/territory of residence and gender.

Methods

AIR and the HPV Register

The Australian Childhood Immunisation Register (ACIR) was established in 1996 by incorporating Medicare data on all children aged <7 years.[136] On 1 January 2016, the ACIR expanded to include all individuals aged up to 20 years, and then on 30 September 2016 expanded further to become the whole-of-life AIR.[137,138] All people registered with Medicare, Australia's universal healthcare system, are automatically added to AIR. Participation in AIR is 'opt-out' and so constitutes a nearly complete population register for Australian residents.[136] Individuals not enrolled in Medicare can

also be added to AIR via a supplementary number. Since 2001, vaccinations given overseas may be recorded if a provider endorses their validity. Data are transferred to AIR when a recognised immunisation provider supplies details of an eligible vaccination. This could occur either via medical practice management software or through direct data entry on the AIR website or by submitting paper encounter or history forms.

The HPV Register was established in 2008 by the VCS Foundation under contract with the Australian Government Department of Health to capture HPV vaccination encounters administered as part of the National HPV Vaccination Program. With the expansion of the ACIR to AIR, all data held in the HPV Register were transferred to AIR in late 2018. All HPV vaccinations given through school-based programs, as well as any HPV vaccinations given by other immunisation providers, are now reported directly to AIR.

Historical estimates of HPV coverage – comparison between HPV Register and AIR estimates

The last published vaccination coverage estimates from the HPV Register were for the cohort of adolescents aged 12–19 years as at 30 June 2017.[33] We compared cumulative HPV vaccination coverage estimates for each vaccine dose calculated using data from the HPV Register with coverage estimates calculated using AIR data. The HPV Register coverage estimates were calculated for female and male adolescents by year of age using the number of adolescents in each age group with a record on the HPV Register of a vaccine received by 30 June 2018 as the numerator and ABS ERP by Single Year of Age[139] data as at 30 June 2017 as the denominator. These estimates were compared with AIR data coverage estimates calculated for female and male adolescents by year of age using the number of adolescents in each age group with an AIR record of a HPV vaccination received by 30 June 2018 as the numerator and the number of Medicare- registered adolescents in each age group as at 30 June 2017 as the denominator.

Assessing current cumulative HPV vaccination coverage

AIR data, as at 29 February 2020, was downloaded from the Services Australia Secure File Transfer Protocol (SFTP) portal and vaccine encounters up to 31 December 2019 were included to assess current cumulative HPV vaccination coverage estimates. This allowed for a 2-month lag period for late notification of HPV vaccinations to AIR. Eligible year-wide birth cohorts for female and male adolescents aged 12 to <20 years as at 31 December 2019 were used to assess cumulative HPV vaccination coverage. The proportion of adolescents vaccinated was calculated using the number of adolescents in each cohort with a record of a HPV vaccine encounter between 1 January 2007 and 31 December 2019 as the numerator and the number of Medicare-registered adolescents in each cohort as the denominator. Cumulative coverage was assessed separately for each dose of HPV vaccine by gender, state/territory of residence, remoteness of area of residence (see details of methods below), SES (see details of methods below) and Aboriginal and Torres Strait Islander status (see details of methods below).

Assessing trends in HPV vaccination coverage at 15 years

The World Health Organization (WHO) recommends assessing coverage at 15 years of age for the purpose of international comparison over time. As HPV vaccination in Australia is delivered routinely in early high school, usually around the age of 12–13 years, all adolescents have had the opportunity to complete the vaccination course by age 15 years. AIR data, as at 29 February 2020, with vaccine encounters up to 31 December 2019, were used to assess trends in HPV vaccination coverage between 2016 and 2019 for females and males aged 15 years. HPV vaccination coverage was calculated using the number of 15-year-olds recorded on AIR to have received dose 1, dose 2 and/or dose 3 of the HPV vaccine as the numerator and the total number of Medicare-registered adolescents in the cohort of 15 years in the year of interest as the denominator. HPV vaccination coverage estimates at 15 years of age were calculated separately for doses 1, 2 and 3 by gender, state/territory of residence and Aboriginal and Torres Strait Islander status. It is important to note that in 2019 the majority of adolescents in New South Wales (NSW, which introduced the 2-dose schedule in 2017), South Australia (SA) and Western Australia (WA) had transitioned to the 2-dose schedule, which had been implemented in 2018, while the majority of adolescents in the Australian Capital Territory (ACT), Victoria (VIC), Queensland (QLD), Tasmania (TAS) and the Northern Territory (NT) were still on the 3-dose schedule.

Assessing uptake of 9vHPV vaccine in adolescents aged <15 years

Using AIR data as at 29 February 2020, the number of HPV vaccination encounters was determined for the 2018 and 2019 calendar years by gender and state/territory of residence for adolescents aged <15 years. The proportion of these HPV vaccines that were recorded as 9vHPV vaccine was then calculated. The age distribution of adolescents receiving the first dose of 9vHPV vaccine was calculated by gender and state/territory of residence. Of the adolescents aged <15 years with 9vHPV vaccine dose 1 recorded on AIR in 2018, the proportion who also received dose 2 by 31 December 2019 was calculated by gender, state/territory of residence, remoteness/SES of area of residence and Aboriginal and Torres Strait Islander status. The number of dose 1 and dose 2 9vHPV vaccinations recorded each month throughout 2018 and 2019 was also determined for those commencing the 2-dose schedule in 2018 by gender and state/territory of residence, as was the interval (length of time) between dose 1 and dose 2. Vaccination encounters for 9vHPV dose 1 and dose 2 in 2018 and 2019 were also analysed by provider type in each state/territory for both female and male adolescents.

Assessing uptake of HPV vaccine in adolescents aged 15 to <20 years

Using AIR data as at 29 February 2020, the number of HPV vaccination encounters recorded on AIR as administered to adolescents aged 15 to <20 years between 1 July 2017 and 31 December 2018 was determined by gender and state/territory of residence for each immunisation provider type and for dose 1, dose 2 and dose 3 separately.

Aboriginal and Torres Strait Islander status

Aboriginal and Torres Strait Islander people represent approximately 3.3% of the Australian population,[140] and status on AIR is recorded as 'Indigenous', 'non-Indigenous' or 'unknown', as reported by the child's parent/carer to Medicare, the young person themselves to Medicare (if 14 years or older) or by the immunisation provider to AIR. The 0.4% of children whose Indigenous status was not specified were classified as non-Indigenous for the purposes of this analysis. When comparing the historical HPV Register data with the AIR data, it should be noted that although the HPV Register collected Indigenous status, this was not a mandatory field, as per the underlying legislation, and was collected directly from consent forms. Data improved markedly over time, but no national estimates were possible.[43,141]

Remoteness of area of residence

Area of residence was defined as 'Major cities', 'Inner regional', 'Outer regional', 'Remote' and 'Very remote' using the Accessibility/Remoteness Index of Australia (ARIA++).[142] For analysis in this report, we combined the two 'Regional' categories ('Inner Regional' and 'Outer Regional') into one category and the two 'Remote' categories ('Remote' and 'Very Remote') into one category. The ARIA Accessibility/Remoteness category was assigned for each individual using their recorded postcode of residence on AIR.

Socioeconomic status

To assess vaccination coverage by SES, we used ABS Socio-Economic Indexes for Areas (SEIFA) Index of Education and Occupation.[143] The SEIFA index category in deciles (with decile one the most disadvantaged) was assigned for each individual using their recorded postcode of residence on AIR.

Results

Cumulative HPV vaccination coverage – comparison between HPV Register and AIR estimates

Vaccination coverage estimates using the HPV Register data for all doses were universally higher than the AIR estimates for females aged 13–18 years (range 0.3–3.4%) and males aged 13–17 years (range 0.8–3.2%) (refer to Tables 21 and 22). This is a consequence of the larger Medicare enrolment population denominator in each of these birth cohorts. For 19-year-old females and 18–19-year-old males, the Medicare enrolment population denominator is lower than the ABS ERP denominator, and the coverage estimates for each dose are higher using AIR data. In females and males aged 13 years, the higher number of doses in AIR than in the HPV Register may reflect the inclusion of doses given in general practice in 2017 and 2018 that were reported directly to AIR. The lower dose numbers recorded in AIR for 16–19-year-old females and males could possibly relate to either a greater ability of AIR to de-duplicate notifications using Medicare numbers and

enrolment history in this age group or possibly to limitations in AIR's ability to match notifications held by the HPV Register in this age group to Medicare enrolments (meaning the notification is excluded) as Medicare number was not a mandatory field in the HPV Register notifications.

Table 21. HPV Register dose 1–3 HPV vaccine coverage estimates versus AIR dose 1–3 HPV vaccine coverage estimates, females

	National HPV Register & ABS Estimated Resident Population Method*					Australian Immunisation Register Method†				Difference between HPV Register and AIR
Age at 30 June 2017, years	Population (ABS ERP as at June 2017)	Number of doses recorded on HPV Register (% coverage)				Population (Medicare enrolment as at June 2017)	Number of doses recorded on AIR (% coverage)			
13	138602	Dose 1:	121862	(87.9%)		143879	Dose 1:	122881	(85.4%)	2.5
		Dose 2:	116038	(83.7%)			Dose 2:	117182	(81.4%)	2.3
		Dose 3:	101325	(73.1%)			Dose 3:	103577	(72.0%)	1.1
14	137916	Dose 1:	122943	(89.1%)		142973	Dose 1:	122542	(85.7%)	3.4
		Dose 2:	118707	(86.1%)			Dose 2:	118891	(83.2%)	2.9
		Dose 3:	110671	(80.2%)			Dose 3:	112022	(78.4%)	1.8
15	137984	Dose 1:	122666	(88.9%)		142570	Dose 1:	121991	(85.6%)	3.3
		Dose 2:	118679	(86.0%)			Dose 2:	118494	(83.1%)	2.9
		Dose 3:	110690	(80.2%)			Dose 3:	111216	(78.0%)	2.0
16	141215	Dose 1:	122430	(86.7%)		143965	Dose 1:	121285	(84.3%)	2.4
		Dose 2:	118280	(83.8%)			Dose 2:	117645	(81.7%)	2.1
		Dose 3:	110882	(78.5%)			Dose 3:	110739	(76.9%)	1.6
17	144001	Dose 1:	122110	(84.8%)		146194	Dose 1:	120642	(82.5%)	2.3
		Dose 2:	117892	(81.9%)			Dose 2:	116996	(80.0%)	1.9
		Dose 3:	109747	(76.2%)			Dose 3:	109367	(74.8%)	1.4

18	146652	Dose 1:	117311	(80.0%)		146658	Dose 1:	115754	(78.9%)	1.1
		Dose 2:	112212	(76.5%)			Dose 2:	111287	(75.9%)	0.6
		Dose 3:	103367	(70.5%)			Dose 3:	102905	(70.2%)	0.3
19	152571	Dose 1:	113799	(74.6%)		147742	Dose 1:	111080	(75.2%)	-0.6
		Dose 2:	108325	(71.0%)			Dose 2:	106234	(71.9%)	-0.9
		Dose 3:	98898	(64.8%)			Dose 3:	97396	(65.9%)	-1.1

* HPV Register estimates calculated using the number of adolescents in each age group with a record on the HPV Register of a vaccine received by 30 June 2018 as the numerator, and the Australian Bureau of Statistics Estimated Resident Population by Single Year of Age as at 30 June 2017 as the denominator.

† AIR data estimates calculated using the number of adolescents in each age group with an AIR record of a HPV vaccine received by 30 June 2018 as the numerator, and the number of Medicare-registered adolescents in each age group as at 30 June 2017 as the denominator.

Table 22. HPV Register dose 1–3 HPV vaccine coverage estimates versus AIR dose 1–3 HPV vaccine coverage estimates, males

	National HPV Register & ABS Estimated Resident Population Method*					Australian Immunisation Register Method†				Difference between HPV Register and& AIR
Age at 30 June 2017, years	Population (ABS ERP as at June 2017)	Number of doses recorded on HPV Register (% coverage)				Population (Medicare enrolment as at June 2017)	Number of doses recorded on AIR (% coverage)			
13	147500	Dose 1:	125318	(85.0%)		152839	Dose 1:	126889	(83.0%)	2.0
		Dose 2:	118513	(80.3%)			Dose 2:	119817	(78.4%)	1.9
		Dose 3:	99875	(67.7%)			Dose 3:	102170	(66.9%)	0.8
14	144913	Dose 1:	124811	(86.1%)		150379	Dose 1:	124621	(82.9%)	3.2
		Dose 2:	120094	(82.9%)			Dose 2:	120404	(80.1%)	2.8
		Dose 3:	111122	(76.7%)			Dose 3:	112454	(74.8%)	1.9
15	145161	Dose 1:	123458	(85.0%)		150114	Dose 1:	123063	(82.0%)	3.0
		Dose 2:	118931	(81.9%)			Dose 2:	119002	(79.3%)	2.6
		Dose 3:	110197	(75.9%)			Dose 3:	110936	(73.9%)	2.0
16	149155	Dose 1:	120750	(81.0%)		152042	Dose 1:	119868	(78.8%)	2.2
		Dose 2:	116489	(78.1%)			Dose 2:	115972	(76.3%)	1.8
		Dose 3:	108424	(72.7%)			Dose 3:	108336	(71.3%)	1.4
17	150325	Dose 1:	114608	(76.2%)		153254	Dose 1:	113601	(74.1%)	2.1

		Dose 2:	110000	(73.2%)			Dose 2:	109313	(71.3%)	1.9
		Dose 3:	98941	(65.8%)			Dose 3:	98705	(64.4%)	1.4
18	154655	Dose 1:	107299	(69.4%)		153925	Dose 1:	106843	(69.4%)	0.0
		Dose 2:	102441	(66.2%)			Dose 2:	102225	(66.4%)	-0.2
		Dose 3:	90703	(58.6%)			Dose 3:	90881	(59.0%)	-0.4
19	160650	Dose 1:	52229	(32.5%)		154979	Dose 1:	51959	(33.5%)	-1.0
		Dose 2:	49110	(30.6%)			Dose 2:	48963	(31.6%)	-1.0
		Dose 3:	42826	(26.7%)			Dose 3:	42893	(27.7%)	-1.0

* HPV Register estimates calculated using the number of adolescents in each age group with a record on the HPV Register of a vaccine received by 30 June 2018 as the numerator and the Australian Bureau of Statistics Estimated Resident Population by Single Year of Age as at 30 June 2017 as the denominator.

† AIR data estimates calculated using the number of adolescents in each age group with an AIR record of a HPV vaccine received by 30 June 2018 as the numerator, and the number of Medicare-registered adolescents in each age group as at 30 June 2017 as the denominator.

Current cumulative HPV vaccine coverage (based on age at 31 December 2019)

Estimated current HPV vaccination coverage, based on AIR data, is shown in Table 23 and Figures 8–11. Coverage in females remains several percentage points higher than in males. Consistent with the HPV Register estimates,[43] dose 1 coverage is roughly equivalent for Aboriginal and Torres Strait Islander and non-Indigenous adolescents, except for 13–14–year-old Aboriginal and Torres Strait Islander males who have 4–5% lower dose 1 coverage than their non-Indigenous peers. Also consistent with the HPV Register estimates, coverage for doses 2 and 3 (lower course completion) is lower in Aboriginal and Torres Strait Islander adolescents.

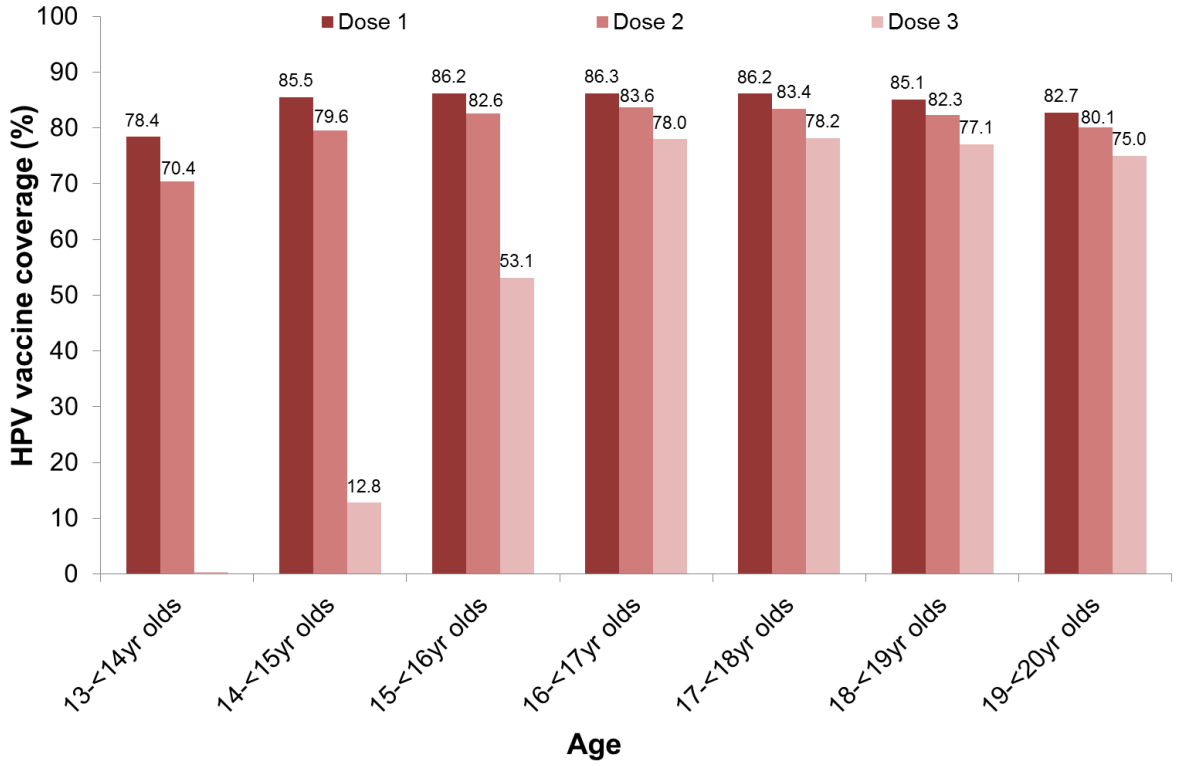
In 2018, the HPV vaccination program changed from a 3-dose schedule to a 2-dose schedule. Table 23 shows 2-dose coverage in the 15-year-old cohort, which was the first cohort to include adolescents vaccinated with two doses of 9vHPV vaccine, was 82.6% in females and 79.9% in males. Compared with the birth cohort 1 year older who received 3 doses, coverage of dose 2 in this younger cohort lies between dose 2 and dose 3 coverage of the older cohort (Figures 8 and 9). This is likely due to the advantage of needing only two doses somewhat offset by the longer interval between the doses.

Table 23. Cumulative coverage (%) for HPV vaccine by first and final dose number,* gender, Indigenous status and birth cohort/age† for vaccination encounters recorded up to 31 December 2019

Females														
Age at 31 Dec 2019 (Birth Cohort)	**13yrs‡ (1 Jan – 31 Dec 2006)**		**14yrs (1 Jan – 31 Dec 2005)**		**15yrs§ (1 Jan – 31 Dec 2004)**		**16yrs (1 Jan – 31 Dec 2003)**		**17yrs (1 Jan – 31 Dec 2002)**		**18yrs (1 Jan – 31 Dec 2001)**		**19yrs (1 Jan – 31 Dec 2000)**	
	Dose 1	Dose 2	Dose 1	Dose 2	Dose 1	Dose 2	Dose 1	Dose 3	Dose 1	Dose 3	Dose 1	Dose 3	Dose 1	Dose 3
All	78.4	70.4	85.5	79.6	86.2	82.6	86.3	78.0	86.2	78.2	85.1	77.1	82.7	75.0
Indigenous	77.2	61.8	85.3	72.5	87.8	77.9	88.8	70.5	87.4	70.4	85.5	69.1	82.4	66.7
Non-Indigenous	78.5	70.9	85.5	80.0	86.2	82.8	86.1	78.3	86.1	78.5	85.0	77.5	82.7	75.4
Males														
Age at 31 Dec 2019 (Birth Cohort)	**13yrs‡ (1 Jan – 31 Dec 2006)**		**14yrs (1 Jan – 31 Dec 2005)**		**15yrs§ (1 Jan – 31 Dec 2004)**		**16yrs (1 Jan – 31 Dec 2003)**		**17yrs (1 Jan – 31 Dec 2002)**		**18yrs (1 Jan – 31 Dec 2001)**		**19yrs (1 Jan – 31 Dec 2000)**	
	Dose 1	Dose 2	Dose 1	Dose 2	Dose 1	Dose 2	Dose 1	Dose 3	Dose 1	Dose 3	Dose 1	Dose 3	Dose 1	Dose 3
All	75.1	66.2	83.4	76.6	84.1	79.9	83.6	74.3	83.2	74.4	80.8	72.3	75.6	67.3
Indigenous	70.0	53.0	79.8	65.9	83.0	71.8	83.7	63.2	82.7	64.5	79.8	62.0	71.4	55.1
Non-Indigenous	75.4	66.9	83.6	77.1	84.2	80.3	83.6	74.8	83.3	74.9	80.8	72.7	75.8	67.8

* Cumulative coverage for dose 1 and dose 3 reported for adolescents aged 16–19 years. Cumulative coverage for dose 1 and dose 2 reported for adolescents aged 13–15 years after the HPV vaccination program changed from a 3-dose schedule to a 2-dose schedule in 2018 (2017 in NSW).
† Age assessed at 31 December 2019. Birth cohort for adolescents aged 12 years not included as 12-year-olds are not eligible for HPV vaccination in some states/territories.
‡ Not all 13-year-olds in 2019 would have been offered HPV vaccine in their 2019 year level, notably those in SA and WA.
§ Coverage at age 15 years is the recommended time point for coverage reporting between jurisdictions and over time.
Source: Australian Immunisation Register, data as at 29 February 2020.

Figure 8: Cumulative coverage (%) of HPV vaccine in Australian females by dose number and, age/birth cohort* for vaccination encounters recorded up to 31 December 2019



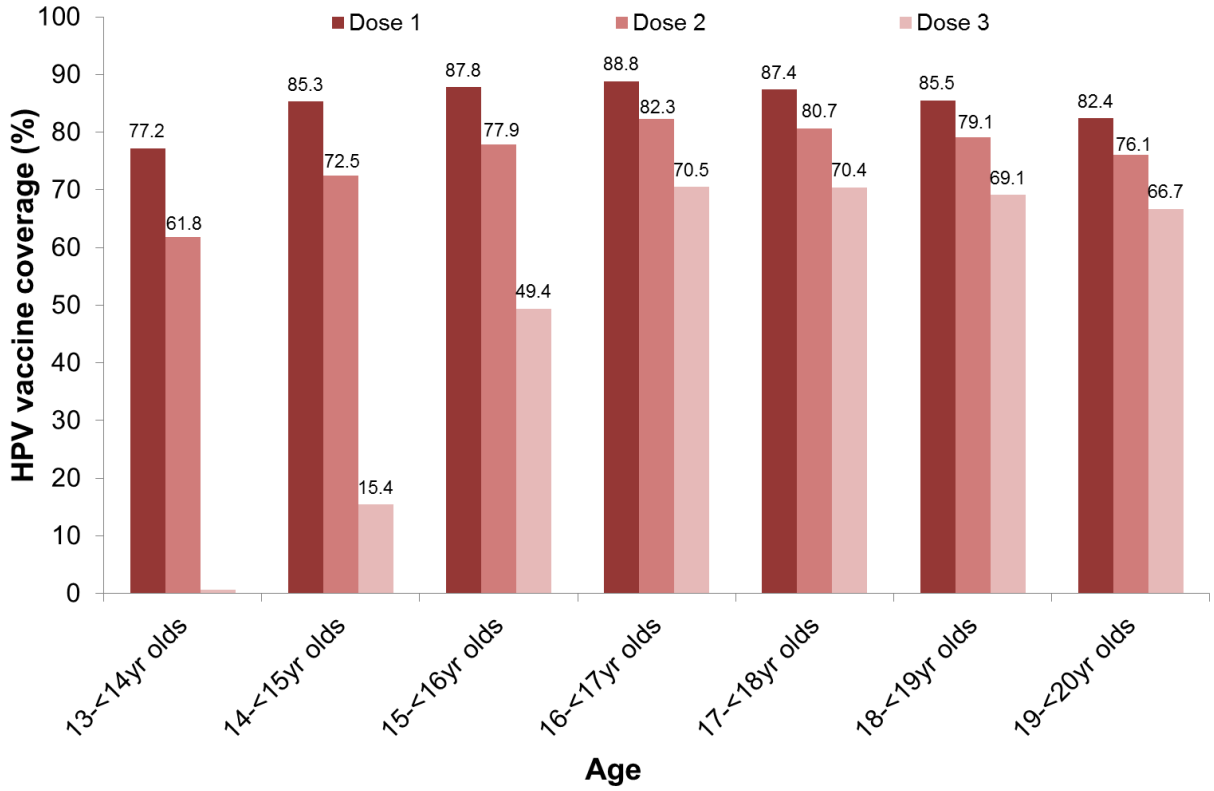
* Age calculated as at 31 December 2019.

Notes:

- Cumulative coverage for adolescents aged 12 years not shown as 12-year-olds are not eligible for HPV vaccination in some states/territories.
- Coverage in 13-year-olds impacted by some 13-year-olds not offered HPV vaccine in 2019, notably in SA and WA cohorts.
- Low dose 3 coverage for adolescents aged 15 years and younger after the HPV vaccination program changed from a 3-dose schedule to a 2-dose schedule in 2018 (2017 in NSW).

Source: Australian Immunisation Register, data as at 29 February 2020.

Figure 9: Cumulative coverage (%) of HPV vaccine in Aboriginal and Torres Strait Islander females by dose number and age/birth cohort* for vaccination encounters recorded up to 31 December 2019



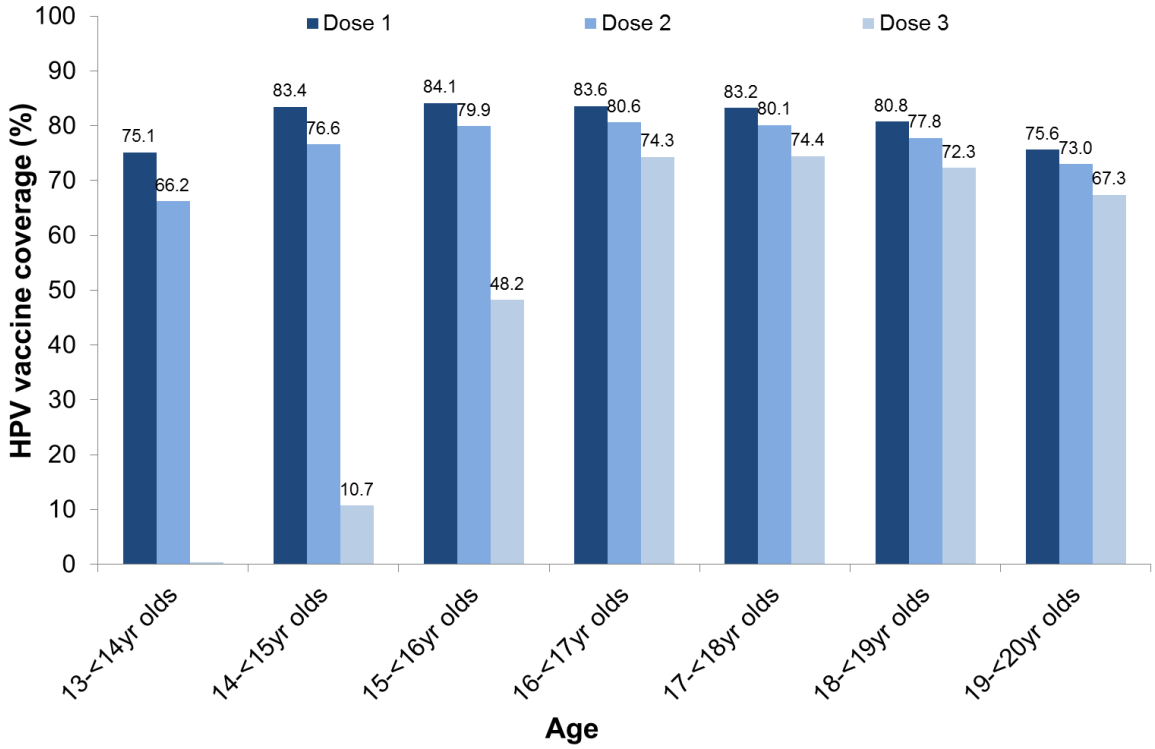
* Age calculated as at 31 December 2019.

Notes:

- Cumulative coverage for adolescents aged 12 years not shown as 12-year-olds are not eligible for HPV vaccination in some states/territories.
- Coverage in 13-year-olds impacted by some 13-year-olds not offered HPV vaccine in 2019, notably in SA and WA cohorts.
- Low dose 3 coverage for adolescents aged 15 years and younger after the HPV vaccination program changed from a 3-dose schedule to a 2-dose schedule in 2018 (2017 in NSW).

Source: Australian Immunisation Register, data as at 29 February 2020.

Figure 10: Cumulative coverage (%) of HPV vaccine in Australian males by dose number and age/birth cohort* for vaccination encounters recorded up to 31 December 2019



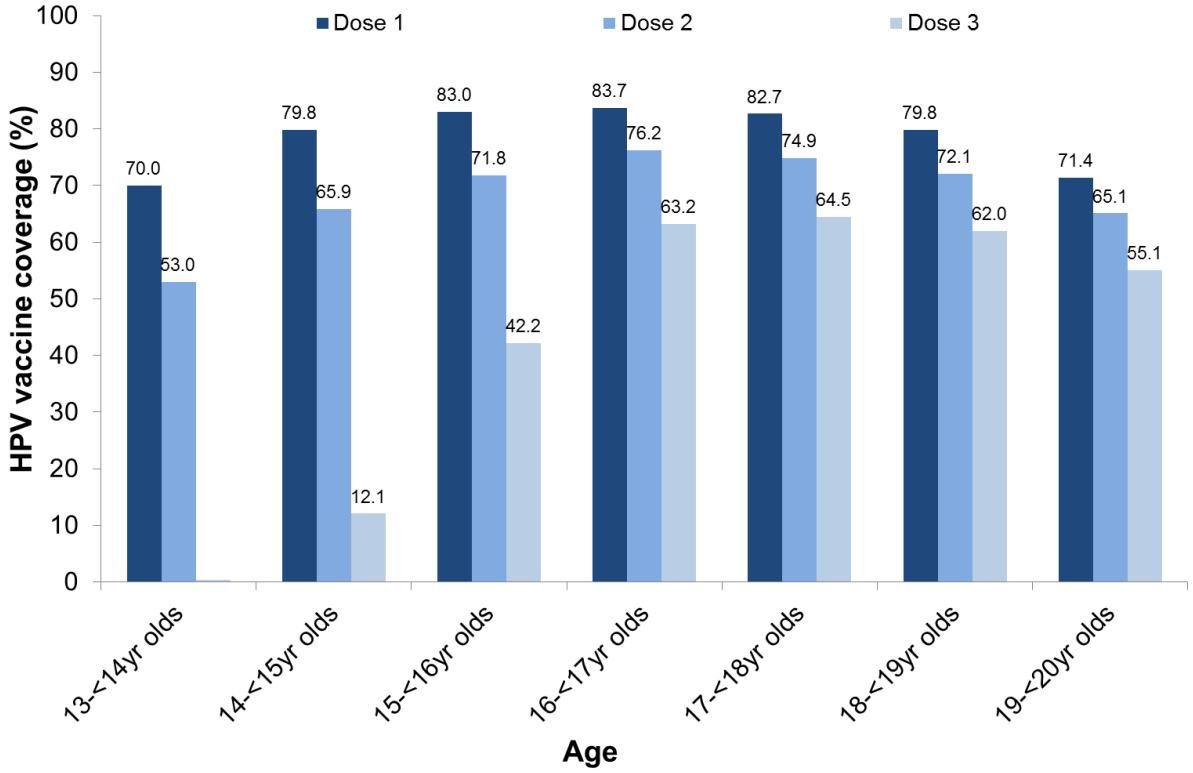
* Age calculated as at 31 December 2019.

Notes:

- Cumulative coverage for adolescents aged 12 years not shown as 12-year-olds are not eligible for HPV vaccination in some states/territories.
- Coverage in 13-year-olds impacted by some 13-year-olds not offered HPV vaccine in 2019, notably in SA and WA cohorts.
- Low dose 3 coverage for adolescents aged 15 years and younger after the HPV vaccination program changed from a 3-dose schedule to a 2-dose schedule in 2018 (2017 in NSW).

Source: Australian Immunisation Register, data as at 29 February 2020.

Figure 11: Cumulative coverage (%) for HPV vaccine in Aboriginal and Torres Strait Islander males by dose number and age/birth cohort* for vaccination encounters recorded up to 31 December 2019, Australia



* Age calculated as at 31 December 2019.
Notes:

- Cumulative coverage for adolescents aged 12 years not shown as 12-year-olds are not eligible for HPV vaccination in some states/territories.
- Coverage in 13-year-olds impacted by some 13-year-olds not offered HPV vaccine in 2019, notably in SA and WA cohorts.
- Low dose 3 coverage for adolescents aged 15 years and younger after the HPV vaccination program changed from a 3-dose schedule to a 2-dose schedule in 2018 (2017 in NSW).

Source: Australian Immunisation Register, data as at 29 February 2020.

Table 24 shows that there is <10% variation in dose 1 coverage by age 15 years across the jurisdictions (female range 83.4% in QLD to 89.0% in ACT; male range 81.0% in QLD to 87.4% in NT). Greater variation (close to 10%) is seen for the final dose (female range 77.7% in TAS to 86.5% in ACT; male range 75.5% in TAS to 84.1% in ACT). Much greater variation by jurisdiction was apparent for coverage in Aboriginal and Torres Strait Islander adolescents (refer to Table 25). Table 26 suggests minimal difference in dose 1 coverage by remoteness of area of residence but lower coverage for the final dose in remote areas. Similar findings are apparent for Aboriginal and Torres Strait Islander adolescents by remoteness of area of residence (refer to Table 27). As shown in Table 28, there was little difference by SES of area of residence for dose 1 coverage in females at age 15 years (<2% variation) but a slightly larger difference in final dose coverage (5% difference between lowest and highest SES). Among males there was a larger gradient by SES at age 15 years for both dose 1 coverage (5% difference) and final dose coverage (almost 10%).

Table 24. Cumulative coverage (%) for HPV vaccine in Australian adolescents by first and final dose number,* gender, jurisdiction and birth cohort/age† for vaccination encounters recorded up to 31 December 2019

Females														
Age at 31 Dec 2019 (Birth Cohort)	**13yrs‡ (1 Jan – 31 Dec 2006)**		**14yrs (1 Jan – 31 Dec 2005)**		**15yrs§ (1 Jan – 31 Dec 2004)**		**16yrs (1 Jan – 31 Dec 2003)**		**17yrs (1 Jan – 31 Dec 2002)**		**18yrs (1 Jan – 31 Dec 2001)**		**19yrs (1 Jan – 31 Dec 2000)**	
	Dose 1	Dose 2	Dose 1	Dose 2	Dose 1	Dose 2	Dose 1	Dose 3	Dose 1	Dose 3	Dose 1	Dose 3	Dose 1	Dose 3
ACT	86.7	77.4	89.5	83.5	89.0	86.5	88.6	80.0	87.9	79.2	86.3	75.3	82.9	72.4
NSW	82.7	75.7	86.7	82.9	87.1	84.0	87.1	80.5	86.2	80.2	84.7	78.4	82.5	76.3
VIC	82.8	74.2	87.3	81.2	88.0	85.2	87.9	79.6	87.7	79.2	86.0	77.6	83.7	75.8
QLD	80.2	71.6	82.5	76.7	83.4	79.9	83.1	73.8	84.1	75.3	83.7	75.5	81.6	73.2
SA	28.6	25.2	84.9	75.7	86.5	79.9	86.8	75.8	86.7	77.8	87.3	77.7	85.1	75.5
WA	81.5	72.8	83.6	75.7	84.1	79.7	85.2	76.6	85.3	76.1	84.5	75.6	81.1	73.8
TAS	76.7	61.6	86.9	72.5	87.7	77.7	87.7	76.9	87.3	74.3	86.8	75.2	83.3	69.4
NT	80.5	64.4	87.2	76.4	88.9	83.6	89.2	76.8	91.1	81.8	89.2	80.2	88.3	79.7
Males														
Age at 31 Dec 2019 (Birth Cohort)	**13yrs‡ (1 Jan – 31 Dec 2006)**		**14yrs (1 Jan – 31 Dec 2005)**		**15yrs§ (1 Jan – 31 Dec 2004)**		**16yrs (1 Jan – 31 Dec 2003)**		**17yrs (1 Jan – 31 Dec 2002)**		**18yrs (1 Jan – 31 Dec 2001)**		**19yrs (1 Jan – 31 Dec 2000)**	
	Dose 1	Dose 2	Dose 1	Dose 2	Dose 1	Dose 2	Dose 1	Dose 3	Dose 1	Dose 3	Dose 1	Dose 3	Dose 1	Dose 3
ACT	85.1	73.9	86.6	80.2	87.2	84.1	87.8	76.8	86.7	77.1	81.5	71.2	77.0	65.3

NSW	78.8	70.8	84.5	79.9	84.5	81.1	83.8	76.3	82.8	76.4	79.3	72.9	73.3	65.9
VIC	78.7	69.4	85.0	77.3	86.1	82.5	85.7	76.4	85.4	76.0	82.3	73.5	78.1	69.9
QLD	77.8	67.8	80.6	73.9	81.0	76.8	80.0	69.7	80.5	70.4	79.3	70.1	75.3	66.4
SA	24.9	21.5	82.7	72.2	83.8	76.5	84.8	72.0	84.8	74.0	83.8	73.3	79.9	70.0
WA	80.9	71.5	82.7	75.0	83.7	79.2	83.3	74.6	83.0	73.7	82.1	72.9	74.3	66.9
TAS	70.1	55.2	83.9	68.1	85.6	75.5	86.0	73.5	84.8	70.9	80.3	65.3	75.5	63.9
NT	73.0	54.5	82.4	70.0	87.4	78.5	86.3	69.3	87.3	74.9	86.0	75.3	81.0	68.6

* Cumulative coverage for dose 1 and dose 3 reported for adolescents aged 16–19 years. Cumulative coverage for dose 1 and dose 2 reported for adolescents aged 13–15 years after the HPV vaccination program changed from a 3-dose schedule to a 2-dose schedule in 2018 (2017 in NSW).

† Age assessed at 31 December 2019. Birth cohort for adolescents aged 12 years not included as 12-year-olds are not eligible for HPV vaccination in some states/territories.

‡ Coverage in 13-year-olds impacted by some 13-year-olds not offered HPV vaccine in 2019, notably in SA and WA cohorts.

§ Coverage at age 15 years is the recommended time point for coverage reporting between jurisdictions and over time.

Source: Australian Immunisation Register, data as at 29 February 2020.

Table 25. Cumulative coverage (%) for HPV vaccine in Indigenous Australian adolescents by dose number,* gender, jurisdiction and birth cohort/age† for vaccination encounters recorded up to 31 December 2019

Females														
Age at 31 Dec 2019 (Birth Cohort)	**13yrs‡ (1 Jan – 31 Dec 2006)**		**14yrs (1 Jan – 31 Dec 2005)**		**15yrs§ (1 Jan – 31 Dec 2004)**		**16yrs (1 Jan – 31 Dec 2003)**		**17yrs (1 Jan – 31 Dec 2002)**		**18yrs (1 Jan – 31 Dec 2001)**		**19yrs (1 Jan – 31 Dec 2000)**	
	Dose 1	Dose 2	Dose 1	Dose 2	Dose 1	Dose 2	Dose 1	Dose 3	Dose 1	Dose 3	Dose 1	Dose 3	Dose 1	Dose 3
ACT	79.1	58.1	86.8	81.1	87.2	79.5	85.7	69.4	83.3	61.9	90.0	60.0	85.9	70.3
NSW	81.7	70.6	89.8	82.1	91.2	82.9	90.8	78.0	88.7	75.4	85.3	73.6	84.1	71.3
VIC	77.5	63.0	86.7	73.9	90.6	83.9	92.7	76.9	88.9	74.3	86.3	71.2	82.9	68.6
QLD	79.1	63.0	83.2	71.4	86.6	78.4	85.3	65.7	86.0	66.4	84.5	66.2	80.0	61.7
SA	26.1	17.5	74.2	52.6	74.3	58.4	84.0	54.6	79.9	60.2	77.4	54.5	69.8	48.5
WA	75.3	55.0	79.4	58.7	83.2	66.9	88.5	61.7	84.5	59.2	83.7	58.0	80.7	60.8
TAS	80.3	61.3	91.5	71.9	87.4	70.1	92.6	77.9	85.3	70.7	87.1	71.6	81.1	66.3
NT	79.12	55.6	88.6	74.0	92.4	83.2	92.6	73.4	94.6	84.6	93.8	83.6	93.1	83.9
Males														
Age at 31 Dec 2019 (Birth Cohort)	**13yrs‡ (1 Jan – 31 Dec 2006)**		**14yrs (1 Jan – 31 Dec 2005)**		**15yrs§ (1 Jan – 31 Dec 2004)**		**16yrs (1 Jan – 31 Dec 2003)**		**17yrs (1 Jan – 31 Dec 2002)**		**18yrs (1 Jan – 31 Dec 2001)**		**19yrs (1 Jan – 31 Dec 2000)**	
	Dose 1	Dose 2	Dose 1	Dose 2	Dose 1	Dose 2	Dose 1	Dose 3	Dose 1	Dose 3	Dose 1	Dose 3	Dose 1	Dose 3
ACT	73.6	52.9	74.5	57.5	80.4	72.6	77.1	60.0	79.1	60.5	78.3	52.2	58.8	52.9
NSW	75.6	63.1	85.8	75.5	83.8	74.0	85.7	69.8	81.8	69.0	77.7	64.6	68.4	53.6
VIC	68.3	49.2	81.4	69.9	87.9	80.2	87.0	69.6	84.5	68.9	82.2	65.5	73.7	58.6

QLD	71.4	55.0	78.2	65.5	81.9	72.3	79.9	59.2	80.5	59.3	77.1	57.6	71.4	53.8
SA	21.3	15.0	62.4	43.2	71.2	53.6	76.4	48.7	74.2	53.6	78.2	54.3	66.9	49.1
WA	70.8	47.3	74.8	55.2	79.2	64.7	83.4	56.9	82.1	57.1	78.6	54.4	65.8	45.6
TAS	73.9	53.1	82.6	62.4	86.0	71.4	88.8	70.0	86.1	71.7	83.0	59.1	75.3	61.5
NT	69.7	42.1	79.8	62.7	90.2	76.0	88.4	63.5	93.2	74.9	90.8	77.1	85.4	71.2

* Cumulative coverage for dose 1 and dose 3 reported for adolescents aged 16–19 years. Cumulative coverage for dose 1 and dose 2 reported for adolescents aged 13–15 years after the HPV vaccination program changed from a 3-dose schedule to a 2-dose schedule in 2018 (2017 in NSW).

† Age assessed at 31 December 2019. Birth cohort for adolescents aged 12 years not included as 12-year-olds are not eligible for HPV vaccination in some states/territories.

‡ Coverage in 13-year-olds impacted by some 13-year-olds not offered HPV vaccine in 2019, notably in SA and WA cohorts.

§ Coverage at age 15 years is the recommended time point for coverage reporting between jurisdictions and over time.

Source: Australian Immunisation Register, data as at 29 February 2020.

Table 26. Cumulative coverage (%) for HPV vaccine in Australian adolescents by dose number,* gender, remoteness and birth cohort/age† for vaccination encounters recorded up to 31 December 2019

Females														
Age at 31 Dec 2019 (Birth Cohort)	**13yrs‡ (1 Jan – 31 Dec 2006)**		**14yrs (1 Jan – 31 Dec 2005)**		**15yrs§ (1 Jan – 31 Dec 2004)**		**16yrs (1 Jan – 31 Dec 2003)**		**17yrs (1 Jan – 31 Dec 2002)**		**18yrs (1 Jan – 31 Dec 2001)**		**19yrs (1 Jan – 31 Dec 2000)**	
	Dose 1	Dose 2	Dose 1	Dose 2	Dose 1	Dose 2	Dose 1	Dose 3	Dose 1	Dose 3	Dose 1	Dose 3	Dose 1	Dose 3
Major Cities	79.1	71.5	85.3	79.9	85.7	82.4	85.7	77.9	85.5	77.9	84.3	76.7	81.8	74.6
Regional	76.8	68.1	86.2	79.3	87.6	83.4	87.6	78.5	87.9	79.2	87.1	78.7	85.3	76.4
Remote	74.8	61.1	84.7	73.2	87.0	78.0	87.1	72.3	87.3	74.5	85.8	73.2	82.4	70.9
Males														
Age at 31 Dec 2019 (Birth Cohort)	**13yrs‡ (1 Jan – 31 Dec 2006)**		**14yrs (1 Jan – 31 Dec 2005)**		**15yrs§ (1 Jan – 31 Dec 2004)**		**16yrs (1 Jan – 31 Dec 2003)**		**17yrs (1 Jan – 31 Dec 2002)**		**18yrs (1 Jan – 31 Dec 2001)**		**19yrs (1 Jan – 31 Dec 2000)**	
	Dose 1	Dose 2	Dose 1	Dose 2	Dose 1	Dose 2	Dose 1	Dose 3	Dose 1	Dose 3	Dose 1	Dose 3	Dose 1	Dose 3
Major Cities	76.3	67.8	83.4	77.1	83.6	79.8	83.0	74.4	82.6	74.1	79.8	71.8	74.6	66.7
Regional	72.5	63.1	83.9	76.0	85.4	80.5	85.2	74.7	85.0	75.6	83.1	73.8	78.6	69.3
Remote	68.7	53.0	80.7	69.5	85.2	75.2	84.2	68.1	84.3	68.4	84.3	71.2	75.2	63.4

* Cumulative coverage for dose 1 and dose 3 reported for adolescents aged 16–19 years. Cumulative coverage for dose 1 and dose 2 reported for adolescents aged 13–15 years after the HPV vaccination program changed from a 3-dose schedule to a 2-dose schedule in 2018 (2017 in NSW).
† Age assessed at 31 December 2019. Birth cohort for adolescents aged 12 years not included as 12-year-olds are not eligible for HPV vaccination in some states/territories.
‡ Coverage in 13-year-olds impacted as some 13-year-olds not offered HPV vaccine in 2019, notably in SA and WA cohorts.
§ Coverage at age 15 years is the recommended time point for coverage reporting between jurisdictions and over time.
Source: Australian Immunisation Register, data as at 29 February 2020.

Table 27. Cumulative coverage (%) for HPV vaccine in Indigenous Australian adolescents by dose number,* gender, remoteness and birth cohort/age† for vaccination encounters recorded up to 31 December 2019

Females														
Age at 31 Dec 2019 (Birth Cohort)	**13yrs‡ (1 Jan – 31 Dec 2006)**		**14yrs (1 Jan – 31 Dec 2005)**		**15yrs§ (1 Jan – 31 Dec 2004)**		**16yrs (1 Jan – 31 Dec 2003)**		**17yrs (1 Jan – 31 Dec 2002)**		**18yrs (1 Jan – 31 Dec 2001)**		**19yrs (1 Jan – 31 Dec 2000)**	
	Dose 1	Dose 2	Dose 1	Dose 2	Dose 1	Dose 2	Dose 1	Dose 3	Dose 1	Dose 3	Dose 1	Dose 3	Dose 1	Dose 3
Major Cities	79.5	65.6	85.7	74.0	87.1	78.2	89.2	72.4	86.7	70.1	84.2	67.7	82.1	66.0
Regional	76.4	62.6	85.5	73.7	87.9	78.4	88.7	71.3	87.5	70.7	85.9	69.8	81.6	66.6
Remote	75.9	52.7	84.5	66.8	88.9	76.0	88.0	63.6	88.0	69.1	87.5	69.1	84.7	66.9
Males														
Age at 31 Dec 2019 (Birth Cohort)	**13yrs‡ (1 Jan – 31 Dec 2006)**		**14yrs (1 Jan – 31 Dec 2005)**		**15yrs§ (1 Jan – 31 Dec 2004)**		**16yrs (1 Jan – 31 Dec 2003)**		**17yrs (1 Jan – 31 Dec 2002)**		**18yrs (1 Jan – 31 Dec 2001)**		**19yrs (1 Jan – 31 Dec 2000)**	
	Dose 1	Dose 2	Dose 1	Dose 2	Dose 1	Dose 2	Dose 1	Dose 3	Dose 1	Dose 3	Dose 1	Dose 3	Dose 1	Dose 3
Major Cities	73.9	57.5	81.9	69.6	82.0	73.3	83.6	65.1	81.8	65.5	78.1	61.2	71.3	55.3
Regional	68.0	53.9	79.4	66.1	83.4	71.6	83.3	63.3	82.2	64.6	78.8	60.4	69.4	53.2
Remote	66.4	40.6	76.5	59.1	83.3	69.3	84.3	59.4	84.4	61.7	84.8	66.7	75.3	58.1

* Cumulative coverage for dose 1 and dose 3 reported for adolescents aged 16–19 years. Cumulative coverage for dose 1 and dose 2 reported for adolescents aged 13–15 years after the HPV vaccination program changed from a 3-dose schedule to a 2-dose schedule in 2018 (2017 in NSW).
† Age assessed at 31 December 2019. Birth cohort for adolescents aged 12 years not included as 12 year olds are not eligible for HPV vaccination in some states/territories.
‡ Coverage in 13-year-olds impacted as some 13-year-olds not offered HPV vaccine in their 2019, notably in SA and WA cohorts.
§ Coverage at 15 years is the recommended time point for coverage reporting between jurisdictions and over time.

Source: Australian Immunisation Register, data as at 29 February 2020.

Table 28. Cumulative coverage (%) for HPV vaccine by dose number,* gender, socioeconomic status of area of residence and birth cohort/age† for vaccination encounters recorded up to 31 December 2019

Females														
Age at 31 Dec 2019 (Birth Cohort)	**13yrs‡ (1 Jan – 31 Dec 2006)**		**14yrs (1 Jan – 31 Dec 2005)**		**15yrs§ (1 Jan – 31 Dec 2004)**		**16yrs (1 Jan – 31 Dec 2003)**		**17yrs (1 Jan – 31 Dec 2002)**		**18yrs (1 Jan – 31 Dec 2001)**		**19yrs (1 Jan – 31 Dec 2000)**	
	Dose 1	Dose 2	Dose 1	Dose 2	Dose 1	Dose 2	Dose 1	Dose 3	Dose 1	Dose 3	Dose 1	Dose 3	Dose 1	Dose 3
Decile 1 -lowest SES	72.3	62.6	84.0	75.3	85.0	78.9	84.9	72.9	84.0	73.6	82.0	71.5	77.6	68.7
Decile 2	73.9	65.8	85.1	78.8	85.9	81.7	85.8	76.2	86.0	77.0	83.9	75.3	81.4	72.7
Decile 3	77.0	68.8	85.4	78.7	86.2	81.9	86.8	77.5	86.1	78.6	85.1	77.0	82.8	74.3
Decile 4	74.7	67.2	85.7	79.6	87.0	83.1	85.6	77.3	86.2	78.3	85.4	77.5	83.2	74.8
Decile 5	76.6	68.7	85.1	78.8	86.0	82.4	85.8	77.1	86.1	78.0	84.7	76.4	82.9	74.6
Decile 6	78.8	71.0	85.1	79.6	86.7	83.1	86.6	79.0	86.6	79.0	85.8	78.5	83.9	76.7
Decile 7	81.0	72.7	85.6	80.0	86.0	82.8	86.4	78.1	86.1	78.3	85.7	78.0	83.2	75.6
Decile 8	80.7	73.3	85.6	81.0	86.4	83.4	86.9	79.5	86.6	78.6	85.7	78.3	83.9	76.7
Decile 9	80.7	72.7	86.8	81.6	86.2	83.5	86.9	79.7	86.8	79.2	86.4	78.8	83.8	76.5
Decile 10 - highest SES	83.7	76.1	86.2	81.5	86.7	84.0	86.6	80.5	86.7	80.1	85.8	78.8	84.1	77.8
Males														
Age at 31 Dec 2019 (Birth Cohort)	**13yrs‡ (1 Jan – 31 Dec 2006)**		**14yrs (1 Jan – 31 Dec 2005)**		**15yrs§ (1 Jan – 31 Dec 2004)**		**16yrs (1 Jan – 31 Dec 2003)**		**17yrs (1 Jan – 31 Dec 2002)**		**18yrs (1 Jan – 31 Dec 2001)**		**19yrs (1 Jan – 31 Dec 2000)**	
	Dose 1	Dose 2	Dose 1	Dose 2	Dose 1	Dose 2	Dose 1	Dose 3	Dose 1	Dose 3	Dose 1	Dose 3	Dose 1	Dose 3

Decile 1 -lowest SES	67.5	57.0	79.6	70.4	80.4	73.5	80.4	67.4	79.6	68.0	76.2	65.6	69.0	58.9
Decile 2	69.0	60.0	82.6	75.2	83.0	78.1	82.3	71.8	82.3	72.4	79.3	70.0	73.8	64.0
Decile 3	72.4	63.6	82.8	75.0	83.9	78.8	83.3	73.8	83.5	73.9	81.3	72.6	75.9	67.5
Decile 4	70.6	62.4	83.3	76.3	84.4	79.8	83.7	73.1	83.5	74.5	80.6	72.1	75.5	67.0
Decile 5	73.9	65.0	82.8	75.8	83.3	79.1	83.7	74.5	82.5	73.7	80.0	71.6	75.2	66.6
Decile 6	76.3	67.7	84.3	78.0	84.6	80.8	84.4	75.7	83.5	75.3	81.3	73.1	77.2	69.3
Decile 7	78.2	69.4	83.6	77.0	84.4	80.6	83.4	74.4	83.6	74.8	81.3	73.2	76.5	68.2
Decile 8	78.2	69.6	84.4	78.3	84.7	81.2	84.3	75.8	83.7	75.4	81.9	74.0	77.4	69.9
Decile 9	78.2	69.0	84.6	78.2	85.9	82.4	85.0	76.6	85.0	77.0	82.6	74.4	78.3	70.4
Decile 10 - highest SES	81.5	73.0	85.2	79.8	85.4	82.6	84.7	77.6	84.5	77.5	82.3	74.9	76.8	69.9

* Cumulative coverage for dose 1 and dose 3 reported for adolescents aged 16-19 years. Cumulative coverage for dose 1 and dose 2 reported for adolescents aged 13-15 years following the HPV vaccination program changing from a 3-dose schedule to a 2-dose schedule in 2018 (2017 in NSW).

† Age assessed at 31 December 2019. Birth cohort for adolescents aged 12 years not included as 12-year-olds are not eligible for HPV vaccination in some states/territories.

‡ Coverage in 13-year-olds impacted as some 13-year-olds not offered HPV vaccine in their 2019, notably in SA and WA cohorts.

§ Coverage at age 15 years is the recommended time point for coverage reporting between jurisdictions and over time.

Source: Australian Immunisation Register, data as at 29 February 2020.

Trends in HPV vaccine coverage at 15 years of age

Table 29, and Figures 12 and 13 show coverage over time at age 15 years using AIR data. As noted previously, use of AIR denominator data results in lower coverage estimates than historic HPV Register data as seen for the 2016 and 2017 15-year-old cohorts. However, trends over time are similar, with dose 1 coverage rising over time (which could be due to a real increase and/or incremental increases in each cohort's denominator per year since vaccination) and dose 3 coverage increasing through 2018. These changes over time apply to both Aboriginal and Torres Strait Islander adolescents. Dose 2 coverage in 2019 has declined in Aboriginal and Torres Strait Islander female and male adolescents relative to the previous year (2018). Tables 30 and 31 show that most 15-year-olds in the 2019 cohort in NSW, SA and WA had already transitioned to the 2-dose schedule because of the earlier implementation of the 2-dose schedule in NSW and the average age of school-based HPV vaccination in SA and WA (more students in this cohort in those states not vaccinated with dose 1 until 2018).

Table 29. Coverage (%) for HPV vaccine in female and male adolescents at age 15 years* by dose number and Indigenous status, 2016–2019

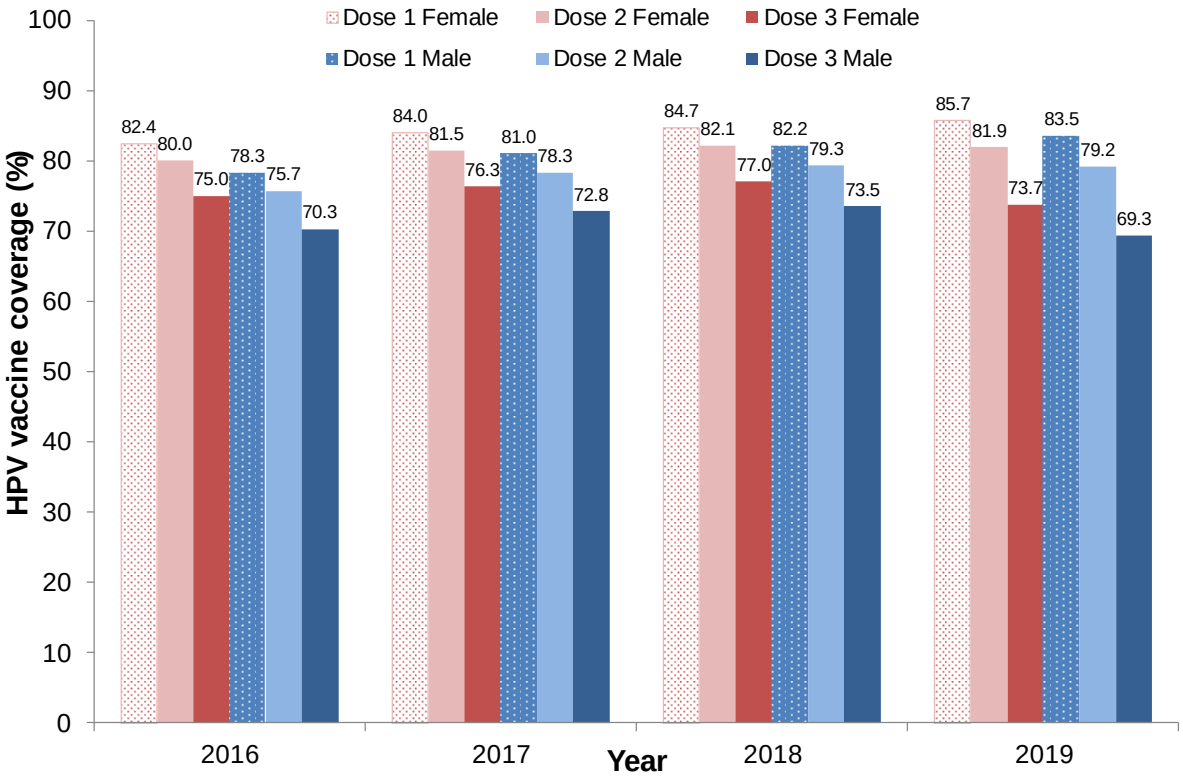
Females												
	2016			2017			2018			2019		
	Dose 1	Dose 2	Dose 3	Dose 1	Dose 2	Dose 3	Dose 1	Dose 2	Dose 3	Dose 1	Dose 2	Dose 3†
All	82.4	80.0	75.0	84.0	81.5	76.3	84.7	82.1	77.0	85.7	81.9	73.7
Indigenous	80.3	74.1	64.2	82.3	75.7	65.2	85.6	78.4	68.0	86.7	76.3	63.2
Non-Indigenous	82.5	80.3	75.5	84.1	81.7	76.7	84.7	82.3	77.5	85.6	82.1	74.2
Males												
	2016			2017			2018			2019		
	Dose 1	Dose 2	Dose 3	Dose 1	Dose 2	Dose 3	Dose 1	Dose 2	Dose 3	Dose 1	Dose 2	Dose 3†
All	78.3	75.7	70.3	81.0	78.3	72.8	82.2	79.3	73.5	83.5	79.2	69.3
Indigenous	72.9	65.8	55.7	76.6	69.2	59.1	80.2	72.4	60.9	81.4	69.9	56.7
Non-Indigenous	78.5	76.1	70.9	81.2	78.7	73.3	82.2	79.6	74.0	83.6	79.6	69.9

* HPV vaccine coverage at 15 years of age based on vaccinations given in the first year of high school, usually at 12–13 years of age.

† Dose 3 coverage in 2019 calculated using Australian Capital Territory, Victoria, Queensland and the Northern Territory data only.

Source: Australian Immunisation Register, data as at 29 February 2020.

Figure 12: Coverage for HPV vaccine in Australian adolescents at age 15 years* by dose number and gender, 2016–2019†

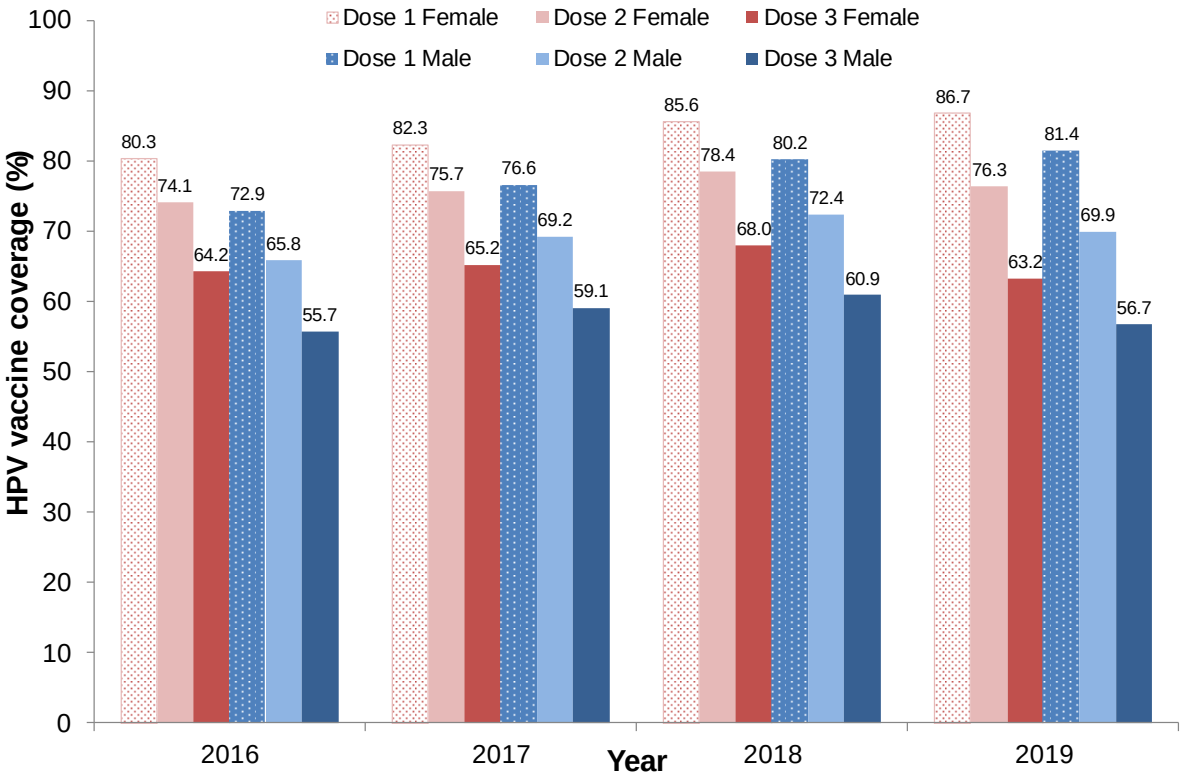


* HPV vaccine coverage at 15 years of age based on vaccinations given in the first year of high school, usually at 12–13 years of age.

† Dose 3 coverage calculated using Australian Capital Territory, Victoria, Queensland and the Northern Territory data only.

Source: Australian Immunisation Register, data as at 29 February 2020.

Figure 13: Coverage of HPV vaccine in Aboriginal and Torres Strait Islander adolescents at age 15 years* by dose number and gender, 2016–2019†



* HPV vaccine coverage at 15 years of age based on vaccinations given in the first year of high school, usually at 12 – 13 years of age.

† Dose 3 coverage calculated using Australian Capital Territory, Victoria, Queensland and the Northern Territory data only.

Source: Australian Immunisation Register, data as at 29 February 2020.

Table 30. Coverage (%) of HPV vaccine in Australian adolescents at age 15 years* by dose number, gender and jurisdiction of residence, 2016–2019

Females												
	2016			2017			2018			2019†		
	Dose 1	Dose 2	Dose 3	Dose 1	Dose 2	Dose 3	Dose 1	Dose 2	Dose 3	Dose 1	Dose 2	Dose 3
ACT	83.1	81.0	73.3	86.2	84.5	77.6	87.2	85.1	79.0	88.5	86.0	74.6
NSW	82.5	80.6	77.2	84.5	82.6	79.3	85.8	83.8	79.9	86.7	83.5	29.8
VIC	83.2	80.9	75.5	85.7	83.1	77.4	86.7	84.1	78.8	87.6	84.5	76.1
QLD	80.8	79.4	72.9	81.4	78.6	72.7	81.1	78.2	72.6	82.7	79.0	71.8
SA	84.9	81.8	74.6	84.0	81.3	74.7	85.2	81.9	74.2	85.7	78.7	26.4
WA	81.1	79.3	72.7	82.7	79.9	73.5	83.4	80.4	75.2	83.5	78.7	37.8
TAS	83.5	79.0	72.4	84.9	81.1	71.9	86.1	82.6	76.1	87.2	77.4	67.8
NT	84.9	81.3	74.3	88.1	84.1	76.9	87.2	82.3	74.9	88.3	82.3	67.9
Males												
	2016			2017			2018			2019†		
	Dose 1	Dose 2	Dose 3	Dose 1	Dose 2	Dose 3	Dose 1	Dose 2	Dose 3	Dose 1	Dose 2	Dose 3
ACT	79.9	78.1	69.9	85.3	82.8	75.7	86.8	83.7	76.2	86.6	83.5	70.5
NSW	77.4	75.5	71.9	81.2	79.0	75.6	82.6	80.4	75.8	84.0	80.6	23.1
VIC	79.7	77.0	71.6	83.2	80.4	74.5	84.5	81.6	75.6	85.6	82.0	71.3
QLD	76.6	73.7	67.7	77.5	74.5	68.2	78.2	74.9	68.7	80.3	76.1	67.9
SA	81.2	78.2	69.8	82.5	79.3	71.2	83.2	79.6	70.4	83.0	75.1	22.4

WA	79.1	76.6	70.4	80.5	77.8	71.3	81.6	78.7	73.4	82.9	78.0	36.5
TAS	77.0	71.6	62.3	82.4	77.9	68.9	85.0	80.5	72.7	85.3	75.3	64.3
NT	80.6	75.1	67.0	83.9	78.1	69.9	83.6	76.3	66.9	86.4	76.9	59.5

* HPV vaccine coverage at 15 years of age based on vaccinations given in the first year of high school, usually at 12–13 years of age.

† In 2019 the majority of female and male adolescents in New South Wales, South Australia and Western Australia had transitioned to the 2-dose schedule (receiving the 2nd dose of HPV ≥5 months after receiving the 1st dose), whereas the majority of female and male adolescents in the Australian Capital Territory, Victoria, Queensland and the Northern Territory were still on the 3-dose schedule (receiving the 2nd dose of HPV <5 months after receiving the 1st dose).

Source: Australian Immunisation Register, data as at 29 February 2020.

Table 31. Coverage (%) of HPV vaccine in Indigenous Australian adolescents at age 15 years* by dose number, gender and jurisdiction of residence, 2016–2019

Females												
	2016			2017			2018			2019†		
	Dose 1	Dose 2	Dose 3	Dose 1	Dose 2	Dose 3	Dose 1	Dose 2	Dose 3	Dose 1	Dose 2	Dose 3
ACT	87.5	70.0	57.5	76.2	73.8	57.1	85.7	85.7	67.4	84.6	76.9	59.0
NSW	82.3	78.0	71.7	85.6	80.5	73.4	89.2	84.3	77.1	90.7	82.3	35.1
VIC	81.9	76.1	68.0	85.4	81.1	70.1	89.5	84.2	74.9	90.1	82.3	66.7
QLD	78.1	72.0	60.5	79.4	72.1	60.8	81.8	73.9	63.1	85.6	76.8	63.6
SA	73.6	60.8	47.5	74.6	66.0	54.5	77.8	66.7	50.7	72.3	56.1	18.5
WA	74.6	65.2	51.0	77.3	66.3	50.3	82.2	70.7	55.9	80.7	64.3	27.6
TAS	82.1	76.6	67.2	80.7	78.0	65.3	89.9	85.2	77.2	86.8	69.5	58.6
NT	89.1	83.9	74.9	89.7	84.7	75.6	89.9	82.3	70.0	91.5	80.6	60.5
Males												
	2016			2017			2018			2019†		
	Dose 1	Dose 2	Dose 3	Dose 1	Dose 2	Dose 3	Dose 1	Dose 2	Dose 3	Dose 1	Dose 2	Dose 3
ACT	71.7	60.9	50.0	76.7	72.1	58.1	74.3	68.6	60.0	80.4	70.6	56.9
NSW	72.7	68.1	62.0	78.1	72.7	66.7	83.6	78.2	68.8	82.7	72.9	23.7
VIC	79.0	71.3	62.3	81.4	75.6	66.7	85.1	79.0	68.1	87.7	79.3	63.4
QLD	70.0	62.4	51.6	71.6	63.7	52.8	75.5	67.8	56.4	80.1	70.9	57.4
SA	70.4	61.8	46.1	68.0	60.5	47.8	74.1	61.6	46.4	69.6	51.1	16.3
WA	67.8	58.3	45.6	74.7	65.2	48.9	77.3	67.9	53.4	75.3	60.2	24.6
TAS	74.4	63.6	51.1	83.3	79.4	68.9	88.1	81.9	68.1	86.0	70.2	56.2

NT	82.8	75.6	63.4	87.0	76.4	64.7	84.6	72.2	59.3	88.4	72.6	49.9

* HPV vaccine coverage at 15 years of age based on vaccinations given in the first year of high school, usually at 12–13 years of age.

† In 2019 the majority of female and male adolescents in New South Wales, South Australia and Western Australia had transitioned to the 2-dose schedule (receiving the 2nd dose of HPV ≥5 months after receiving the 1st dose), whereas the majority of female and male adolescents in the Australian Capital Territory, Victoria, Queensland and the Northern Territory were still on the 3-dose schedule (receiving the 2nd dose of HPV <5 months after receiving the 1st dose).

Source: Australian Immunisation Register, data as at 29 February 2020.

Uptake of 9vHPV vaccine in adolescents aged <15 years

In 2018 9vHPV vaccine replaced 4vHPV vaccine. Stocks of 4vHPV vaccine continued to be used to complete courses initiated with that vaccine and until replacement stock of 9vHPV vaccine was available. Some 4vHPV vaccine stocks were redirected to support immunisation of men who have sex with men (MSM) in some jurisdictions. Therefore in 2018 a mix of HPV vaccine types were in use. By 2019 all HPV vaccine supplies in Australia should have been of 9vHPV vaccine, with no further distribution of 4vHPV vaccine. Data reported in Table 32 may reflect actual HPV vaccine type administered or reporting error by providers more familiar with 4vHPV vaccine. Figures 14 and 15 indicate variation in the routine age for immunisation with HPV vaccine by jurisdiction, which depends on school programs and the routine school year level of administration as well as other access through primary care programs.

Table 32. Number of HPV vaccines administered in 2018 and 2019 to female and male adolescents aged <15 years* and the proportion recorded as 9vHPV vaccine by dose number and jurisdiction of residence

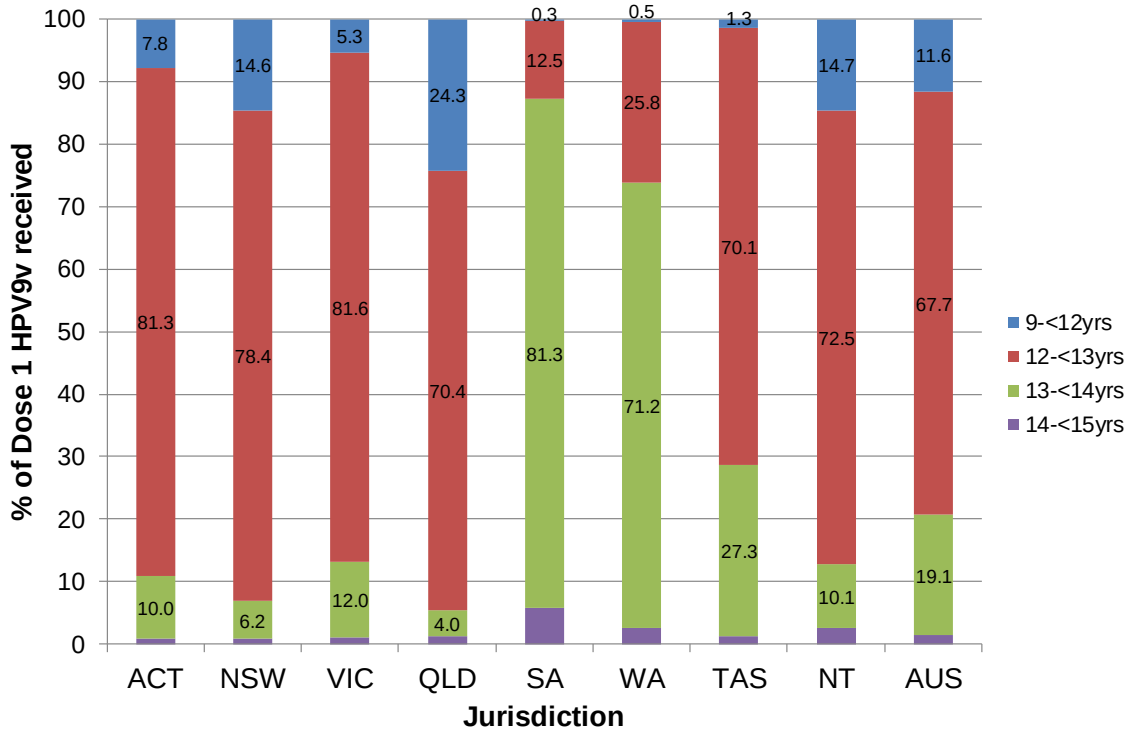
2018								
	Females				Males			
	Dose 1		Dose 2		Dose 1		Dose 2	
	Any brand (n)	% 9vHPV	Any brand (n)	% 9vHPV	Any brand (n)	% 9vHPV	Any brand (n)	% 9vHPV
ACT	2358	98.6	1984	99.5	2324	98.5	1964	99.1
NSW	41975	97.6	36209	99.2	43133	97.7	36155	99.2
VIC	32917	95.9	28971	98.7	33495	96.3	28964	98.9
QLD	27627	97.1	23262	99.3	28298	97.3	23443	99.3
SA	8171	97.4	7109	98.4	8350	97.6	7176	98.6
WA	13476	97.0	11785	99.0	14125	97.5	12401	99.2
TAS	2845	84.8	2173	95.5	2870	84.7	2137	95.7
NT	1488	85.4	962	95.5	1467	84.6	898	96.3
AUS	130857	96.6	112455	98.9	134062	96.8	113138	99.0
2019								
	Females				**Males**			
	Dose 1		Dose 2		Dose 1		Dose 2	
	Any brand (n)	% 9vHPV	Any brand (n)	% 9vHPV	Any brand (n)	% 9vHPV	Any brand (n)	% 9vHPV
ACT	2417	99.3	2277	99.2	2611	99.5	2534	99.2
NSW	42617	99.0	41354	99.4	43133	99.0	41825	99.5

VIC	34052	98.8	31236	99.1	34809	98.9	31359	99.2
QLD	29189	99.0	26715	99.3	30317	99.0	26947	99.4
SA	8775	98.9	7998	99.1	9107	99.0	8129	99.2
WA	28376	99.0	25955	99.6	29485	99.1	26795	99.7
TAS	2612	97.9	2248	97.8	2606	97.8	203	98.7
NT	1513	98.0	1312	98.7	498	98.7	1217	98.6
AUS	149551	98.9	139095	99.3	153566	99.0	140829	99.4

* Adolescents aged less than 15 years of age at time of dose 1 receipt.

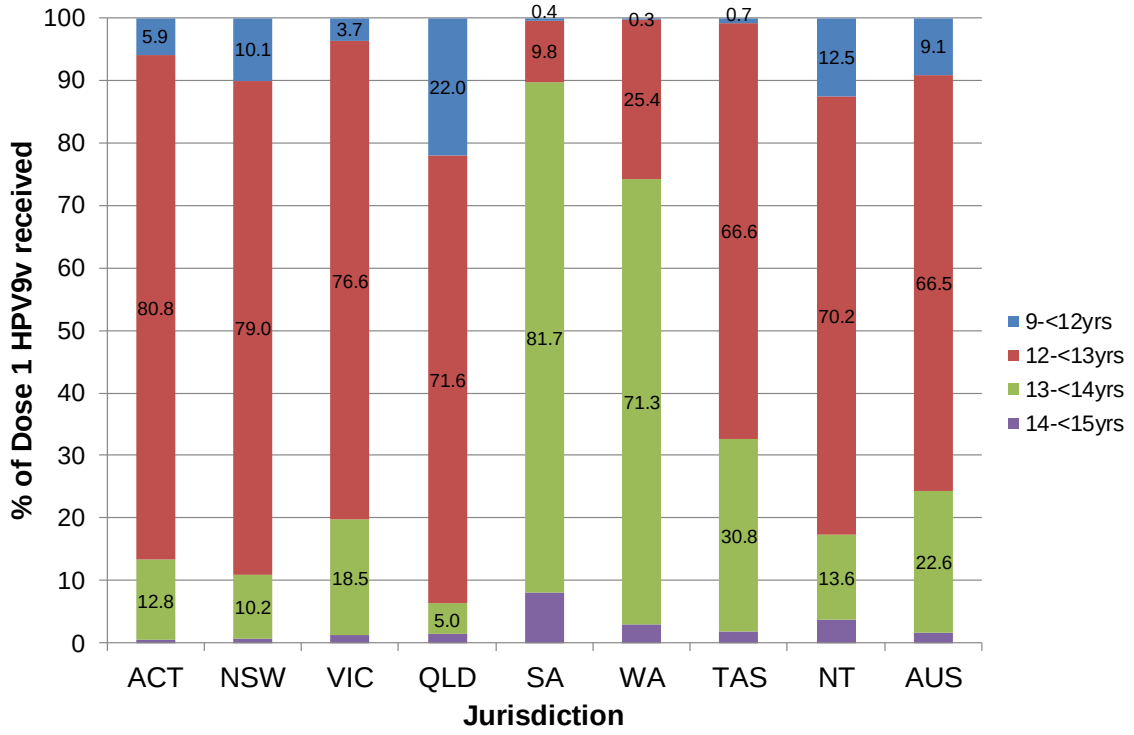
Source: Australian Immunisation Register, data as at 29 February 2020.

Figure 14: Age distribution of female adolescents aged <15 years receiving the first dose of 9vHPV vaccine in 2018 by jurisdiction of residence



Source: Australian Immunisation Register, data as at 29 February 2020.

Figure 15: Age distribution of male adolescents aged <15 years receiving the first dose of 9vHPV vaccine in 2018 by jurisdiction of residence



Source: Australian Immunisation Register, data as at 29 February 2020.

Course completion refers to receipt of the second dose of 9vHPV vaccine only among those adolescents who received dose 1. It is therefore a different measure from population coverage and requires different interpretation. Tables 33 and 34 highlight that while the majority of vaccination courses are completed in the same calendar year/school year in which they are initiated, a considerable amount of vaccination occurs in the following year (7.2% increase in course completion for females and 7.7% for males nationally). Estimation of coverage or course completion restricted to that achieved within the same calendar year will underestimate population level uptake/coverage achieved. This also emphasises the rationale for measuring vaccination coverage at age 15 years, allowing time for follow-up public health activities, such as register reminders, to reach those who still need to complete the course. The largest increase in course completion by jurisdiction between the end of 2018 and 2019 for courses started in 2018 was in NT (20.3% for females and 19.0% for males). Course completion increased most in remote areas and increases were seen across all SES deciles. For Aboriginal and Torres Islander adolescents (refer to Table 34), the extra year provided large increases in course completion (17.2% increase in females and 17.9% in males), with particularly notable increases in NT and in remote areas.

Table 33. Number of Australian adolescents aged <15 years commencing 9vHPV vaccination in 2018 and the percentage completing the 2-dose schedule by 31 December 2019, by gender, Indigenous status, jurisdiction and remoteness/socioeconomic status of area of residence

		Females			Males		
		Number receiving dose 1 in 2018	**% of dose 1 recipients also receiving dose 2 by 31 Dec 2018**	**% of dose 1 recipients also receiving dose 2 by 31 Dec 2019**	**Number receiving dose 1 in 2018**	**% of dose 1 recipients also receiving dose 2 by 31 Dec 2018**	**% of dose 1 recipients also receiving dose 2 by 31 Dec 2019**
AUSTRALIA	All	126349	86.2	93.4	129802	84.8	92.5
State of residence	ACT	2326	84.3	92.2	2290	84.6	90.9
	NSW	40955	86.7	96.1	42139	84.3	95.6
	VIC	31553	88.4	92.9	32254	86.9	91.4
	QLD	26811	84.3	91.6	27531	83.2	90.4
	SA	7956	86.9	91.2	8149	85.7	90.0
	WA	13067	87.8	94.0	13767	88.3	94.6
	TAS	2411	72.7	80.3	2431	71.3	78.5
	NT	1270	65.2	85.5	1241	64.5	83.5
Remoteness category	Major Cities	89022	87.4	94.1	91913	85.9	93.3
	Regional	34035	84.5	91.9	34487	83.0	90.9
	Remote	2171	67.0	85.0	2257	69.3	84.9
	Decile 1	10692	80.7	90.4	10853	79.7	89.8

SEIFA decile	Decile 2	10848	84.8	92.5	10816	83.1	91.0
	Decile 3	10779	84.4	92.2	10965	82.9	91.1
	Decile 4	10380	85.3	93.4	10805	83.2	91.9
	Decile 5	11621	85.5	93.0	12105	84.4	92.3
	Decile 6	12436	87.4	94.3	12849	85.2	93.3
	Decile 7	13628	87.0	93.0	13610	86.0	92.4
	Decile 8	15044	87.8	93.9	15460	85.9	93.1
	Decile 9	12538	88.2	94.3	13006	86.7	92.9
	Decile 10	16956	88.8	95.3	17913	88.0	95.0

Source: Australian Immunisation Register, data as at 29 February 2020.

Table 34. Number of Indigenous adolescents aged <15 years commencing 9vHPV vaccination in 2018 and the percentage completing the 2-dose schedule by 31 December 2019, by gender, jurisdiction and remoteness/socioeconomic status of area of residence.

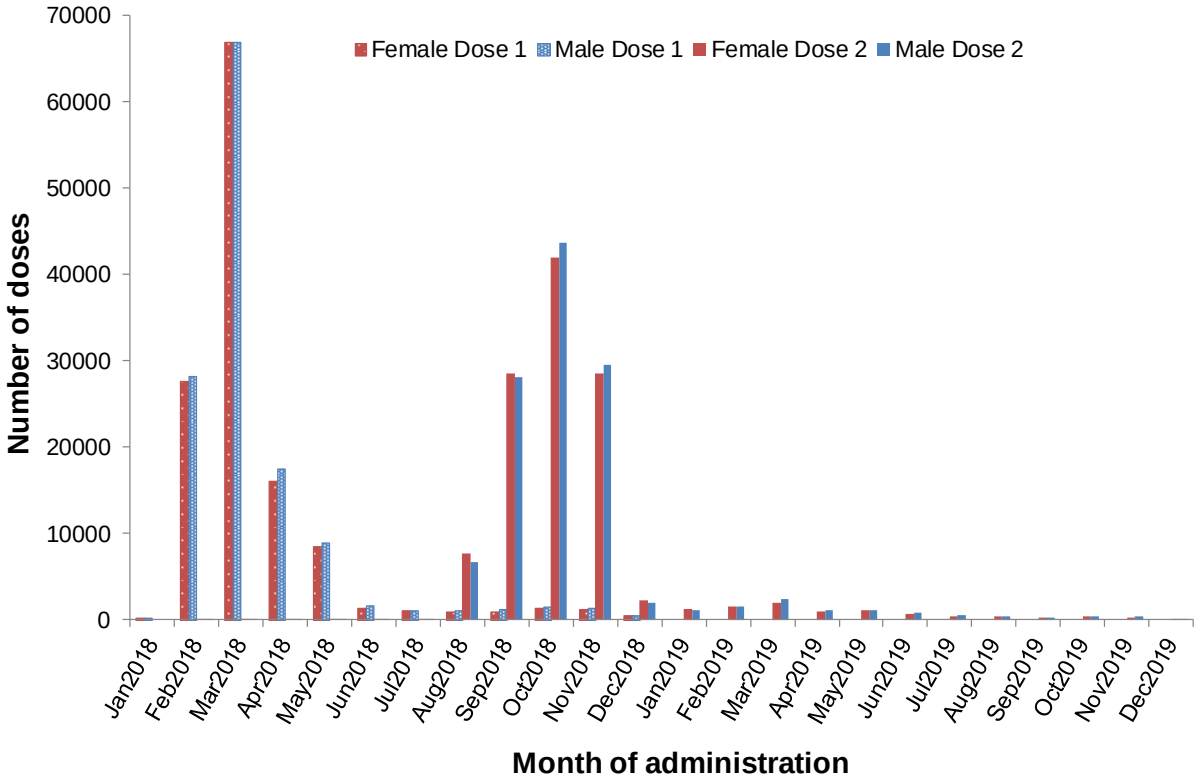
		Females			Males		
		Number receiving dose 1 in 2018	**% of dose 1 recipients also receiving dose 2 by 31 Dec 2018**	**% of dose 1 recipients also receiving dose 2 by 31 Dec 2019**	**Number receiving dose 1 in 2018**	**% of dose 1 recipients also receiving dose 2 by 31 Dec 2018**	**% of dose 1 recipients also receiving dose 2 by 31 Dec 2019**
AUSTRALIA	Indigenous	5962	68.7	85.9	5604	66.4	84.3
State of residence	ACT	51	78.4	90.2	36	63.9	69.4
	NSW	2070	75.7	92.3	2009	71.7	90.6
	VIC	489	77.3	86.9	428	74.1	84.4
	QLD	1844	70.4	84.3	1685	68.4	82.8
	SA	191	63.4	75.9	186	66.1	75.8
	WA	666	61.4	81.4	689	61.7	82.3
	TAS	185	58.4	70.8	150	62.0	71.3
	NT	466	36.7	79.4	421	34.4	73.4
Remoteness category	Major Cities	2106	73.7	88.7	2083	71.9	87.4
	Regional	2882	72.4	86.1	2599	68.8	84.3
	Remote	840	45.1	79.1	782	44.8	76.2

SEIFA decile	Decile 1	1094	54.0	80.4	1054	51.8	78.0
	Decile 2	792	72.2	86.5	686	69.8	87.2
	Decile 3	720	72.1	86.0	640	72.3	86.6
	Decile 4	726	72.7	88.6	680	69.7	83.8
	Decile 5	617	69.5	87.0	623	64.2	82.8
	Decile 6	534	74.3	88.2	498	70.1	88.0
	Decile 7	379	74.7	86.3	357	69.7	81.8
	Decile 8	449	70.2	86.4	423	71.4	89.6
	Decile 9	238	76.9	88.7	243	77.0	86.8
	Decile 10	230	79.6	93.9	226	77.0	89.4

Source: Australian Immunisation Register, data as at 29 February 2020.

Figure 16 shows that most first HPV vaccine doses in 2018 were given in March, with dose 2 administration peaking in October. Figure 17 shows the interval between receipt of doses 1 and 2 for female and male adolescents commencing the 2-dose course in 2018. The median interval between the two doses was 6.9 months for both female and male adolescents. The interval between dose 1 and dose 2 did not vary by gender but did vary by jurisdiction (Figures 18–19), with the median interval ranging from 6.0 months in NT to 7.6 months in QLD.

Figure 16: Monthly administration of 9vHPV vaccine dose 1 during 2018 and dose 2* during 2018 and 2019 in Australian adolescents aged <15 years† by gender

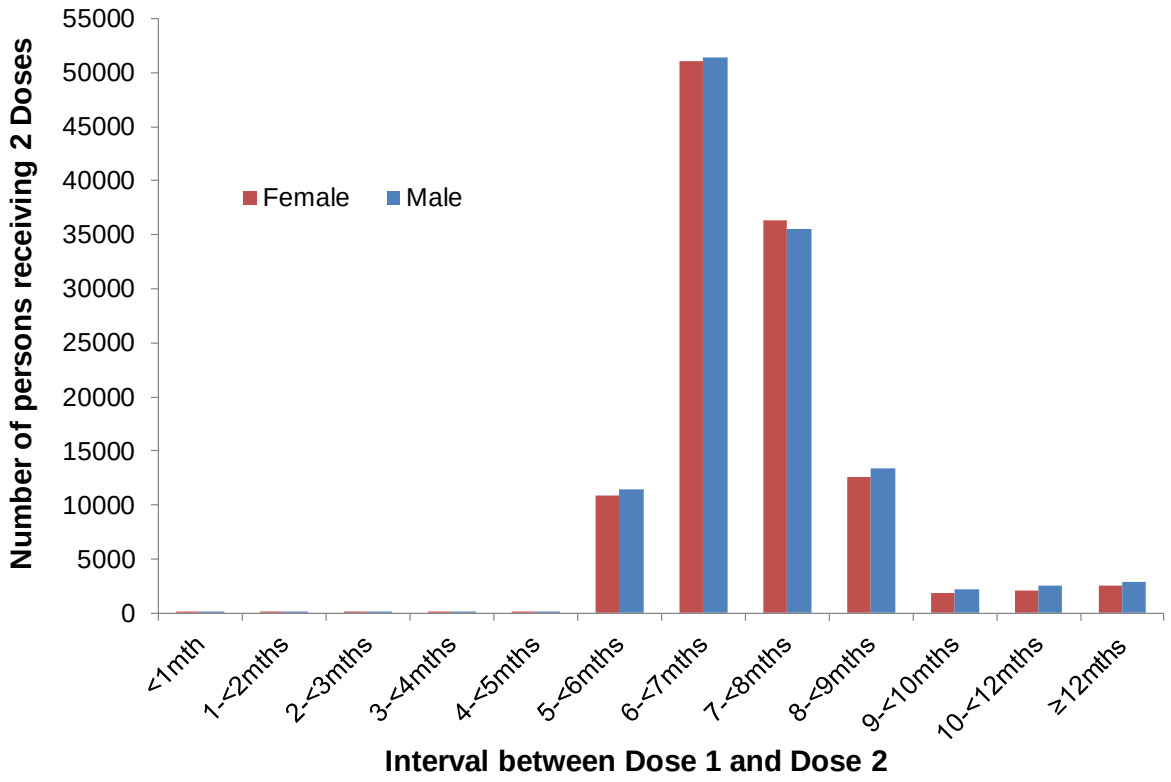


* Dose 2 counts are for only those who received dose 1 in 2018.

† Adolescents aged <15 years at time of dose 1 receipt.

Source: Australian Immunisation Register, data as at 29 February 2020.

Figure 17: Interval between dose 1 and dose 2* of 9vHPV vaccine administered during 2018 and 2019 to Australian adolescents aged <15 years†

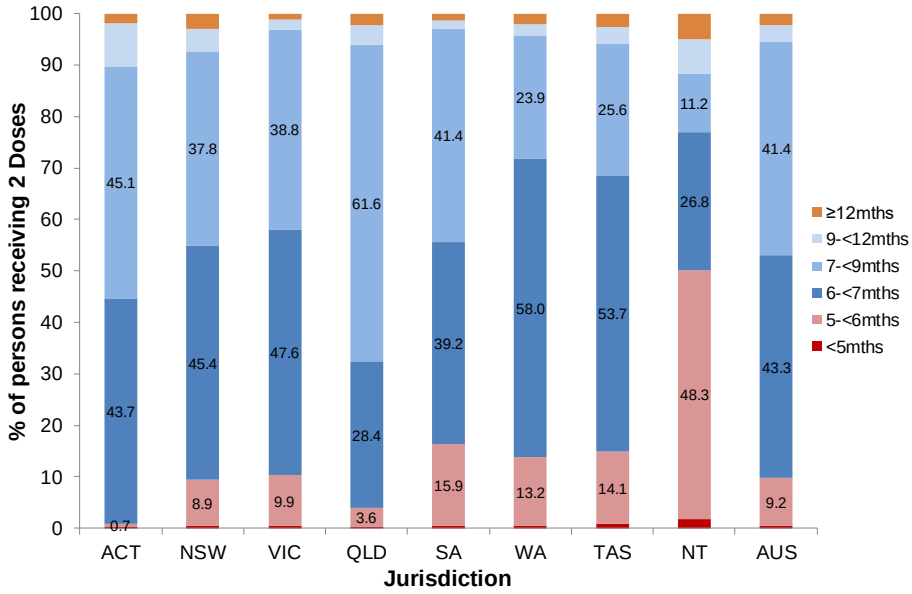


* Dose 2 counts are for only those who received dose 1 in 2018.

† Adolescents aged <15 years at time of dose 1 receipt.

Source: Australian Immunisation Register, data as at 29 February 2020.

Figure 18: Interval between dose 1 and dose 2* of 9vHPV vaccine administered during 2018 and 2019 to female adolescents aged less than 15 years,† by jurisdiction



* Dose 2 counts are for only those who received dose 1 in 2018.

† Adolescents aged <15 years age at time of dose 1 receipt.

Source: Australian Immunisation Register, data as at 29 February 2020

Figure 19: Interval between dose 1 and dose 2* of 9vHPV vaccine administered during 2018 and 2019 to male adolescents aged less than 15 years,† by state of residence, Australia

* Dose 2 counts are for only those who received dose 1 in 2018.

† Adolescents aged <15 years at time of dose 1 receipt.

Source: Australian Immunisation Register, data as at 29 February 2020

Tables 35 and 36 indicate setting of HPV vaccination/provider type by jurisdiction for adolescents aged <15 years and reflect immunisation service structures in each jurisdiction. Of note QLD and TAS have the largest proportion of GP doses for both doses 1 and 2.

Table 35. Percentage* of 9vHPV vaccine dose 1 and dose 2 administered during 2018 and 2019 to female adolescents aged <15 years† by provider type and jurisdiction

Dose 1							
	% administered in						
	Number of Doses	Community Health	Council	General Practice	Public/Private Hospital	State Health/PHU	Aboriginal Health Service
ACT	4727	93.4	1.4	4.4	0.2	0.5	0.0
NSW	83150		1.0	7.3	8.4	19.7	0.2
VIC	65178	1.0	89.0	9.2	0.4	0.4	0.0
QLD	55697	34.2	43.7	17.9	3.0	1.1	0.1
SA	16635	7.8	82.3	7.5	1.2	0.9	0.3
WA	41172	74.4	15.8	6.9	0.8	1.9	0.1
TAS	4967	1.4	79.5	17.5	0.1	1.3	0.0
NT	2752	11.6	3.8	7.0	0.8	61.0	15.7
AUS	274278	39.8	39.2	10.0	3.5	7.3	0.3
Dose 2							
	% administered in						
	Number of Doses	Community Health	Council	General Practice	Public/Private Hospital	State Health/PHU	Aboriginal Health Service
ACT	4210	91.2	1.4	6.7	0.2	0.5	0.0
NSW	76366		0.9	5.4	3.0	27.2	0.2
VIC	58538	0.9	90.4	8.1	0.3	0.4	0.0

QLD	48939	35.1	44.8	16.1	2.7	1.3	0.1
SA	14801	7.3	83.9	6.7	1.2	0.8	0.2
WA	37102	76.3	16.0	5.7	0.7	1.1	0.1
TAS	3919	1.5	81.2	16.1	0.1	1.1	0.0
NT	2061	9.8	4.1	6.1	0.4	69.2	10.3
AUS	245936	40.5	39.5	8.5	1.7	9.6	0.2

* Where the percentage for a state/territory does not add up to 100%, the remainder of doses are in the 'Other' provider type category.

† Adolescents aged <15 years at time of dose 1 receipt.

Note: The high number of doses administered in community health in NSW appears to be a data issue associated with some PHUs being incorrectly categorised as community health (versus State Health/PHU) on AIR.

Source: Australian Immunisation Register, data as at 29 February 2020.

Table 36. Percentage* of 9vHPV vaccine dose 1 and dose 2 administered during 2018 and 2019 to male adolescents aged <15 years† by provider type and jurisdiction

Dose 1							
	% administered in						
	Number of Doses	**Community Health**	**Council**	**General Practice**	**Public/Private Hospital**	**State Health/PHU**	**Aboriginal Health Service**
ACT	4887	94.1	1.1	3.9	0.1	0.7	0.0
NSW	84855		1.1	7.0	8.6	19.5	0.2
VIC	66675	1.0	90.0	8.2	0.4	0.4	0.0
QLD	57553	34.9	42.9	17.6	3.4	1.2	0.1
SA	17169	8.8	82.2	6.8	1.2	0.8	0.3

WA	42999	75.1	16.0	6.0	0.7	2.0	0.2
TAS	4980	1.4	80.9	16.5	0.2	0.9	0.0
NT	2719	11.2	3.9	7.7	0.7	58.4	18.1
AUS	281837	40.3	39.3	9.4	3.6	7.1	0.3
Dose 2							
% administered in							
	Number of Doses	**Community Health**	**Council**	**General Practice**	**Public/Private Hospital**	**State Health/PHU**	**Aboriginal Health Service**
ACT	4263	92.2	1.1	5.9	0.0	0.7	0.0
NSW	76914		1.0	4.4	2.6	27.3	0.2
VIC	58886	0.8	92.0	6.5	0.3	0.3	0.0
QLD	49477	36.3	44.2	15.2	3.0	1.3	0.1
SA	15020	8.5	84.1	5.5	1.2	0.6	0.1
WA	38660	77.4	16.4	4.3	0.7	1.2	0.1
TAS	3870	1.6	83.9	13.4	0.1	1.0	0.0
NT	1921	10.3	4.5	5.5	0.9	69.4	9.5
AUS	249011	41.5	39.8	7.3	1.7	9.5	0.2

* Where the percentage for a state/territory does not add up to 100%, the remainder of doses are in the 'Other' provider type category.
† Adolescents aged <15 years of age at time of dose 1 receipt.

Note: The high number of doses administered in community health in NSW appears to be a data issue associated with some PHUs being incorrectly categorised as community health (versus State Health/PHU) on AIR.

Source: Australian Immunisation Register, data as at 29 February 2020.

Uptake of 9vHPV vaccine in adolescents aged 15 to <20 years

Tables 37 and 38 show that general practices administer most HPV vaccine doses to those aged 15 to <20 years in every jurisdiction except NT where community health and Aboriginal Health Services provide the majority of HPV vaccines.

Table 37. Percentage* of HPV vaccine doses administered between 1 July 2017 and 31 December 2019 to females aged 15 to <20 year† by provider type and jurisdiction

Female Dose 1							
% administered in							
	Number of Doses	Community Health	Council	General Practice	Public/Private Hospital	State Health/PHU	Aboriginal Health Service
ACT	185	6.5	0.5	89.7	0.5	2.7	0.0
NSW	2658		0.3	87.6	1.2	6.4	0.7
VIC	2438	0.9	14.6	79.8	1.6	2.8	0.3
QLD	2946	7.9	2.6	84.6	1.8	1.7	1.1
SA	760	10.8	17.0	65.8	1.5	2.6	2.4
WA	1310	24.6	1.1	66.3	2.2	4.4	1.5
TAS	239	0.4	4.2	94.1	0.4	0.0	0.4
NT	156	19.9	0.6	41.0	1.92	6.4	30.1
AUS	10692	7.5	5.6	80.3	1.6	3.6	1.3
Female Dose 2							
% administered in							
	Number of Doses	Community Health	Council	General Practice	Public/Private Hospital	State Health/PHU	Aboriginal Health Service
ACT	148	5.4	0.7	91.2	1.4	1.4	0.0
NSW	2248		0.4	87.3	1.3	6.3	0.8
VIC	2304	0.6	17.4	77.5	1.7	2.5	0.4
QLD	2617	5.1	2.3	87.5	2.0	2.2	0.6
SA	788	9.9	27.0	57.9	1.5	1.8	1.8
WA	1285	25.6	2.2	65.2	1.0	4.2	1.8
TAS	218	0.9	2.8	92.7	0.9	2.3	0.0
NT	213	18.3	0.0	33.8	0.9	8.5	38.5
AUS	9821	7.0	7.3	78.8	1.5	3.6	1.6
Female Dose 3							
% administered in							

	Number of Doses	Community Health	Council	General Practice	Public/Private Hospital	State Health/PHU	Aboriginal Health Service
ACT	131	1.5	1.5	93.9	1.5	0.8	0.8
NSW	1346		0.6	90.2	0.8	3.9	0.7
VIC	1828	0.4	19.5	75.6	1.9	2.2	0.3
QLD	1998	5.6	3.2	84.3	3.4	2.5	0.9
SA	676	8.6	31.1	55.9	1.0	2.4	1.0
WA	1023	28.5	3.0	59.4	1.7	5.5	2.0
TAS	187	0.5	9.1	88.8	1.1	0.5	0.0
NT	195	22.1	0.5	23.1	0.5	11.3	42.6
AUS	7384	7.7	9.3	75.8	1.9	3.2	1.9

* Where the percentage for a state/territory does not add up to 100%, the remainder of doses are in the 'Other' provider type category.

† Age assessed at 31 December 2019.

Note: The high number of doses administered in community health in NSW appears to be a data issue associated with some PHUs being incorrectly categorised as community health (versus State Health/PHU) on AIR.

Source: Australian Immunisation Register, data as at 29 February 2020.

Table 38. Percentage* of HPV vaccine doses administered between 1 July 2017 and 31 December 2019 to males aged 15 to <20 years† by provider type and jurisdiction

Male Dose 1							
% administered in							
	Number of Doses	Community Health	Council	General Practice	Public/Private Hospital	State Health/PHU	Aboriginal Health Service
ACT	138	8.0	1.5	86.2	0.7	3.6	0.0
NSW	2544		0.3	83.2	1.6	8.1	0.4
VIC	2349	0.5	18.1	75.5	2.9	2.5	0.5
QLD	2938	11.9	3.2	77.8	2.4	3.8	0.7
SA	705	17.5	19.3	56.5	1.8	3.0	2.0
WA	1286	28.4	1.3	55.9	1.9	11.0	1.5
TAS	228	1.3	4.0	90.8	0.4	3.1	0.0
NT	198	15.2	0.0	28.8	1.5	11.1	43.4
AUS	10386	10.1	6.7	73.9	2.1	5.5	1.6
Male Dose 2							
% administered in							

	Number of Doses	Community Health	Council	General Practice	Public/Private Hospital	State Health/PHU	Aboriginal Health Service
ACT	121	5.0	1.7	90.9	0.0	1.7	0.8
NSW	1948		0.3	82.2	1.8	7.5	0.5
VIC	2013	0.6	19.9	74.3	2.1	2.6	0.5
QLD	2323	10.0	3.4	80.8	2.0	2.6	0.7
SA	765	12.9	34.5	47.1	1.6	2.1	1.8
WA	1249	29.5	1.8	54.8	2.2	10.3	1.4
TAS	194	1.0	3.6	91.2	1.0	2.6	0.0
NT	284	16.9	0.0	16.2	0.7	13.0	53.2
AUS	8897	10.3	8.8	71.4	1.9	5.1	2.5
Male Dose 3							
% administered in							
	Number of Doses	**Community Health**	**Council**	**General Practice**	**Public/Private Hospital**	**State Health/PHU**	**Aboriginal Health Service**
ACT	88	2.3	1.1	95.5	0.0	1.1	0.0
NSW	1098		1.0	85.2	1.3	5.3	0.3
VIC	1505	0.6	23.8	71.7	2.1	1.6	0.2
QLD	1737	13.6	3.3	76.2	3.1	2.9	0.6
SA	626	8.3	37.5	47.1	3.0	2.1	1.9
WA	945	34.9	2.7	49.8	0.6	10.2	1.8
TAS	172	0.0	4.7	91.9	0.6	2.9	0.0
NT	235	14.5	1.7	11.5	1.3	15.3	55.7
AUS	6406	11.6	10.9	68.3	2.0	4.4	2.8

* Where the percentage for a state/territory does not add up to 100%, the remainder of doses are in the 'Other' provider type category.

† Age assessed at 31 December 2019.

Note: The high number of doses administered in community health in NSW appears to be a data issue associated with some PHUs being incorrectly categorised as community health (versus State Health/PHU) on AIR.

Source: Australian Immunisation Register, data as at 29 February 2020.

Summary/discussion

Current cumulative HPV vaccine coverage (based on age at 31 December 2019) is broadly consistent with historical data trends from previous coverage derived from the HPV Register. The 15-year-old cohort in 2019, the first cohort that included some adolescents vaccinated with two doses of 9vHPV vaccine, shows 2-dose coverage of 82.6% in females and 79.9% in males. Coverage remains several percentage points higher in females than in males. Consistent with the

HPV Register estimates,[43] first dose coverage is roughly equivalent for Aboriginal and Torres Strait Islander and non-Indigenous adolescents, except in 13–14-year-old Aboriginal and Torres Strait Islander males who have 4–5% lower dose 1 coverage than their non-Indigenous peers. Also consistent with the HPV Register data, there is a lower coverage for second and third doses (lower course completion) for Aboriginal and Torres Strait Islander adolescents.

HPV vaccine coverage at 15 years of age increased over time to 2018, in both Aboriginal and Torres Strait Islander and non-Indigenous adolescents. In 2019, dose 2 coverage declined in Aboriginal and Torres Strait Islander female and male adolescents relative to the previous year. Dose 2 and dose 3 coverage in 2019 shows that most adolescents in NSW, SA and WA had transitioned to the 2-dose schedule because of the earlier implementation of the 2-dose schedule in NSW and the age of vaccination in SA and WA.

Adolescents aged 15 to <20 years received their 9vHPV vaccine doses predominantly in general practice in all jurisdictions except NT where community health and Aboriginal Health Services provided the majority of HPV vaccines.

The overall comparison between the HPV Register and AIR estimates shows that the HPV Register vaccination coverage estimates for all doses are universally higher than the AIR estimates for females aged 13–18 years and males aged 13–17 years. However, for females aged 19 years and males aged 18–19 years, the coverage estimates for each dose are higher using the AIR data. The last published cohort for coverage estimates from the HPV Register was for adolescents aged 12–19 years in 2017, with data as notified to mid-2018. Notably by this time WA had ceased reporting to the HPV Register directly and the HPV Register was receiving large numbers of notifications from AIR, many of which duplicated state-based notifications. Best efforts were made to identify and remove such duplicates but because of missing data or data quality issues, this was not always possible.

The differences in ABS ERP and Medicare denominator estimates in Tables 21 and 22 are notable and require a wider discussion regarding the interpretation/differences in the population captured in either denominator. In each of the 13- and 14-year-old cohorts in 2017, Medicare denominator data included over 10,000 more individuals than ERP data. This is in direct contrast to an earlier study assessing the impacts on HPV vaccine coverage of the two alternative denominators, which found that in 2007 there was only a minor difference of <250 individuals in these younger age groups and that it was older adolescents where there was the greatest discrepancy.[15]

Estimation and monitoring of HPV vaccination coverage poses several challenges different from those for monitoring coverage of childhood vaccines. Unlike vaccines given in early childhood, there is no necessity to give the HPV vaccine at an exact scheduled age and the recommended age for the routine delivery of HPV vaccine (in Australia 12–13 years) reflects both the local median age of sexual debut (HPV vaccine effectiveness greatest if given before then) and the practicalities/method of administration in our setting (in the early high school vaccine program). In the school-based HPV vaccination programs, not all children are offered HPV vaccine at the same age, with children in one year level with a range of ages (typically the first or second year of high school) in each state usually offered vaccination per year. This makes measuring vaccination coverage by age or birth cohort at a state or national level problematic compared with that for

childhood age scheduled vaccines because not all children aged 12 or 13 would have been offered the vaccine or would have had the time required to be offered the second dose. Recognising this challenge, and the varying ages at which countries routinely administer HPV vaccines, WHO recommends vaccination coverage achieved in each birth cohort by age 15 as a metric that will allow comparison of coverage between countries and over time.[144] However, this metric is too lagged to identify any drop in coverage or program issues in a timely way, making monitoring of coverage with the best available program data enumerating the targeted school-based cohort in each area important. According to the HPV Register coverage estimates, 3-dose coverage in those aged 15 years has gradually improved over time in Australia and had reached 80% for females and 76% for males by 2017.

Monitoring of HPV vaccination coverage in birth cohorts of adult women is likely to be of high interest in future, because cervical screening practices may become dependent on vaccination status once those vaccinated with 9vHPV vaccine reach 25 years of age (the age at which screening starts). When extracting data for such cohorts from AIR in future, it is to be expected that apparent coverage will have fallen markedly from that estimated originally at age 15 years in the same cohort because of the ongoing increase in the Medicare-eligible denominator population as a result of migration.

Vaccine safety

Aims

To evaluate vaccine safety issues relating to HPV vaccines.

Therapeutic Goods Administration Adverse Events Management System data

The Therapeutic Goods Administration (TGA) Adverse Events Management System (AEMS) is a spontaneous surveillance system for monitoring adverse events associated with the use of a medicine or vaccine. Vaccine adverse event reports received by the TGA are entered into AEMS.[145] Information recorded in the database includes the adverse event(s), the vaccine(s) involved and other relevant information provided by the reporter, such as relevant medical history, laboratory results and how the adverse event was treated.[145]

We analysed data on adverse events following 4vHPV vaccine doses administered between April 2007 and December 2017, reported by March 2018.

AusVaxSafety

AusVaxSafety is an enhanced active surveillance system for adverse events following immunisation (AEFI) coordinated by NCIRS and funded by the Australian Government Department of Health.[146]

AusVaxSafety monitors the safety of vaccines through sentinel active SMS-based surveillance.[146] Vaccine recipients (or their caregivers) are sent an SMS in the days following vaccination and asked whether any adverse events were experienced. If an adverse event is reported, additional SMS are sent asking whether medical attention was sought for the adverse event and providing a link to an online survey for more details. Signal detection methods are employed to monitor for any safety signals. AusVaxSafety data were reviewed and summarised from two surveillance systems, SmartVax (for the overall surveillance period 1 February 2018 – 31 December 2019) and Vaxtracker (for the period 15 October 2019 – 7 November 2019).

Methods

AEMS

We focused on determining age- and sex-specific AEFI reporting rates, analysed the impact of enhanced surveillance and examined adverse events of special interest (AESI).

Study population and surveillance system characteristics

Australia has a population of approximately 25 million, and over nine million doses of HPV vaccine were administered between 2007 and 2017, according to the National HPV Vaccination Program Register (HPV Register). The majority of doses were given through the school-based vaccination program (94% for males, 69% for females overall and 92% for females once early community catch-up programs ceased).

Pharmaceutical companies (Australian sponsors) are required to report adverse events to the TGA within mandated timeframes. However, anyone can voluntarily report a suspected adverse event to the TGA, including immunisation providers, consumers and parents. In most jurisdictions (comprising eight states and territories) that have responsibility for administering school-based vaccination programs, adverse event reporting is a statutory obligation for healthcare providers and predominantly occurs via state/territory vaccine safety surveillance mechanisms.[147] Reporters are requested to provide patient identifiers, including date of birth or age, details of the product involved and the suspected adverse event, including dates. The reporter is also able to provide contact details, if consent is provided, to enable communication to seek additional information, if required. Reports are coded by the TGA using the internationally recognised Medical Dictionary for Regulatory Activities (MedDRA®) standardised terms, including preferred terms,[148] and stored in the AEMS database.

Australian sponsors are required to apply seriousness coding to ensure legislated requirements are met. Other reports are coded (typically on initial receipt) as 'serious' based on criteria similar to the World Health Organization (WHO) definition[149] and available information, where any of the following outcomes are documented: death; inpatient hospitalisation or prolongation of existing hospitalisation; persistent or significant disability; life-threatening; or congenital anomaly/birth defect. Any event that requires medical intervention to prevent one of these outcomes (a medically important event or reaction) may also be considered as serious. The TGA identifies and reviews medically important cases, which are flagged for review by the TGA clinical staff. Where a 'serious' adverse event report lacks information, TGA routinely requests follow-up information from the reporter with assistance from the relevant state or territory health department, including medical record information where required; however, this may not always be provided.

Using the TGA AEMS database, we analysed adverse event following 4vHPV vaccine doses administered between 1 April 2007 and 31 December 2017 for females, and between 1 February 2013 and 31 December 2017 for males, and reported by March 2018 to allow for reporting lag. Reports following nonavalent (9vHPV) or bivalent (2vHPV) HPV vaccines were excluded. 9vHPV vaccine was not available until 1 January 2018 after which it was added to the National Immunisation Program (NIP), replacing 4vHPV vaccine. The bivalent vaccine was not supplied under the NIP and thus only administered to a small number of women within primary care over the study period. Where no vaccine type was specified, reports were included and presumed to be related to 4vHPV vaccine. Reports following vaccination during pregnancy were identified using methods described previously.[150]

For reports that were missing vaccination date, the date of reaction onset was used (the median lag time between vaccination date and reaction onset date was 0 days in this cohort). Where the

reaction onset date was missing, the vaccination date was replaced with the date the report was received minus 15 days (the median lag time from vaccination to report in this cohort). Vaccination date was only used to determine annual rates and changes in rates over time. For description of individual AESI, additional free text data was used to review time between vaccination and reaction onset. Where multiple 4vHPV doses were recorded within one report, the date of latest vaccination was used.

Descriptive analysis

Adverse event reports were described for males and females by age group, reporter type, concomitant vaccination and seriousness code. We identified the top 10 most commonly reported MedDRA Preferred Terms by sex. Crude adverse event reporting rates per 100,000 doses administered were calculated across the entire program, with age- and sex-specific adverse event rates calculated for the NIP cohorts (refer to Table 39). Rates for females and males in the primary target cohort were analysed separately during the enhanced surveillance period. Doses administered by vaccine type, age, sex and time period were obtained from the National HPV Vaccination Program Register (HPV Register).

Table 39. NIP-funded age groups, vaccination program type and year of program delivery for 4vHPV vaccine in Australia, 2007 to 2017

Program delivery type	NIP-funded age group	Year of program delivery
Primary Program		
Female	12 to 13-years	2007 to 2017
Male		2013 to 2017
Catch-up program		
Female	14 to 26-years	2007 to 2009
Male	14 to 15-years	2013 to 2014

Adverse events of special interest

Adverse events of special interest (AESI) were determined by reviewing literature[151-153] and from recent analyses of the United States (US) Vaccine Adverse Events Reporting System (VAERS).[154] The following conditions were selected: syncope, venous thromboembolism (VTE), anaphylaxis, autoimmune disease (AID), postural orthostatic tachycardia syndrome (POTS), complex regional pain syndrome (CRPS) and Guillain-Barré syndrome (GBS). To allow comparison with international data, MedDRA Preferred Terms were selected in VAERS analyses[154] (refer to Appendix 8) with the exception of GBS, where the term ‘chronic inflammatory demyelinating polyradiculoneuropathy’ (CIDP) was added (CIPD is considered a chronic form of GBS).[155] These MedDRA terms were used as a sensitive search for potentially relevant cases, which were then further reviewed to determine whether cases met published criteria for the specific condition. De-identified cases were obtained, where available, from the TGA for all AESI except syncope. TGA case details included those obtained during investigation of the adverse event. Reports of

anaphylaxis had been classified according to Brighton Collaboration criteria by the TGA on the basis of available data.[156]

Signal detection methods were not applied in this retrospective analysis; this is undertaken continuously and prospectively by the TGA.

AusVaxSafety

Data collection

Participant-reported adverse event data were obtained via two surveillance tools, SmartVax and Vaxtracker, installed at sentinel sites across Australia. As at February 2020, SmartVax was installed at over 325 GP, hospital, council, community clinic and Aboriginal Medical Service (AMS) sites, and several of the council sites using SmartVax also deliver school-based immunisations.

Vaxtracker was used for HPV vaccine safety surveillance in school-based immunisation programs delivered by five public health units in NSW only. Both tools automatically send an SMS message to a vaccinated adolescent's caregiver that enquired about AEFI.

For SmartVax users, this initial SMS (SMS1) stated: "We would like to know if there were any reactions to the vax. Please reply with 'Y' for Yes, 'N' for No or 'STOP' to opt out."

Caregivers who responded 'Y' to SMS1 received a second SMS message (SMS2) that asked, "As a result of the vaccination reaction, did you visit a doctor, medical centre, after hours service, or hospital emergency dept [sic]?" These caregivers also received an additional SMS message that contained a link to a short online survey where the caregiver could report specific solicited and unsolicited adverse events and details of medical attention sought.

Caregivers of adolescents vaccinated at Vaxtracker sites received only one SMS that contained a link to an online survey. In this survey, caregivers were asked: "Did [your child] experience any kind of reaction, illness or discomfort after the vaccination?" If caregivers responded 'Yes', further questions appeared that sought details about specific solicited adverse events and also whether medical attention was sought for the reaction. Participants could unsubscribe after enrolling/clicking on the survey link.

De-identified, line-listed data containing demographic, vaccination and SMS/survey response information were obtained from both the SmartVax and Vaxtracker tools by the NCIRS for cleaning and analysis.

Surveillance design and study population

AusVaxSafety active HPV vaccine safety surveillance commenced on 1 February 2018. The HPV vaccine funded under the NIP from this time was the 9-valent Gardasil brand, but residual 4-valent Gardasil was also available for the third dose in catch-up programs.

At this time, only SmartVax collected HPV vaccine safety data for AusVaxSafety.

Vaxtracker was implemented to collect HPV vaccine safety data for school-based immunisation programs in NSW in late 2019, and contributed data only for school term 4 (October–November) in 2019. HPV vaccine safety data were analysed for the overall surveillance period 1 February 2018 – 31 December 2019 for SmartVax, and 15 October 2019 – 7 November 2019 for Vaxtracker.

Inclusion criteria were as follows:

- adolescent aged 11–14 years
- adolescent received an HPV vaccine (including 2-valent Cervarix, 4-valent Gardasil, 9-valent Gardasil, or HPV vaccine with brand unspecified) at a sentinel SmartVax or Vaxtracker site (including schools whose vaccinations were delivered by SmartVax or Vaxtracker sites)
- caregiver responded within 7 days post vaccination to an SMS message and/or survey enquiring about their adolescent's adverse events following immunisation.

Definitions

A report of any AEFI was defined as responding 'Y' to SMS1 for SmartVax or 'Yes' to the survey question asking about any reactions for Vaxtracker.

A participant was defined as an adolescent whose caregiver participated by responding 'Y' or 'N' to SMS1 for SmartVax, or 'Yes' or 'No' to the survey question asking about any reactions for Vaxtracker. A caregiver was considered to have participated if they responded to SMS1 or the Vaxtracker survey. Participants may have had multiple vaccination encounters during the surveillance period, and may not represent unique individuals.

For SmartVax, note that not all caregivers who reported any adverse event responded to SMS2 and/or the online survey; these participants have been included in calculations involving SMS1, but excluded from calculations involving SMS2 and/or the survey.

A report of medical attendance (MA) was defined as responding 'Y' to SMS2 for SmartVax, or indicating presentation to a general practice (GP) or an emergency department (ED) in the online survey question: "As a result of your reaction, did you visit, or were you visited by, any of the following: GP/medical centre, after hours/locum, ED?" For Vaxtracker, an MA report was defined as responding to the medical attention question ("Did you seek medical attention for the reaction?") in the online survey.

Data analysis

Data were cleaned and analysed using Stata version 14.2. Figures were prepared in Microsoft Excel 2010.

Analyses performed included a descriptive analysis of participant demographic information (age, sex, Aboriginal and Torres Strait Islander status and location), adverse events reported and MAs reported.

Surveillance captured vaccination encounters from a wide range of settings where multiple vaccines were often given at the same visit (e.g. HPV and dTpa vaccines, which are scheduled

together in school-based immunisation programs). For SmartVax data, analyses were stratified according to whether adolescents received only HPV vaccine, only HPV and dTpa vaccines, or HPV and other vaccines (e.g. influenza vaccine). Note that an encounter where an adolescent received HPV, dTpa and another vaccine (e.g. influenza vaccine) was included in 'HPV and other vaccine(s)' group.

Multiple HPV vaccine brands (Gardasil9, Gardasil and Cervarix) were available during the surveillance period and we assumed that vaccine brands were given as recorded. Data were not validated, and therefore, data entry errors (e.g. mis-recorded brands) were possible.

Unsolicited AEFI reported via free text were manually reviewed and classified to MedDRA® (Medical Dictionary for Regulatory Activities) version 21.0 preferred terms using MedDRA Desktop Browser© version beta 4.0.0.97.

Statistical analyses

Pearson's chi-square test was performed to compare the rates of any adverse event and MA by sex, Aboriginal and Torres Strait Islander status, additional vaccine status and brand (SmartVax only), except in the case with cell counts <5, in which Fisher's exact test was performed. These analyses were performed using Stata version 14.2. A p-value of less than 0.05 was considered significant

Results

Adverse Events Management System (AEMS)

For 4vHPV vaccine doses given between 1 April 2007 and 31 December 2017, the TGA received 4,556 adverse event reports up to 31 March 2018. Five reports for males were excluded from the main analysis (three for males vaccinated before the 2013 NIP expansion and two for male infants whose mothers were vaccinated). During the entire study period, 4,402 doses of 2vHPV vaccine were administered in Australia, with 18 adverse event reported; these reports were not further examined.

Most reports were for the primary NIP-funded cohort (12- to 13-year-old males and females) and the most common reporters were the respective state and territory health departments, reflecting established pathways for reporting to the TGA (refer to Table 40). The most commonly reported MedDRA Preferred Terms were similar among males and females, with headache and syncope the most common (refer to Table 41).

Table 40. Summary of adverse event reports to the TGA following 4vHPV vaccine given to females (2007 to 2017) and males (2013 to 2017)

	Female n (%)	Male n (%)	Unknown n (%)	Total n (%)
Total reports	3221 (70.8)	1298 (28.5)	32 (0.7)	4551
Coded as serious	295 (9.2)	54 (4.2)	5 (15.6)	354 (7.8)

4vHPV only	2167 (67.3)	604 (46.5)	22 (68.8)	2793 (61.4)
Reporter type				
Health Professional	447 (13.9)	53 (4.1)	6 (18.8)	506 (11.1)
Patient/Consumer	180 (5.6)	38 (2.9)	2 (6.2)	220 (4.8)
Sponsor	106 (3.3)	1 (0.1)	8 (25.0)	115 (2.5)
State/Territory surveillance system	2488 (77.2)	1206 (92.9)	16 (50.0)	3710 (81.5)
Age group (years)				
Under 12 years	99 (3.1)	39 (3.0)	3 (9.4)	141 (3.1)
12-13 years	1740 (54.0)	960 (74.0)	7 (21.9)	2707 (59.5)
14-17 years	695 (21.6)	277 (21.3)	5 (15.6)	977 (21.5)
18 years and over	627 (19.5)	9 (0.7)	4 (12.5)	640 (14.1)
Unknown	60 (1.9)	13 (1.0)	13 (40.6)	86 (1.9)

Table 41. Top 10 Preferred Terms and as a percentage of all MedDRA Preferred Terms for adverse events following 4vHPV vaccine reported to TGA for females (2007– 2017) and males (2013–2017)*

Females	n (%)	Males	n (%)
Headache	550 (6.5)	Syncope	362 (13.8)
Syncope	467 (5.5)	Headache	188 (7.2)
Nausea	460 (5.5)	Pyrexia	156 (6.0)
Dizziness	423 (5.0)	Nausea	133 (5.1)
Pyrexia	324 (3.8)	Injection site reaction	120 (4.6)
Injection site reaction	307 (3.6)	Dizziness	111 (4.2)
Vomiting	262 (3.1)	Vomiting	108 (4.1)
Rash	255 (3.0)	Pre-syncope	85 (3.2)
Urticaria	212 (2.5)	Rash	64 (2.4)
Malaise	210 (2.5)	Urticaria	62 (2.4)

* Note that total number of Preferred Terms will not equal total number of AE reports as there may be more than one Preferred Term per report.

Most reports (92.2%) were not coded as serious in AEMS (refer to Table 40). Of the 354 reports that were coded as serious, all met at least one criterion of the WHO definition for a serious adverse event; most (n = 224) were coded as serious due to the criterion 'caused or prolonged hospitalisation'. The proportion of reports coded as serious changed over the study period, with the

highest proportion for females in 2009 (13.9%) and 2017 (13.2%), and the lowest proportion during the enhanced surveillance period (3.9% for females and 2.7% for males) (data not shown).

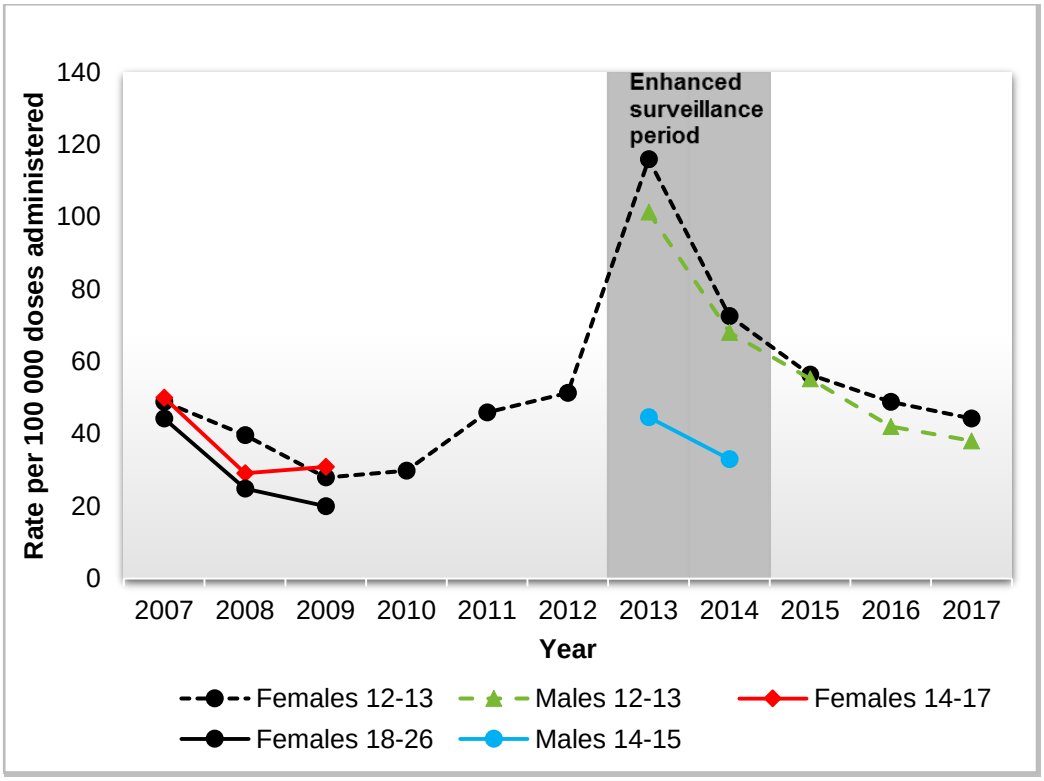
Adverse event reporting rates in target cohorts

Between 1 April 2007 and 31 December 2017, almost 9.4 million doses of 4vHPV vaccine were recorded by the HPV Register in Australia, with an overall adverse event reporting rate of 48.5 per 100,000 doses administered across all age groups and 3.8 reports per 100,000 doses coded as serious.

One hundred and two reports had either missing age, sex or both and were not included in age- and sex- specific AE rates. Vaccination date was missing in five per cent of cases (n = 243) and was substituted with reaction onset date for calculation of annual rates.

The reporting rate among primary and catch-up NIP cohorts (refer to Table 39) was 39.8 per 100,000 doses, excluding the enhanced surveillance period (2013–2014) when adverse event reporting rates were higher overall (72.3 per 100,000 doses). During the enhanced surveillance period, the rate was notably lower among older males (14 to 15 years) than in younger males and females (39.1 compared with 88.4 per 100 000 doses) (refer to Figure 20, Appendix 9). Following the conclusion of enhanced surveillance, reporting rates for females aged 12–13 years were maintained at slightly higher levels than those before 2013.

Figure 20: Rates of adverse events following 4vHPV vaccine given to females (2007 to 2017) and males (2013 to 2017), reported by year; before, during and after an enhanced surveillance period (2013 to 2014)



Pregnancy reports

Thirteen of the 4,556 reports (including 3,221 reports for females and two for infant males) were identified as occurring during or following pregnancy. Four of the 13 reports identified spontaneous abortion and one was a report of preterm labor.

There were four reports of vaccination in pregnancy that specified the adverse event as one of various infant congenital anomalies. Three of these reports involved individuals who did not yet know they were pregnant when they received the vaccine, and the fourth report did not contain enough narrative detail to determine this information. There was one report of eczema in an infant following administration of 4vHPV vaccine to the infant's mother during pregnancy. Other medical conditions were noted in data contained in these reports. No adverse outcomes were reported for the remaining pregnancy reports.

Adverse events of special interest

Of pre-defined AESI, syncope (as a composite measure defined by the MedDRA Preferred Terms 'syncope', 'syncope vasovagal' or 'loss of consciousness' [refer to Appendix 8]) was the most commonly reported (refer to Table 42). One death was reported with the cause stated as being cervical cancer years following HPV vaccination as an adult; the information provided in the report (which was based on a press article) was insufficient to determine causality.

Table 42. Number and rate of identified adverse events of special interest (AESI) following 4vHPV vaccine in females (2007 to 2017) and males (2013 to 2017), in Australia

AESI*	N†	Rate in overall surveillance period (enhanced surveillance period)‡
Syncope	856	9.11 (23.78)
Anaphylaxis	30	0.32 (0.26)
Guillain–Barre syndrome	5	0.05
Postural orthostatic tachycardia syndrome	13	0.14
Autoimmune disease	13	0.14
Primary ovarian insufficiency	12	0.17§
Complex regional pain syndrome	4	0.04
Venous thromboembolism	3	0.03

*AESI were identified using grouped Preferred Terms as identified in Appendix 8.

† Number of cases based on all those identified using prescribed search terms; not all cases are clinically confirmed, and causality is not assumed.

‡ Rate per 100,000 doses administered in overall surveillance period (2007–2017); rate during enhanced surveillance period (2013–2014) for AESI that are likely to occur on the day of vaccination (therefore responsive to enhanced surveillance methodology)

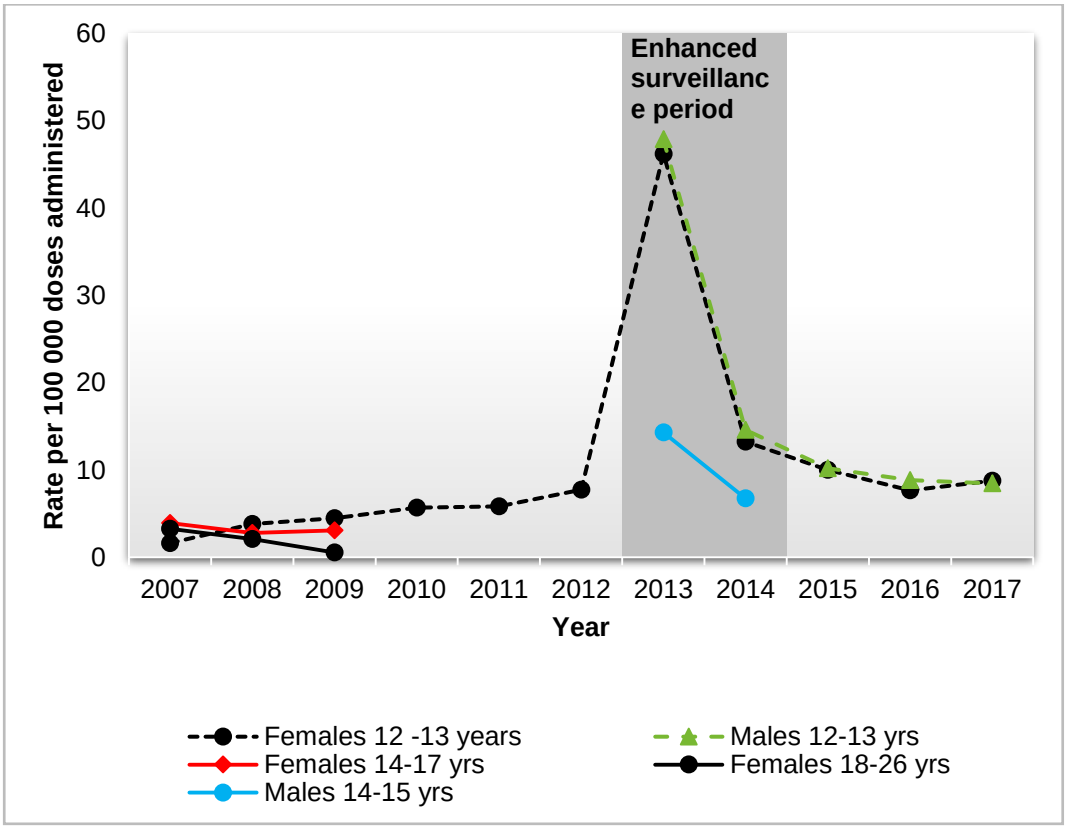
§ Denominator includes female doses administered only (DA = 7,014,406)

Syncope

Of 856 adverse events classified as syncope, 825 were coded with the MedDRA Preferred Term ‘syncope’; 23 were coded as ‘loss of consciousness’; and eight were coded with both preferred terms. Preferred terms that may relate to seizures (‘seizure’, ‘partial seizures’, ‘generalised tonic-clonic seizure’, ‘clonic convulsion’, ‘tonic convulsion’ and/or ‘tonic clonic movements’) were also assigned in a subset of reports coded with ‘loss of consciousness’ (n = 15) and a small proportion of reports coded as ‘syncope’ (n = 23). There were 14 reports coded with both ‘syncope’ and injury (including Preferred Terms ‘concussion’, ‘contusion’ and ‘head injury’) of which 13 were on the same day as vaccination.

Over half of syncope cases (n = 453) were reported during the enhanced surveillance period. During the enhanced surveillance period, the rate of reported syncope in the primary target cohort (12- to 13-year-old males and females) was 29.6 per 100,000 doses administered, over four-fold higher than the rate during the remaining study period for this same age group (7.1 per 100,000 doses) and around three times higher than the rate in 14- to 15-year-old males during enhanced surveillance (10.7 per 100,000 doses) (refer to Figure 21 and Appendix 10). Rates decreased in 2014, following a peak in 2013 (from 47.1 to 13.9 per 100,000 doses in the primary target cohort).

Figure 21: Syncope (including MedDRA Preferred Terms ‘syncope’, ‘syncope vasovagal’ and ‘loss of consciousness’)



Anaphylaxis

All 30 cases of anaphylaxis were coded using the MedDRA Preferred Term ‘anaphylactic reaction’ and all were confirmed by TGA coders as meeting the Brighton Collaboration case definition. Of the 24 cases that had reaction onset date and vaccination date documented, all occurred on the day of vaccination; six reported concomitant administration of another vaccine (DTPa, hepatitis B and/or influenza vaccines). The median age was 14 years; of the 28 cases where sex was reported, 26 were females.

Over one third of the total cases of anaphylaxis (n = 11) were reported in 2007. Low annual numbers were reported following 2007 (one to four cases per year), including during the enhanced surveillance period. The rate over the entire program was 0.32 per 100,000 doses administered and 0.26 per 100,000 doses during the enhanced surveillance period (refer to Table 42).

Guillain–Barré syndrome

Four cases were reported as Guillain–Barré syndrome (GBS) and confirmed by a specialist during hospital admission; one GBS diagnosis was subsequently reclassified to chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) and one additional case of CIDP was reported. All four GBS cases (three females and one male; median age 13 years) were reported to have had undergone nerve conduction studies as part of the diagnostic workup. Two of the four cases were reported to have had evidence of an antecedent illness (viral infection, mycoplasma infection) and one reported concomitant vaccination with dTpa vaccine.

Postural orthostatic tachycardia syndrome and other postural dizziness

Of 13 cases identified using the MedDRA Preferred Terms ‘postural orthostatic tachycardia syndrome’ (POTS), ‘dizziness postural’ or ‘postural reflex impairment’, most (n = 11) were in females. Six had been coded with the Preferred Term ‘dizziness postural’, of which five were self-limiting and occurred at the time of, or shortly after, vaccination; three had also received concomitant vaccination (hepatitis B, DTPa and/or influenza vaccine).

For the remaining seven cases coded with the MedDRA Preferred Term ‘postural orthostatic tachycardia syndrome’, all were reported from 2015 and there was insufficient information on symptoms, heart rate, blood pressure, investigations and/or duration of illness to establish a diagnosis of POTS according to published criteria.[157] Three cases were reported as being treated for orthostatic intolerance; two cases were reported to have also been diagnosed with chronic fatigue syndrome (CFS). Reaction onset dates were varied, but where documented, ranged from 6 months to over 1 year following vaccination.

Autoimmune disease

All 13 reports of autoimmune disease (AID) were in females; the median age at vaccination was 15 years. Three had documented pre-existing AID and reported escalation in symptoms following 4vHPV vaccination. Of the remaining new onset cases, conditions reported included arthritis,

systemic lupus erythematosus, dermatomyositis, autoimmune hemolytic anemia, ulcerative colitis, thyroiditis, diabetes mellitus, multiple sclerosis (coded with the preferred term 'autoimmune disorder') and non-specific diagnoses. There was no pattern regarding time of onset following vaccination, which was reported in seven cases and varied from 1 week to 3 months.

Primary ovarian insufficiency

Of 12 reports of primary ovarian insufficiency (POI) identified using the MedDRA Preferred Terms 'premature menopause', 'ovarian disorder' and 'amenorrhea' (refer to Appendix 8), three were published previously in an Australian case series.[158] Of the remaining cases, none had sufficient information to confirm a diagnosis and two had other generalised symptoms. Among the 12 cases, the median age at vaccination was 16 years; where documented, amenorrhea was reported to have occurred at variable times following vaccination.

Complex regional pain syndrome

All of the four reported cases of complex regional pain syndrome (CRPS) were in females with a median age of 14 years and occurred in the individual's vaccinated arm. Three of the cases were also identified in a case series from a jurisdictional surveillance system[159] and were considered confirmed based on the clinical review. The remaining case was reported to have been diagnosed with CRPS by a pediatrician; there was a history of injury to the hand before vaccination.

Venous thromboembolism

The three cases of venous thromboembolism (VTE) were in females with a median age of 19 years; two were documented to be taking the oral contraceptive pill and confirmed to have thrombophilia.

AusVaxSafety

Overall results

During the period 1 February 2018 – 31 December 2019, AusVaxSafety sentinel surveillance captured 73,627 HPV vaccination encounters in adolescents aged 11–14 years using SmartVax and Vaxtracker. The majority of encounters (91.1%) were captured by the SmartVax tool, which included individuals vaccinated at 269 national sentinel sites. The Vaxtracker encounters were all in NSW and captured via the state's school-based immunisation program.

Of the 73,627 vaccination encounters, the caregivers of 42,067 (57.1%) adolescents participated by responding to SmartVax's SMS1 or the Vaxtracker survey. Of these, 3,690 (8.8%) reported any adverse event and 235 (0.6%) reported seeking medical attention for an adverse event. The caregivers for 114 adolescents provided details about their child's reported medical attendance; of these, 106 (88.6%) presented to a GP and 13 (11.4%) to an ED.

SmartVax

During the period 1 February 2018 – 31 December 2019, AusVaxSafety sentinel surveillance captured 67,155 SmartVax HPV vaccination encounters in adolescents aged 11–14 years. Caregivers participated by responding to SMS1 following 39,359 (58.6%) of these vaccination encounters.

Demographic summary – SmartVax

Of the 39,359 adolescents, 19,422 (49.4%) were female; 19,930 (50.6%) were male; and 781 of 27,884 (2.8%) were Aboriginal and Torres Strait Islander. Information regarding sex and Indigenous status was not available for seven adolescents (0.02%) and 11,475 adolescents (29.2%), respectively.

The median age of the adolescents was 12 years, with a range of 11–14 years.

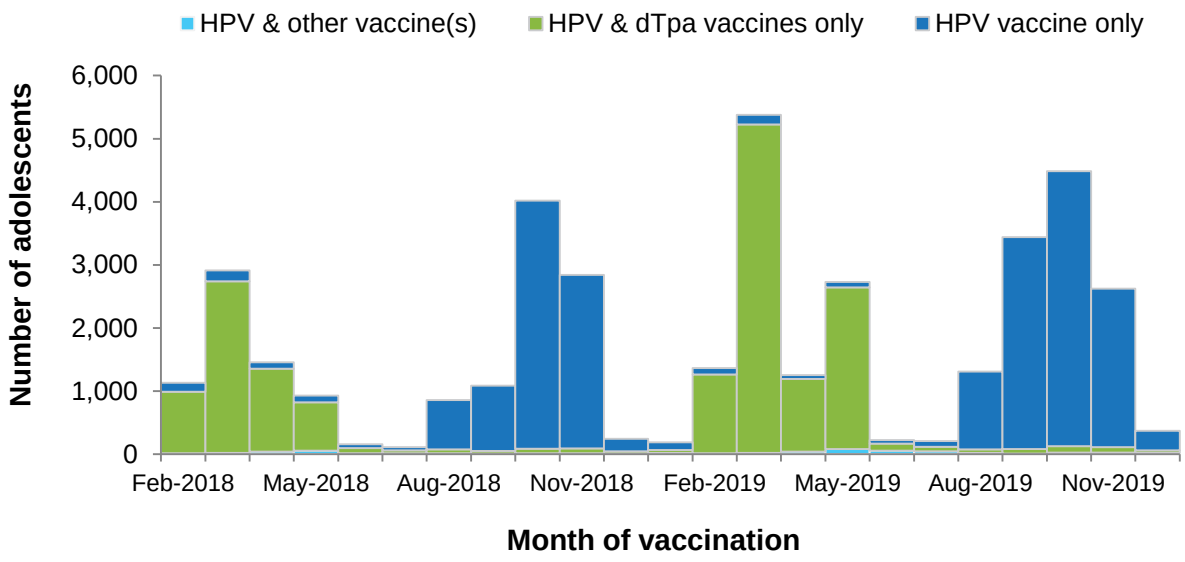
Most adolescents (94%) were vaccinated in WA or QLD (refer to Table 43), which had 77 and 68 sentinel sites, respectively. A large proportion of vaccinations captured in these states and Victoria were delivered in schools. In other states (ACT, NSW, NT, SA and TAS), vaccinations were only captured outside the school setting (e.g. at general practices).

Table 43**. Distribution of 39,359 participants during the surveillance period February 2018 – December 2019, by state/territory**

State/territory	Number of adolescents	Percentage of adolescents
ACT	89	0.2
NSW	664	1.7
NT	16	0.04
QLD	14,336	36.4
SA	68	0.2
TAS	292	0.7
VIC	1,221	3.1
WA	22,673	57.6
Australia	39,359	100.0

The number of participants over the surveillance period followed a cyclical pattern due to the school-based delivery of HPV vaccine. The number increased as more sentinel immunisation provider sites were recruited over time (refer to Figure 22).

Figure 22: Distribution of 39,359 participants during the surveillance period February 2018 – December 2019, by month of vaccination and vaccine group



'HPV & other vaccines' included HPV given without dTpa and with other vaccine(s) (13vPCV, 23vPPV, DT, DTPa, DTPa-HepB-IPV-Hib, DTPa-IPV, dTpa-IPV, HepA, HepB, HepA-HepB, Hib, Hib-MenC, influenza, JE, MenACWY, MenB, MenC, MMR, MMRV, polio, rabies, typhoid, typhoid-HepA, and varicella vaccines) and HPV given with dTpa and other vaccine(s) (13vPCV, 23vPPV, HepA, HepB, influenza, MenACWY, MenB, MenC, MMR, MMRV, polio, typhoid and varicella vaccines).

Vaccine brands (data obtained using Smartvax tool under AusVaxSafety)

The majority of adolescents received the 9vHPV vaccine brand (refer to Table 44). The 4vHPV vaccine brand was received most often in the beginning of the surveillance period (refer to Figure 23) in catch-up programs at general practices (refer to Figure 24). Few adolescents (n = 3) received the 2vHPV vaccine, and for 254 adolescents the HPV vaccine type was not specified (refer to Table 44).

Table 44. Number of adolescents who received HPV vaccine, by HPV vaccine brand and vaccine group (N=39,359)

HPV vaccine brand	HPV vaccine only	HPV & dTpa vaccines only	HPV & other vaccines	Total
9vHPV	21,330	16,695	619	38,644
4vHPV	230	188	40	458
2vHPV	2	0	1	3
Unspecified	198	35	21	254
Any HPV	21,760	16,918	681	39,359

Brands were analysed as recorded by immunisation provider site, and were not reviewed for accuracy.

'HPV & other vaccines' included HPV given without dTpa and with other vaccine(s) (13vPCV, 23vPPV, DT, DTPa, DTPa-HepB-IPV-Hib, DTPa-IPV, dTpa-IPV, HepA, HepB, HepA-HepB, Hib, Hib-MenC, influenza, JE, MenACWY, MenB, MenC, MMR, MMRV, polio, rabies, typhoid, typhoid-HepA, and varicella vaccines) and HPV given with dTpa and other vaccine(s) (13vPCV, 23vPPV, HepA, HepB, influenza, MenACWY, MenB, MenC, MMR, MMRV, polio, typhoid, and varicella vaccines).

Figure 23: Distribution of HPV vaccine brands received by 39,359 adolescents during the surveillance period 1 February 2018 – 31 December 2019

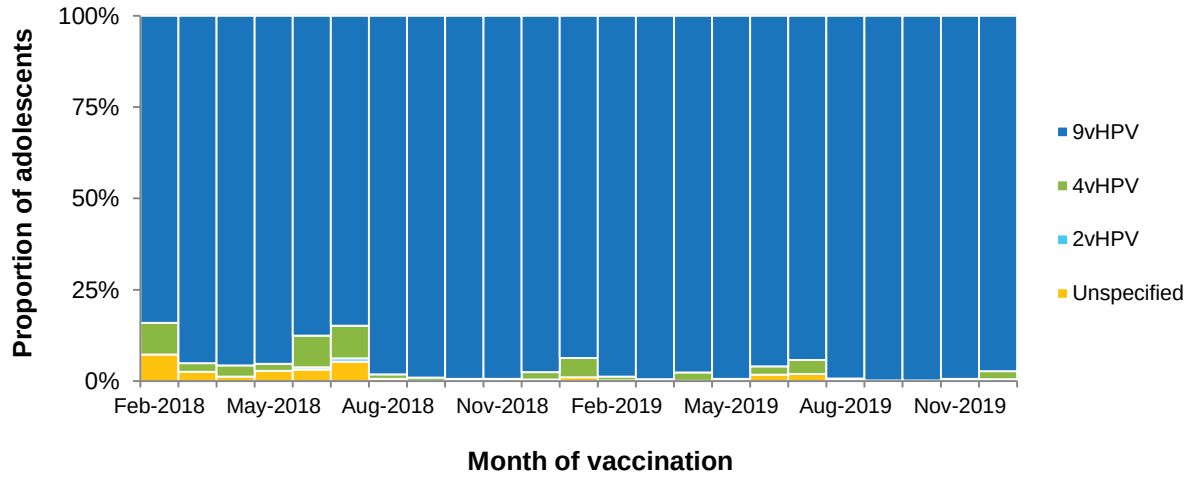
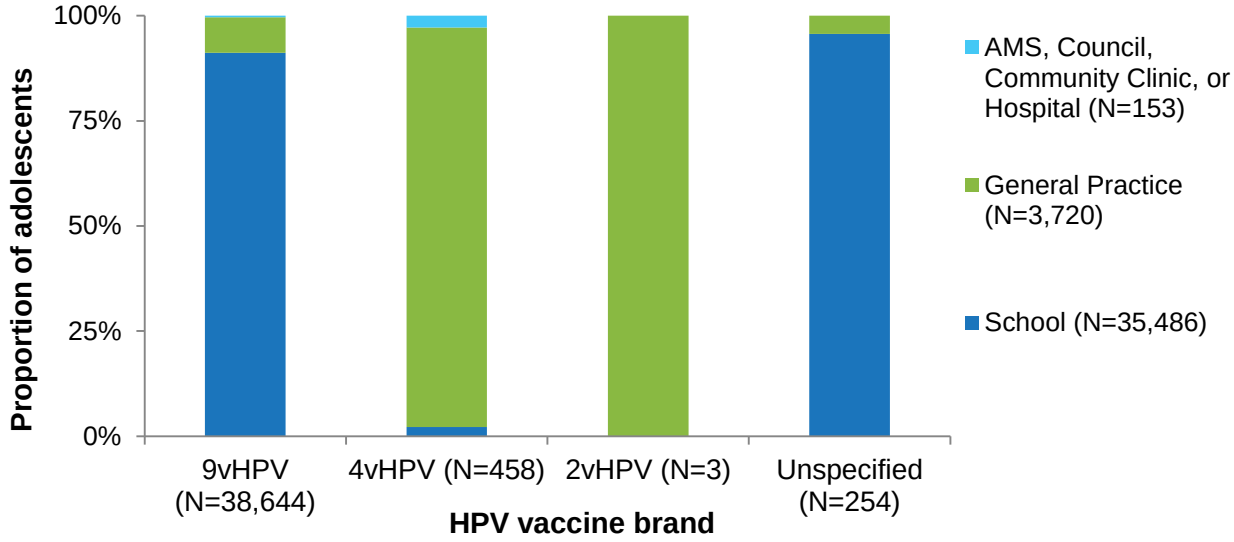


Figure 24: Distribution of immunisation provider types where HPV vaccine was received by 39,359 adolescents, by HPV vaccine type



HPV vaccine types were analysed as recorded by immunisation provider site and were not reviewed for accuracy.

Other vaccines

In addition to HPV vaccine, 17,599 adolescents (44.7%) received another vaccine or vaccines. Of these, the majority received one additional vaccine (n=17,233; 97.9%), while 296 (1.7%) received two additional vaccines, and 70 (0.4%) received three or more additional vaccines. The most common additional vaccine was dTpa vaccine, which was received by 43.7% of adolescents (refer to Table 45).

Table 45. Number and percentage of adolescents who received vaccine(s) in addition to HPV vaccine, by vaccine type (N=39,359)

Type of additional vaccine	Number of adolescents	Percentage of adolescents, %
dTpa	17,212	43.7
Influenza	288	0.7
MenACWY	144	0.4
Varicella	100	0.3
MMR	79	0.2
HepB	65	0.2
Polio	30	0.1
HepA	22	0.1
13vPCV	18	0.05
23vPPV	14	0.04
MenC	14	0.04
MMRV	13	0.03
MenB	12	0.03
Typhoid	8	0.02
dTpa-IPV	7	0.02
DTPa	5	0.01
DTPa-IPV	4	0.01
DT	2	0.01
Rabies	2	0.01
DTPa-HepB-IPV-Hib	1	0.003
HepA-HepB	1	0.003
Hib-MenC	1	0.003
Hib	1	0.003
Typhoid-HepA	1	0.003
JE	1	0.003

Adolescents who received more than one additional vaccine are included in the count for each additional vaccine.

Adverse events

Any adverse event

Following vaccination, caregivers of 3,453 adolescents (8.8%) reported any adverse event. The rates of any adverse event were similar by Indigenous status (p=0.59). Caregivers of female adolescents reported any adverse event slightly more often than caregivers of male adolescents (9.1% versus 8.5%; p=0.04). Caregivers of adolescents who received vaccine(s) in addition to HPV vaccine (including dTpa and/or other vaccine(s)) reported any adverse event more often than caregivers of adolescents who received only HPV vaccine (10.1% versus 7.7%; p<0.001).

The rates of any adverse event by vaccine group are given in Table 46. Among participants who received HPV vaccine only, caregivers of adolescents who received 9vHPV vaccine reported any adverse event more often (1,658/21,330; 7.8%) than caregivers of adolescents who received 4vHPV vaccine (9/230; 3.9%; p=0.03).

Table 46. Reports of any adverse event in adolescents who received HPV vaccine, by vaccine group

Vaccine group	Number of adverse event reports	Number of adolescents	Adverse event rate (%)
HPV vaccine only	1,680	21,760	7.7
HPV & dTpa vaccines only	1,725	16,918	10.2
HPV & other vaccine(s)*	48	681	7.0
Total	3,453	39,359	8.8

'HPV & other vaccines' included HPV given without dTpa and with other vaccine(s) (13vPCV, 23vPPV, DT, DTPa, DTPa-HepB-IPV-Hib, DTPa-IPV, dTpa-IPV, HepA, HepB, HepA-HepB, Hib, Hib-MenC, influenza, JE, MenACWY, MenB, MenC, MMR, MMRV, polio, rabies, typhoid, typhoid-HepA, and varicella vaccines) and HPV given with dTpa and other vaccine(s) (13vPCV, 23vPPV, HepA, HepB, influenza, MenACWY, MenB, MenC, MMR, MMRV, polio, typhoid, and varicella vaccines).

Specified adverse events

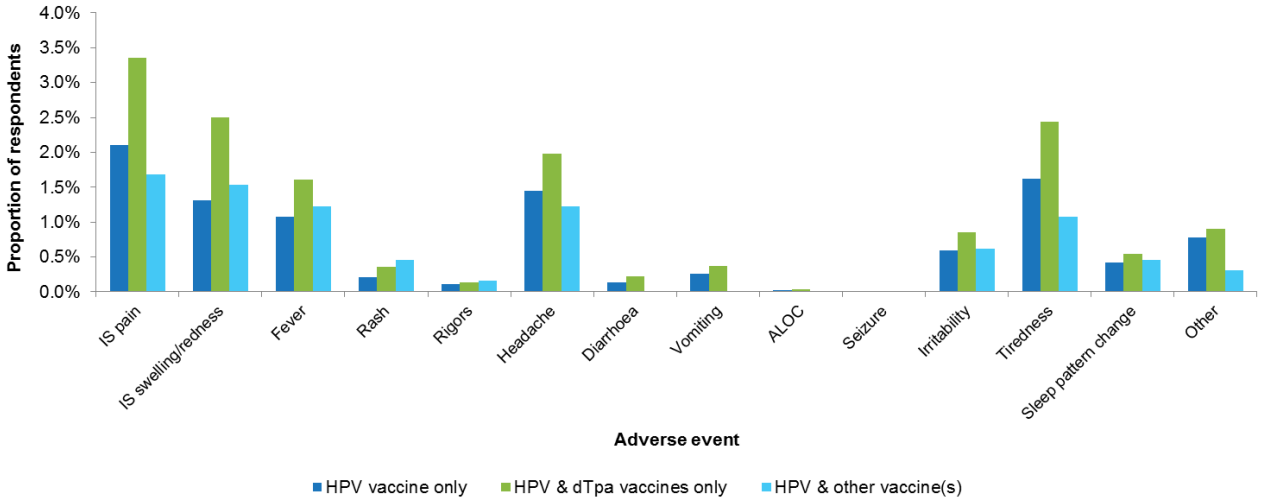
After reporting any adverse event, the caregivers of 1,404 adolescents (40.7%) provided further details by responding to the online survey.

Solicited adverse events

The most common solicited adverse events reported were injection site reactions, headache and tiredness (refer to Figure 25).

The caregivers of nine adolescents reported altered level of consciousness ('non-responsiveness/loss of consciousness') following HPV vaccination, and the caregivers of three adolescents reported seizure following HPV vaccination. Details of these AEFI are reported in Table 47.

Figure 25: Percentage of solicited adverse events reported following HPV vaccination in adolescents, by vaccine group



ALOC: altered level of consciousness; IS: injection site

Table 47. Details of altered level of consciousness or seizure following HPV vaccination reported by caregivers of adolescents

ID	Vaccines received	Onset time post vaccination	Duration	Other AEFI reported	MA	Treatment, outcome
Altered level of consciousness						
1	9vHPV; dTpa	3 min	Unsure	Fever, pain at IS, tired, headache	No	Resolved
2	9vHPV; dTpa	6 min	Unsure	Fever, pain at IS, tired, sleep pattern change, headache, nausea, cough, rhinorrhoea	No	Pain/fever medication; resolved
3	9vHPV; dTpa	Unsure	Unsure	Nil	No	Resolved
4	9vHPV	1 hour	Unsure	Fever, pain at IS, headache	No	Resolved
5	9vHPV	15 min	3 min	Nil	No	Resolved
6	9vHPV; dTpa	2 days	6 min	Fever, pain at IS, tired, sleep pattern change	Yes (ED)	Pain/fever medication

7	9vHPV	30 min	Unsure	Pain at IS, tired, irritable	Yes (GP)	Pain/fever medication; resolved
8	9vHPV; dTpa	6 min	12 min	Pain at IS, tired, sleep pattern change, headache, diarrhoea	Yes (GP)	Pain/fever medication
9	9vHPV	15 min	3 hours	Pain at IS, headache	Yes (GP)	Pain/fever medication; resolved
Seizure						
10	9vHPV	N/A	N/A	Pain at IS, tired, syncope	No	Resolved
11	9vHPV; dTpa	1 day	2 days	Tired, irritable, sleep pattern change	No	N/A
12	9vHPV	8 hours	1 day	Pain and swelling/redness at IS, tired, sleep pattern change	No	Pain/fever medication; resolved

AEFI: adverse event following immunisation, MA: medical attendance, IS: injection site, min: minutes, N/A: not available

Unsolicited ('other') events

The caregivers of 307 adolescents (0.8%) reported an unsolicited adverse event. The most commonly reported unsolicited adverse events were nausea (n=87; 19.4% of unsolicited AEFI reports), dizziness (n=53; 11.8%) and lymphoedema (n=23; 5.1%). All other unsolicited adverse events are detailed in the Appendix 11.

Medical attendances

The caregivers of 227 adolescents reported MA for an adverse event (N= 38,850; 0.6%). MA rates were similar by sex (p=0.70), Indigenous status (p=0.32) and additional vaccine status (p=0.07; Table 10). Rates were also similar by vaccine type (4vHPVvaccine or 9vHPV vaccine) among adolescents who received HPV vaccine alone (Fisher's p=1.0).

Table 48. Reports of medical attendance in adolescents who received HPV vaccine, by vaccine group

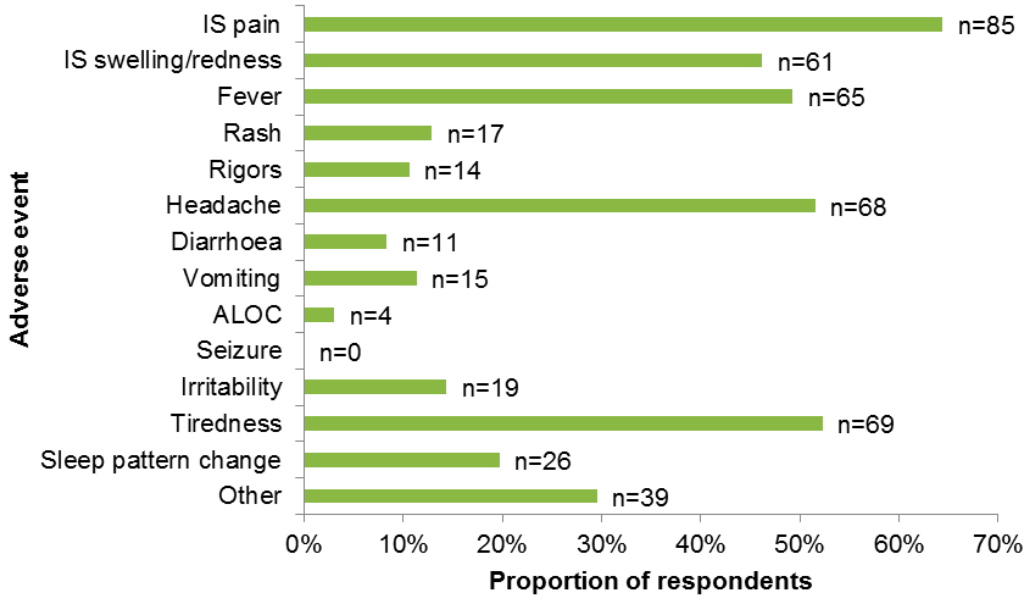
Vaccine group	Number of MA reports	Number of adolescents	MA rate (%)
HPV vaccine only	112	21,504	0.5
HPV & dTpa vaccines only	110	16,676	0.7
HPV & other vaccine(s)*	5	670	0.7
Total	227	38,850	0.6

'HPV & other vaccines' included HPV given without dTpa and with other vaccine(s) (13vPCV, 23vPPV, DT, DTPa, DTPa-HepB-IPV-Hib, DTPa-IPV, dTpa-IPV, HepA, HepB, HepA-HepB, Hib, Hib-MenC, influenza, JE, MenACWY, MenB, MenC, MMR, MMRV, polio, rabies, typhoid, typhoid-HepA, and varicella vaccines) and HPV given with dTpa and other vaccine(s) (13vPCV, 23vPPV, HepA, HepB, influenza, MenACWY, MenB, MenC, MMR, MMRV, polio, typhoid, and varicella vaccines).

The majority of caregivers who reported MA and provided details in the online survey (N=106) reported taking their child to a GP (n=94; 88.7%), while 12 caregivers (11.3%) reported taking their child to an ED.

The caregivers of 132 of these adolescents (58.1%) provided further details by responding to the online survey. The AEFI profile was similar for children whose caregivers reported MA compared with children whose caregivers did not report MA (refer to Figure 26).

Figure 26: Number and percentage of solicited adverse events reported by medical attendances following HPV vaccination (N=132)



Vaxtracker

The Vaxtracker tool captured 6,472 adolescent vaccination encounters. Caregivers of 2,708 (41.8%) adolescents participated in surveillance.

Demographic summary

Of the 2,708 adolescents, 1,178 (43.5%) were female; 1,530 were male (56.5%); and 64 of 2,708 (2.4%) were Aboriginal and Torres Strait Islander. The median age of the adolescents was 13 years, with a range of 12–14 years.

All Vaxtracker participants were vaccinated in NSW as part of school-based HPV immunisation programs. The majority (74.8%) were vaccinated in October 2019, with the remainder (25.2%) vaccinated in November 2019.

Vaccine details

All participants received only the 9vHPV vaccine. For the majority of participants (99.1%), this was recorded as a second dose of HPV vaccine; it was recorded as the first dose of HPV vaccine for 24 participants (0.9%). No information was available regarding additional vaccines, but as dose 2 of the 9vHPV vaccine delivered in NSW schools is typically administered alone, it is likely that most participants received only 9vHPV vaccine and no additional vaccines. No additional vaccines were recorded as given to any participant in this cohort.

Adverse events

Any adverse event

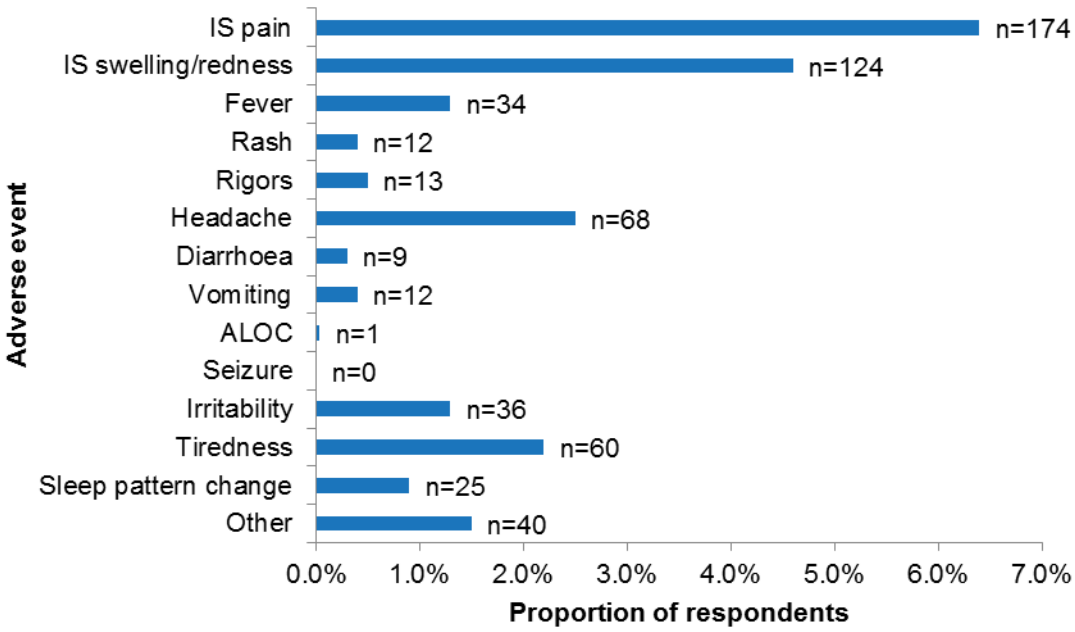
Following vaccination, caregivers of 237 adolescents (8.8%) reported any adverse event. The rates of any adverse event were similar by Indigenous status (p=0.128). Caregivers of female adolescents reported any adverse event slightly more often than caregivers of male adolescents (10.0% versus 7.8%; p=0.04).

Solicited adverse events

The most common solicited adverse events reported were injection site reactions, headache and tiredness (refer to Figure 27).

There was one reported case of altered level of consciousness. The caregiver of a 12-year-old male reported that he experienced pain at the injection site and fainted after the injection was administered.

Figure 27: Number and percentage of solicited adverse events reported following HPV vaccination in adolescents



The caregivers of 40 adolescents (1.5%) reported an unsolicited adverse event. The most commonly reported unsolicited adverse events were nausea (n=13; 22.8% of unsolicited AEFI reports), dizziness (n=7; 12.3%) and pain in extremity (n=4; 7.0%). All other unsolicited adverse events are detailed in the Appendix 12.

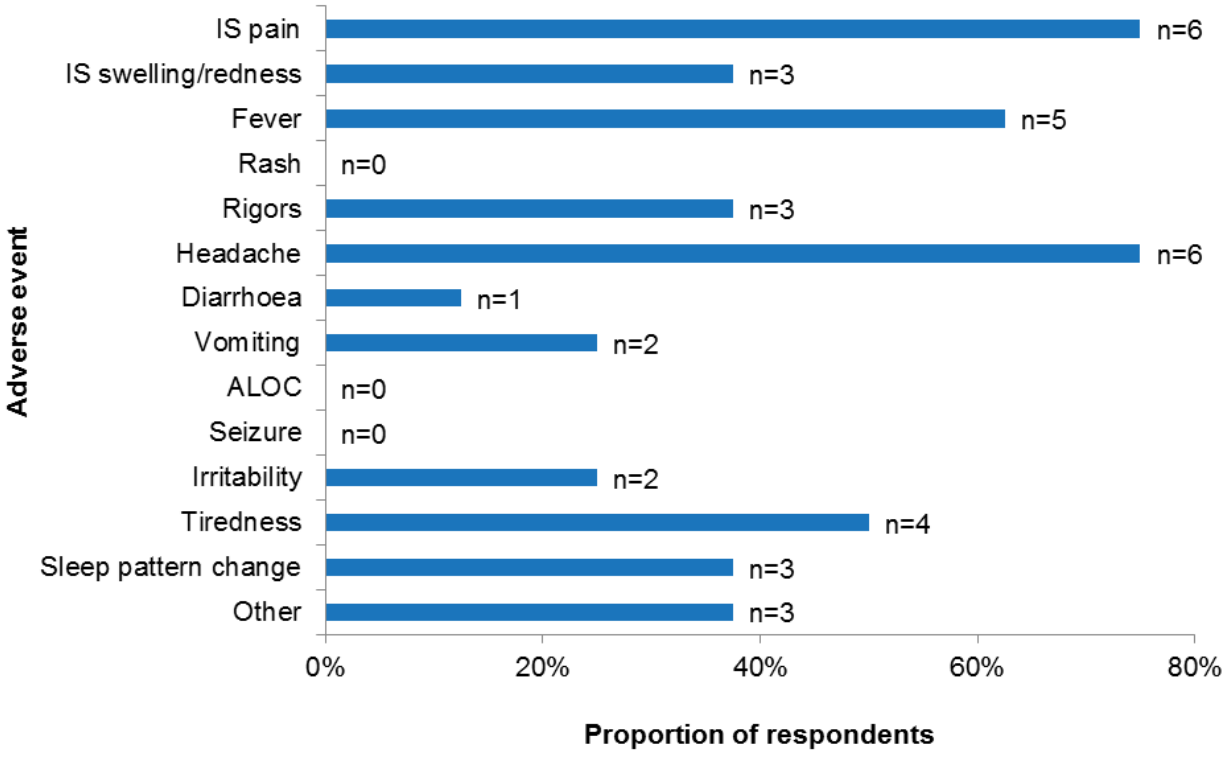
Medical attendances

The caregivers of eight adolescents (0.3%) reported MA for an adverse event (refer to Figure 28). MA rates were similar by sex (p=0.512) and Indigenous status (p=0.826).

The majority of caregivers who reported MA and provided details reported taking their child to a GP (n=7; 87.5%), while one caregiver (12.5%) reported taking their child to an ED.

The AEFI profile was similar for children whose caregivers reported MA compared with children whose caregivers did not report MA.

Figure 28: Number and percentage of solicited adverse events reported by medical attendances following HPV vaccination (n = 8)



ALOC: altered level of consciousness; IS: injection site

Summary/discussion

This review of 11 years of post-marketing vaccine safety surveillance data from Australia's spontaneous adverse event reporting system AEMS and nearly 2 years of active surveillance data from AusVaxSafety has provided valuable information on HPV vaccine safety.

While the overall adverse event reporting rate from AEMS (48.5 per 100,000 doses administered)[160] was higher than the rate of reporting to the US VAERS (32.7 per 100,000 doses distributed),[154] this was because of higher reporting rates during the enhanced surveillance period. Excluding the enhanced surveillance period, the reporting rate (39.8 per 100,000 doses) among all funded primary and catch-up cohorts was similar to that of VAERS and is robust due to the use of denominator data obtained from the HPV Register on doses administered. Reporting rates were maintained at slightly higher levels following the enhanced surveillance period which likely reflects continued improvements in the reporting system and the commensurate increased awareness of and reporting of adverse events, as has been seen for other NIP vaccines over time.[161] While the increase in reporting during the enhanced surveillance period may suggest underreporting at other

times, the higher proportion of reports that were non-serious during enhanced surveillance, as a result of instructions to nurses to report simple syncope, is reassuring.

Syncope was notable as the adverse event detected at an increased rate during the period of enhanced nurse-led school-based surveillance. For the composite outcome of 'syncope' (including the MedDRA preferred terms 'syncope', 'syncope vasovagal' and 'loss of consciousness'), nearly half of all reported cases occurred during the 2-year enhanced surveillance period, and the rate was over four times higher among both females and males in the primary target cohort during this time than in the periods of routine surveillance. Inclusion of data from this enhanced surveillance period likely explains why the overall rate of syncope in this study was nearly double the rate reported by VAERS in 2018 using the same preferred terms.[154] Analysis of enhanced surveillance data also revealed that syncope was about three times as likely to occur in younger adolescents (aged 12 to 13 years) than in older males (14 to 15 years), as noted in a preliminary report by the TGA.[162] However, syncope rates in 12- to 13-year-old females were similar to those in males of the same age. This suggests an age-related relationship with this well-recognised immunisation stress–related reaction that has not previously been noted in population-level post-marketing surveillance, to our knowledge.

These comprehensive data on syncope in both sexes of young adolescent vaccine recipients during the enhanced surveillance period allowed for a greater awareness of this condition among immunisation program staff. As a result, these staff then ensured management protocols were in place to mitigate syncope and prevent syncope-induced injury. The proportion of reports of syncope associated with a preferred term indicating injury was low in this study. Similarly, the TGA review of the enhanced surveillance period identified very few syncopal episodes resulting in injury or requiring further medical review, such that a decision was made not to request school-based reporting of simple syncopal events in the second year of enhanced surveillance.[162] Syncope can create concern among vaccine recipients and/or carers and lead to negative perceptions of vaccination. However, in many instances, it is preventable or the risk of injury minimised. It is important that immunisation providers are aware of the frequency at which this can occur, particularly in younger adolescents, to avoid unduly negative outcomes.[163]

The rate of anaphylaxis was higher in our study than the rate reported to VAERS (0.32 per 100,000 doses administered compared with 0.06 per 100,000 doses administered for VAERS),[154] but was similar to previously reported rates from Australia (0.32 per 100,000),[83] Canada (0.3 per 100,000)[164] and Europe (0.22 per 100,000).[165] This was likely due to high awareness and reporting of anaphylaxis following initial signal investigation early in the HPV vaccination program in Australia.[166] In this context, it was considered possible that there was a reduced threshold for using adrenaline and that syncope cases were more likely to meet the Brighton Collaboration criteria for anaphylaxis where anaphylaxis code was based on the treatment given. The reporting rate for anaphylaxis was not elevated during the enhanced surveillance period, during which it was a specified condition, which further supported our impression that anaphylaxis is rare after HPV vaccination, occurring in fewer than 1 in 300,000 young adolescent 4vHPV vaccine recipients.

We selected a number of other AESI to analyse in detail. Notably, while many reports were not confirmed to meet diagnostic criteria for the various conditions, reporting rates were nonetheless

low and comparable with rates using similar surveillance methods.[154] Spontaneous reporting systems like AEMS have specific characteristics, including incomplete and selective reporting, which means it is almost never possible to conclusively determine causality for an individual case on the basis of available data. The absence of detailed clinical data, despite requests initiated by the TGA, made it difficult to assess a causal relationship to vaccination for the reports in this study. Importantly, these conditions occur at a background rate in the population, irrespective of vaccination,[167] although data on local and age-specific prevalence and incidence are variably available.[82]

Only four cases of GBS were reported following immunisation with Gardasil (4vHPV), two of which had documented infection prior to disease onset, during the entire 11-year surveillance period. The incidence of acute flaccid paralysis in Australia (of which GBS is the diagnosis in almost half of cases) has been estimated to be 0.8 per 100,000 children aged <15 years.[168] An early possible signal for GBS following HPV vaccine was identified and investigated in the US[169] but was not confirmed in analyses of either VAERS[154] or the Vaccine Safety Datalink (VSD).[152,170] While a cohort study in France suggested an elevated hazard ratio for GBS in vaccinated versus unvaccinated females,[171] a UK self-controlled case series subsequently found no evidence of an increased risk in the 3 months following vaccination,[172] and a Canadian study did not identify any increased risk of GBS-related hospitalisation in HPV-target cohorts.[173] Evidence from our analysis is consistent with these studies in suggesting no increase in GBS in association with the introduction of HPV vaccination.

Adverse events identified using the search criteria that may suggest POTS, a syndrome of orthostatic intolerance associated with an increase in heart rate in the absence of orthostatic hypotension that is associated with light-headedness, palpitations and weakness,[157] were reported at a low rate in our study, similar to that from two analyses of US VAERS data (0.11 and 0.16 per 100,000 doses distributed, respectively).[154,174] Many of the adverse events in our study described simple postural dizziness on the day of vaccination; for those reported as POTS specifically, it was not possible to establish a diagnosis of POTS according to published criteria in any case. While some published reports have suggested an association between POTS and HPV vaccination,[151] neither the WHO's Global Advisory Committee on Vaccine Safety (GACVS)[175] nor the American Autonomic Society found evidence to support a causal association.[176] Although the prevalence of POTS in Australia is not well described, globally it is estimated to affect 0.2% of the population, supporting the observation of low rates in our cohort.[157] POTS is a heterogeneous condition that is prevalent in the same population that receives HPV vaccine (adolescents and females), and symptoms can overlap with other syndromes that occur in adolescence, such as fatigue syndromes.[176] No association between HPV vaccination and increased risk of fatigue syndromes has been identified in epidemiological studies.[177,178]

We found insufficient clinical information to confirm the diagnosis of POTS in any of the cases identified using this search strategy. Similarly, in a recent study based on VAERS data, only 29.5% (n=29) of reports (using the preferred terms that we also used in our study) met POTS diagnostic criteria, and a pre-existing medical condition was documented in 20 cases, including five cases of CFS.[174] Most reports in our study were made after 2015, which may reflect the responsiveness of spontaneous reporting systems to media interest and public concern; clusters of non-specific

symptoms attributed to POTS and CFS were reported in Denmark and increased following heightened media reporting in 2013 and 2015.[179] Concern arising from causal attribution given to such temporal associations has led to declines in vaccine uptake in some countries,[180,181] resulting in lost opportunities to prevent cervical and other cancers.

Of the other AESI examined, no vaccine safety signals were identified. Although disease flare in individuals with pre-existing AID was reported in three cases, clinical trials have not identified any difference in the risk of disease flare between vaccinated and unvaccinated individuals with pre-existing AID.[151] New-onset AID was reported rarely, with no consistent pattern and variable syndromes reported. Similarly, large population-based studies have not demonstrated any increased risk of new-onset AID following 4vHPV vaccine.[182,183] The rate of complex regional pain syndrome was similar to that reported from the US (0.28 per million doses distributed).[154] The reported rate of POI was low with lack of clinical and diagnostic data, similar to that in a recent population-based epidemiological study which found no significant risk of POI following 4vHPV vaccine (HR 0.30; 95% CI: 0.07–1.36).[184] This lack of significant risk of POI associated with HPV vaccine was further supported by a 2017 statement issued by the GACVS declaring there was no evidence of a causal association between HPV vaccine and POI.[175] The rate of VTE in our study, based on just three cases, was comparable to the rate reported to VAERS;[154] recent evidence[183,185] has not supported any increased risk of VTE following the early safety signal identified in VAERS data.[186]

While HPV vaccines are not recommended for use in pregnancy, data from spontaneous reporting systems as well as registries have not identified fetal loss or congenital anomalies above background rates or any concerning pattern of fetal loss following 4vHPV vaccine;[150,151,187] our study findings supports this conclusion. In 2017, the GACVS concluded that inadvertent administration of 4vHPV during pregnancy has not been shown to be associated with adverse outcomes.[175]

AusVaxSafety also captured post-licensure surveillance data, especially in school-delivered vaccination settings in 2018–2019. AusVaxSafety data showed that more AEFI were reported when HPV vaccine was given with other vaccine(s), than HPV alone, but this did not affect the medical attendance rates (proxy for more serious adverse events) and rates overall were low. It was noted that caregivers of female children reported slightly more AEFI than caregivers of male children. Furthermore there were more AEFI post 9vHPV vaccine than 4vHPV vaccine when HPV vaccine was given alone, but 4vHPV vaccine numbers were much smaller than 9vHPV vaccine numbers and caution should be taken in interpreting these data.

There are several limitations in our vaccine safety evaluation. A limitation of the AEMS data is interpretation of the seriousness code for reported adverse event which, while included for completeness, is primarily used as a guide for sponsor reporting. Although multiple attempts are made to obtain additional information from the reporter, coding may not be based on review of detailed and verified clinical data in every case and may not capture all medically important events.[188] These limitations should be considered in interpreting the code and it should not be considered definitive of the seriousness of the event. As it is not necessarily applied based on review of detailed and verified clinical data, and may not capture all medically important events,

reporting rates of serious adverse event are unlikely to be robust. Identification of potential AESI was limited by the search terms selected, which may not have captured all potentially relevant cases. Review of individual AESI was limited by the case details provided by the reporter during investigation; despite multiple attempts, sufficient detail is not always obtained. Our study is also subject to the inherent limitations of spontaneous reporting systems, including incomplete and selective reporting. While essential for signal detection and hypothesis generation (which is undertaken prospectively by the TGA and may lead to investigation and regulatory action), spontaneous reporting systems do not allow comparison to rates in unvaccinated populations; epidemiological studies are required to explore a potential association.[189] The use of national vaccine registry data as a denominator for doses administered may slightly underestimate total doses because of under-notification from predominantly catch-up vaccination delivered by primary care practices, which may have modestly inflated rate estimates.

In conclusion, the data reported here are consistent with an overall high level of safety of HPV vaccines since their inclusion in the NIP schedule. Over the evaluation period, reporting rates of adverse events following HPV vaccine administration in Australia were consistent with data from similar surveillance systems internationally and did not reveal any new or concerning safety issues. However, during a period of enhanced surveillance implemented to monitor introduction of the vaccine to adolescent males in addition to females, syncope was noted to occur at a higher rate in younger adolescents than previously observed. AESI, except for syncope (a common adverse event), were reported rarely and no new or concerning patterns were identified. This comprehensive analysis further contributes to the large body of existing data affirming the safe post-marketing profile of the HPV vaccine in both males and females and the value and characteristics of long-term spontaneous reporting systems in monitoring vaccine safety.

Impact on disease burden: Cervical abnormalities and tumours

Aims

To assess the impact of the HPV vaccination program, that commenced in 2007, on the epidemiology of disease outcomes, including cervical high-grade abnormalities (HGA), HPV-associated cancers and recurrent respiratory papillomatosis (RRP).

Specific objectives

To detect any significant changes in incidence and hospitalisation rates due to each disease outcome, between the pre- and post-vaccine periods, with stratification by age group (based on eligibility for the vaccine program), gender, Aboriginal and Torres Strait Islander status and jurisdiction.

Methods

In our analysis, we used an ecological design with 'before and after' comparisons.

Section 1 of this report describes the impact of the HPV vaccination program on HPV-associated disease burden using published literature. This chapter contains HPV vaccination impact assessment based on primary analyses of relevant data from several data sources. The following are the data sources used for cervical abnormalities, associated cancers and RRP:

- Reports and data published by the Australian Institute of Health and Welfare (AIHW) 2004–2017, including incidence rates of HGA (defined as cervical intraepithelial neoplasia [CIN] 2 and 3 or adenocarcinoma in situ [AIS]) detected by histology, incidence rates for cancers of the cervix and mortality rates of cervical cancer.[190, 191]
- Incidence data of cancers (anus, penis, vagina, vulva, oral cavity, oropharynx and larynx) downloaded from the AIHW Australian Cancer Database 2002–2016.[191]
- AIHW hospitalisation datasets 2002–2017 for hospital separations containing International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification (ICD-10-AM) and the Australian Classification of Health Interventions (ACHI) coded diagnoses for each condition or disease as listed in Table 49. For anal, vaginal, vulval and penile disease both cancers and high-grade intraepithelial lesions (i.e. grade 3 precancerous lesions, coded as carcinoma in situ) were included. Note that there is no specific ICD code for RRP and codes to which hospitalisations due to the disease are likely to be mapped are used as proxies to indicate probable RRP. Principal diagnosis was used in the analysis for HGA and cancers.
- Cause of death dataset 2006–2017 using underlying cause of death for the selected diseases and conditions listed in Table 49. Death data were obtained from the Cause of Death Unit

Record File (COD URF) from the Australian Coordinating Registry (ACR). The Queensland Registry of Births, Deaths and Marriages (RBDM) is the ACR for COD URF data. The ACR coordinates the approval and release of COD URF files on behalf of the data custodians – Australian Registrars of Births, Deaths and Marriages (RBDM), State/Chief Coroners and the National Coronial Information System (NCIS). Since 1997, ICD-10 has been used to identify the cause of death.

Data were tabulated and examined by gender, age group (<20; 20–24; 25–29; ≥30 years), Aboriginal and Torres Strait Islander status and jurisdiction, where applicable. For each disease outcome incidence rates and rate ratios (RR), pre- to post-vaccine introduction with 95% confidence intervals (CI) and p values, were calculated. Rates were presented, where relevant, as either per 1,000 females screened or per 100,000 females, males or population using Australian Bureau of Statistics (ABS) census data as the denominator (June 2019, 3101.0 Australian Demographic Statistics, Tables 59–51). Statistical tests for trends were used to evaluate changes from before HPV vaccination program introduction (2002–2007) to after (2008–2017).

Where the year of hospital admission was not available (11,382/857,211, 1.3%), the separation year was used as a proxy.

Subgroup analysis by Aboriginal and Torres Strait Islander status was undertaken to assess whether vaccine impact on disease burden is equitable. Of note, because of the incompleteness of Aboriginal and Torres Strait Islander status reporting on pathology forms, cervical screening program outcomes are not reported by Aboriginal and Torres Strait Islander status.

The time periods for which different data elements were available across the data sources varied. For AIHW datasets the relevant time periods were: HGA incidence 2004 – June 2017, cervical cancer incidence by age group 2000–2015, cervical cancer incidence by state and territory 2010–2014, cervical cancer mortality 2000–2017, anogenital, oropharynx, larynx and oral cavity cancer incidence 2002–2016.

Table 49. ICD-10-AM/ACHI codes used in this study and their corresponding clinical condition or disease[132, 133, 192-194]

Condition / Disease	ICD-10-AM or ACHI code	Description
HGA (CIN2) HGA (CIN3)	N87.1 D06	Dysplasia of cervix uteri Carcinoma in situ of cervix uteri
Cervical cancer[30,31]	C53	Malignant neoplasm of cervix uteri
Anal cancer[30,31]	C21 D01.3	Malignant neoplasm of anus and anal canal Carcinoma in situ of anus and anal canal
Penile cancer[30,31]	C60 D07.4	Malignant neoplasm of penis Carcinoma in situ of penis
Vaginal cancer[30,31]	C52	Malignant neoplasm of vagina

	D07.2	Carcinoma in situ of vagina
Vulval cancer[30,31]	C51.x D07.1	Malignant neoplasm of vulva Carcinoma in situ of vulva
Cancers in the oropharynx[30,31]	C01 C09 C10	Malignant neoplasm of base on tongue Malignant neoplasm of tonsil Malignant neoplasm of oropharynx
Oral cavity[30,31]	C02 C03 C04 C05 C06.	Malignant neoplasm of other and unspecified parts of the tongue Malignant neoplasm of gum Malignant neoplasm of floor of mouth Malignant neoplasm of palate Malignant neoplasm of other and unspecified parts of mouth
Larynx[30,31]	C32	Malignant neoplasm of larynx
RRP[28,32,33]	D14.1* D14.2 D14.3 D14.4 4187000 4186100	Benign neoplasm of larynx Benign neoplasm of trachea Benign neoplasm of bronchus and lung Benign neoplasm of respiratory system, unspecified Administration of agent into larynx or vocal cord Microlaryngoscopy with removal of lesion by laser

ACHI – Australian Classification of Health Interventions, CIN – cervical intraepithelial neoplasia, HGA – high grade abnormality, HPV – human papillomavirus, ICD-10-AM – International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification, RRP – recurrent respiratory papillomatosis.

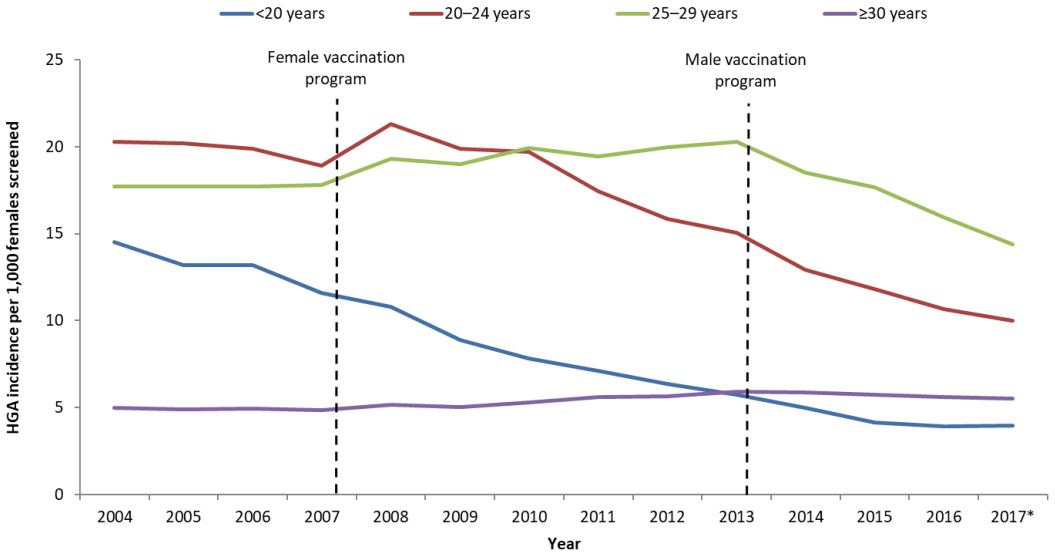
* The diagnosis code D14.1 was highly sensitive (97.7%) for RRP admissions and had a high positive predictive value (98.1%) in children.[32]

Results

Cervical abnormalities

Cervical HGA incidence rate decreased in vaccine-eligible age groups, by 48% and 20% in females aged <20 years and 20–24 years, respectively (refer to Figure 29). However, cervical HGA incidence rate increased by 5% and 13% in females aged 25–29 years and ≥30 years, respectively. There was a progressive decline in the proportion of cervical HGA that was diagnosed in individuals aged <30 years, from 53% in 2004–2006 to 50% in 2007–2012 and then to 41% in 2013 – June 2017. The overall age-standardised cervical HGA rate declined from 8.4 per 1,000 females screened in 2007 to 5.8 per 1,000 females screened in the first half of 2017. The cervical HGA incidence rate in women aged ≥35 years gradually increased over the time period.

Figure 29: Trends in high-grade cervical abnormalities (CIN2/3) in females by age group, Australia, 2004–2017*



Source: AIHW histology data table – S4.8. *2017 January–June annualised

The hospitalisation rates of cervical HGA (as principal diagnosis) in non-Indigenous females aged <30 years decreased from pre-vaccine (2002–2007) to post-vaccine (2008–2017) period, by 69%, 36% and 9% in the age groups of <20, 20–24 and 25–29 years, respectively (refer to Table 50). A small but significant increase was noted among women aged ≥30 years. In Aboriginal and Torres Strait Islander females aged <25 years, the cervical HGA hospitalisation rates declined over the same period by 58% and 14% in the age groups of <20 and 20–24 years, respectively, which were eligible for vaccination. Conversely there were concomitant increases in cervical HGA hospitalisation rates in older Aboriginal and Torres Strait Islander females of 11% and 15% in the age groups of 25–29 years and ≥30 years, respectively.

Table 50. Hospitalisation rates of high-grade cervical abnormality (CIN2 and CIN3) (recorded as principal diagnosis), pre-vaccine (2002–2007) to post-vaccine (2008–2017) introduction, by Aboriginal and Torres Strait Islander status and age group, Australia

Age group	Hospitalisation rate (per 100,000 females)		RR	95% CI
	2002–2007	2008–2017		
Aboriginal and Torres Strait Islander				
<20 years	29.4	12.4	0.42	0.35–0.51
20–24 years	401.9	346.3	0.86	0.78–0.95
25–29 years	400.7	446.3	1.11	1.01–1.23
≥30 years	140.7	162.1	1.15	1.07–1.24
Total	128.4	132.0	1.03	0.98–1.08
Non-Indigenous				
<20 years	23.6	7.2	0.31	0.29–0.32

20–24 years	385.9	248.8	0.64	0.63–0.66
25–29 years	421.3	382.0	0.91	0.89–0.92
≥30 years	102.8	105.4	1.03	1.01–1.04
Total	123.3	111.8	0.91	0.90–0.91

Source: AIHW hospitalisation datasets; high grade cervical abnormality diagnosis codes N87.1 (CIN2) and D06 (CIN3).

Cervical cancer

As shown in Table 51, overall the cervical cancer incidence rate was not significantly different in the post-vaccine period compared with the pre-vaccine period. Overall, the mortality rate decreased by 12% in the post-vaccine period compared with the pre-vaccine period.

Table 51. Cervical cancer incidence and mortality rates pre-vaccine (2000–2007) to post-vaccine (2008–2015) introduction, by age group, Australia

Age group	Rate per 100,000 females		RR	95% CI
	2000–2007	2008–2015		
Incidence rate				
<20 years	0.1	0.0	0.51	0.15–1.50
20–24 years	1.5	1.7	1.14	0.85–1.53
25–29 years	6.0	8.1	1.37	1.19–1.57
≥30 years	11.4	10.8	0.95	0.91–0.98
Total	7.4	7.3	0.99	0.95–1.02
Mortality rate				
<20 years	0.0	0.0	2.80	0.22–146.79
20–24 years	0.1	0.1	0.49	0.11–1.92
25–29 years	0.5	0.6	1.41	0.84–2.41
≥30 years	3.8	3.2	0.86	0.80–0.92
Total	2.3	2.0	0.88	0.82–0.94

Source: AIHW National Cervical Screening Program monitoring report 2019: supplementary data tables

Age-standardised cervical cancer incidence rate in Aboriginal and Torres Strait Islander women aged 20–69 years was more than double that of their non-Indigenous counterparts in 2011–2015.

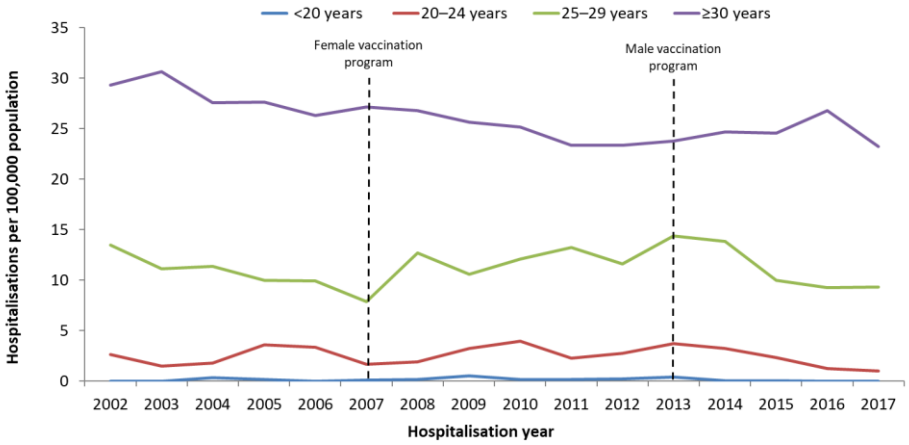
In Australian females, the cervical cancer hospitalisation rate (as principal diagnosis) in the post-vaccine period was lower than in the pre-vaccine period (refer to Table 52).The rate was statistically significantly lower in women aged ≥30 years (both Aboriginal and Torres Strait Islander and non-Indigenous) and in Aboriginal and Torres Strait Islander women aged 25–29 years, but higher in non-Indigenous females aged 25–29 years (refer to Table 52 and Figure 30).

Table 52. Cervical cancer hospitalisation rates (recorded as principal diagnosis) pre-vaccine (2002–2007) to post-vaccine (2008–2017) introduction, by Indigenous status and age group, Australia

Age group	Hospitalisation rate per 100,000 females		RR	95% CI
	2002–2007	2008–2017		
Aboriginal and Torres Strait Islander				
<20 years	0.0	0.1	N/A	N/A
20–24 years	6.7	5.8	0.87	0.38–2.09
25–29 years	33.4	14.6	0.44	0.28–0.69
≥30 years	63.9	53.2	0.83	0.74–0.94
Total	27.3	22.5	0.82	0.74–0.92
Non-Indigenous				
<20 years	0.1	0.2	1.63	0.89–3.16
20–24 years	2.3	2.4	1.07	0.83–1.39
25–29 years	9.8	11.6	1.18	1.04–1.33
≥30 years	27.4	24.1	0.88	0.86–0.90
Total	17.6	16.0	0.91	0.89–0.93
All Australians				
<20 years	0.1	0.2	1.70	0.93–3.28
20–24 years	2.4	2.6	1.06	0.83–1.35
25–29 years	10.6	11.7	1.10*	0.98–1.23
≥30 years	28.1	24.7	0.88*	0.86–0.90
Total	17.9	16.2	0.90*	0.88–0.93

Source: AIHW hospitalisation datasets; cervical cancer diagnosis codes C53.

Figure 30: Trends in cervical cancer (principal diagnosis) hospitalisations in females by age group, Australia, 2002–2017



Source: AIHW hospitalisation datasets; cervical cancer diagnosis codes C53.

Anogenital and oropharyngeal cancers

Incidence and hospitalisation rates of anogenital cancers and their immediate precursor lesions (including anal, penile, vaginal and vulval) and oropharyngeal cancers, as the principal diagnosis, are provided in Appendices 13 and 14. The number of new cases and incidence rates for anogenital cancers and oropharyngeal cancers were very small in both pre- and post-vaccine periods for those aged <30 years, hence any observed changes in these age groups are likely due to chance. Hospitalisation rates also fluctuated during these periods.

Recurrent respiratory papillomatosis

The hospitalisation rate for probable RRP (as principal diagnosis or procedure code) in females decreased in those aged <20 years (3.1 to 2.4 per 100,000) and increased in those aged ≥30 years (3.9 to 5.7 per 100,000) from pre- to post-vaccine period (refer to Table 53). The rate in males decreased in those aged <30 years (4.2 to 2.7 per 100,000) and increased in those aged ≥30 years (11.5 to 13.0 per 100,000) from pre- to post-vaccine period. Probable RRP hospitalisation rates were low in Aboriginal and Torres Strait Islander populations, with only 123 male and 104 female hospitalisations in the 16-year study period. Note that the diagnosis code D14.1 was found to be highly sensitive (97.7%) for RRP admissions and had a high positive predictive value (98.1%) in children in a NSW study.[132] D14.1 made up the majority of cases in these data (97.8%). However, none of these codes have been validated in adults who may have multiple hospitalisations/treatments with RRP. Other causes of benign disease at these sites in adults or children may utilise these codes.

Table 53. Recurrent respiratory papillomatosis hospitalisation rates (recorded as principal diagnosis) pre-vaccine (2002–2007) to post-vaccine (2008–2017) introduction, by gender, Indigenous status and age group, Australia

Age group	Hospitalisation rate per 100,000 population		RR	95% CI
	2002–2007	2008–2017		
Males				
Aboriginal and Torres Strait Islander				
<20 years	0.7	1.7	2.51	1.03–7.41
20–24 years	1.4	0.3	0.22	0.00–4.19
25–29 years	3.0	1.4	0.48	0.09–2.56
≥30 years	2.1	4.7	2.20	1.22–4.25
Total	1.4	2.6	1.86	1.19–2.98
Non-Indigenous				
<20 years	3.5	2.4	0.70	0.63–0.79
20–24 years	3.8	2.1	0.54	0.43–0.67
25–29 years	8.6	4.7	0.54	0.47–0.63
≥30 years	11.7	13.2	1.12	1.08–1.17
Total	8.7	9.0	1.03	1.00–1.07
Females				
Aboriginal and Torres Strait Islander				
<20 years	2.1	1.9	0.93	0.50–1.75
20–24 years	nc	0.6	N/A	N/A
25–29 years	nc	1.1	N/A	N/A
≥30 years	1.4	2.7	1.89	0.93–4.25
Total	1.5	2.0	1.35	0.87–2.17
Non-Indigenous				
<20 years	3.2	2.5	0.78	0.69–0.88
20–24 years	1.8	1.6	0.85	0.63–1.16
25–29 years	2.5	2.8	1.11	0.87–1.43
≥30 years	4.0	5.8	1.46	1.37–1.55
Total	3.5	4.5	1.27	1.21–1.34
All Australians				
<20 years	3.2	2.4	0.75	0.69–0.81
20–24 years	2.8	1.8	0.64	0.53–0.76
25–29 years	5.4	3.7	0.67	0.59–0.76
≥30 years	7.6	9.3	1.22	1.18–1.25
Total	6.0	6.6	1.10	1.07–1.14

Source: AIHW hospitalisation datasets; RRP diagnosis codes D14.1, D14.2, D14.3x and D14.4. N/A - not applicable, nc - no cases

Summary/discussion

This report summarises relevant diseases that are potentially attributable to HPV. [192,193] We have highlighted the successes observed thus far while acknowledging that success for some outcomes, such as cancers in adults, will only become discernible with time and these data primarily serve as observation of trends in cancer incidence before expected impact of HPV vaccination in the coming decades.

Cervical pre-cancerous HGA have significantly declined in females age-eligible for HPV vaccine, although in Aboriginal and Torres Strait Islander females this decline has only been observed in females aged <25 years to date (unlike in non-Indigenous females in whom declines are now also being observed in females aged 25–29 years). In older cohorts with lower levels of vaccination coverage there have been significant increases in HGA over time, continuing pre-vaccine trends. The decline in HGA incidence by age group is consistent with expected trends by vaccine-eligible cohort as they age, with a decline in incidence evident from 2009 in women aged 20–24 years and from 2014 in those aged 25–34 years. No decline was observed in women aged >35 years who were not eligible for funded HPV vaccine either through the school-based or community catch-up programs. The declining trend in all-age HGA incidence was observed across all Australian states and territories. Data linkage studies have shown that fully vaccinated females in 2007–2014 had lower rates of HGA compared with unvaccinated females of the same age, a trend that was consistent across jurisdictions, remoteness and socioeconomic areas.[195] The rate of HGA in the pre-vaccine cohort was significantly higher than in unvaccinated females in the post-vaccine cohort, indicating herd benefit effect.[195]

In addition, a recent Australian study showed that one dose of the HPV vaccine had comparable effectiveness as two or three doses in preventing HGA in a high coverage setting.[196] Also, a comparison with a historical cohort of age-matched women showed that the result was not due to herd protection alone.[196]

In Australia, incidence rates of cervical cancer in Aboriginal and Torres Strait Islander women aged 20–69 years were more than double that of their non-Indigenous counterparts.[190] A previous study found that of the 101 cervical cancers diagnosed in fully HPV-vaccinated females in Australia between 2007 and 2012,[99] occurred in females estimated (based on age, date of vaccination and date of commencing screening) to have been exposed to HPV before vaccination and the other two were cancers not caused by HPV.[195]

As expected, the all-age cervical cancer incidence rate has not declined since the vaccine introduction, although the mortality rate has declined in this period in those aged over ≥30 years (who were not vaccine-eligible).[190] The age-standardised mortality rate of cervical cancer in females decreased from 5.2 to an estimated 1.8 per 100,000 females between 1982 and 2019.[190] This decrease was greatest in women aged 20–69 years (targeted screening age group), in whom the mortality rates (per 100,000 women) were 5.5 in 1982 and 1.7 in 2015 and is likely to be attributable to cervical screening.[190]

Our findings show that cervical cancer hospitalisation rates were lower in the post-vaccine period than in the pre-vaccine period in Australian females aged ≥30 years, among both the Aboriginal and Torres Strait Islander and non-Indigenous populations. In Aboriginal and Torres Strait Islander females, the lower rate of cervical cancer hospitalisations in the post-vaccine period was seen also in the younger age group (25–29 years). Note that interpretation of hospitalisation data needs to take into account that there could be multiple hospitalisations per patient for use of inpatient and outpatient services over time.

These reductions seen in cervical cancer hospitalisations and mortality without a similar decline in the overall cervical cancer incidence may be a reflection of the reduction in severity of cervical cancer in cases and earlier detection and effective treatments.

The Northern Territory (NT) had the highest cervical cancer incidence rate overall.[190] This disparity may be due to the greater proportion of the population that are of Aboriginal and Torres Strait Islander origin, given that they currently bear a disproportionate burden of cervical cancer.[190] Remoteness also affects cervical cancer incidence, with a higher rate in 'remote and very remote' locations than in 'major cities'.[190] A study that used data from the New South Wales (NSW) Cancer Registry from 2001 to 2014 found that incidence rates in Aboriginal and Torres Strait Islander women were significantly higher than in non-Indigenous women in all 10-year age groups from 30 to 79 years.[197] Linked cervical screening and hospitalisation data showed that in 2010–2011, Aboriginal and Torres Strait Islander women in Queensland who attended screening had a significantly higher prevalence of cytological low- and high-grade abnormalities and histologically confirmed high-grade abnormalities than non-Indigenous women.[112] A study exploring factors associated with cervical cancer in women in New South Wales, the NT, QLD, VIC, SA and WA reported that Aboriginal and Torres Strait Islander women with cervical cancer were more likely to have associated comorbidities, including congestive heart failure, chronic pulmonary disease, diabetes and moderate–severe kidney disease.[198] The survival rate for cervical cancer was lower in Aboriginal and Torres Strait Islander women between 2003–2007 and 2008–2012.[198]

HPV has been estimated to cause 85% of anal cancers, 50% of penile cancers, 70% of vaginal cancer, 40% of vulval cancer and 35% of mouth and oropharyngeal cancers.[199] The transition from 4vHPV vaccine to 9vHPV vaccine in Australia has been predicted to prevent a further 15% of cervical cancers and 11% of anal cancers.[200] However, this proposed reduction in cancer incidence is not expected to be evident possibly for decades, given the difference in the mean age of disease diagnosis of these cancers and the current age of fully vaccinated adults.[200]

A more recently identified impact of the National HPV Vaccination Program is the significant reduction in juvenile-onset RRP (JoRRP), a condition associated with vertical transmission of HPV infection before or during birth, particularly type 6 or 11.[12,132,133] Our estimated hospitalisation rates (given there is no unique ICD code for RRP and no validation of these codes has been undertaken in adults) follow the expected pattern that JoRRP predominantly affects children aged <12 years and adult-onset RRP (AoRRP) predominantly affects adults aged 20–30 years and >60 years. Since the introduction of the HPV vaccination program, hospitalisation rates for probable RRP (i.e. ICD codes likely to be associated with RRP) have decreased in females aged <20 years and males aged <30 years, while ICD codes likely to be associated with RRP in adults increased in

both males and females aged ≥30 years. This declining incidence in JoRRP supports reduced mother–child HPV transmission and Australia was the first globally to document this impact of a 4vHPV vaccination program on JoRRP.[201]

Previous studies have demonstrated declines in prevalence of 4vHPV vaccine genotypes, and also potential herd protection in the older unvaccinated age groups.[50,94,95,96,98,202,203,204] The decrease in prevalence of HPV infection following vaccination among Australian Aboriginal and Torres Strait Islander females was only observed in those aged <25 years but the prevalence of HPV infection remains higher than in non-Indigenous females in each age group.[100]

The decline in prevalence of 4vHPV vaccine genotypes in males in the younger age groups is supported by prevalence and serosurveillance studies in Australia.[101,102,103,104]

In conclusion, we found significant reductions in cervical high-grade lesions and also in probable RRP that may be attributable to the female and male HPV immunisation programs in Australia.

Impact on disease burden: Genital warts

Aims

To estimate the hospitalisation rates for anogenital warts by gender, age, jurisdiction and Aboriginal and Torres Strait Islander status, and to assess changes in hospitalisation rates for anogenital warts following introduction of the HPV vaccination program in Australia.

Methods

We used data from the National Hospital Morbidity Database of the Australian Institute of Health and Welfare (AIHW) for this analysis. Data included age, gender and Aboriginal and Torres Strait Islander status of hospitalised patients and hospital diagnoses coded using the International Statistical Classification of Diseases, Tenth Revision, Australian Modification; (ICD-10-AM).

The population estimates used as denominators for rate calculations were obtained from the Australian Bureau of Statistics (cat no. 3101.0, release date 19 March 2020). All AIHW hospitalisation data that included ICD-10-AM code A63.0 ('anogenital warts') as the principal or any of the additional diagnoses, for the years 2003–2017, were included.

Most genital warts do not result in hospitalisation and these data represent the most severe cases. Some individuals could have multiple episodes of treatment which cannot be identified as belonging to a single individual in these data. Hospitalisation rates were calculated per 100,000 people on the basis of total hospital admissions over a relevant 12-month period and the corresponding mid-year resident population estimate. Hospitalisations were stratified by sex and by age group (<10 years, 10–19 years, 20–29 years, 30–39 years and ≥40 years).

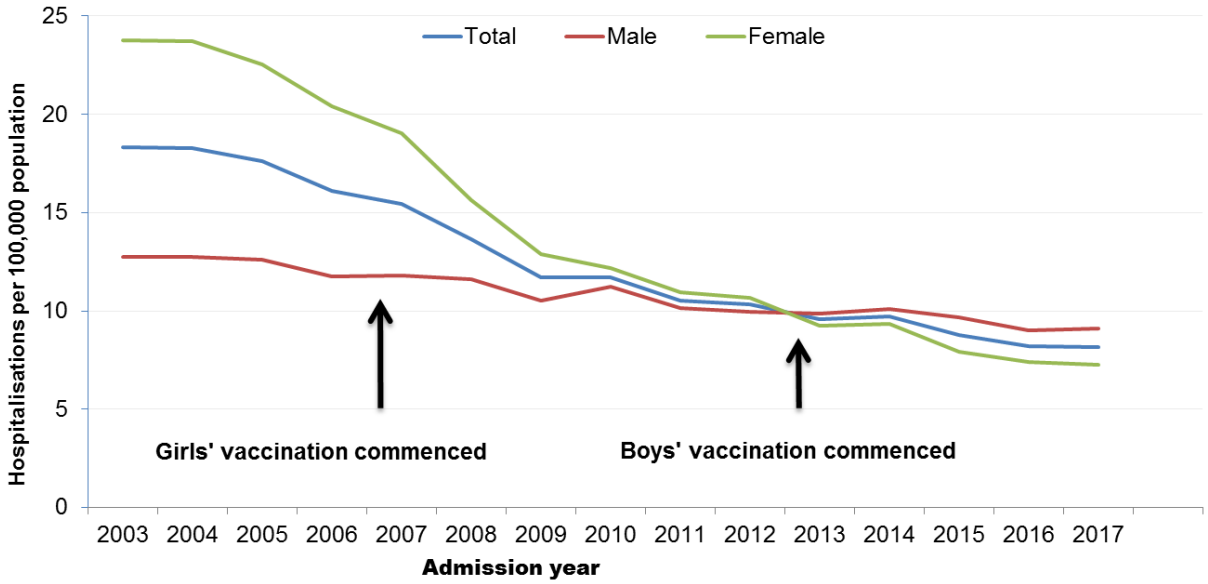
Complete data for both numerators and denominators for all Australian states and territories, and for both Aboriginal and Torres Strait Islander and non-Indigenous populations, were available for the period 2003–2017. Average annual hospitalisation rates in the pre-vaccine period of 2003–2007 were compared with those in two post-vaccine periods: 2008–2013 and 2014–2017.

Results

Between 2003 and 2017, a total of 40,612 hospitalisations that had a diagnosis of anogenital warts (ICD-10-AM code A 63.0) were identified across Australia. Of those hospitalisations 22,924 (56.4%) were in females and 17,688 (43.6%) in males. There were 960 (1.2%) hospitalisations in Aboriginal and Torres Strait Islander people: 679 (70.7%) in females and 281 (29.3%) in males.

Overall, there was a gradual decline in anogenital warts hospitalisations across the study period in both females and males. This decline was more pronounced in females (refer to Figure 31).

Figure 31: Anogenital warts hospitalisation rates (all ages)* by gender, 2003 to 2017

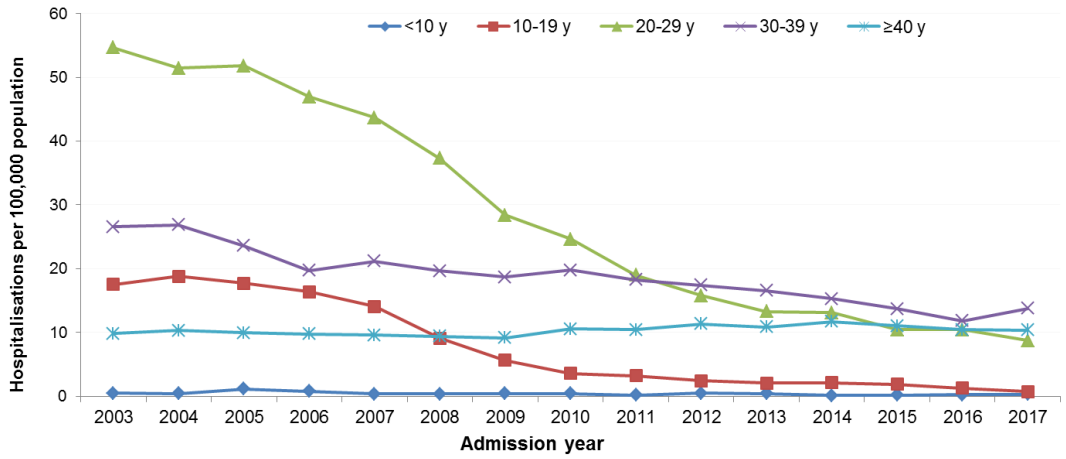


* Per 100,000 population

Hospitalisations by age group

Overall, for both genders combined, there was a decline in hospitalisation rates in age groups 10–19 years, 20–29 years and 30–39 years (refer to Table 54, Figure 32). There was no significant change in the rates in <10 years and ≥40 years age groups. The greatest reduction in rate was in the 10–19 years age group followed by 20–29 and 30–39 years. Annual average hospitalisation rates per 100,000 population for anogenital warts in the age groups 10–19 years, 20–29 years and 30–39 years in the pre-vaccine period (2003–2007) were 16.9, 49.6 and 23.6, and these rates decreased to 4.3, 22.8 and 18.4 in the post-vaccine period, equating to declines of 74.4%, 54.1% and 22.1%, respectively. Hospitalisation rates decreased further in the 2014–2017 period, compared with the 2008–2017 period, to 1.5, 10.6 and 13.6 per 100,000 population in the age groups 10–19 years, 20–29 years and 30–39 years, respectively, equating to further declines of 65.5%, 53.2% and 25.8%, respectively.

Figure 32: Anogenital warts hospitalisation rates* by age group, 2003 to 2017



* Per 100,000 population

In females, the highest decline was in the 10–19 years age group, followed by 20–29 years. Annual average hospitalisation rates in the 10–19 years and 20–29 years age groups declined from 31.7 and 70.1 per 100,000 population in pre-vaccine period (2003–2007) to 6.3 and 26.3 in the post-vaccine period (2008–2013), equating to a reduction of 80.3% and 62.5%, respectively. Rates in the 2014–2017 period declined to 1.6 and 8.0 per 100,000 population in the 10–19 and 20–29 years age groups, respectively, equating to a further 74.0% and 69.5% decline compared with the 2008–2013 period.

In males, annual hospitalisation rates in the years 2003–2013 (corresponding to the period before the commencement of the male HPV vaccination program) were 2.6 and 24.1 per 100,000 population in the 10–19 years and 20–29 years age groups, respectively. These rates decreased by 48.0% and 45.2% to 1.4 and 13.2 per 100,000 population in the 10–19 and 20–29 years age groups, respectively, in the 2014–2017 period.

Hospitalisations by Aboriginal and Torres Strait Islander status

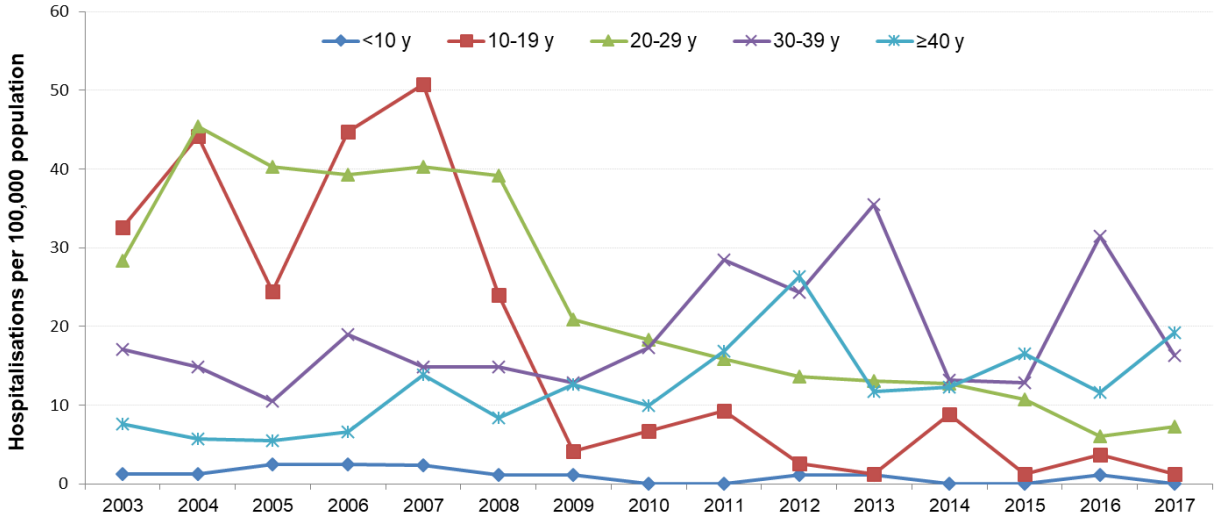
In Aboriginal and Torres Strait Islander people, there was a significant decline in hospitalisation rates for anogenital warts from pre- to post-HPV vaccine introduction in the 10–19 and 20–29 years age groups (refer to Table 54), in both females and males (refer to Figure 33 and Figure 34).

However, in the 30–39 years age group there was a significant increase in hospitalisation rate in the post-vaccine period (2008–2017) compared with the pre-vaccine period (2003–2007), and the rate was significantly higher in Aboriginal and Torres Strait Islander people compared with their non-Indigenous counterparts (refer to Table 55).

In Aboriginal and Torres Strait Islander males aged 10-19 years and 20-29 years, hospitalisation rates in the 2003-2013 period were 1.9 and 9.9 per 100,000 population and these rates decreased by 52.7% and 14.9%, respectively, to 0.9 and 8.4 per 100,000. Refer to Figure 34 for

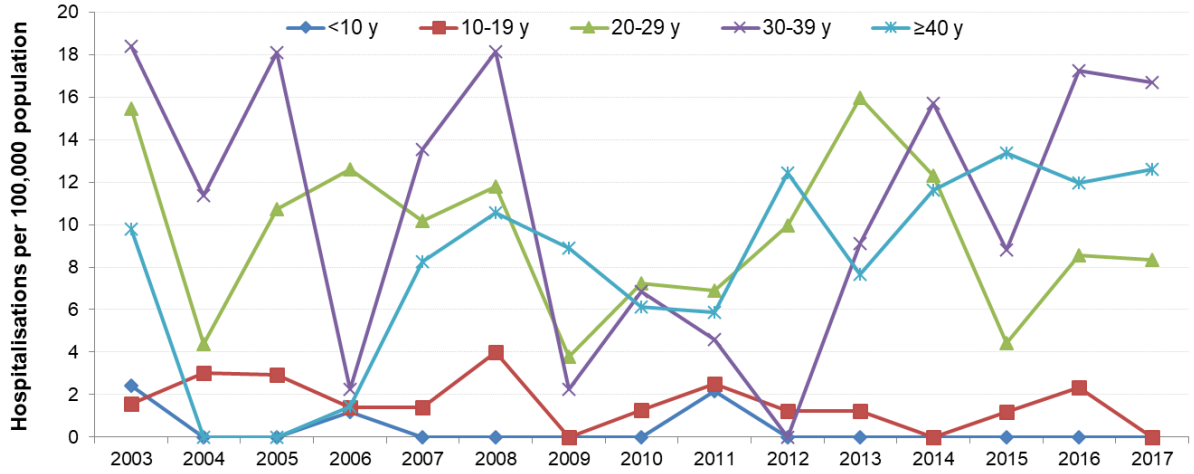
hospitalisation rates for Aboriginal and Torres Strait Islander males by age group from 2003 to 2017.

Figure 33: Anogenital warts hospitalisation rates* for Aboriginal and Torres Strait Islander females by age group, 2003 to 2017



* Per 100,000 population

Figure 34: Anogenital warts hospitalisation rates* for Aboriginal and Torres Strait Islander males by age group, 2003 to 2017



* Per 100,000 population

Table 54. Anogenital warts hospitalisation rates* pre-vaccine (2003–2007) to post-vaccine (2008–2017) introduction, by Indigenous status and age group

	2003–2007 (a)	2008–2017 (b)	Rate Ratio (b/a)	95% CI
Aboriginal and Torres Strait Islander				
<10 years	1.3	0.4	0.45	0.04-5.01
10–19 years	20.4	3.8	0.19	0.08-0.45
20–29 years	24.8	12.4	0.51	0.27-0.97
30–39 years	19.7	43.5	2.17	1.02-4.61
≥40 years	6.0	12.7	2.2	0.99-4.94
Total	12.4	8.6	0.7	0.50-0.98
Non-Indigenous				
<10 years	0.6	0.3	0.51	0.21-1.21
10–19 years	16.7	3.1	0.19	0.15-0.24
20–29 years	50.5	17.9	0.36	0.32-0.39
30–39 years	23.7	16.1	0.68	0.61-0.76
≥40 years	9.9	10.5	1.10	0.97-1.16
Total	17.3	10.2	0.59	0.56- 0.62
All Australians				
<10 years	0.6	0.3	0.50	0.22-1.13
10–19 years	16.9	3.2	0.19	0.15-0.24
20–29 years	49.6	17.7	0.36	0.32-0.39
30–39 years	23.6	16.4	0.70	0.62-0.78
≥40 years	9.9	10.5	1.07	0.98-1.17
Total	17.1	10.2	0.59	0.56-0.63

* Per 100,000 population

Table 55. Anogenital warts hospitalisation rates* in Aboriginal and Torres Strait Islander people and non-Indigenous populations, by age groups and pre- and post-vaccine periods

	Aboriginal and Torres Strait Islander (a)	Non-Indigenous (b)	Rate Ratio (a/b)	95% CI
2003–2007				
<10 years	1.3	0.6	2.11	0.48-9.27
10–19 years	20.4	16.7	1.21	0.82-1.78
20–29 years	24.8	50.5	0.48	0.32-0.73
30–39 years	19.7	23.7	0.85	0.49-1.47

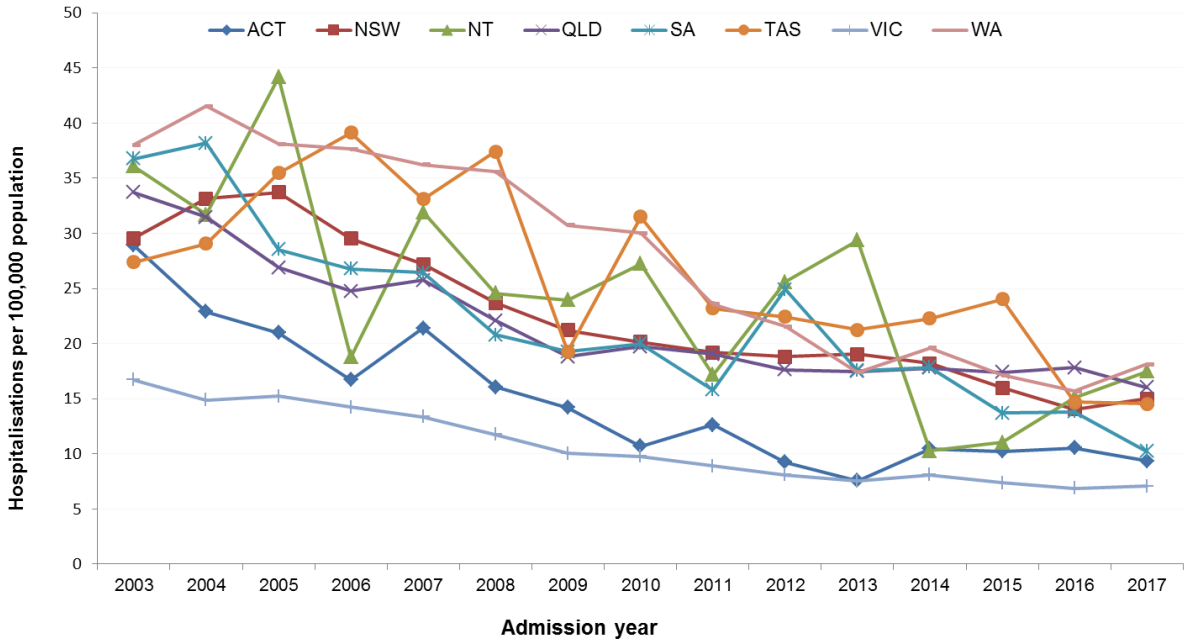
≥40 years	6.0	9.9	0.58	0.29-1.16
Total	12.4	17.3	0.72	0.57-0.90
2008–2013				
<10 years	0.6	0.4	1.48	0.19-11.57
10–19 years	4.7	4.3	1.06	0.49-2.27
20–29 years	14.5	23.1	0.62	0.38-1.01
30–39 years	44.3	18.1	2.41	1.39-4.18
≥40 years	11.7	10.3	1.16	0.75-1.79
Total	8.9	11.3	0.79	0.61-1.02
2014–2017				
<10 years	0.1	0.2	1.04	0.06-18.24
10–19 years	2.3	1.4	1.65	0.59-4.61
20–29 years	8.8	10.7	0.84	0.47-1.49
30–39 years	42.9	13.3	3.33	2.02-5.48
≥40 years	13.8	10.8	1.30	0.89-1.87
Total	8.2	8.7	0.94	0.73-1.22

* Per 100,000 population

Hospitalisations rates by jurisdiction

Hospitalisation rates for anogenital warts decreased over the years, from 2003 to 2017, in all Australian states and territories; however, the decline was more pronounced in some jurisdictions and age groups (refer to Figure 35, Table 56). There were statistically significant reductions in the 20–29 years age groups in all jurisdictions and in the 10–19 years age group in all except the Australian Capital Territory (ACT), where the number of hospitalisations was very small (refer to Table 56). In states with larger populations (i.e. New South Wales, Victoria and Queensland) there were also significant reductions in hospitalisations in the 30–39 years age group. In the <10 and ≥40 years age groups there were no significant changes except in Queensland where there was an increased rate in the ≥40 years age group in the post-vaccine period (refer to Table 56). Average annual hospitalisation rates per 100,000 population by individual state/territory, age and Aboriginal and Torres Strait Islander status are summarised in Appendices 15–22.

Figure 35: Anogenital warts hospitalisation rates* by state/ territory, 2003 to 2017



* Per 100,000 population

Table 56. Anogenital warts hospitalisation rates* pre-vaccine (2003–2007) and post-vaccine (2008–2017) introduction, by state/territory and age group

	2003–2007	2008–2017	RR	95% CI
New South Wales				
<10 years	0.5	0.3	0.69	0.15-3.10
10–19 years	14.8	2.7	0.18	0.12-0.28
20–29 years	46.2	16.8	0.36	0.31-0.43
30–39 years	22.1	15.8	0.71	0.58-0.87
≥40 years	9.7	10.1	1.03	0.89-1.21
Total	16.0	9.6	0.60	0.55-0.66
Victoria				
<10 years	0.7	0.4	0.52	0.13-2.19
10–19 years	16.0	2.7	0.17	0.10-0.28
20–29 years	59.4	19.2	0.32	0.27-0.39
30–39 years	28.6	18.5	0.64	0.53-0.80
≥40 years	11.2	11.3	1.01	0.85-1.19
Total	19.9	11.1	0.56	0.50- 0.62
Queensland				
<10 years	0.6	0.4	0.57	0.10-3.42

10–19 years	18.2	3.3	0.18	0.11-0.30
20–29 years	40.9	14.6	0.36	0.28-0.45
30–39 years	20.0	14.6	0.73	0.55-0.95
≥40 years	7.9	10.8	1.37	1.11-1.70
Total	14.7	9.5	0.65	0.57-0.73
Australian Capital Territory				
<10 years	0	0	0.87	0.02-43.90
10–19 years	22.8	0.4	0.09	0.01-1.65
20–29 years	57.7	20.0	0.37	0.15-0.91
30–39 years	30.7	17.5	0.55	0.18-1.67
≥40 years	11.9	11.2	0.96	0.39-2.36
Total	22.1	11.0	0.51	0.30-0.86
South Australia				
<10 years	0.3	0.2	0.31	0.01-7.65
10–19 years	17.0	3.9	0.23	0.11-0.50
20–29 years	52.0	15.3	0.30	0.20-0.44
30–39 years	21.8	16.4	0.75	0.48-1.16
≥40 years	9.4	9.1	0.95	0.69-1.32
Total	16.5	9.2	0.55	0.45-0.68
Tasmania				
<10 years	1.0	0.2	0.33	0.01-8.14
10–19 years	27.6	5.5	0.22	0.07-0.65
20–29 years	62.4	23.7	0.39	0.21-0.71
30–39 years	16.9	22.7	0.74	0.34-1.63
≥40 years	7.7	11.4	1.49	0.83-2.68
Total	17.3	12.1	0.70	0.51-0.97
Northern Territory				
<10 years	1.2	0.3	0.95	0.02-47.67
10–19 years	10.1	2.5	0.33	0.03-3.17
20–29 years	32.7	14.0	0.44	0.16-1.20
30–39 years	24.8	13.1	0.50	0.17-1.49
≥40 years	12.5	12.5	1.00	0.41-2.41
Total	15.7	9.6	0.63	0.37-1.07
Western Australia				
<10 years	1.0	0.4	0.28	0.03-2.66
10–19 years	21.7	4.9	0.23	0.13-0.40

20–29 years	53.2	23.8	0.45	0.34-0.58
30–39 years	25.7	16.8	0.65	0.46-0.91
≥40 years	11.8	10.9	0.92	0.71-1.20
Total	19.6	11.6	0.59	0.51-0.69

* per 100,000 population

Summary/discussion

This analysis corroborates and confirms findings from previous studies that showed a remarkable decline in all diagnoses and hospitalisations for anogenital warts in Australia, across populations within and outside of major cities, males and females and whether vaccinated at school or in the community.[120, 124, 125, 205-208] Our data demonstrate ongoing incremental declines in genital warts hospitalisation following extension of the HPV vaccination program to males and gradually rising female coverage. Our data are also in concordance with data from Europe and North America where a significant reduction in diagnoses or hospitalisations for genital warts have been noted in age groups eligible for vaccination. [209-211] These declines are believed to be a reliable early marker of disease reduction due to HPV vaccination and associated herd protection.[212, 213] For the first time in Australian data analyses, we found a significant decrease in hospitalisations for genital warts in the 30–39 years age group, likely because the earliest vaccinated cohorts are now reaching that age. However, Aboriginal and Torres Strait Islander people aged 30–39 years had increased rates of hospitalisations in the post-vaccine period (2008–2017) than in the pre-vaccine period (RR 2.2; 95% CI: 1.0–4.6) and were twice as likely to be hospitalised with anogenital warts compared with their non-Indigenous counterparts in both the 2008–2013 (RR 2.4; 95% CI: 1.4–4.2 1.4-4.18-4.2) and 2014–2017 (RR 3.3; 95% CI: 2.0–5.5) periods. This may be due to lower uptake of vaccination in Aboriginal and Torres Strait Islander people during the adult catch-up program in 2007–2009 than in non-Indigenous people.[34]

We did not find any significant change in hospitalisation rates in those aged ≥40 years, consistent with other studies that noted no significant decreases as yet in older age groups.[207,214]

Our analysis used national data up to 5 years after the extension of HPV vaccination program to males, but has some limitations. We did not include hospital admissions coded as procedures related to genital warts or explore program impact by either socioeconomic or geographic factors beyond state of residence, as we did not have access to postcode-level data. We were unable to assess impact on men who have sex with men (MSM),[215] as it was not possible to identify MSM through hospitalisation data.

Appendices

Appendix 1. Sampling matrix of key stakeholders interviewed

Stakeholder group	National	QLD	NSW	ACT	VIC	TAS	SA	WA	NT
Department of Health- Immunisation Branch	X								
Department of Health- Screening	X								
Department of Health- AIR Policy	X								
TGA	X								
Juriasdcitional immunisartion program managers		X	X	X	X	X	X	X	N/A
Other state/ territory health department immunisation staff		X			X	X	X		X
State/ territory school immunisation program co-ordinator			X						
Remote area immunisation co-ordinator		X							X
Local council Immunisation Staff					X (2)				
ACCHS staff						X	X		X
Jurisdictional cervical screening program manager	X (jurisdiction not identified)								
Sexual Health Physician									
HPV Researcher	X (2)								
Seqirus	X								

ACCHS= Aboriginal Community Controlled Health Service

Appendix 2. Questionnaire used for state and territory immunisation program managers

NCIRS National Centre for Immunisation Research and Surveillance

Impact Evaluation of the National Human Papillomavirus Vaccination Program

Stakeholder Interview Questionnaire

- The National Centre for Immunisation Research and Surveillance is currently conducting an impact evaluation of the national human papillomavirus (HPV) vaccination program on behalf of the Australian Government Department of Health
- This questionnaire will form the basis for a telephone interview and is being provided now to allow you time to reflect and collect any supporting information to inform your responses
- The focus of this questionnaire is to identify factors that are positively or negatively influencing the outcomes and impacts of the program and the questions are intended to be answered based on your experiences and perceptions
- All information you provide will be kept confidential and the final report to the Department of Health will contain de-identified information only
- You will be provided with a transcript of your completed interview and permitted to make any amendments that you deem necessary

is questionnaire will cover the following areas:

- ✓ Participant details
- ✓ Vaccination coverage
- ✓ Vaccine safety
- ✓ Vaccination reporting
- ✓ Cervical screening
- ✓ Program strengths and challenges
- ✓ Recommendations

Appendix 3. The SurveyMonkey questionnaire

Evaluation of the National HPV Vaccination Program

Participant Details

* 1. What is your age group?

- ◯ <25 years
- ◯ 25-34 years
- ◯ 35-44 years
- ◯ 45-54 years
- ◯ 55 years and over

* 2. What is your gender?

- ◯ Female
- ◯ Male
- ◯ Other (please specify):

* 3. Where do you work?

- ☐ Nationally
- ☐ NSW
- ☐ QLD
- ☐ VIC
- ☐ WA
- ☐ SA
- ☐ NT
- ☐ TAS
- ☐ ACT

* 4. Which best describes where you work?

- ◯ Major city
- ◯ Regional
- ◯ Remote

* 5. What is your role in HPV control and cervical cancer prevention?

- ○ General practitioner
- ○ Practice nurse
- ○ School-based nurse immuniser
- ○ Aboriginal Health Worker
- ○ Aboriginal Health Practitioner
- ○ Sexual health physician
- ○ Cervical screening program manager
- ○ Other (please specify):

Evaluation of the National HPV Vaccination Program

Vaccination Coverage

* 6. How often is school-based HPV vaccination coverage in your area impacted by:

	Never	Rarely	Sometimes	Frequently	Don't Know or N/A
Absenteeism on vaccination day	○	○	○	○	○
Consent forms not returned	○	○	○	○	○
Inadequate education for parents before vaccination day	○	○	○	○	○
Parents choosing not to consent	○	○	○	○	○
Student refusal on vaccination day	○	○	○	○	○
Staffing shortages	○	○	○	○	○

Additional comments:

Vaccination Coverage

In 2018 the 9-valent HPV (9vHPV) vaccine Gardasil9® replaced the quadrivalent HPV vaccine Gardasil® in the national HPV vaccination program.

* 7. Have you experienced any issues with implementing the 9vHPV vaccination program? (e.g. vaccine supply, safety rumours, confusion about eligibility or if people require re-vaccination)

- ◯ Yes
- ◯ No
- ◯ Not Applicable

If yes, please describe the issues:

* 8. Have you experienced any advantages of implementing the 9vHPV vaccination program? (e.g. support for the increased valency or reduction to 2 doses)

- ◯ Yes
- ◯ No
- ◯ Not Applicable

If yes, please describe the advantages:

* 9. How do you believe the change to a 2-dose schedule has influenced HPV vaccination coverage for adolescents aged under 15 years in your area?

	Increased coverage	No change	Decreased coverage	Don't Know
First dose HPV vaccine	◯	◯	◯	◯
Second dose HPV vaccine	◯	◯	◯	◯

Additional comments:

* 10. In your school immunisation program or practice what is the usual interval between doses in the 2-dose schedule?

- ◯ 6-7 months
- ◯ 8-10 months
- ◯ 11-12 months
- ◯ Don't Know
- ◯ Other (please specify):

11. What new strategies do you think could improve school-based HPV vaccination coverage in your area? (e.g. digital technology like electronic consent forms or reminder messages, changed timing of doses, community partnerships, coverage targets, increased education for parents, students or schools)

* 12. Do you believe the option for HPV vaccine catch-up through primary care up to age 19 years (e.g. through GP or AMS) is being adequately utilised in your area? (e.g. parents and young people know about it and practices implement it effectively)

	Yes	No	Don't Know
Age <15 years (2 doses)	◯	◯	◯
Age ≥15 years (3 doses)	◯	◯	◯

If no, please describe the barriers and how this could be improved:

* 13. Are you satisfied with the relationship between the school-based HPV vaccination program and primary care providers in your area?

- ◯ Yes
- ◯ No
- ◯ Don't Know

If no, please describe why not and how this could be improved:

14. Does your work include HPV vaccination in schools or communities with significant representation of any of the following population groups? (select any or all that apply)

- [ ] Aboriginal and/or Torres Strait Islander people
- [ ] Culturally and linguistically diverse people
- [ ] Socioeconomically disadvantaged people
- [ ] Other diverse population groups (please specify):

15. If you selected any of the above population groups, please describe your experience and any particular successes or challenges of HPV vaccination in these groups:

Vaccine Safety

* 20. Have you perceived any change in FREQUENCY of adverse events following immunisation with 9vHPV vaccine compared to quadrivalent HPV vaccine?

- ◯ Yes- Increased adverse events
- ◯ Yes- Decreased adverse events
- ◯ No change
- ◯ Don't know

If yes, please describe your answer including any data sources relevant to your observation:

* 21. Have you perceived any change in TYPE of adverse events following immunisation with 9vHPV vaccine compared to quadrivalent HPV vaccine?

- ◯ Yes- Change in type of adverse event
- ◯ No change
- ◯ Don't know

If yes, please describe your answer including any data sources relevant to your observation:

Vaccination Reporting

In 2018 vaccination reporting on the National HPV Vaccination Program Register ceased and transitioned to the Australian Immunisation Register (AIR).

* 22. Please indicate how strongly you agree or disagree with each statement:

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree	Don't Know
I am satisfied with the transition of HPV vaccination reporting to the AIR	○	○	○	○	○	○
All HPV vaccinations I provide get reported to the AIR	○	○	○	○	○	○

Additional comments (e.g. enablers or barriers to reporting):

23. Have you experienced any benefits with the transition of HPV vaccination reporting to the AIR?

24. Have you experienced any challenges with the transition of HPV vaccination reporting to the AIR?

Cervical Screening

* 25. Does your work involve cervical screening?

- ○ Yes
- ○ No

Cervical Screening

* 26. From your experience, please indicate how strongly you agree or disagree with each statement:

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree	Don't Know
Receiving HPV vaccine influences the uptake of cervical screening	○	○	○	○	○	○
Females who have received HPV vaccine are MORE likely to undergo cervical screening than unvaccinated females	○	○	○	○	○	○
Females who have received HPV vaccine are LESS likely to undergo cervical screening than unvaccinated females	○	○	○	○	○	○
Females who have received HPV vaccine have adequate knowledge that they still require cervical screening	○	○	○	○	○	○

Additional comments:

* 27. Do you believe the change to HPV-based cervical screening could have any impact on HPV vaccination uptake in Australia?

- ○ Yes
- ○ No
- ○ Don't Know

If yes, please describe how:

Disease Impact

* 28. Do you see patients with HPV-related conditions?

- ○ Yes
- ○ No

Disease Impact

* 29. In your work, have you observed any decrease in the following conditions since the introduction of HPV vaccination in Australia?

	No decrease	Small decrease	Moderate decrease	Large decrease	Don't Know or N/A
High-grade cervical abnormalities	○	○	○	○	○
Genital warts in females	○	○	○	○	○
Genital warts in males	○	○	○	○	○

Additional comments:

Program Strengths and Challenges

* 30. How important do you consider the following factors are in POSITIVELY influencing the coverage and impacts of the national HPV vaccination program?

	Not Important	Slightly Important	Moderately Important	Very Important	Don't Know
Funded on the NIP	○	○	○	○	○
School-based program	○	○	○	○	○
Community catch-up option	○	○	○	○	○
Gender-neutral program	○	○	○	○	○
Reduction to 2-dose schedule	○	○	○	○	○
Promotion of HPV vaccination as cancer prevention	○	○	○	○	○

Other factors (please specify):

31. Can you identify any factors that could positively influence the program in future?

* 32. How important do you consider the following factors are in NEGATIVELY influencing the coverage and impacts of the national HPV vaccination program?

	Not Important	Slightly Important	Moderately Important	Very Important	Don't Know
School absenteeism	○	○	○	○	○
Return of consent forms	○	○	○	○	○
Lack of agreed national HPV vaccine coverage target	○	○	○	○	○
Social stigma around HPV as an STI	○	○	○	○	○
Parental concern about HPV vaccine safety	○	○	○	○	○
Parental concern about promoting promiscuity or early sexual initiation	○	○	○	○	○
Cultural or religious barriers	○	○	○	○	○

Other factors (please specify):

33. Can you identify any factors that could negatively influence the program in future?

* 34. To achieve elimination of cervical cancer as a public health problem by 2030 (rate <4 per 100, 000) the World Health Organization has set a target of 90% of girls fully vaccinated with HPV vaccine by age 15 years. Do you think this is achievable in Australia?

- ○ Yes
- ○ No
- ○ Don't Know

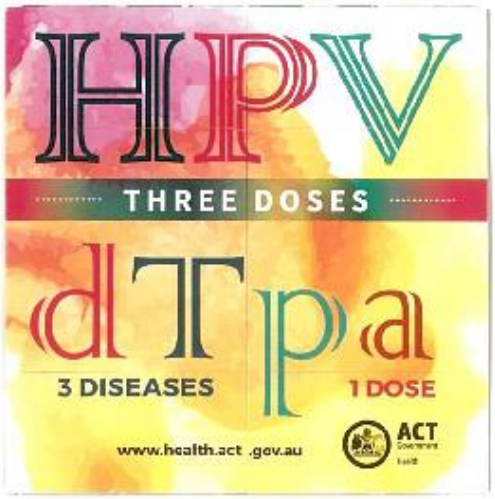
Additional comments (e.g. how Australia could achieve this target or why this is not achievable):

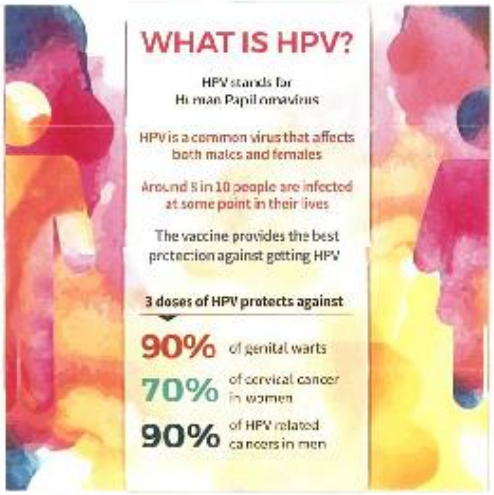
* 35. How satisfied are you with the following achievements to date of the national HPV vaccination program?

	Very Dissatisfied	Dissatisfied	Neutral	Satisfied	Very Satisfied	Don't Know
Local vaccine coverage	○	○	○	○	○	○
National vaccine coverage	○	○	○	○	○	○
Impact on disease burden	○	○	○	○	○	○

36. Do you have any further comments?

Appendix 4. Infinity cards provided to children in recovery post-vaccination in ACT





Appendix 5. Simplified consent form with dual HPV/dTpa consent for students from remote communities in NT

NORTHERN TERRITORY GOVERNMENT

Please complete and **return this form** to school. It is a legal requirement for a parent/guardian to sign this consent form for your child to receive vaccines at school.

School Vaccination Program

In the Northern Territory, **all students in Year 7** are eligible to receive

- A course of Human Papillomavirus (HPV) vaccine and
- One dose of diphtheria, tetanus, pertussis vaccine

If your child can't be vaccinated at school or misses out because of illness or absence, you can visit a health clinic for the missed vaccines.

Information and Consent for Vaccination

■ Human Papillomavirus (HPV) and the vaccine

HPV is a very common virus in women and men. HPV is spread from one person to another during all types of sexual activity. Most people (4 out of 5) will have HPV at some point in their lives and never know it. The HPV vaccine (Gardasil®) helps protect against 4 types of HPV which cause cervical cancer and cancers of the vulva, vagina, penis and anus, HPV also causes genital warts.

The vaccine does not protect people already infected with HPV. The vaccine is given as a course of injections over a period of 6-12 months.

■ What are the possible side effects of the vaccines?

Common side effects are discomfort, redness, pain and swelling at the injection site for 1-2 days. Other symptoms may include headache, fever, tiredness and nausea. Putting a cool wet cloth on the injection site and giving paracetamol helps to relieve symptoms. Fainting, the most common immediate reaction to any vaccine in older children and teenagers may occur 5-30 minutes following vaccination. Severe allergic reactions are rare.

It is safe to give more than 1 vaccine on the same day. If more than 1 vaccine is required they may be given in separate arms.

■ Diphtheria, tetanus, pertussis and the vaccine

A single vaccine protects against diphtheria, tetanus and pertussis infections.

- Diphtheria infection can cause breathing difficulty and damage to the heart. About 10% of people with diphtheria will die. Others may have permanent heart damage.
- Tetanus infection causes painful muscle spasms that cause trouble breathing and can lead to death. Tetanus spores live in the soil and infection can occur from injuries, sometimes minor.
- Pertussis (Whooping Cough) can be passed between people either by coughing and sneezing or during kissing or sharing eating utensils. The infection causes severe coughing, spasms and vomiting. Pneumonia, fitting and brain swelling can occur.

www.health.nt.gov.au

See overleaf ►

NORTHERN TERRITORY GOVERNMENT

School Vaccination Program

Student Details

Student First Name: _____ Student Last Name: _____

Other Legal Names (if applicable): _____

Sex: ☐ Male ☐ Female Date of Birth: ___ / ___ / ___

Community: _____

Medicare No: ☐☐☐☐ ☐☐☐☐☐ ☐☐

☐ Non-Aboriginal ☐ Aboriginal ☐ Aboriginal and Torres Strait Islander ☐ Torres Strait Islander

School: _____ Class/Year: _____

Any severe reactions to previous vaccines ☐ No ☐ Yes - list

Pre-Vaccination Checklist

Your consent is required before your child can be immunised at school. Your child should not be immunised if any of the following apply:

- They are known to have had a severe reaction to any vaccine; or part of a vaccine
- They have a fever of 38.5ºC or above on the day of immunisation
- They have had a serious allergic reaction to yeast
- They are taking a medication or have a disease which lowers immunity (for example leukaemia or cancer)
- They are pregnant or could be pregnant.

Consent for Vaccination - For Parent / Guardian to complete

I consent for my child to receive:

a course of **Human Papillomavirus (HPV)** vaccine and
1 dose of **Adult diphtheria, tetanus, pertussis** vaccine

and the information being recorded*. *Tick one box only.*

▶ ☐ **YES** ☐ **NO**

Parent / Guardian Name: _____ Daytime phone contact: _____

Parent / Guardian Signature: _____ Date: _____

Privacy Information

*The information on this form will be recorded on the NT Immunisation Register and later transferred to the Australian Immunisation Register (AIR). Inclusion on these registers is voluntary. All personal information collected by the NT Department of Health will be handled in accordance with the *Information Act* and the Department's Privacy Policy. Personal information disclosed to AIR is subject to the *Privacy Act* (Commonwealth).

For further information on privacy laws, visit: https:/nt.gov.au/law/rights/freedom-of-information.

Office use only

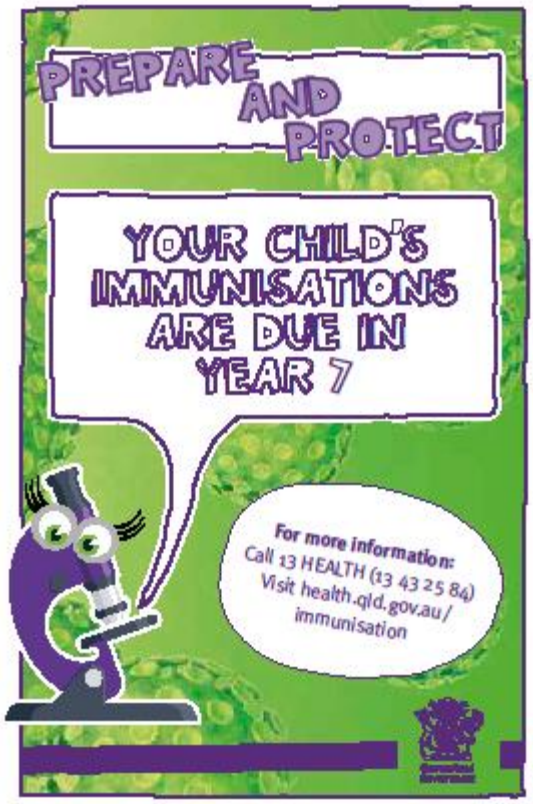
Vaccine Dose	Date Given	Batch Number	Site		Vaccinator Name
HPV # 1			Left	Right	
HPV # 2			Left	Right	
HPV # 3			Left	Right	
dTpa # 1			Left	Right	

Reason not vaccinated: ☐ Absent ☐ Refused ☐ Unwell ☐ No consent ☐ Other _____

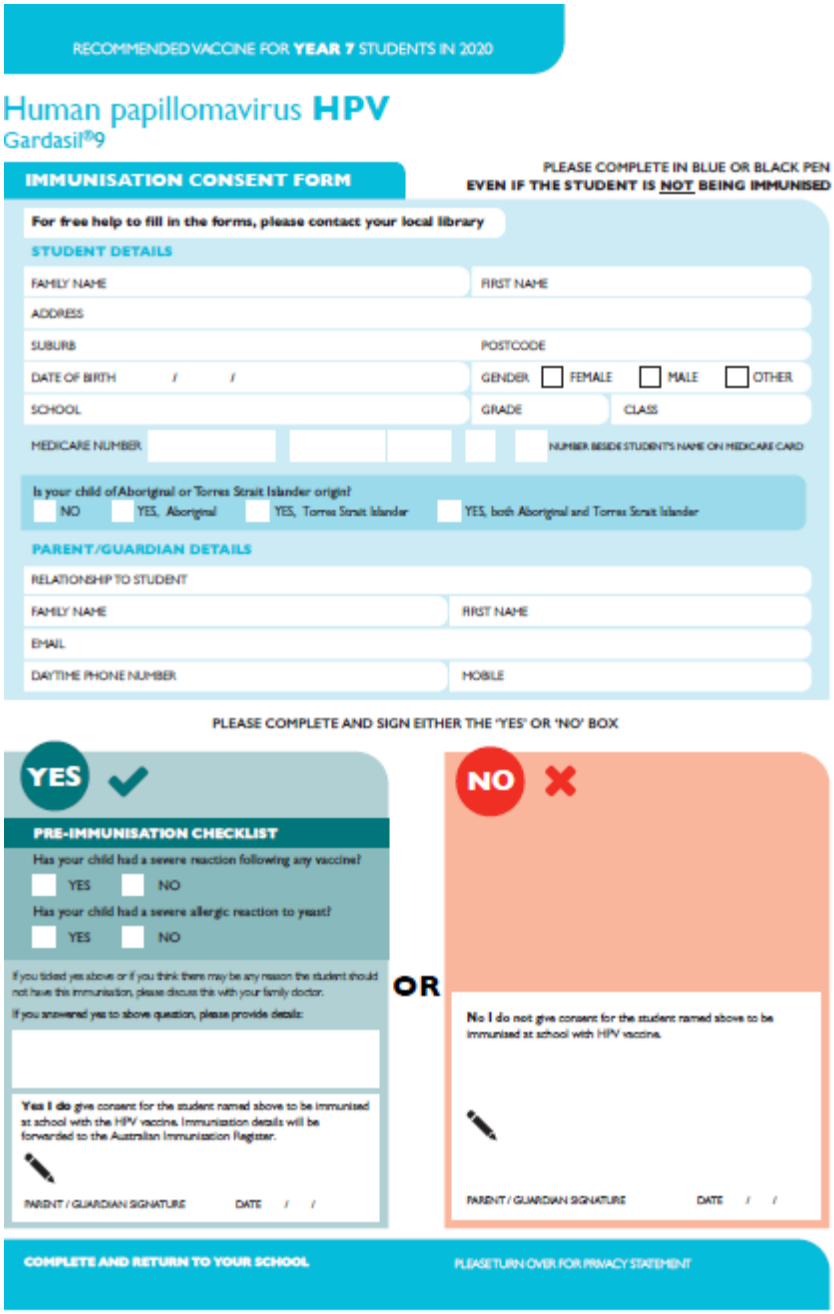
For further information regarding the School Vaccination Program please contact > Darwin **8922 8044** or Regional Centres: Katherine **8973 9049**; Alice Springs **8951 7549**; Nhulunbuy **8987 0357**; Tennant Creek **8962 4259** or visit **www.hpvvaccine.org.au**.

www.health.nt.gov.au Approved for use in 2020

Appendix 6. Postcards used in Queensland reminding about HPV vaccination



Appendix 7. Consent form for HPV vaccination used in Tasmania



RECOMMENDED VACCINE FOR **YEAR 7** STUDENTS IN 2020

Human papillomavirus **HPV**
Gardasil®9

IMMUNISATION CONSENT FORM

PLEASE COMPLETE IN BLUE OR BLACK PEN
EVEN IF THE STUDENT IS NOT BEING IMMUNISED

For free help to fill in the forms, please contact your local library

STUDENT DETAILS

FAMILY NAME | FIRST NAME
ADDRESS
SUBURB | POSTCODE
DATE OF BIRTH / / | GENDER ☐ FEMALE ☐ MALE ☐ OTHER
SCHOOL | GRADE | CLASS
MEDICARE NUMBER | NUMBER BESIDE STUDENT'S NAME ON MEDICARE CARD

Is your child of Aboriginal or Torres Strait Islander origin?
☐ NO ☐ YES, Aboriginal ☐ YES, Torres Strait Islander ☐ YES, both Aboriginal and Torres Strait Islander

PARENT/GUARDIAN DETAILS

RELATIONSHIP TO STUDENT
FAMILY NAME | FIRST NAME
EMAIL
DAYTIME PHONE NUMBER | MOBILE

PLEASE COMPLETE AND SIGN EITHER THE 'YES' OR 'NO' BOX

YES

PRE-IMMUNISATION CHECKLIST

Has your child had a severe reaction following any vaccine?
☐ YES ☐ NO
Has your child had a severe allergic reaction to yeast?
☐ YES ☐ NO

If you ticked yes above or if you think there may be any reason the student should not have this immunisation, please discuss this with your family doctor.
If you answered yes to above question, please provide details:

Yes I do give consent for the student named above to be immunised at school with the HPV vaccine. Immunisation details will be forwarded to the Australian Immunisation Register.

PARENT / GUARDIAN SIGNATURE DATE / /

OR

NO

No I do not give consent for the student named above to be immunised at school with HPV vaccine.

PARENT / GUARDIAN SIGNATURE DATE / /

COMPLETE AND RETURN TO YOUR SCHOOL

PLEASE TURN OVER FOR PRIVACY STATEMENT

Appendix 8: Preferred terms used to identify adverse events of special interest (AESI)

- Syncope: Syncope, syncope vasovagal, loss of consciousness
- Anaphylaxis: Anaphylactic shock, anaphylactic reaction, anaphylactoid reaction, anaphylactoid shock
- Autoimmune disorders (AID): Antinuclear antibody positive, autoantibody positive, autoimmune disorder, autoimmune hemolytic anemia, autoimmune thyroiditis, autoimmune thrombocytopenia, Bechet's syndrome, colitis ulcerative, dermatomyositis, mixed connective tissue disease, myasthenia gravis, polymyalgia rheumatica, Reiter's syndrome, rheumatoid arthritis, scleroderma, sicca syndrome, Sjogren's syndrome, systemic lupus erythematosus, polymyalgia rheumatica
- Venous thromboembolism (VTE): Thrombosis, deep vein thrombosis, mesenteric vein thrombosis, cerebral venous thrombosis, cavernous sinus thrombosis, intracranial venous sinus thrombosis, pulmonary embolism, embolism venous, axillary vein thrombosis, venous thrombosis
- Guillain-Barré syndrome (GBS): Guillain-Barré syndrome, Miller Fisher syndrome, demyelinating polyneuropathy, chronic inflammatory demyelinating polyradiculoneuropathy
- Postural orthostatic tachycardia syndrome (POTS): Postural orthostatic tachycardia syndrome, dizziness postural, postural reflex impairment
- Complex regional pain syndrome (CRPS): Complex regional pain syndrome, mononeuropathy multiplex
- Primary ovarian insufficiency (POI): Premature menopause, ovarian disorder, amenorrhea

Appendix 9: Reported adverse event rates per 100 000 doses administered to females and males in Australia within funded primary and catch-up programs by specified surveillance periods

Year of vaccination		**2007–2009**	**2010–2012**	**2013–2014 Enhanced surveillance period**		**2015–2017**	
Program	Age group	Female Rate (n/DA)	Female Rate (n/DA)	Female Rate (n/DA)	Male Rate (n/DA)	Female Rate (n/DA)	Male Rate (n/DA)
Primary	12-13 years	37.0 (317/856,802)	42.7 (377/883,335)	93.1 (561/602,666)	83.8 (513/612,057)	49.7 (485/975,043)	44.8 (447/996,689)
Catch up	14-15 years	NA	NA	NA	39.1 (230/588,958)	NA	NA
	14-17 years	41.0 (605/1,475,484)	NA	NA	NA	NA	NA
	18-26 years	30.5 (543/1,777,470)	NA	NA	NA	NA	NA

DA: doses administered; NA: not applicable as not funded program (small denominators)

Appendix 10: Reported rate of syncope per 100 000 doses administered to females and males in Australia within funded primary and catch-up programs by specified surveillance periods

Year of vaccination		2007–2009	2010–012	2013–2014 Enhanced surveillance period		2015–2017	
Program	Age group	Female Rate (n/DA)	Female Rate (n/DA)	Female Rate (n/DA)	Male Rate (n/DA)	Female Rate (n/DA)	Male Rate (n/DA)
Primary	12-13 years	3.7 (32/856,802)	6.5 (57/883,335)	28.9 (174/602,666)	30.4 (186/612,057)	8.72 (85/975,043)	9.13 (91/996,689)
Catch up	14-15 years	NA	NA	NA	10.7 (63/588,958)	NA	NA
	14-17 years	3.5 (51/1,475,484)	NA	NA	NA	NA	NA
	18-26 years	2.2 (39/1,777,470)	NA	NA	NA	NA	NA

Appendix 11. Unsolicited adverse events reported by SmartVax respondents in free text, classified to MedDRA preferred terms

Unsolicited adverse event (MedDRA Preferred Term)	Number of reports	Percent of reports
Nausea	87	19.4%
Dizziness	53	11.8%
Lymphoedema	23	5.1%
Oropharyngeal pain	16	3.6%
Abdominal pain upper	15	3.3%
Pain in extremity	13	2.9%
Lymph node pain	11	2.5%
Pain in extremity	11	2.5%
Lymph node pain	9	2.0%
Malaise	9	2.0%
Injection site bruising	8	1.8%
Nasopharyngitis	8	1.8%
Pain (body)	8	1.8%
Cough	7	1.6%
Rhinorrhoea	7	1.6%
Influenza like illness	6	1.3%
Myalgia	6	1.3%
Neck pain	5	1.1%
Pallor	5	1.1%
Pyrexia	5	1.1%
Syncope	5	1.1%
Fatigue	4	0.9%
Vision blurred	4	0.9%
Abdominal pain	3	0.7%
Arthralgia	3	0.7%
Headache	3	0.7%
Hypoaesthesia	3	0.7%
Injection site haemorrhage	3	0.7%

Injection site movement impairment	3	0.7%
Pain (unspecified)	3	0.7%
Pruritus	3	0.7%
Blank	3	0.7%
Asthenia	2	0.4%
Back pain	2	0.4%
Cold sweat	2	0.4%
Decreased appetite	2	0.4%
Disorganized speech	2	0.4%
Dysarthria	2	0.4%
Dysgeusia	2	0.4%
Eye pain	2	0.4%
Injection site mass	2	0.4%
Injection site nodule	2	0.4%
Injection site pain	2	0.4%
Injection site swelling	2	0.4%
Injection site warmth	2	0.4%
Lymphadenopathy	2	0.4%
Lymphadenopathy	2	0.4%
Musculoskeletal stiffness	2	0.4%
Skin warm	2	0.4%
Anxiety	1	0.2%
Blindness	1	0.2%
Blindness transient	1	0.2%
Body temperature decrease	1	0.2%
Superficial vein prominence	1	0.2%
Chest discomfort	1	0.2%
Contusion	1	0.2%
Crying	1	0.2%
Cyanosis	1	0.2%
Depressed mood	1	0.2%

Disorganised speech	1	0.2%
Dyspnoea	1	0.2%
Ear pain	1	0.2%
Epistaxis	1	0.2%
Erythema (face)	1	0.2%
Erythema (hands and feet)	1	0.2%
Erythema (unspecified)	1	0.2%
Eye swelling	1	0.2%
Feeling hot	1	0.2%
Flushing (cheeks and forehead)	1	0.2%
Flushing (cheeks)	1	0.2%
Hallucination	1	0.2%
Hyperhidrosis	1	0.2%
Hyperventilation	1	0.2%
Hypoaesthesia	1	0.2%
Influenza	1	0.2%
Injection site erythema	1	0.2%
Injection site haematoma	1	0.2%
Injection site hypoaesthesia	1	0.2%
Injection site induration	1	0.2%
Injection site joint swelling	1	0.2%
Injection site nerve damage	1	0.2%
Injection site papule	1	0.2%
Injection site pustule	1	0.2%
Lacrimation increased	1	0.2%
Lethargy	1	0.2%
Limb discomfort	1	0.2%
Limb discomfort	1	0.2%
Muscle contusion	1	0.2%
Muscle spasms	1	0.2%
Musculoskeletal pain	1	0.2%

Musculoskeletal stiffness	1	0.2%
Musculoskeletal stiffness (neck)	1	0.2%
Neuralgia	1	0.2%
Ocular hyperaemia	1	0.2%
Oral herpes	1	0.2%
Pain in jaw	1	0.2%
Pain injection site	1	0.2%
Pain of skin	1	0.2%
Paraesthesia (hands and face)	1	0.2%
Peripheral coldness	1	0.2%
Peripheral swelling	1	0.2%
Pruritus (face)	1	0.2%
Pruritus (hands and feet)	1	0.2%
Slow movement	1	0.2%
Swelling (hands and feet)	1	0.2%
Swelling (neck)	1	0.2%
Swelling (unspecified)	1	0.2%
Swelling face	1	0.2%
Tissue clot inside eye	1	0.2%
Tonsillitis	1	0.2%
Yellow skin	1	0.2%
Total	448	100.0%

Appendix 12. Unsolicited adverse events reported by Vaxtracker respondents in free text, classified to MedDRA preferred terms

Unsolicited adverse event (MedDRA Preferred Term)	Number of reports	Percent of reports
Nausea	13	22.8%
Dizziness	7	12.3%
Pain in extremity	4	7.0%
Abdominal pain upper	2	3.5%
Injection site pruritus	2	3.5%
Lymph node pain	2	3.5%
Angina pectoris	1	1.8%
Back pain	1	1.8%
Chest discomfort	1	1.8%
Chest pain	1	1.8%
Cough	1	1.8%
Dyspnoea	1	1.8%
Headache	1	1.8%
Hyperhidrosis	1	1.8%
Injection site bruising	1	1.8%
Injection site dryness	1	1.8%
Injection site erythema	1	1.8%
Injection site haemorrhage	1	1.8%
Lymphadenopathy	1	1.8%
Lymphoedema	1	1.8%
Nasopharyngitis	1	1.8%
Neck pain	1	1.8%
Nipple pain	1	1.8%
Oropharyngeal pain	1	1.8%
Pain (unspecified)	1	1.8%
Pharyngeal erythema	1	1.8%
Poor quality sleep	1	1.8%
Pyrexia	1	1.8%

Rhinorrhoea	1	1.8%
Sneezing	1	1.8%
Syncope	1	1.8%
Tiredness	1	1.8%
Urticaria	1	1.8%
Total	57	100.0%

Appendix 13. Incidence rates (per 100,000 males*/females†/population‡) for cancers pre-vaccine (2002–2007) to post-vaccine (2008–2016) introduction, by age group, Australia

Cancer by age group	Number (Rate per 100,000 population)		RR	95% CI
	2002–2007	2008–2016		
Anus‡				
<20 years	0 (0.00)	2 (0.00)	–	-
20–24 years	4 (0.05)	3 (0.02)	0.43	0.06 to 2.54
25–29 years	1 (0.01)	13 (0.09)	7.06	1.06 to 299.83
≥30 years	1700 (2.37)	3664 (2.98)	1.26	1.19 to 1.34
Total	1705 (1.41)	3682 (1.80)	1.27	1.20 to 1.35
Penis*				
<20 years	1 (0.01)	0 (0.00)	–	–
20–24 years	0 (0.00)	0 (0.00)	–	–
25–29 years	0 (0.00)	3 (0.04)	–	–
≥30 years	444 (1.27)	874 (1.46)	1.15	1.02 to 1.29
Total	445 (0.74)	877 (0.86)	1.16	1.03 to 1.30
Vagina†				
<20 years	5 (0.03)	8 (0.03)	0.99	0.29 to 3.85
20–24 years	2 (0.05)	0 (0.00)	0.00	0.00 to 3.07
25–29 years	2 (0.05)	7 (0.09)	1.91	0.36 to 18.82
≥30 years	403 (1.09)	669 (1.06)	0.97	0.86 to 1.10
Total	412 (0.68)	684 (0.66)	0.98	0.87 to 1.11
Vulva†				
<20 years	1 (0.01)	3 (0.01)	1.86	0.15 to 97.58
20–24 years	3 (0.07)	5 (0.07)	0.96	0.19 to 6.19
25–29 years	6 (0.15)	18 (0.24)	1.64	0.62 to 5.03
≥30 years	1495 (4.06)	3030 (4.82)	1.19	1.11 to 1.26
Total	1505 (2.48)	3056 (2.97)	1.20	1.13 to 1.28
Oropharynx‡				
<20 years	1 (0.00)	4 (0.01)	2.48	0.25 to 121.92
20–24 years	2 (0.02)	4 (0.03)	1.15	0.16 to 12.68
25–29 years	3 (0.04)	9 (0.06)	1.63	0.41 to 9.35
≥30 years	3123 (4.35)	7913 (6.44)	1.48	1.42 to 1.54
Total	3129 (2.59)	7930 (3.87)	1.49	1.43 to 1.56
Oral cavity‡				
<20 years	13 (0.04)	32 (0.06)	1.52	0.78 to 3.16

20–24 years	20 (0.24)	30 (0.21)	0.86	0.47 to 1.60
25–29 years	32 (0.39)	77 (0.51)	1.31	0.85 to 2.04
≥30 years	4795 (6.68)	9253 (7.53)	1.13	1.09 to 1.17
Total	4860 (4.03)	9392 (4.59)	1.14	1.10 to 1.18
Larynx‡				
<20 years	1 (0.00)	4 (0.01)	2.48	0.25 to 121.92
20–24 years	2 (0.02)	3 (0.02)	0.86	0.10 to 10.30
25–29 years	4 (0.05)	3 (0.02)	0.41	0.06 to 2.41
≥30 years	3511 (4.89)	5315 (4.33)	0.88	0.85 to 0.92
Total	3518 (2.92)	5325 (2.60)	0.89	0.85 to 0.93

Source: AIHW 2016 Australian Cancer Database; cancer diagnosis codes C21 (anus), C60 (penis), C52 (vagina), C51 (vulva), C01, C09–C10 (oropharynx), C02–C06 (oral cavity) and C32 (larynx).

Appendix 14. Hospitalisation rate (principal diagnosis) for specified cancers and premalignant lesions pre-vaccine (2002–2007) to post-vaccine (2008–2017) introduction by age group, Australia

Cancer by Age group	Hospitalisation rate per 100,000 population		RR	95% CI
	2002–2007	2008–2017		
Anus*				
<20 years	0.0	0.0	0.55	0.10–2.97
20–24 years	0.1	0.2	3.18	1.33–9.23
25–29 years	0.4	0.4	1.15	0.74–1.83
≥30 years	6.7	7.7	1.15	1.11–1.19
Total	4.0	4.7	1.16	1.12–1.20
Penis†				
<20 years	0.0	0.0	0.92	0.30–3.08
20–24 years	0.1	0.1	0.68	0.21–2.39
25–29 years	0.2	0.4	1.78	0.83–4.22
≥30 years	3.3	4.2	1.27	1.18–1.36
Total	2.0	2.5	1.28	1.19–1.37
Vagina‡				
<20 years	0.5	0.3	0.54	0.39–0.75
20–24 years	0.8	0.3	0.38	0.22–0.66
25–29 years	0.7	0.6	0.89	0.55–1.47
≥30 years	4.8	4.4	0.92	0.86–0.97
Total	3.1	2.8	0.90	0.85–0.95
Vulva‡				
<20 years	0.2	0.3	1.72	1.13–2.66
20–24 years	2.1	0.7	0.33	0.23–0.46
25–29 years	2.2	2.2	1.00	0.77–1.30
≥30 years	17.5	19.8	1.13	1.09–1.16
Total	11.0	12.4	1.13	1.10–1.16
Oropharynx*				
<20 years	0.0	0.1	2.55	1.27–5.66
20–24 years	0.1	0.1	0.51	0.18–1.46
25–29 years	0.2	0.1	0.46	0.23–0.90
≥30 years	12.6	15.2	1.21	1.18–1.24
Total	7.5	9.1	1.22	1.19–1.25
Oral cavity‡				

<20 years	0.3	0.3	1.09	0.84–1.42
20–24 years	1.0	0.4	0.44	0.32–0.62
25–29 years	0.8	0.8	0.94	0.69–1.28
≥30 years	14.4	14.3	0.99	0.97–1.02
Total	8.8	8.8	1.00	0.98–1.02
Larynx*				
<20 years	0.0	0.1	4.15	1.46–16.23
20–24 years	0.1	0.0	0.21	0.06–0.65
25–29 years	0.1	0.1	1.45	0.55–4.47
≥30 years	12.2	9.9	0.81	0.79–0.83
Total	7.3	6.0	0.82	0.79–0.84

Source: AIHW hospitalisation datasets; cancer diagnosis codes C21.x and D01.3 (anus), C60 and D07.4 (penis), C52 and D07.2 (vagina), C51 and D07.1 (vulva), C01, C09–C10 (oropharynx), C02–C06 (oral cavity) and C32 (larynx). * per 100,000 population, † per 100,000 males, ‡ per 100,000 females.

Appendix 15: Average annual hospitalisation rates per 100,000 population: NSW, by age and Indigenous status

Average annual hospitalisation rate	<10 years	10–19 years	20–29 years	30–39 years	≥40 years
2003-2007					
Non-Aboriginal male	0.2	2.7	31.5	22.3	11.6
Non-Aboriginal female	0.8	27.8	62.9	22.4	8.2
Aboriginal male	0	1.0	7.1	13.2	1.7
Aboriginal female	0	25.5	27.9	13.1	7.3
2008-2013					
Non-Aboriginal male	0.3	2.2	19.9	15.0	11.8
Non-Aboriginal female	0.5	4.9	23.5	19.3	8.7
Aboriginal male	0.5	0.6	15.6	7.3	10.3
Aboriginal female	0	9.4	18.1	16.1	6.9
2014-2017					
Non-Aboriginal male	0.0	1.5	13.5	15.0	11.3
Non-Aboriginal female	0.2	1.6	7.1	12.6	8.5
Aboriginal male	0	1.7	10.3	13.1	9.7
Aboriginal female	0.8	1.8	5.9	25.7	19.4

Appendix 16: Average annual hospitalisation rates per 100,000 population: Victoria, by age and Indigenous status

Average annual hospitalisation rate	<10 years	10-19 years	20-29 years	30-39 years	≥40 years
2003-2007					
Non-Aboriginal male	0.7	3.1	34.1	24.8	11.2
Non-Aboriginal female	0.5	29.5	86.1	32.5	11.3
Aboriginal male	0	7.0	11.3	18.5	12.0
Aboriginal female	13.6	30.2	34.4	24.4	0
2008-2013					
Non-Aboriginal male	0.2	2.3	21.9	20.2	12.0
Non-Aboriginal female	0.4	5.1	28.4	23.9	9.5
Aboriginal male	0	5.5	3.8	5.3	19.0
Aboriginal female	5.4	11.6	19.7	31.3	14.8
2014-2017					
Non-Aboriginal male	0.2	1.2	15.1	15.1	13.1
Non-Aboriginal female	0.5	1.2	7.7	12.5	10.8
Aboriginal male	0	0.0	4.9	23.7	48.5
Aboriginal female	0.0	0.0	20.2	7.8	22.5

Appendix 17: Average annual hospitalisation rates per 100,000 population: Queensland, by age and Indigenous status

Average annual hospitalisation rate	<10 years	10–19 years	20–29 years	30–39 years	≥40 years
2003-2007					
Non-Aboriginal male	0.1	2.6	19.4	15.2	7.5
Non-Aboriginal female	1.2	34.7	64.6	25.7	8.4
Aboriginal male	0	0	6.5	11.8	0
Aboriginal female	1.7	34.3	40.3	7.8	7.4
2008-2013					
Non-Aboriginal male	0.4	2.4	14.6	12.0	10.1
Non-Aboriginal female	0.4	6.4	22.5	18.9	10.0
Aboriginal male	0.6	1.5	3.4	5.6	9.2
Aboriginal female	0.6	6.3	15.6	11.8	8.9
2014-2017					
Non-Aboriginal male	0.2	1.6	12.0	11.9	12.5
Non-Aboriginal female	0.4	1.7	7.9	15.2	11.2
Aboriginal male	0	0	8.2	16.3	11.6
Aboriginal female	0	3.2	4.2	15.7	14.6

Appendix 18: Average annual hospitalisation rates per 100,000 population: South Australia, by age and Indigenous status

Average annual hospitalisation rate	<10 years	10-19 years	20-29 years	30-39 years	≥40 years
2003–2007					
Non-Aboriginal male	0.2	2.6	26.6	15.8	9.0
Non-Aboriginal female	0.5	30.6	78.7	28.4	9.7
Aboriginal male	0	0	16.4	8.7	16.9
Aboriginal female	0	78.0	76.2	15.3	10.4
2008–2013					
Non-Aboriginal male	0.3	3.3	13.0	5.1	8.4
Non-Aboriginal female	0.2	7.9	27.8	9.1	10.2
Aboriginal male	0	0	5.4	7.7	0
Aboriginal female	0	0	39.0	47.1	10.1
2014–2017					
Non-Aboriginal male	0	1.3	7.9	11.0	9.5
Non-Aboriginal female	0.3	0.8	9.3	13.8	7.8
Aboriginal male	0	0	6.9	31.8	14.9
Aboriginal female	0	11.3	14.0	30.5	26.1

Appendix 19: Average annual hospitalisation rates per 100,000 population: Northern Territory, by age and Indigenous status

Average annual hospitalisation rate	<10 years	10-19 years	20-29 years	30-39 years	≥40 years
2003-2007					
Non-Aboriginal male	2	4	30	22	14.6
Non-Aboriginal female	0	7	61.2	30.5	10.9
Aboriginal male	2.8	2.9	0.0	12.5	0
Aboriginal female	0	30.9	11.3	28.3	19.6
2008-2013					
Non-Aboriginal male	0	0	20	9	13.0
Non-Aboriginal female	0	2	22.5	16.2	12.8
Aboriginal male	0	4.7	7.6	3.3	6.5
Aboriginal female	2.4	2.6	11.0	43.3	49.7
2014-2017					
Non-Aboriginal male	0	3	8	11	11.1
Non-Aboriginal female	0	3	9.0	8.3	5.3
Aboriginal male	0	3.4	10.4	4.5	2.7
Aboriginal female	0	3.8	11.4	18.6	4.7

Appendix 20: Average annual hospitalisation rates per 100,000 population: Tasmania, by age and Indigenous status

Average annual hospitalisation rate	<10 years	10–19 years	20–29 years	30–39 years	≥40 years
2003–2007					
Non-Aboriginal male	0	3.0	32.8	12.2	7.5
Non-Aboriginal female	2.2	55.1	92.3	22.0	7.6
Aboriginal male	0	0	68.6	12.8	13.1
Aboriginal female	0	30.4	59.1	11.8	13.6
2008–2013					
Non-Aboriginal male	0.6	2.6	16.9	16.5	14.1
Non-Aboriginal female	0	11.7	49.0	30.1	9.1
Aboriginal male	0	0	0	22.4	4.7
Aboriginal female	0	13.8	26.7	31.5	31.8
2014–2017					
Non-Aboriginal male	0	1.7	10.1	21.8	8.3
Non-Aboriginal female	0	4.5	15.1	20.2	13.3
Aboriginal male	0	0	0	17.6	6.4
Aboriginal female	0	8.9	11.6	29.6	11.8

Appendix 21: Average annual hospitalisation rates per 100,000 population: ACT, by age and Indigenous status

Average annual hospitalisation rate	<10 years	10–19 years	20–29 years	30–39 years	≥40 years
2003–2007					
Non-Aboriginal male	0	2.6	16.5	9.5	7.7
Non-Aboriginal female	0	20.0	40.4	21.9	5.7
Aboriginal male	0	0	40.4	0.0	0.0
Aboriginal female	0	25.9	38.0	0.0	0
2008-2013					
Non-Aboriginal male	0	0.0	13.9	7.2	7.4
Non-Aboriginal female	0	0.8	7.5	12.0	4.7
Aboriginal male	0	0	24.7	0	0
Aboriginal female	0	0	0	116.7	0
2014-2017					
Non-Aboriginal male	0	0	11.4	3.2	6.8
Non-Aboriginal female	0	0	3.8	9.5	6.1
Aboriginal male	0	0	62.8	58.5	28.4
Aboriginal female	0	0	35.0	0	0

Appendix 22. Average annual hospitalisation rates per 100,000 population: Western Australia, by age and Indigenous status

Average annual hospitalisation rate	<10 years	10-19 years	20-29 years	30-39 years	≥40 years
2003-2007					
Non-Aboriginal male	1.8	7.5	87.5	63.1	27.9
Non-Aboriginal female	1.4	72.8	228.0	86.9	0
Aboriginal male	3.9	6.4	17.2	13.5	7.4
Aboriginal female	4.0	82.6	60.8	22.9	4.3
2008-2013					
Non-Aboriginal male	0.6	5.4	51.8	47.8	29.0
Non-Aboriginal female	1.0	12.1	70.0	59.5	0
Aboriginal male	0	1.7	14.0	8.3	3.2
Aboriginal female	0	10.8	30.4	16.7	17.1
2014-2017					
Non-Aboriginal male	0.5	3.0	37.8	35.4	31.9
Non-Aboriginal female	1.3	3.0	19.7	30.5	0
Aboriginal male	0	0	2.7	11.6	8.3
Aboriginal female	0	7.5	14.7	7.9	5.5

References

1. Brotherton JML, Bloem PN. Population-based HPV vaccination programmes are safe and effective: 2017 update and the impetus for achieving better global coverage. B*est Practice & Research: Clinical Obstetrics & Gynaecoloy*. 2018; 47:42-58.
2. Bouvard V, Baan R, Straif K, Grosse Y, Secretan B, El Ghissassi F, et al. A review of human carcinogens--Part B: biological agents. *The Lancet Oncology*. 2009; 10:321-2.
3. Garland SM, Steben M, Sings HL, James M, Lu S, Railkar R, et al. Natural history of genital warts: analysis of the placebo arm of 2 randomized phase III trials of a quadrivalent human papillomavirus (types 6, 11, 16, and 18) vaccine. *Journal of Infectious Diseases*. 2009; 199:805-14.
4. Vu M, Yu J, Awolude OA, Chuang L. Cervical cancer worldwide. *Current Problems in Cancer*. 2018; 42:457-65.
5. Serrano B, Brotons M, Bosch FX, Bruni L. Epidemiology and burden of HPV-related disease. *Best Practice & Research: Clinical Obstetrics & Gynaecoloy*. 2018; 47:14-26.
6. World Health Organization. Cervical cancer. [4 September 2019]; Available from: https://www.who.int/cancer/cervical-cancer.
7. World Health Organization. Draft: Global strategy towards the elimination of cervical cancer as a public health problem. [4 September 2019]; Available from: https://www.who.int/docs/default-source/documents/cervical-cancer-elimination-draft-strategy.pdf?sfvrsn=380979d6_4.
8. Hall MT, Simms KT, Lew JB, Smith MA, Brotherton JM, Saville M, et al. The projected timeframe until cervical cancer elimination in Australia: a modelling study. T*he Lancet Public Health*. 2019; 4:e19-e27.
9. National Centre for Immunisation Research and Surveillance (NCIRS). Evaluation of the National HPV Program. 2014 [09 Jan 2020]; Available from: https://beta.health.gov.au/news-and-events/news/evaluation-of-the-national-hpv-program.
10. Patel C, Brotherton JM, Pillsbury A, Jayasinghe S, Donovan B, Macartney K, et al. The impact of 10 years of human papillomavirus (HPV) vaccination in Australia: what additional disease burden will a nonavalent vaccine prevent? *Eurosurveillance*. 2018; 23:1560-7917.
11. Australian Government Department of Health. Preventing human papillomavirus (HPV) cancers and diseases by vaccination. [updated 14/2/201331 May 2019]; Available from: https://beta.health.gov.au/news-and-events/news/preventing-human-papillomavirus-hpv-cancers-and-diseases-by-vaccination.
12. Australian Technical Advisory Group on Immunisation (ATAGI). Australian Immunisation Handbook, Australian Government Department of Health, Canberra, 2018. [31 May 2019]; Available from: https://immunisationhandbook.health.gov.au/.
13. Peyton DJ, Scicchitano M. Devil is in the details: Using logic models to investigate program process. *Evaluation and Program Planning*. 2017; 65:156-62.
14. HPV Surveillance Working Group, Communicable Diseases Network Australia (CDNA). Human Papillomavirus (HPV) Surveillance Plan – an integrated approach to monitoring the impact of HPV vaccine in Australia. . 2013 [27 April 2020]; Available from: https://www1.health.gov.au/internet/main/publishing.nsf/content/e5b543ce209e55c3ca257f48001d65ef/$file/hpv-surveillance-plan.pdf.
15. Barbaro B, Brotherton JM. Measuring HPV vaccination coverage in Australia: comparing two alternative population-based denominators. *Australian and New Zealand Journal of Public Health*. 2015; 39:326-30.
16. President's Cancer Panel, United States. HPV vaccination for cancer prevention: progress, opportunities, and a renewed call to action. [4 September 2019]; Available from: https://prescancerpanel.cancer.gov/report/hpvupdate/.

17. Australian Governement Department of Health. Fourth National Sexually Transmissible Infections Strategy 2018-2022. 2018 [24 Dec 2019]; Available from: https://www1.health.gov.au/internet/main/publishing.nsf/Content/ohp-bbvs-1/$File/STI-Fourth-Nat-Strategy-2018-22.pdf.
18. Australian Governement Department of Health. Fifth National Aboriginal and Torres Strait Islander Blood Borne Viruses and Sexually Transmissible Infections Strategy 2018 [24 Dec 2019]; Available from: https://www1.health.gov.au/internet/main/publishing.nsf/Content/ohp-bbvs-1/$File/ATSI-Fifth-Nat-Strategy-2018-22.pdf.
19. The Kirby Institute. National blood-borne viruses and sexually transmissible infections surveillance and monitoring report, 2017. 2017 [24 Dec 2019]; Available from: https://kirby.unsw.edu.au/sites/default/files/kirby/report/National-BBV%26STI-Surveillance%26Monitoring-Report-2017.pdf.
20. Cancer Australia. National Framework for Gynaecological Cancer Control. 2016 [24 Jan 2020]; Available from: https://canceraustralia.gov.au/sites/default/files/publications/national-framework-gynaecological-cancer-control/pdf/2016_gcnf_gynae_framework.pdf.
21. Victorian Government Health and Human Services. Victorian Cancer Plan 2016-2020. 2016 [14 Jan 2020]; Available from: https://www2.health.vic.gov.au/about/health-strategies/cancer-care/victorian-cancer-plan.
22. Tasmanian Government Department of Health and Human Services. Cancer Framework and Strategic Cancer Plan 2010-2013. 2010 [24 Dec 2019]; Available from: https://www.dhhs.tas.gov.au/__data/assets/pdf_file/0006/74229/UPDATED_2010-07-27_Tasmanias_Cancer_Framework_and_Strategic_Plan_2010-20131.pdf.
23. South Australia Health. Aboriginal Cancer Control Plan 2016-2021. 2016 [24 Dec 2019]; Available from: https://www.sahealth.sa.gov.au/wps/wcm/connect/f09df30045a67ceb8f8baf9f9859b7b1/SA+Aboriginal+Cancer+Control+Plan+2016_21_Final.pdf?MOD=AJPERES&CACHEID=ROOTWORKSPACE-f09df30045a67ceb8f8baf9f9859b7b1-mMz955M.
24. ACT Government Health. Hepatitis B, Hepatitis C, HIV, and Sexually Transmissible Infections. ACT Statement of Priorities 2016-2020. 2016 [24 Dec 2019]; Available from: https://www.health.act.gov.au/sites/default/files/2018-09/Hepatitis%20B,%20Hepatitis%20C,%20HIV%20and%20Sexually%20Transmissible%20Infections%20ACT%20Statement%20of%20Priorities%202016-2020.pdf.
25. National HPV Vaccination Program Register. Coverage Data. [10 Jan 2020]; Available from: http://www.hpvregister.org.au/research/coverage-data.
26. Queensland Health. Queensland Sexual Health Strategy 2016-2021. 2016 [24 Dec 2019]; Available from: https://www.health.qld.gov.au/__data/assets/pdf_file/0024/601935/qh-sexual-health-strategy.pdf.
27. New South Wales Health. NSW STI Strategy 2016-2020. 2016 [24 Dec 2019]; Available from: https://www1.health.nsw.gov.au/pds/ActivePDSDocuments/IB2016_005.pdf.
28. Northern Territory Government Department of Health. Northern Territory Sexually Transmissible Infections and Blood Borne Viruses Strategic and Operational Plan 2019-2023. 2019.
29. Government of South Australia Department for Health and Ageing. South Australian Sexually Transmissible Infection Implementation Plan 2016-2018. 2016 [24 Dec 2019]; Available from: https://www.sahealth.sa.gov.au/wps/wcm/connect/535381004c974616b366b3a496684d9f/STI_ImpPlan20162018-CDCB-20161103.pdf?MOD=AJPERES&CACHEID=ROOTWORKSPACE-535381004c974616b366b3a496684d9f-mN5-vMw.
30. Government of Western Australia Department of Health. Western Australian Sexually Transmissible Infections (STI) Strategy 2019-2023. 2019 [24 Dec 2019]; Available from: https://ww2.health.wa.gov.au/~/media/Files/Corporate/general%20documents/Sexual%20Health/PDF/Strategy/2019-2023/STI-strategy.pdf.

31. Government of Western Australia Department of Health. Western Australian Aboriginal Sexual Health and Blood-borne Virus Strategy 2019-2023. 2019 [24 Dec 2019]; Available from: https://ww2.health.wa.gov.au/~/media/Files/Corporate/general%20documents/Sexual%20Health/PDF/Strategy/2019-2023/Aboriginal-STI-BBV-strategy.pdf.
32. Hull B, Hendry A, Dey A, McIntyre P, Macartney K, Beard F. Annual Immunisation Coverage Report 2018. 2019 [13 Dec 2019]; Available from: http://ncirs.org.au/sites/default/files/2019-11/NCIRS%20Annual%20Immunisation%20Coverage%20Report%202018.pdf.
33. Australian Government Department of Health. Historical data from the National HPV Vaccination Program Register. 2020 [24 Jan 2020]; Available from: https://www.health.gov.au/resources/collections/historical-data-from-the-national-hpv-vaccination-program-register.
34. Hull B, Hendry A, Dey A, Brotherton J, Macartney K, Beard F. Annual Immunisation Coverage Report 2017. *Communicable Diseases Intelligence*. (2018). 2019; 43.
35. Hull B, Hendry A, Dey A, Beard F, Brotherton J, McIntyre P. Annual Immunisation Coverage Report 2016. *Communicable Diseases Intelligence*. (2018). 2019; 43.
36. Hull B, Hendry A, Dey A, Beard F, Brotherton J, McIntyre P. Immunisation coverage annual report, 2015. *Communicable Diseases Intelligence*. (2018). 2019.
37. Hull BP, Hendry AJ, Dey A, Beard FH, Brotherton JM, McIntyre PB. Immunisation coverage annual report, 2014. *Communicable Diseases Intelligence Quarterly Report*. 2017; 41:E68-E90.
38. Hull BP, Dey A, Beard FH, Menzies RI, Brotherton JM, McIntyre PB. Immunisation coverage annual report, 2013. *Communicable Diseases Intelligence Quarterly Report*. 2016; 40:E146-69.
39. Hull BP, Dey A, Menzies RI, Brotherton JM, McIntyre PB. Immunisation coverage, 2012. *Communicable Diseases Intelligence Quarterly Report*. 2014; 38:E208-31.
40. Hull B, Dey A, Menzies R, McIntyre P. Annual immunisation coverage report, 2010. *Communicable Diseases Intelligence Quarterly Report*. 2013; 37:E21-39.
41. Hull BP, Dey A, Menzies RI, Brotherton JM, McIntyre PB. Immunisation coverage annual report, 2011. *Communicable Diseases Intelligence Quarterly Report*. 2013; 37:E291-312.
42. Brotherton JM, Winch KL, Bicknell L, Chappell G, Saville M. HPV vaccine coverage is increasing in Australia. *Medical Journal of Australia*. 2017; 206:262.
43. Brotherton JM, Winch KL, Chappell G, Banks C, Meijer D, Ennis S, et al. HPV vaccination coverage and course completion rates for Indigenous Australian adolescents, 2015. *Medical Journal of Australia*. 2019; 211:31-6.
44. Wnukowski-Mtonga P, Jayasingh S, Chiu C, Macartney K, Brotherton J, Donovan B, et al. Scientific evidence supporting recommendations on the use of the 9-valent HPV vaccine in a 2-dose vaccine schedule in Australia. *Communicable Diseases Intelligence* 2020;44. https://doiorg/1033321/cdi20204433.
45. Sonawane K, Nyitray AG, Nemutlu GS, Swartz MD, Chhatwal J, Deshmukh AA. Prevalence of Human Papillomavirus Infection by Number of Vaccine Doses Among US Women. *JAMA Network Open*. 2019; 2:e1918571.
46. Markowitz LE, Naleway AL, Klein NP, Lewis RM, Crane B, Querec TD, et al. Human Papillomavirus Vaccine Effectiveness Against HPV Infection: Evaluation of One, Two, and Three Doses. *Journal of Infectious Diseases*. 2020; 221:910-8.
47. Batmunkh T, Dalmau MT, Munkhsaikhan ME, Khorolsuren T, Namjil N, Surenjav U, et al. A single dose of quadrivalent human papillomavirus (HPV) vaccine is immunogenic and reduces HPV detection rates in young women in Mongolia, six years after vaccination. *Vaccine*. 2020; 38:4316-24.
48. Sankaranarayanan R, Joshi S, Muwonge R, Esmy PO, Basu P, Prabhu P, et al. Can a single dose of human papillomavirus (HPV) vaccine prevent cervical cancer? Early findings from an Indian study. *Vaccine*. 2018; 36:4783-91.

49. Toh ZQ, Russell FM, Reyburn R, Fong J, Tuivaga E, Ratu T, et al. Sustained Antibody Responses 6 Years Following 1, 2, or 3 Doses of Quadrivalent Human Papillomavirus (HPV) Vaccine in Adolescent Fijian Girls, and Subsequent Responses to a Single Dose of Bivalent HPV Vaccine: A Prospective Cohort Study. *Clinical Infectious Diseases*. 2017; 64:852-9.
50. Tabrizi SN, Brotherton JM, Kaldor JM, Skinner SR, Liu B, Bateson D, et al. Assessment of herd immunity and cross-protection after a human papillomavirus vaccination programme in Australia: a repeat cross-sectional study. *The Lancet Infectious Diseases*. 2014; 14:958-66.
51. Osborne SL, Tabrizi SN, Brotherton JM, Cornall AM, Wark JD, Wrede CD, et al. Assessing genital human papillomavirus genoprevalence in young Australian women following the introduction of a national vaccination program. *Vaccine*. 2015; 33:201-8.
52. Garland SM, Cornall AM, Brotherton JML, Wark JD, Malloy MJ, Tabrizi SN. Final analysis of a study assessing genital human papillomavirus genoprevalence in young Australian women, following eight years of a national vaccination program. *Vaccine*. 2018; 36:3221-30.
53. Brotherton JML, Malloy M, Budd AC, Saville M, Drennan KT, Gertig DM. Effectiveness of less than three doses of quadrivalent human papillomavirus vaccine against cervical intraepithelial neoplasia when administered using a standard dose spacing schedule: Observational cohort of young women in Australia. *Papillomavirus Research*. 2015; 1:59-73.
54. Brotherton JM, Budd A, Rompotis C, Bartlett N, Malloy MJ, Andersen RL, et al. Is one dose of human papillomavirus vaccine as effective as three?: A national cohort analysis. *Papillomavirus Research* (Amsterdam, Netherlands). 2019; 8:100177.
55. Canfell K, Egger S, Velentzis LS, Brown JD, O'Connell DL, Banks E, et al. Factors related to vaccine uptake by young adult women in the catch-up phase of the National HPV Vaccination Program in Australia: Results from an observational study. *Vaccine*. 2015; 33:2387-94.
56. Gunasekaran B, Jayasinghe Y, Brotherton JM, Fenner Y, Moore EE, Wark JD, et al. Asking about human papillomavirus vaccination and the usefulness of registry validation: a study of young women recruited using Facebook. *Vaccine*. 2015; 33:826-31.
57. Tung IL, Machalek DA, Garland SM. Attitudes, Knowledge and Factors Associated with Human Papillomavirus (HPV) Vaccine Uptake in Adolescent Girls and Young Women in Victoria, Australia. *PLoS ONE*. 2016; 11:e0161846.
58. Brotherton JML, Liu B, Donovan B, Kaldor JM, Saville M. Human papillomavirus (HPV) vaccination coverage in young Australian women is higher than previously estimated: independent estimates from a nationally representative mobile phone survey. *Vaccine*. 2014; 32:592-7.
59. Australian Government Department of Health. National HPV vaccination coverage by socio-economic status [27 April 2020]; Available from: https://www.health.gov.au/resources/publications/national-hpv-vaccination-coverage-by-socio-economic-status.
60. Brotherton JM, Piers LS, Vaughan L. Estimating human papillomavirus vaccination coverage among young women in Victoria and reasons for non-vaccination. *Sex Health*. 2016; 13:190-2.
61. Burns S, Selvey L. Increasing HPV vaccinations in WA schools. [13 Dec 2019]; Available from: https://az659834.vo.msecnd.net/eventsairaueprod/production-ashm-public/8a6eb4ca1fe940069751e3fdb4515a8b.
62. Nickel B, Dodd RH, Turner RM, Waller J, Marlow L, Zimet G, et al. Factors associated with the human papillomavirus (HPV) vaccination across three countries following vaccination introduction. *Preventive Medicine Reports*. 2017; 8:169-76.
63. Marshall HS, Collins J, Sullivan T, Tooher R, O'Keefe M, Skinner SR, et al. Parental and societal support for adolescent immunization through school based immunization programs. *Vaccine*. 2013; 31:3059-64.
64. Staples C, Butler M, Nguyen J, Durrheim DN, Cashman P, Brotherton JML. Opportunities to increase rates of human papillomavirus vaccination in the New South Wales school program through enhanced catch-up. *Sex Health*. 2016; 13:536-9.

65. O'Neill J, Newall F, Antolovich G, Lima S, Danchin M. The uptake of adolescent vaccinations through the School Immunisation Program in specialist schools in Victoria, Australia. *Vaccine*. 2019; 37:272-9.
66. Mak DB, Bulsara MK, Wrate MJ, Carcione D, Chantry M, Efller PV. Factors determining vaccine uptake in Western Australian adolescents. J Paediatr Child Health. 2013; 49:895-900.
67. Selvey LA, Roux F, Burns S. Potential process improvements to increase coverage of human papillomavirus vaccine in schools - A focus on schools with low vaccine uptake. *Vaccine*. 2020; 38:2971-7.
68. Davies C, Skinner SR, Stoney T, Marshall HS, Collins J, Jones J, et al. 'Is it like one of those infectious kind of things?' The importance of educating young people about HPV and HPV vaccination at school. *Sex Education*. 2017; 17:256-75.
69. Tull F, Borg K, Knott C, Beasley M, Halliday J, Faulkner N, et al. Short Message Service Reminders to Parents for Increasing Adolescent Human Papillomavirus Vaccination Rates in a Secondary School Vaccine Program: A Randomized Control Trial. *Journal of Adolescent Health*. 2019; 65:116-23.
70. Brotherton JM, Batchelor M, Winch K. Utility of reports and routine correspondence from the National HPV Vaccination Program Register. *Medical Journal of Australia*. 2013; 199:463.
71. McGrath L, Fairley CK, Cleere EF, Bradshaw CS, Chen MY, Chow EPF. Human papillomavirus vaccine uptake among young gay and bisexual men who have sex with men with a time-limited targeted vaccination programme through sexual health clinics in Melbourne in 2017. *Sexually Transmitted Infections*. 2019; 95:181-6.
72. Shapiro GK, Surian D, Dunn AG, Perry R, Kelaher M. Comparing human papillomavirus vaccine concerns on Twitter: a cross-sectional study of users in Australia, Canada and the UK. *BMJ Open*. 2017; 7:e016869.
73. Dyda A, Shah Z, Surian D, Martin P, Coiera E, Dey A, et al. HPV vaccine coverage in Australia and associations with HPV vaccine information exposure among Australian Twitter users. *Human Vaccines and Immunotherapeutics*. 2019; 15:1488-95.
74. Young EJ, Tabrizi SN, Brotherton JM, Wark JD, Pyman J, Saville M, et al. Measuring effectiveness of the cervical cancer vaccine in an Australian setting (the VACCINE study). *BMC Cancer*. 2013; 13:296.
75. Mahajan D, Dey A, Cook J, Harvey B, Menzies RI, Macartney KM. Surveillance of adverse events following immunisation in Australia, 2012. *Communicable Diseases Intelligence Quarterly Report*. 2014; 38:E232-46.
76. Mahajan D, Dey A, Cook J, Harvey B, Menzies R, Macartney K. Surveillance of adverse events following immunisation in Australia annual report, 2013. Communicable diseases intelligence quarterly report. 2015; 39:E369-86.
77. Dey A, Wang H, Quinn HE, Hill R, Macartney KK. Surveillance of adverse events following immunisation in Australia annual report, 2014. *Communicable Diseases Intelligence Quarterly Report*. 2016; 40:E377-e90.
78. Dey A, Wang H, Quinn H, Cook J, Macartney K. Surveillance of adverse events following immunisation in Australia, 2015. *Communicable Diseases Intelligence Quarterly Report*. 2017; 41:E264-e78.
79. Dey A, Wang H, Quinn H, Cook J, Macartney K. Surveillance of adverse events following immunisation in Australia annual report, 2016. *Communicable Diseases Intelligence* (2018). 2018; 42.
80. Dey A, Wang H, Quinn H, Hiam R, Wood N, Beard F, et al. Surveillance of adverse events following immunisation in Australia annual report, 2017. *Communicable Diseases Intelligence* (2018). 2019; 43.
81. Therapautic Goods Administration. Enhanced school-based surveillance of acute adverse events following immunisation with human papillomavirus vaccine in males and females, 2013. Canberra 2015.

82. Clothier HJ, Lee KJ, Sundararajan V, Buttery JP, Crawford NW. Human papillomavirus vaccine in boys: background rates of potential adverse events. *Medical Journal of Australia*. 2013; 198:554-8.
83. Cheng DR, Perrett KP, Choo S, Danchin M, Buttery JP, Crawford NW. Pediatric anaphylactic adverse events following immunization in Victoria, Australia from 2007 to 2013. *Vaccine*. 2015; 33:1602-7.
84. Clothier HJ, Crawford NW, Russell M, Kelly H, Buttery JP. Evaluation of 'SAEFVIC', A Pharmacovigilance Surveillance Scheme for the Spontaneous Reporting of Adverse Events Following Immunisation in Victoria, Australia. *Drug Safety*. 2017; 40:483-95.
85. Crawford NW, Hodgson K, Gold M, Buttery J, Wood N. Adverse events following HPV immunization in Australia: Establishment of a clinical network. *Human Vaccines & Immunotherapeutics*. 2016; 12:2662-5.
86. MacIntyre CR, Shaw P, Mackie FE, Boros C, Marshall H, Barnes M, et al. Immunogenicity and persistence of immunity of a quadrivalent Human Papillomavirus (HPV) vaccine in immunocompromised children. *Vaccine*. 2016; 34:4343-50.
87. MacIntyre CR, Shaw PJ, Mackie FE, Boros C, Marshall H, Seale H, et al. Long term follow up of persistence of immunity following quadrivalent Human Papillomavirus (HPV) vaccine in immunocompromised children. *Vaccine*. 2019; 37:5630-6.
88. Lee VY, Booy R, Skinner SR, Fong J, Edwards KM. The effect of exercise on local and systemic adverse reactions after vaccinations - Outcomes of two randomized controlled trials. *Vaccine*. 2018; 36:6995-7002.
89. Lee VY, Booy R, Skinner R, Edwards KM. The effect of exercise on vaccine-related pain, anxiety and fear during HPV vaccinations in adolescents. *Vaccine*. 2018; 36:3254-9.
90. AusVaxSafety. Adolescents vaccine safety surveillance. 2019 [updated 13 Dec 201909 Jan 2020]; Available from: http://www.ausvaxsafety.org.au/safety-data/adolescents.
91. Macartney KK, Chiu C, Georgousakis M, Brotherton J. Safety of human papillomavirus vaccines: a review. *Drug Safety*. 2013; 36:393-412.
92. Phillips A, Patel C, Pillsbury A, Brotherton J, Macartney K. Safety of Human Papillomavirus Vaccines: An Updated Review. *Drug Safety*. 2018; 41:329-46.
93. Australian Institute of Health and Welfare. The burden of vaccine preventable diseases in Australia. 2019 [23 Dec 2019]; Available from: https://www.aihw.gov.au/getmedia/49809836-8ead-4da5-81c4-352fa64df75b/aihw-phe-263.pdf.aspx?inline=true.
94. Chow EP, Danielewski JA, Fehler G, Tabrizi SN, Law MG, Bradshaw CS, et al. Human papillomavirus in young women with Chlamydia trachomatis infection 7 years after the Australian human papillomavirus vaccination programme: a cross-sectional study. *The Lancet Infectious Diseases*. 2015; 15:1314-23.
95. Machalek DA, Garland SM, Brotherton JML, Bateson D, McNamee K, Stewart M, et al. Very Low Prevalence of Vaccine Human Papillomavirus Types Among 18- to 35-Year Old Australian Women 9 Years Following Implementation of Vaccination. *Journal of Infectious Diseases*. 2018; 217:1590-600.
96. Brotherton JM, Hawkes D, Sultana F, Malloy MJ, Machalek DA, Smith MA, et al. Age-specific HPV prevalence among 116,052 women in Australia's renewed cervical screening program: A new tool for monitoring vaccine impact. *Vaccine*. 2019; 37:412-6.
97. Tabrizi SN, Brotherton JM, Stevens MP, Condon JR, McIntyre P, Smith D, et al. HPV genotype prevalence in Australian women undergoing routine cervical screening by cytology status prior to implementation of an HPV vaccination program. *Journal of Clinical Virology*. 2014; 60:250-6.
98. Velentzis LS, Sitas F, O'Connell DL, Darlington-Brown J, Egger S, Sinha R, et al. Human papillomavirus 16/18 seroprevalence in unvaccinated women over 30 years with normal cytology and with high grade cervical abnormalities in Australia: results from an observational study. *BMC Infectious Diseases*. 2014; 14:3861.

99. Machalek DA, Roberts JM, Garland SM, Thurloe J, Richards A, Chambers I, et al. Routine cervical screening by primary HPV testing: early findings in the renewed National Cervical Screening Program. *Medical Journal of Australia*. 2019; 211:113-9.
100. McGregor S, Saulo D, Brotherton JML, Liu B, Phillips S, Skinner SR, et al. Decline in prevalence of human papillomavirus infection following vaccination among Australian Indigenous women, a population at higher risk of cervical cancer: The VIP-I study. *Vaccine*. 2018; 36:4311-6.
101. Pillsbury AJ, Quinn HE, Evans TD, McIntyre PB, Brotherton JML. Population-Level Herd Protection of Males From a Female Human Papillomavirus Vaccination Program: Evidence from Australian Serosurveillance. *Clinical Infectious Diseases*. 2017; 65:827-32.
102. Chow EPF, Tabrizi SN, Fairley CK, Wigan R, Machalek DA, Regan DG, et al. Prevalence of human papillomavirus in teenage heterosexual males following the implementation of female and male school-based vaccination in Australia: 2014-2017. *Vaccine*. 2019; 37:6907-14.
103. Chow EPF, Machalek DA, Tabrizi SN, Danielewski JA, Fehler G, Bradshaw CS, et al. Quadrivalent vaccine-targeted human papillomavirus genotypes in heterosexual men after the Australian female human papillomavirus vaccination programme: a retrospective observational study. *The Lancet Infectious Diseases*. 2017; 17:68-77.
104. Machalek DA, Chow EP, Garland SM, Wigan R, Cornall AM, Fairley CK, et al. Human Papillomavirus Prevalence in Unvaccinated Heterosexual Men After a National Female Vaccination Program. *Journal of Infectious Diseases*. 2017; 215:202-8.
105. Chow EPF, Danielewski JA, Murray GL, Fehler G, Chen MY, Bradshaw CS, et al. Anal human papillomavirus infections in young unvaccinated men who have sex with men attending a sexual health clinic for HPV vaccination in Melbourne, Australia. *Vaccine*. 2019; 37:6271-5.
106. Poynten IM, Tabrizi SN, Jin F, Templeton DJ, Machalek DA, Cornall A, et al. Vaccine-preventable anal human papillomavirus in Australian gay and bisexual men. Papillomavirus research (Amsterdam, Netherlands). 2017; 3:80-4.
107. Australian Institute of Health and Welfare. Cervical screening in Australia 2019. 2019 [23 Dec 2019]; Available from: https://www.aihw.gov.au/getmedia/6a9ffb2c-0c3b-45a1-b7b5-0c259bde634c/aihw-can-124.pdf.aspx?inline=true.
108. Brotherton JM, Saville AM, May CL, Chappell G, Gertig DM. Human papillomavirus vaccination is changing the epidemiology of high-grade cervical lesions in Australia. *Cancer Causes Control*. 2015; 26:953-4.
109. Robertson G, Robson SJ. Excisional Treatment of Cervical Dysplasia in Australia 2004-2013: A Population-Based Study. *Journal of Oncology*. 2016; 2016:3056407.
110. Brotherton JM, Gertig DM, May C, Chappell G, Saville M. HPV vaccine impact in Australian women: ready for an HPV-based screening program. *Medical Journal of Australia*. 2016; 204:184-e1.
111. Gertig DM, Brotherton JM, Budd AC, Drennan K, Chappell G, Saville AM. Impact of a population-based HPV vaccination program on cervical abnormalities: a data linkage study. *BMC Medicine* 2013; 11:227.
112. Whop LJ, Baade P, Garvey G, Cunningham J, Brotherton JM, Lokuge K, et al. Cervical Abnormalities Are More Common among Indigenous than Other Australian Women: A Retrospective Record-Linkage Study, 2000-2011. *PLoS ONE*. 2016; 11:e0150473.
113. Australian Institute of Health and Welfare. Analysis of cervical cancer and abnormality outcomes in an era of cervical screening and HPV vaccination in Australia. 2019 [23 Dec 2019]; Available from: https://www.aihw.gov.au/getmedia/479cc5bb-d698-4ff7-92fa-4be451b1897b/aihw-can-129.pdf.aspx?inline=true.
114. Budd AC, Brotherton JM, Gertig DM, Chau T, Drennan KT, Saville M. Cervical screening rates for women vaccinated against human papillomavirus. *Medical Journal of Australia*. 2014; 201:279-82.
115. Crowe E, Pandeya N, Brotherton JML, Dobson AJ, Kisely S, Lambert SB, et al. Effectiveness of quadrivalent human papillomavirus vaccine for the prevention of cervical

abnormalities: case-control study nested within a population based screening programme in Australia. *British Medical Journal*. 2014; 348:g1458.
116. Brotherton JML, Tabrizi SN, Phillips S, Pyman J, Cornall AM, Lambie N, et al. Looking beyond human papillomavirus (HPV) genotype 16 and 18: Defining HPV genotype distribution in cervical cancers in Australia prior to vaccination. *International Journal of Cancer*. 2017; 141:1576-84.
117. Hall MT, Simms KT, Lew JB, Smith MA, Saville M, Canfell K. Projected future impact of HPV vaccination and primary HPV screening on cervical cancer rates from 2017-2035: Example from Australia. *PLoS ONE*. 2018; 13:e0185332.
118. Smith MA, Canfell K. Projected impact of HPV vaccination and primary HPV screening on cervical adenocarcinoma: Example from Australia. *Papillomavirus Research* (Amsterdam, Netherlands). 2017; 3:134-41.
119. Smith M, Canfell K. Impact of the Australian National Cervical Screening Program in women of different ages. *Medical Journal of Australia*. 2016; 205:359-64.
120. Ali H, McManus H, O'Connor CC, Callander D, Kong M, Graham S, et al. Human papillomavirus vaccination and genital warts in young Indigenous Australians: national sentinel surveillance data. *Medical Journal of Australia*. 2017; 206:204-9.
121. The Kirby Institute. Genital Warts Surveillance Network Report 2004-2015. 2016 [17 Dec 2019]; Available from: https://kirby.unsw.edu.au/sites/default/files/kirby/report/SHP_Genital-Warts-Surveillance-Network-Report-2004-2015.pdf.
122. The Kirby Institute. HIV, viral hepatitis and sexually transmissible infections in Australia: Annual surveillance report 2018. 2018 [24 Dec 2019]; Available from: https://kirby.unsw.edu.au/sites/default/files/kirby/report/KI_Annual-Surveillance-Report-2018.pdf.
123. The Kirby Institute. Blood-borne viral and sexually transmissible infections in Aboriginal and Torres Strait Islander people.: Annual surveillance report 2018. 2018 [24 Dec 2019]; Available from: https://kirby.unsw.edu.au/sites/default/files/kirby/report/KI_Aboriginal-Surveillance-Report-2018.pdf.
124. Smith MA, Liu B, McIntyre P, Menzies R, Dey A, Canfell K. Fall in genital warts diagnoses in the general and indigenous Australian population following implementation of a national human papillomavirus vaccination program: analysis of routinely collected national hospital data. *Journal of Infectious Diseases*. 2015; 211:91-9.
125. Smith MA, Liu B, McIntyre P, Menzies R, Dey A, Canfell K. Trends in genital warts by socioeconomic status after the introduction of the national HPV vaccination program in Australia: analysis of national hospital data. *BMC Infectious Diseases*. 2016; 16:52.
126. Chow EP, Read TR, Wigan R, Donovan B, Chen MY, Bradshaw CS, et al. Ongoing decline in genital warts among young heterosexuals 7 years after the Australian human papillomavirus (HPV) vaccination programme. *Sexually Transmitted Infections*. 2015; 91:214-9.
127. Harrison C, Britt H, Garland S, Conway L, Stein A, Pirotta M, et al. Decreased management of genital warts in young women in Australian general practice post introduction of national HPV vaccination program: results from a nationally representative cross-sectional general practice study. *PLoS ONE*. 2014; 9:e105967.
128. Liu B, Donovan B, Brotherton JM, Saville M, Kaldor JM. Genital warts and chlamydia in Australian women: comparison of national population-based surveys in 2001 and 2011. *Sexually Transmitted Infections*. 2014; 90:532-7.
129. Chow EPF, Fairley CK. Association between sexual mixing and genital warts in heterosexual men in Australia: the herd protection from the female human papillomavirus vaccination program. Sex Health. 2016; 13:489-90.
130. Drolet M, Laprise JF, Brotherton JML, Donovan B, Fairley CK, Ali H, et al. The Impact of Human Papillomavirus Catch-Up Vaccination in Australia: Implications for Introduction of Multiple Age Cohort Vaccination and Postvaccination Data Interpretation. *Journal of Infectious Diseases*. 2017; 216:1205-9.

131. Korostil IA, Ali H, Guy RJ, Donovan B, Law MG, Regan DG. Near elimination of genital warts in Australia predicted with extension of human papillomavirus vaccination to males. *Sexually Transmitted Diseases*. 2013; 40:833-5.
132. Novakovic D, Cheng AT, Baguley K, Walker P, Harrison H, Soma M, et al. Juvenile recurrent respiratory papillomatosis: 10-year audit and Australian prevalence estimates. *Laryngoscope*. 2016; 126:2827-32.
133. Novakovic D, Cheng ATL, Zurynski Y, Booy R, Walker PJ, Berkowitz R, et al. A Prospective Study of the Incidence of Juvenile-Onset Recurrent Respiratory Papillomatosis After Implementation of a National HPV Vaccination Program. *Journal of Infectious Diseases*. 2018; 217:208-12.
134. Nunez C, Morris A, Teutsch S, McGregor S, Brotherton J, Novakovic D, et al. Australian Paediatric Surveillance Unit Annual Report, 2018. *Communicable Diseases Intelligence*. 2019 Volume 43, https://doiorg/1033321/cdi20194353.
135. World Health Organization. 73rd World Health Assembly Decisions: Cervical cancer prevention and control. 2020 [16 October 2020]; Available from: https://www.who.int/news-room/feature-stories/detail/73rd-world-health-assembly-decisions.
136. Hull BP, McIntyre PB, Heath TC, Sayer GP. Measuring immunisation coverage in Australia: a review of the Australian Childhood Immunisation Register. *Australian Family Physician*. 1999; 28:55-60.
137. Australian Government Australian Digital Health Agency. Australian Immunisation Register. 2019 [cited 2019 27 August 2019]; Available from: https://developer.digitalhealth.gov.au/products/australian-immunisation-register.
138. Australian Government Department of Health. Using the Australian Immunisation Register. Canberra 2018 [updated 27 November 2018; cited 2019 08 April 2019]; Available from: https://beta.health.gov.au/health-topics/immunisation/health-professionals/using-the-australian-immunisation-register.
139. Australian Bureau of Statistics. 3101.0 - Australian Demographic Statistics, Jun 2018 Canberra: Australian Bureau of Statistics; [4/05/2020]; Available from: https://www.abs.gov.au/AUSSTATS/abs@.nsf/DetailsPage/3101.0Jun%202018?OpenDocument.
140. Australian Bureau of Statistics. 3238.0 - Estimates and Projections, Aboriginal and Torres Strait Islander Australians, 2006 to 2031 Canberra: Australian Bureau of Statistics; 2019 [updated 11/07/2019; cited 2019 20/09/2019]; Available from: https://www.abs.gov.au/ausstats/abs@.nsf/Latestproducts/3238.0Main%20Features402006%20to%202031?opendocument&tabname=Summary&prodno=3238.0&issue=2006%20to%202031&num=&view=.
141. Brotherton JM, Murray SL, Hall MA, Andrewartha LK, Banks CA, Meijer D, et al. Human papillomavirus vaccine coverage among female Australian adolescents: success of the school-based approach. *Medical Journal of Australia*. 2013; 199:614-7.
142. Hugo Centre for Migration and Population Research. Accessibility/Remoteness Index of Australia - ARIA++(2011). 2011 [cited 2017 17 November 2017]; Available from: https://www.adelaide.edu.au/hugo-centre/spatial_data/.
143. Australian Bureau of Statistics. Socio Economic Indexes for Areas (SEIFA). Canberra: Australian Bureau of Statistics; 2013 [updated 23 September 2013; cited 2018 26/02/2018]; Available from: http://www.abs.gov.au/websitedbs/censushome.nsf/home/seifa.
144. Brotherton JML, Bloem PN. Population-based HPV vaccination programmes are safe and effective: 2017 update and the impetus for achieving better global coverage. *Best Practice & Research: Clinical Obstetrics & Gynaecology*. 2018; 47:42-58.
145. Therapeutic Goods Administration. Reporting adverse events. [21 June 2018]; Available from: https://www.tga.gov.au/reporting-adverse-events.
146. National Centre for Immunisation Research and Surveillance. AusVaxSafety. [21 June 2018]; Available from: http://www.ausvaxsafety.org.au/.

147. National Centre for Immunisation Research and Surveillance. Vaccine Safety. Sydney: NCIRS; 2019 [cited 2020 12 January]; Available from: http://www.ncirs.org.au/health-professionals/vaccine-safety.
148. Brown EG, Wood L, Wood S. The medical dictionary for regulatory activities (MedDRA). Drug Safety. 1999; 20:109-17.
149. World Health Organisation. Global manual on surveillance of adverse events following immunisation. Geneva: World Health Organisation 2016 Contract No.: ISBN 978 92 4 150776 9.
150. Moro PL, Zheteyeva Y, Lewis P, Shi J, Yue X, Museru OI, et al. Safety of quadrivalent human papillomavirus vaccine (Gardasil) in pregnancy: adverse events among non-manufacturer reports in the Vaccine Adverse Event Reporting System, 2006-2013. *Vaccine*. 2015; 33:519-22.
151. Phillips A, Patel C, Pillsbury A, Brotherton J, Macartney K. Safety of Human Papillomavirus Vaccines: An Updated Review. *Drug Safety*. 2018; 41:329-46.
152. Gee J, Naleway A, Shui I, Baggs J, Yin R, Li R, et al. Monitoring the safety of quadrivalent human papillomavirus vaccine: findings from the Vaccine Safety Datalink. *Vaccine*. 2011; 29:8279-84.
153. Gee J, Weinbaum C, Sukumaran L, Markowitz LE. Quadrivalent HPV vaccine safety review and safety monitoring plans for nine-valent HPV vaccine in the United States. *Human Vaccines & Immunotherapeutics*. 2016; 12:1406-17.
154. Arana JE, Harrington T, Cano M, Lewis P, Mba-Jonas A, Rongxia L, et al. Post-licensure safety monitoring of quadrivalent human papillomavirus vaccine in the Vaccine Adverse Event Reporting System (VAERS), 2009-2015. *Vaccine*. 2018; 36:1781-8.
155. Odaka M, Yuki N, Hirata K. Patients with chronic inflammatory demyelinating polyneuropathy initially diagnosed as Guillain-Barre syndrome. *Journal of Neurology*. 2003; 250:913-6.
156. Ruggeberg JU, Gold MS, Bayas JM, Blum MD, Bonhoeffer J, Friedlander S, et al. Anaphylaxis: case definition and guidelines for data collection, analysis, and presentation of immunization safety data. *Vaccine*. 2007; 25:5675-84.
157. Sheldon RS, Grubb BP, 2nd, Olshansky B, Shen WK, Calkins H, Brignole M, et al. 2015 heart rhythm society expert consensus statement on the diagnosis and treatment of postural tachycardia syndrome, inappropriate sinus tachycardia, and vasovagal syncope. *Heart Rhythm*. 2015; 12:e41-63.
158. Little DT, Ward HRG. Adolescent Premature Ovarian Insufficiency Following Human Papillomavirus Vaccination: A Case Series Seen in General Practice. *Journal of Investigative Medice High Impact Case Reports*. 2014; 2:2324709614556129-.
159. Richards S, Chalkiadis G, Lakshman R, Buttery JP, Crawford NW. Complex regional pain syndrome following immunisation. *Archives of Diseases in Childhood*. 2012; 97:913-5.
160. Phillips A, Hickie M, Totterdell J, Brotherton J, Dey A, Hill R, et al. Adverse events following HPV vaccination: 11 years of surveillance in Australia. *Vaccine*. 2020; 38:6038-46.
161. Dey A, Wang H, Quinn H, Hiam R, Wood N, Beard F, et al. Surveillance of adverse events following immunisation in Australia annual report, 2017. *Communicable Diseases Intelligence* 2019; 43.
162. Therapeutic Goods Administration. Enhanced school-based surveillance of acute adverse events following immunisation with human papillomavirus vaccine in males and females, 2013. Canberra: Australian Government Department of Health.2015.
163. Kuntz JL, Firemark A, Schneider J, Henninger M, Bok K, Naleway A. Development of an Intervention to Reduce Pain and Prevent Syncope Related to Adolescent Vaccination. *The Permanante Journal*. 2019; 23:17-136.
164. Harris T, Williams DM, Fediurek J, Scott T, Deeks SL. Adverse events following immunization in Ontario's female school-based HPV program. *Vaccine*. 2014; 32:1061-6.

165. Oberle D, Pavel J, Rieck T, Weichert S, Schroten H, Keller-Stanislawski B, et al. Anaphylaxis After Immunization of Children and Adolescents in Germany. *Pediatric Infectious Diseases Journal*. 2016; 35:535-41.
166. Brotherton JM, Gold MS, Kemp AS, McIntyre PB, Burgess MA, Campbell-Lloyd S. Anaphylaxis following quadrivalent human papillomavirus vaccination. *Canadian Medical Association Journal*. 2008; 179:525-33.
167. Siegrist C-A. Autoimmune diseases after adolescent or adult immunization: what should we expect? *Canadian Medical Association Journal*. 2007; 177:1352-4.
168. Morris AM, Elliott EJ, D'Souza RM, Antony J, Kennett M, Longbottom H. Acute flaccid paralysis in Australian children. *Journal of Paediatrics and Child Health*. 2003; 39:22-6.
169. Souayah N, Michas-Martin PA, Nasar A, Krivitskaya N, Yacoub HA, Khan H, et al. Guillain-Barre syndrome after Gardasil vaccination: data from Vaccine Adverse Event Reporting System 2006-2009. *Vaccine*. 2011; 29:886-9.
170. Gee J, Sukumaran L, Weintraub E. Risk of Guillain-Barre Syndrome following quadrivalent human papillomavirus vaccine in the Vaccine Safety Datalink. *Vaccine*. 2017; 35:5756-8.
171. Miranda S, Chaignot C, Collin C, Dray-Spira R, Weill A, Zureik M. Human papillomavirus vaccination and risk of autoimmune diseases: A large cohort study of over 2million young girls in France. *Vaccine*. 2017; 35:4761-8.
172. Andrews N, Stowe J, Miller E. No increased risk of Guillain-Barre syndrome after human papilloma virus vaccine: A self-controlled case-series study in England. *Vaccine*. 2017; 35:1729-32.
173. Deceuninck G, Sauvageau C, Gilca V, Boulianne N, De Serres G. Absence of association between Guillain-Barre syndrome hospitalizations and HPV-vaccine. *Expert Review of Vaccines*. 2018; 17:99-102.
174. Arana J, Mba-Jonas A, Jankosky C, Lewis P, Moro PL, Shimabukuro TT, et al. Reports of Postural Orthostatic Tachycardia Syndrome After Human Papillomavirus Vaccination in the Vaccine Adverse Event Reporting System. *Journal of Adolescent Health*. 2017; 61:577-82.
175. World Health Organisation. Meeting of the Global Advisory Committee on Vaccine Safety, 7–8 June 2017. *Weekly Epidemiological Record*. 2017; 92:393–404.
176. Barboi A, Gibbons CH, Axelrod F, Benarroch EE, Biaggioni I, Chapleau MW, et al. Human papillomavirus (HPV) vaccine and autonomic disorders: a position statement from the American Autonomic Society. *Clinical Autonomic Research*. 2019.
177. Donegan K, Beau-Lejdstrom R, King B, Seabroke S, Thomson A, Bryan P. Bivalent human papillomavirus vaccine and the risk of fatigue syndromes in girls in the UK. *Vaccine*. 2013; 31:4961-7.
178. Feiring B, Laake I, Bakken IJ, Greve-Isdahl M, Wyller VB, Haberg SE, et al. HPV vaccination and risk of chronic fatigue syndrome/myalgic encephalomyelitis: A nationwide register-based study from Norway. *Vaccine*. 2017; 35:4203-12.
179. Ward D, Thorsen NM, Frisch M, Valentiner-Branth P, Molbak K, Hviid A. A cluster analysis of serious adverse event reports after human papillomavirus (HPV) vaccination in Danish girls and young women, September 2009 to August 2017. *Eurosurveillance*. 2019; 24.
180. Larson H. The world must accept that the HPV vaccine is safe. Nature. 2015; 528:9.
181. World Health Organisation. Global Advisory Committee on Vaccine Safety, 5–6 June 2019. *Weekly Epidemiological Record*. 2019; 28:306-16.
182. Arnheim-Dahlstrom L, Pasternak B, Svanstrom H, Sparen P, Hviid A. Autoimmune, neurological, and venous thromboembolic adverse events after immunisation of adolescent girls with quadrivalent human papillomavirus vaccine in Denmark and Sweden: cohort study. *BMJ* 2013; 347:f5906.
183. Frisch M, Besson A, Clemmensen KKB, Valentiner-Branth P, Molbak K, Hviid A. Quadrivalent human papillomavirus vaccination in boys and risk of autoimmune diseases, neurological diseases and venous thromboembolism. *International Journal of Epidemiology*. 2018; 47:634-41.

184. Naleway AL, Mittendorf KF, Irving SA, Henninger ML, Crane B, Smith N, et al. Primary Ovarian Insufficiency and Adolescent Vaccination. *Pediatrics*. 2018; 142: e20180943.
185. Naleway AL, Crane B, Smith N, Daley MF, Donahue J, Gee J, et al. Absence of venous thromboembolism risk following quadrivalent human papillomavirus vaccination, Vaccine Safety Datalink, 2008-2011. *Vaccine*. 2016; 34:167-71.
186. Slade BA, Leidel L, Vellozzi C, Woo EJ, Hua W, Sutherland A, et al. Postlicensure Safety Surveillance for Quadrivalent Human Papillomavirus Recombinant Vaccine. *JAMA*. 2009; 302:750-7.
187. Goss MA, Lievano F, Buchanan KM, Seminack MM, Cunningham ML, Dana A. Final report on exposure during pregnancy from a pregnancy registry for quadrivalent human papillomavirus vaccine. *Vaccine*. 2015; 33:3422-8.
188. Dey A, Wang H, Quinn H, Pillsbury A, Glover C, Hickie M, et al. Surveillance of adverse events following immunisation in Australia annual report, 2018. *Communicable Diseases Intelligence*. 2020; In press.
189. Tomianovic D, Bauwens J, Heininger U, Bonhoeffer J. Global Vaccine Safety Assessment: Challenges and Opportunities. *Pediatric Infectious Diseases Journal*. 2016; 35:446-8.
190. Australian Institute of Health and Welfare. Cervical screening in Australia 2019. Canberra: AIHW2019.
191. Australian Institute of Health and Welfare (AIHW). 2016 Australian Cancer Database pivot table. Canberra: AIHW. 2020; Available from: http://www.aihw.gov.au/cancer-data.
192. de Martel C, Plummer M, Vignat J, Franceschi S. Worldwide burden of cancer attributable to HPV by site, country and HPV type. *International Journal of Cancer*. 2017; 141:664-70.
193. de Martel C, Georges D, Bray F, Ferlay J, Clifford GM. Global burden of cancer attributable to infections in 2018: a worldwide incidence analysis. *The Lancet Global Health*. 2020; 8:e180-e90.
194. Novakovic D, Cheng ATL, Cope DH, Brotherton JML. Estimating the prevalence of and treatment patterns for juvenile onset recurrent respiratory papillomatosis in Australia pre-vaccination: a pilot study. *Journal of Sexual Health*. 2010; 7:253-61.
195. Australian Institute of Health and Welfare. Analysis of cervical cancer and abnormality outcomes in an era of cervical screening and HPV vaccination in Australia 2019.
196. Brotherton JML, Budd A, Rompotis C, Bartlett N, Malloy MJ, Andersen RL, et al. Is one dose of human papillomavirus vaccine as effective as three?: A national cohort analysis. *Papillomavirus Research*. 2019; 8:100177.
197. Tervonen HE, Morrell S, Roder D, You H, Currow DC. Differences in cancer incidence by age at diagnosis between Aboriginal and non-Aboriginal people for cancer types included in Australian national screening programs. *Cancer Epidemiology*. 2019; 60:102-5.
198. Diaz A, Baade PD, Valery PC, Whop LJ, Moore SP, Cunningham J, et al. Comorbidity and cervical cancer survival of Indigenous and non-Indigenous Australian women: A semi-national registry-based cohort study (2003-2012). *PLoS One*. 2018; 13:e0196764.
199. Grulich AE, Jin F, Conway EL, Stein AN, Hocking J. Cancers attributable to human papillomavirus infection. *Sexual Health*. 2010; 7:244-52.
200. Patel C, Brotherton JM, Pillsbury A, Jayasinghe S, Donovan B, Macartney K, et al. The impact of 10 years of human papillomavirus (HPV) vaccination in Australia: what additional disease burden will a nonavalent vaccine prevent? *Eurosurveillance*. 2018; 23.
201. Nunez CA, Morris A, Teutsch SM, McGregor S, Brotherton J, Novakovic D, et al. Australian Paediatric Surveillance Unit Annual Report 2018. *Communicable Diseases of Intelligence* (2018). 2019; 43.
202. Shilling H, Murray G, Brotherton JML, Hawkes D, Saville M, Sivertsen T, et al. Monitoring human papillomavirus prevalence among young Australian women undergoing routine chlamydia screening. *Vaccine*. 2019.
203. Tabrizi SN, Brotherton JM, Stevens MP, Condon JR, McIntyre P, Smith D, et al. HPV genotype prevalence in Australian women undergoing routine cervical screening by cytology

status prior to implementation of an HPV vaccination program. *Journal of Clinical Virology*. 2014; 60:250-6.
204. Garland SM, Cornall AM, Brotherton JML, Wark JD, Malloy MJ, Tabrizi SN, et al. Final analysis of a study assessing genital human papillomavirus genoprevalence in young Australian women, following eight years of a national vaccination program. *Vaccine*. 2018; 36:3221-30.
205. Fairley CK, Hocking JS, Gurrin LC, Chen MY, Donovan B, Bradshaw CS. Rapid decline in presentations of genital warts after the implementation of a national quadrivalent human papillomavirus vaccination programme for young women. *Sexually Transmitted Infections*. 2009; 85:499-502.
206. Ali H, Donovan B, Wand H, Read TR, Regan DG, Grulich AE, et al. Genital warts in young Australians five years into national human papillomavirus vaccination programme: national surveillance data. *BMJ*. 2013; 346:f2032.
207. Ali H, Guy RJ, Wand H, Read TR, Regan DG, Grulich AE, et al. Decline in in-patient treatments of genital warts among young Australians following the national HPV vaccination program. *BMC Infectious Diseases*. 2013; 13:140.
208. Donovan B, Franklin N, Guy R, Grulich AE, Regan DG, Ali H, et al. Quadrivalent human papillomavirus vaccination and trends in genital warts in Australia: analysis of national sentinel surveillance data. *The Lancet Infectious Diseases*. 2011; 11:39-44.
209. Checchi M, Mesher D, Mohammed H, Soldan K. Declines in anogenital warts diagnoses since the change in 2012 to use the quadrivalent HPV vaccine in England: data to end 2017. *Sexually Transmitted Infections*. 2019; 95:368-73.
210. Cocchio S, Baldovin T, Bertoncello C, Buja A, Furlan P, Saia M, et al. Decline in hospitalization for genital warts in the Veneto region after an HPV vaccination program: an observational study. *BMC Infectious Diseases*. 2017; 17:249.
211. Flagg EW, Torrone EA. Declines in Anogenital Warts Among Age Groups Most Likely to Be Impacted by Human Papillomavirus Vaccination, United States, 2006-2014. *American Journal of Public Health*. 2018; 108:112-9.
212. Steben M, Garland SM. Genital warts. *Best Practice & Research: Clinical Obstetrics & Gynaecology*. 2014; 28:1063-73.
213. Drolet M, Benard E, Perez N, Brisson M. Population-level impact and herd effects following the introduction of human papillomavirus vaccination programmes: updated systematic review and meta-analysis. *The Lancet*. 2019; 394:497-509.
214. Read TR, Hocking JS, Chen MY, Donovan B, Bradshaw CS, Fairley CK. The near disappearance of genital warts in young women 4 years after commencing a national human papillomavirus (HPV) vaccination programme. *Sexually Transmitted Infections*. 2011; 87:544-7.
215. Chow EP, Lin AC, Read TR, Bradshaw CS, Chen MY, Fairley CK. Ratio of anogenital warts between different anatomical sites in homosexual and heterosexual individuals in Australia, 2002-2013: implications for susceptibility of different anatomical sites to genital warts. *Epidemiology and Infection*. 2015; 143:1495-9.