Active vaccine safety surveillance:
monitoring the switch to 9-valent HPV vaccine in Australian adolescents

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Background:

HPV vaccine

Australia has led the world with HPV vaccination, from early vaccine development and having been the first country to immunise both girls (from 2007) and boys (from 2013) in school-based programs. Changes to the National Immunisation Program (NIP) are detailed in Table 1.

Table 1. HPV vaccination schedules pre- and from 2018

2007-2018:	2018-present:
3 doses of 4-valent HPV vaccine (Gardasil)	2 doses of 9-valent HPV vaccine (Gardasil9)

AusVaxSafety active vaccine safety surveillance system

Australia's automated vaccine safety surveillance system surveys participants immunised at sentinel immunisation-providing sites via opt-out SmartVax SMS message. Participants receive an SMS approximately 3 days after immunisation asking for details about any adverse events following immunisation (AEFI). AusVaxSafety currently monitors AEFI for seasonal influenza, pertussis booster, zoster and HPV vaccines.[1-4]

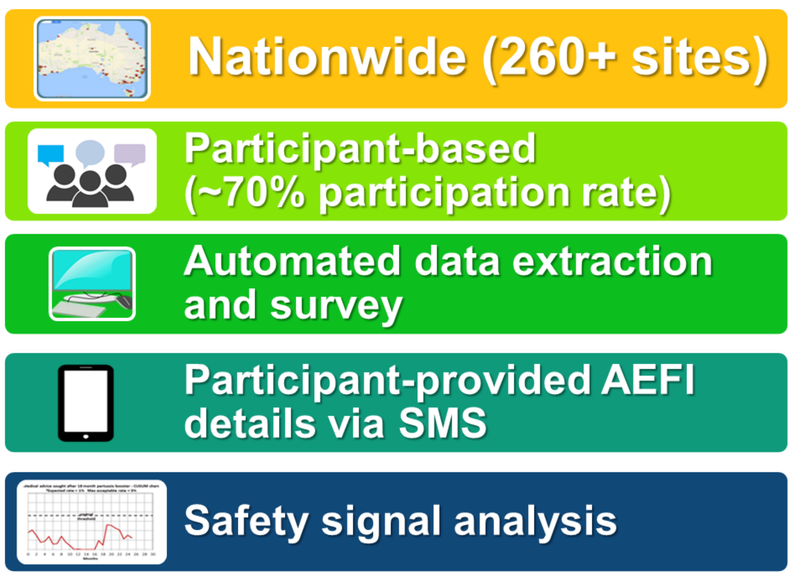


Figure 1. AusVaxSafety attributes

Aim:

To compare the safety profiles of Gardasil and Gardasil9 administered to adolescents captured by AusVaxSafety active vaccine safety surveillance.

Methods:

- De-identified data from the period of 1 February-31 July for both 2017 (Gardasil) and 2018 (Gardasil9) were obtained via the automated reporting tool SmartVax from the parents/caregivers of adolescents aged 11-14 years vaccinated at participating sentinel schools/primary care providers.
- Rates of AEFI occurring within days of immunisation as well as rates of medical attendance sought for an adverse event (as a proxy for serious adverse event) were summarised and compared.

Results:

Data from 6,418 participants who received Gardasil (2017) were compared with 6,640 participants receiving Gardasil9 (2018). Participants receiving Gardasil9 had a higher rate of reporting any AEFI than participants receiving Gardasil (9.8% versus 7.5%; p<0.001).

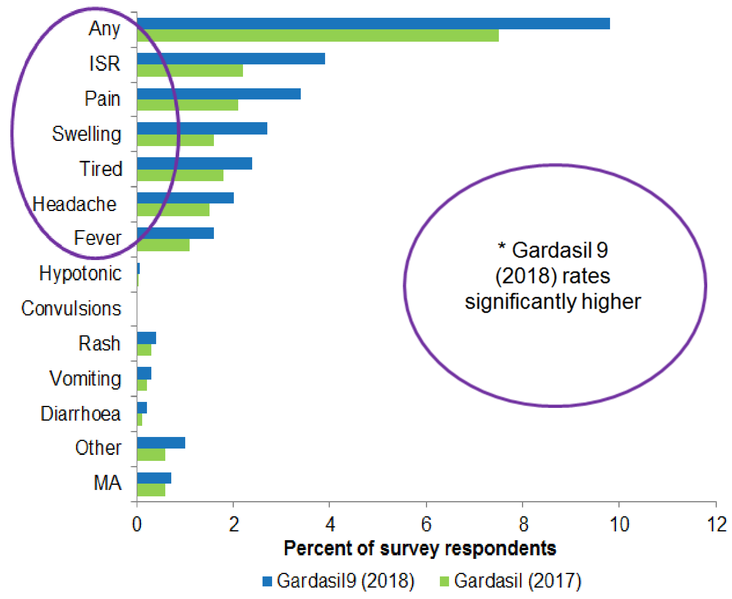
Results:

Table 2. Details of participants in HPV active vaccine safety surveillance

Vaccine/	Participants*	Sex	Median age	Concomitant vaccination
Gardasil	6,418/9,986 (64.3%)	50.3% female	12 years	70.9%
Gardasil9	6,640/9,877 (67.2%)	49.7% female	12 years	95.2%

*Participants were those who responded to the survey. Denominators represent all vaccination encounters.

Rates of fever (1.6% versus 1.1%; p=0.03), headache (2.0% versus 1.5%; p=0.04), tiredness (2.4% versus 1.8%; p=0.02) and injection site reaction (ISR; 3.9% versus 2.2%; p<0.001) were higher for Gardasil9 compared with Gardasil. Rates of medical attention sought within days of immunisation were low and comparable: 0.7% for Gardasil9 and 0.6% for Gardasil. Of those participants for which medical attendance was reported and the survey completed, most reported ISR, headache or fever.



Note: "Other" symptoms includes unsolicited events provided in free text.

Figure 2. Percentage of solicited AEFI reported by vaccine

Conclusion:

AEFI rates following Gardasil and Gardasil9 vaccines, including rates of medical attendance sought for an AEFI, were low. Though slightly higher AEFI rates associated with Gardasil9 are consistent with clinical trial data, overall, the rates of AEFI from this post-marketing surveillance system are lower than those reported from clinical trial data.[5] In this analysis, the pattern of AEFI reported by participants who sought medical attention for their AEFI was consistent with the pattern reported overall.

The 2018 cohort had predominantly received dose 1 and not dose 2. Moreover, 95% of adolescents in the 2018 cohort received a concomitant vaccine (typically Boostrix), compared to only 70% in 2017. These limitations may contribute to confounding and require further analysis.

AusVaxSafety data provide reassurance of HPV vaccine safety, with respect to events occurring within the first few days post-vaccination, and contribute to the global HPV vaccine safety evidence base.

Participant-driven vaccine safety surveillance = **Transparency and reassurance** ➡ **Continued high vaccination coverage and positive public health outcomes**

Acknowledgements:

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5. Moreira et al. Safety profile of the 9-valent HPV vaccine: a combined analysis of 7 Phase III clinical trials. *Pediatrics*.2016; 138(2).

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