Measuring the impact of the HPV vaccination program in Australia

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Overview

- Global perspective
- Australia’s position and role in the region
- HPV vaccination programs- where are we at?
- Cervical cancer screening
- Data collection and register systems
- Data linkage
- Evaluations (including modelling)

Global and regional burden of cancers caused by HPV

International Agency Research on Cancer

World Health Organization

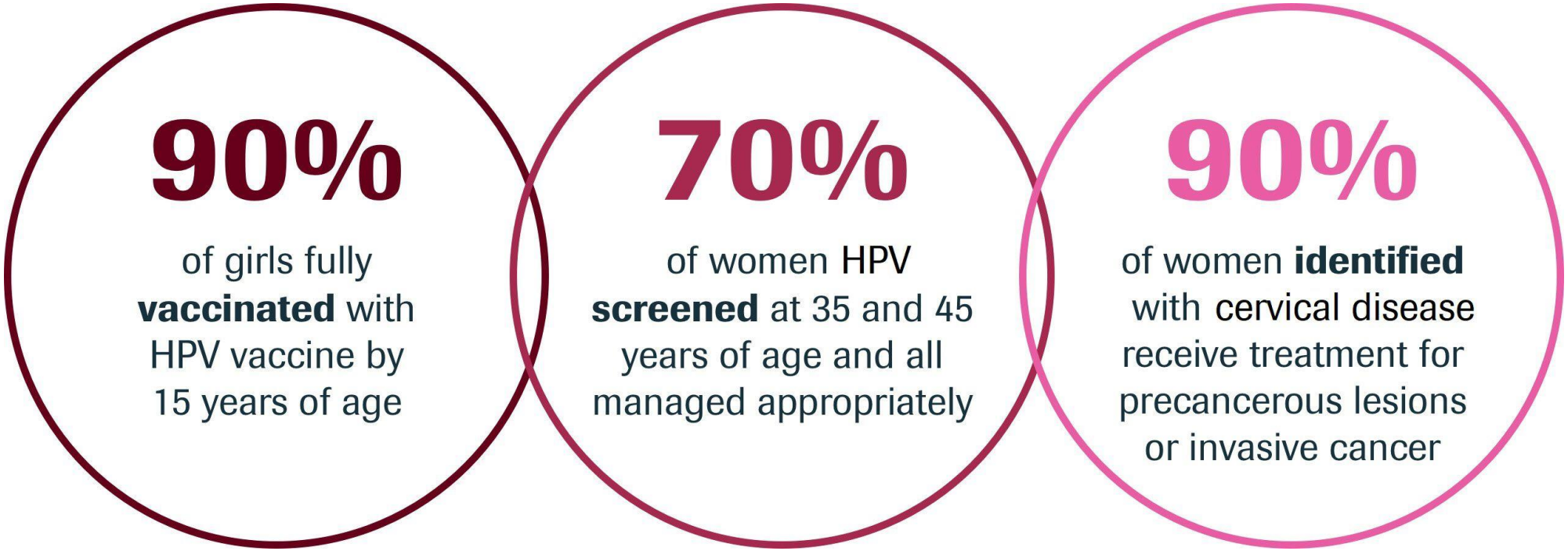
- Burden, incidence and mortality
  - Source of data: IARC
  - New cases (2018) 569,571 cervix (100% HPV attributable)
  - All **HPV attributable related cancers** though (eg vulva, penis, anus) **684,068 in 2018**
  - 6 WHO regions: SEARO (incidence 15.8) and WPRO (incidence 10.7) account for **53% of global burden** of cervical cancer (globally 13.1/100,000 women)
  - Total deaths 311,365 globally in 2018; SEARO (account for 30.8% of deaths) and WPRO (20.5%) account for **51% of global deaths**
  - Mortality rate globally 6.9/100,000
  - Overall cervical cancer is the 5th most common cancer, 4th most common type of cancer causing death among women (after breast, colorectal, lung)

WHO 2017 HPV vaccine position paper

- HPV should be included in national immunization programmes
- HPV vaccines should be introduced as part of a coordinated and comprehensive strategy to prevent cervical cancer
    - Primary prevention : HPV vaccine, education: delay age first intercourse, condoms
    - Secondary prevention: screening , early diagnosis
    - Tertiary prevention: treatment
- Target population girls aged 9-14 prior to sexual debut
- Targeting multiple age cohorts eg 9-18 would result in faster and greater population impact

May 2018 the WHO Director General called to eliminate cervical cancer

- Draft strategy towards elimination of cervical cancer
  - Vision: a world without cervical cancer
  - Threshold: all countries reach <4 cases/100,000
  - 2030 control targets



Current status of HPV vaccine introduction globally

- 100 countries have introduced HPV vaccination
    - Some national roll outs, some pilot
    - **Only cover one third of girls globally (goal 90%)**
- Proportions differ according to region and income level
- Challenges
    - HPV vaccine introduced in 52% of countries but access in highest burden countries is lagging eg Indonesia, Philippines
    - Global vaccine shortage
    - Price variation
    - Anti-vaccination groups and preparedness
    - Advocacy and awareness programmes to maintain demand
    - Despite NITAG recommendations resource allocation lagging as is political will

Australian context

- One of the lowest rates of cervical cancer incidence and mortality in the world
- Predominantly occurs now in unscreened or under screened women
- Indigenous women have >double the risk of developing cervical cancer and >5X mortality rate c.f. non-indigenous

Cervical Cancer Prevention in Australia - screening

- National Cervical Screening Program (NCSP) established in 1991.
- The NCSP aims to reduce morbidity and mortality from cervical cancer in a cost effective manner through an organised approach to screening
- Initially recommended two yearly conventional cytology tests for women aged 18 to 69 years
- In December 2017, moved to five yearly primary HPV testing with liquid based cytology triage.
- Delivered through primary healthcare, subsidised by Government funding
- A population based register supports the collection of screening histories and sends invitations and reminders for screening and clinical follow-up

Impact of the NCSP

Participation

2 yearly - 57%

3 yearly - 70%

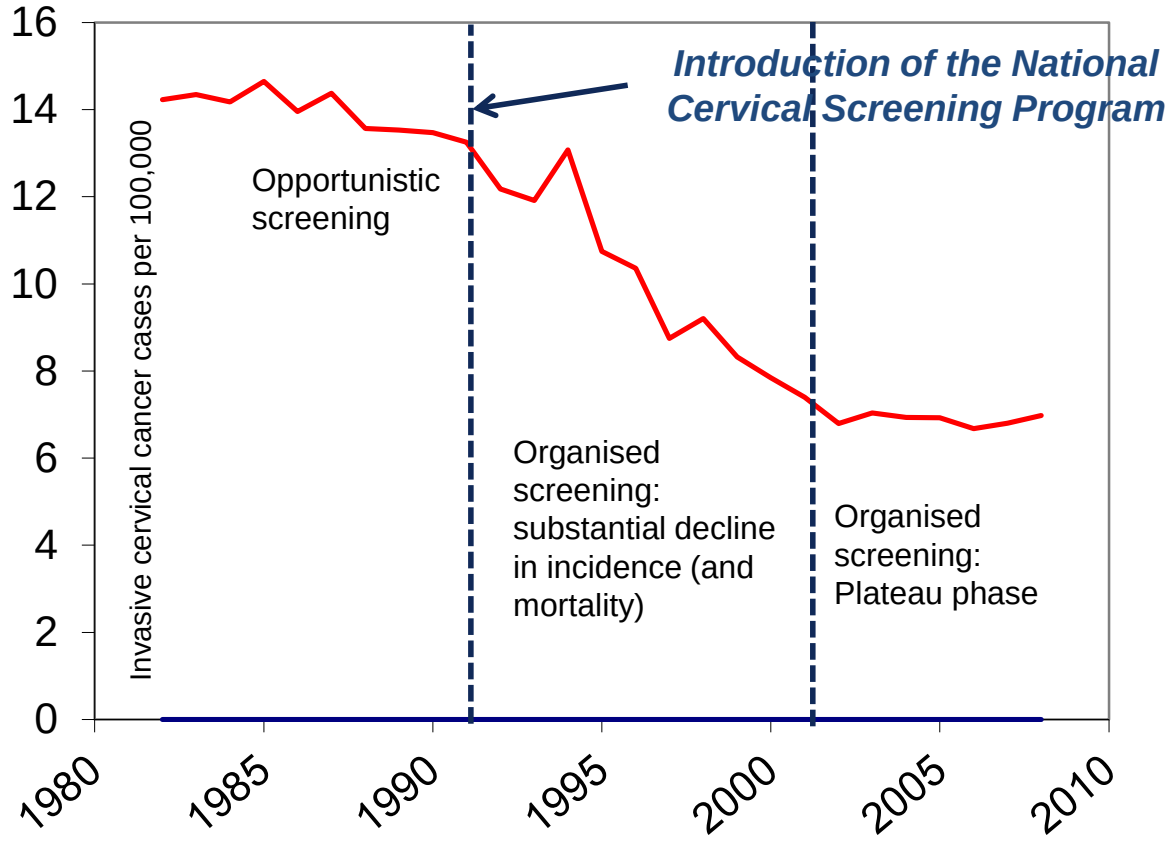
5 yearly - 83%

Incidence

6.8 per 100,000

Mortality

1.7 per 100,000



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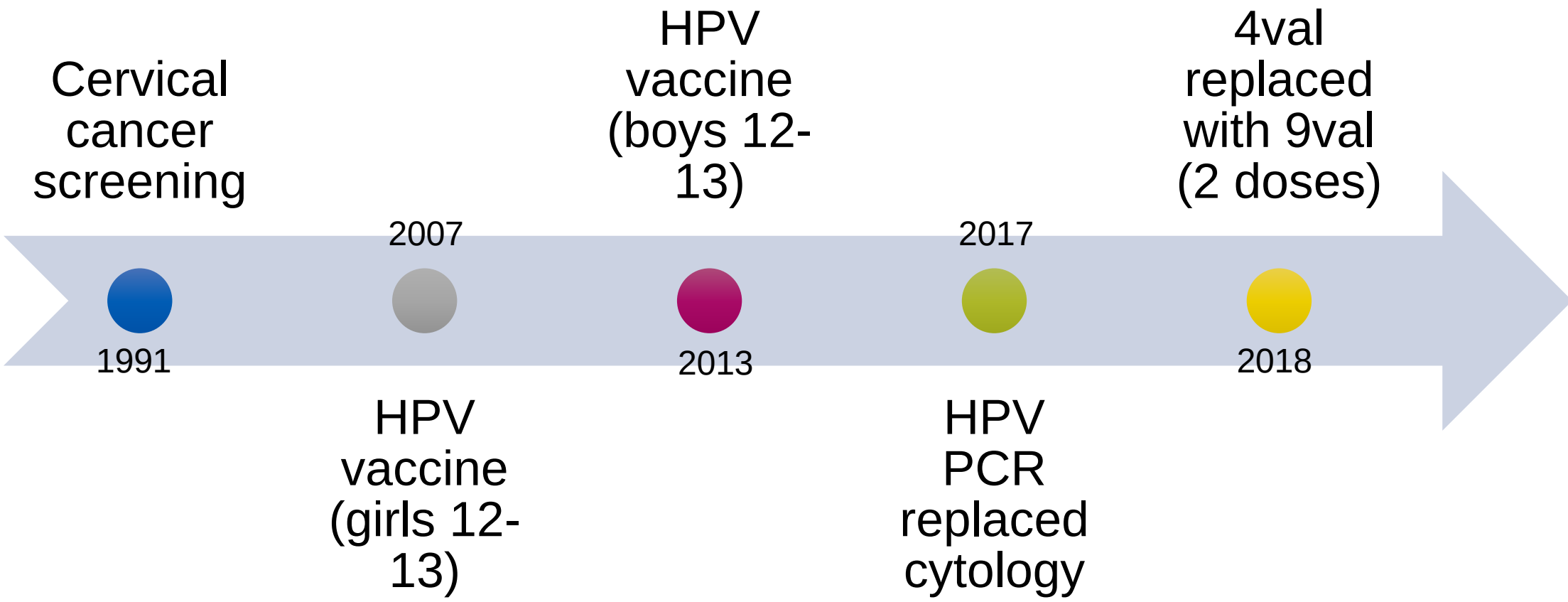
Since commencement there has been a 50% reduction in incidence and mortality

Cervical Cancer Prevention in Australia - vaccination

- Australia was the first country to implement a fully funded National HPV Vaccination Programme
- Free human papillomavirus (HPV) vaccines are provided through the National Immunisation Program (NIP) to adolescent females and males, aged 12 to 13 years
- Commenced in 2007 for girls and expanded in 2013 to include boys
- Delivered via a school based program to adolescents
- Catch up program available up to 19 years of age through General Practice and other vaccination providers
- In 2018, Australia switched from using the 4-valent Gardasil vaccine to using the 9-valent Gardasil 9 vaccine, the schedule was reduced from 3 doses to 2
- Register supports the collection of HPV vaccination history and sends reminders

Timeline of cervical cancer prevention program



Cervical Cancer Prevention in Australia - vaccination

- HPV immunisation coverage rates in 2017:
  - 80.2% of girls and 75.9% of males aged 15 years fully vaccinated.
- From 2007 to 2017, among Australian-born women and heterosexual men aged 21 years or younger attending sexual health clinics, there has been a 96 and 88% per cent reduction, respectively in genital warts.
- High grade cervical abnormalities have also declined, with detection rates declining between 2006 and 2016 by 70 per cent in women aged 20 years or younger, and 47 per cent in women aged 20–24 years.
- Evaluation of HPV vaccination in Australian completed in 2014.

Evaluation of the HPV vaccination program

Evaluation	Methodology	Outcome
Process – program implementation	Interviews: online survey and semi-structured telephone interviews	• Successful implementation • Short lead time to implement • Community concerns regarding safety
Vaccination Coverage	Number of doses notified divided by estimated resident population	• School coverage 83/78/70% for doses 1/2/3 (girls only)
Adverse Events Following Immunisation	Passive Surveillance notification through the Adverse Drug Reaction System (ADRS)	• 2,460 AEFIs reported between 1 April 2007 and 30 June 2013 • Headache, nausea, dizziness • 7% Serious AEFI, no deaths
Disease Impact: high-grade cervical abnormalities and anogenital warts	Ecologic design – pre-vaccination compared to post vaccination using screening outcomes and hospitalisation data	• Decline in rates of high grade abnormalities and anogenital warts in females < 20 years over time

2014. *Evaluation of the National HPV Vaccination Program Final Report.* National Centre for Immunisation Research and Evaluation. Accessed at: http://www.ncirs.org.au/our-work/program-evaluation

Process Evaluation

- Survey and interviews covered the following areas
  - Stakeholders experience with implementation including
    - Communication and resources
    - Program planning and rollout
    - Service delivery
    - Data collection and reporting
    - Strengths and challenges
    - Recommendations for future National Immunisation Programs
  - National cervical screening program managers completed an online survey about their organisations involvement in the HPV program and impact of program on activities

Key findings

- Major challenge for the program was initial acceptance by community and parents
- Effective consent strategies were central to the success of the program
- Early apprehension seen with the female program not seen with the male program
- It was ‘more acceptable’ to promote an “STI vaccine” for adolescent males than for females
- Gender neutral increased the program’s acceptibility

Coverage

- Females only (males introduced in 2013, evaluation 2014)
- Number of doses notified/estimated resident population for females
- Number of doses (as recorded on the National HPV Vaccination Program Register (NHVPR)- established in 2008 and collects reports of doses for the purpose of notifying individuals/parents/providers and coverage data
- Estimated resident population from the Australian Bureau of Statistics
- Stratified according to
  - Age
  - Socioeconomic status
  - Remoteness
- Timeliness (0,2,6 month schedule)
  - Proportion who completed course within 6-12 months of first dose

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

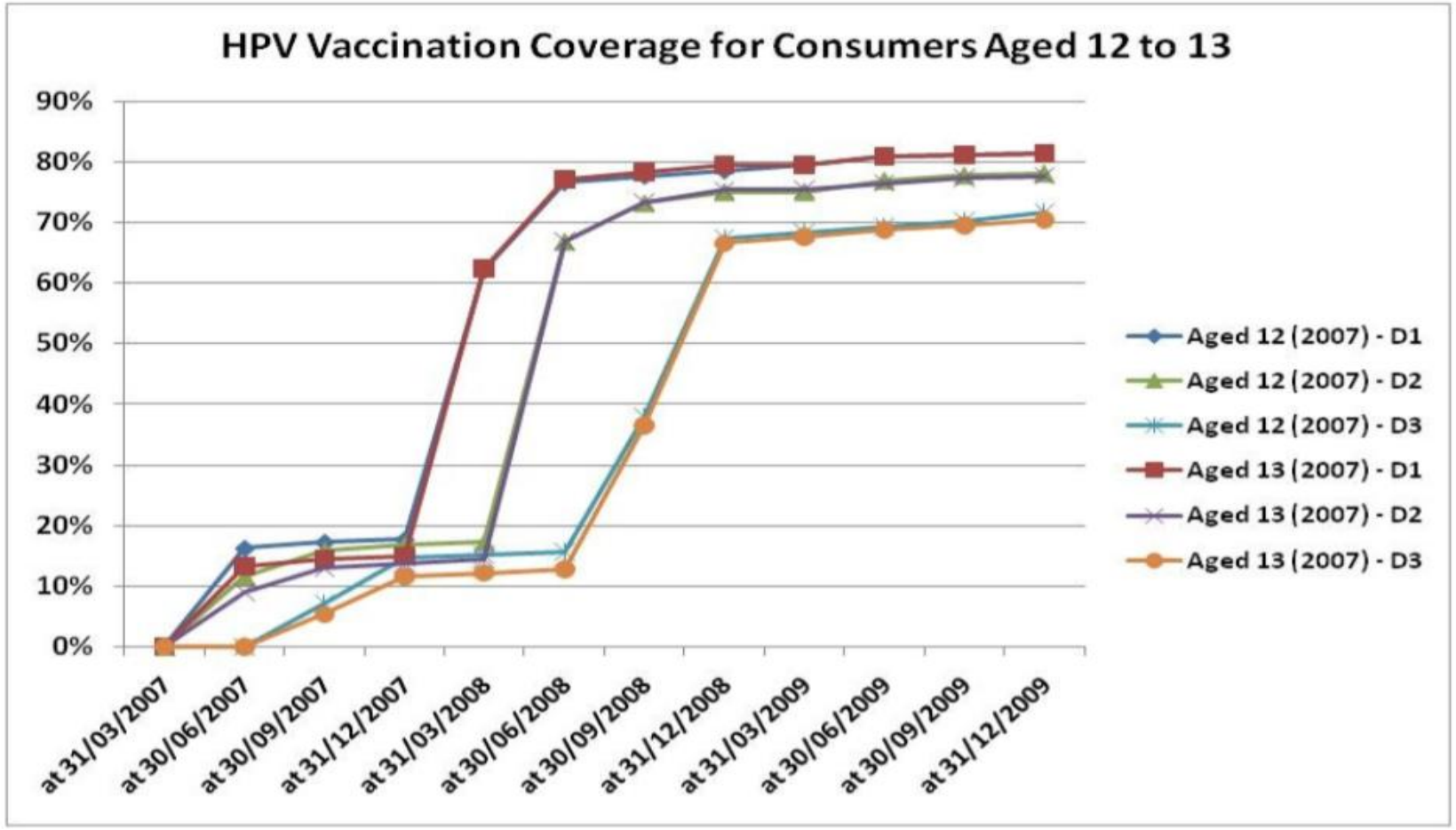
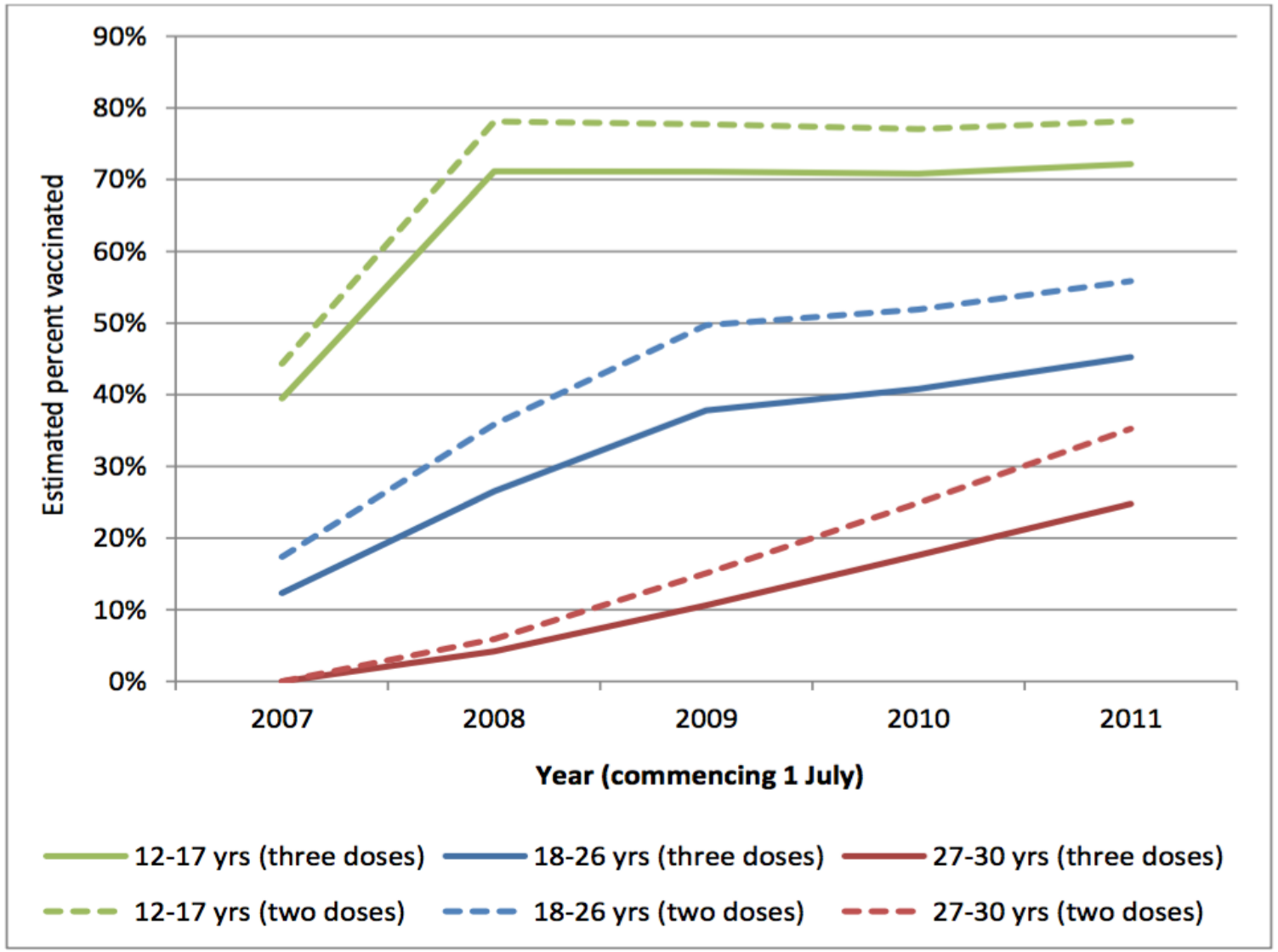


Figure A6.2.1. Estimated* percentage of females in each age group ever vaccinated, by year

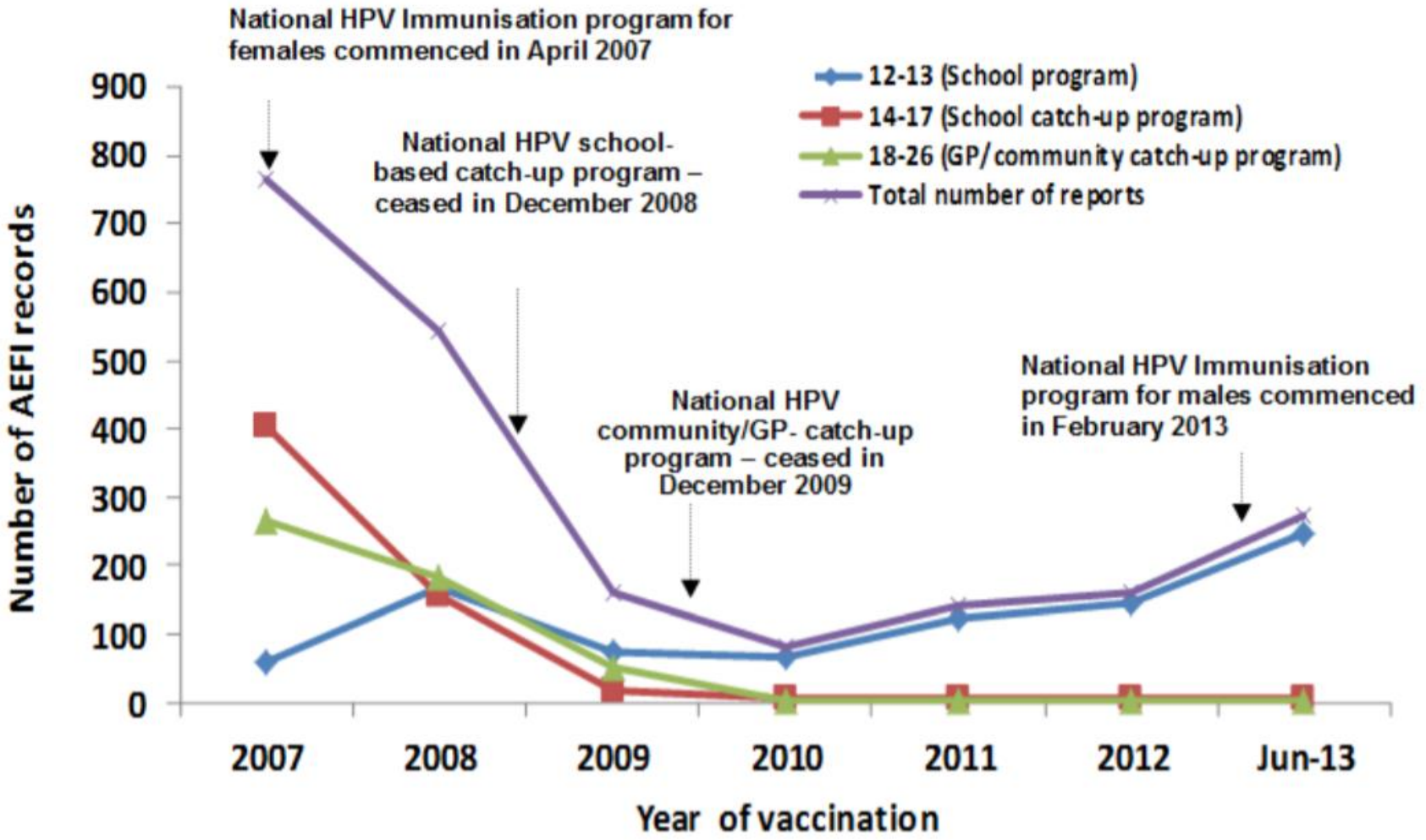


* Estimated from published coverage data and population estimates.[38,41,113,114] Coverage data for females aged 12–13 years in 2011 is not yet available so estimates are based on similar coverage to those aged 14–15 years in 2011. Percentage effectively immunised may be lower due to some prior exposure.

AEFI

- In Australia a passive surveillance system is used
- Reports can be made by any provider to either their local jurisdiction or the Therapeutic Goods Administration (TGA)
- All reports to the TGA between 1/4/07 and 30/6/13 released for analysis in 2014
- Additional activities
  - Review of published case series/literature
  - Rapid school based reporting for 4 key conditions (anaphylaxis, generalised allergic reaction, LOC, hospitalisation/ED presentation)
  - Expert panel convened
  - Rapid responses to potential safety signal
  - Protocol for National HPV program action and communication to ensure consistency in response to a potential safety signal
  - AEFI-CAN

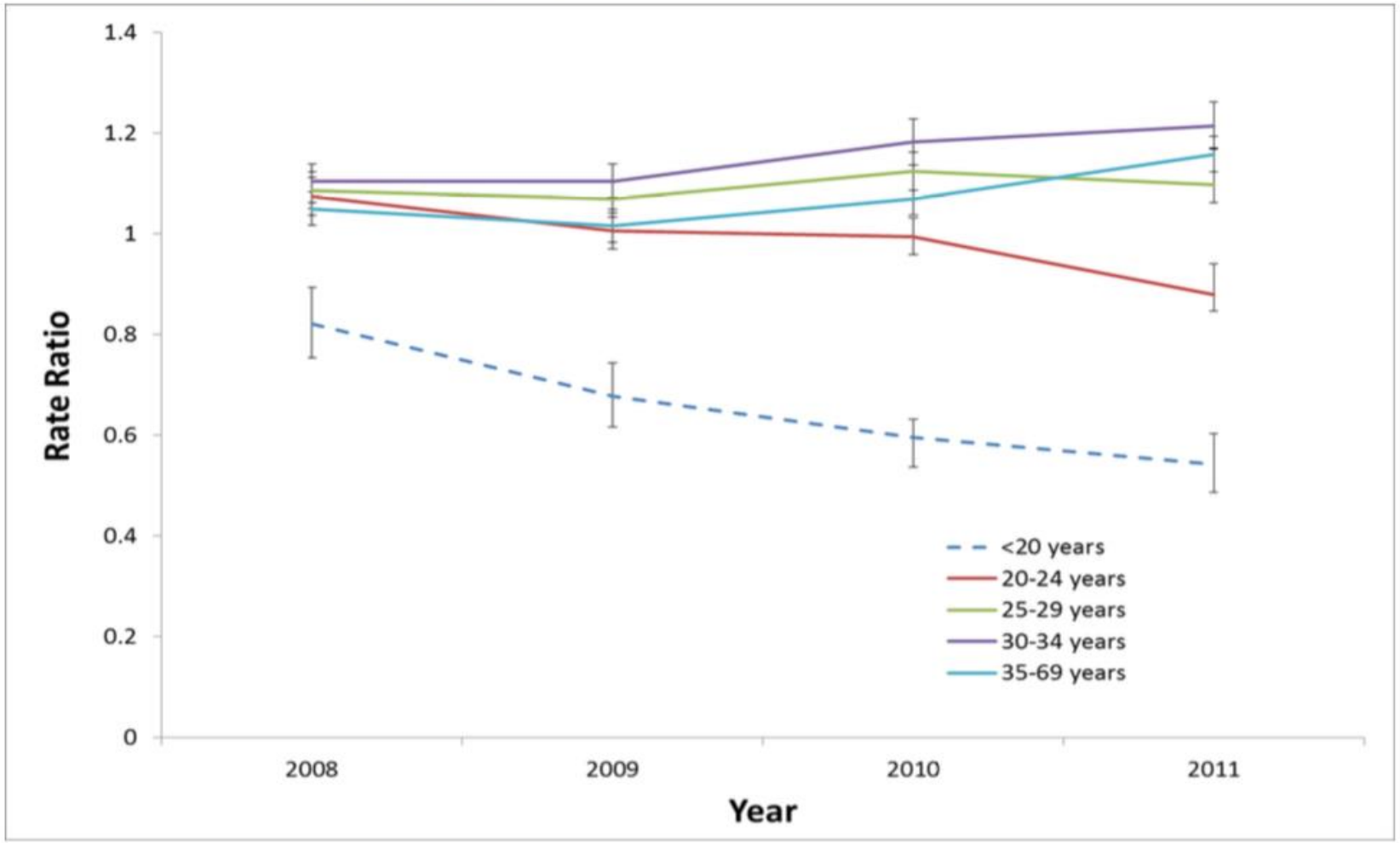
Figure 4.1. Number of reports of adverse events following HPV vaccination for females aged 12–13 years, 14–17 years and 18–26 years, TGA Adverse Drug Reaction System database, 1 April 2007 to 30 June 2013, by year of vaccination



Impact on disease

- The disease impact was assessed using 2 sources of data
  - 1. high grade cervical (CIN 2 or CIN3 or adenocarcinoma in situ or endocervical dysplasia) from the National Cervical Screening in Australia reports (2004-2007 c.f. 2008-2011)
  - 2. Hospitalisation data including diagnosis of genital warts from 1//7/1999 to 30/6/2011

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

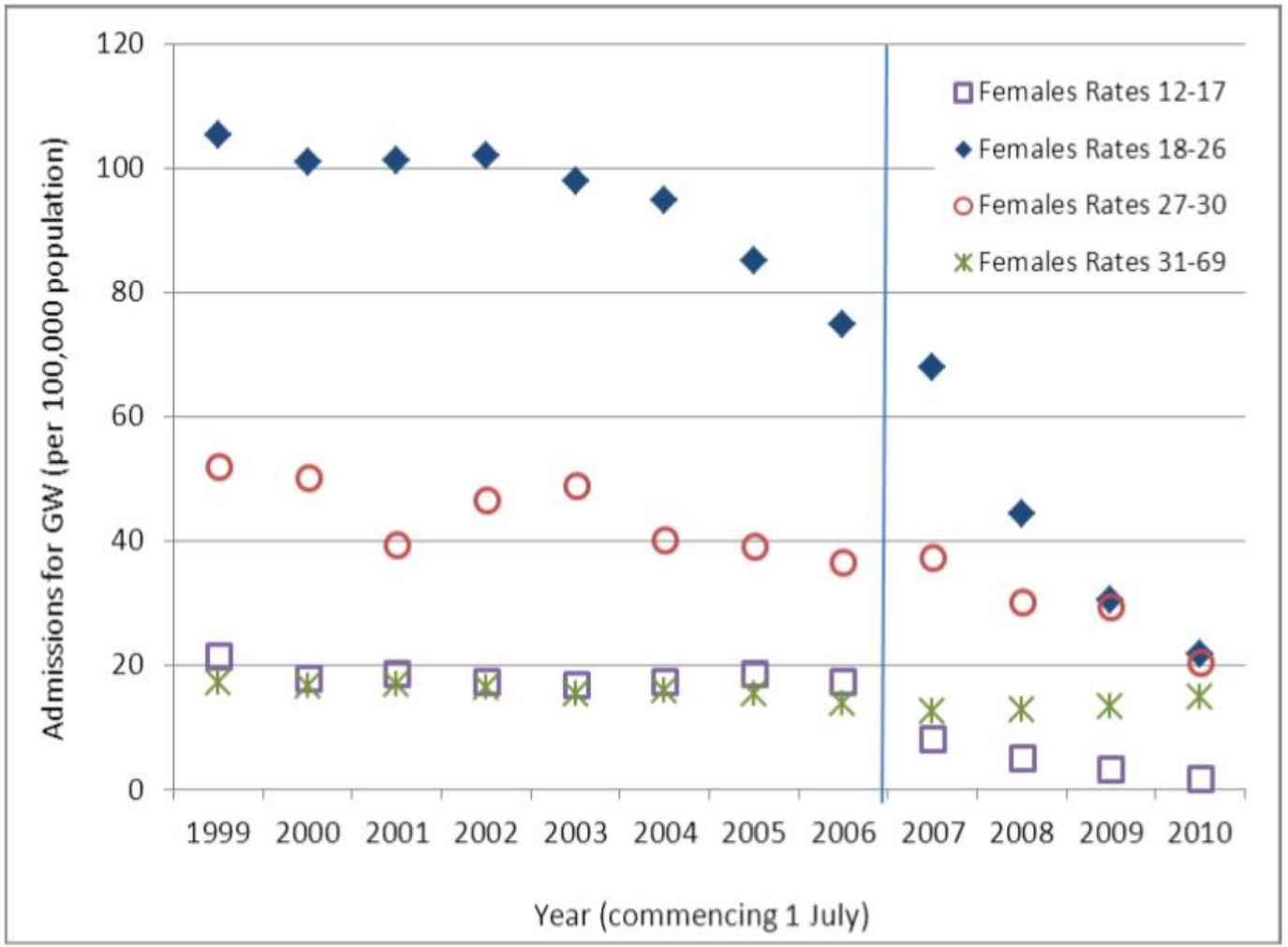


Source: *Cervical screening in Australia 2010–2011*, AIHW and ABS census data

* 95% confidence intervals displayed.

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

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



Line indicates commencement of National HPV Vaccination Program

Data collection and register systems

- State and territory registries
  - Births, deaths and marriages registries
  - Cancer registries
- National registries
  - National Death Index – includes data from Births, deaths and marriage registries
  - Australian Cancer Database – includes data from cancer registries
  - National Cancer Screening Register (NCSR) – cervical* and bowel screening
  - Australian Immunisation Register (AIR) – all immunisations, including HPV^
- Register systems standalone
- Research requires ethics approval and approval from data custodians
- Currently, no routine reporting of cervical screening outcomes by vaccination status.
- Future – routine linkage of AIR with NCSR for routine reporting and evaluation

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*State and territory cervical screening registers operated until December 2017
^National HPV Vaccination Program Register operated until 2018

Modelled evaluations

- Modelled evaluations can inform effectiveness and cost-effectiveness of health interventions
- Recent changes to the National Cervical Screening Program was informed by a modelled evaluation developed by Professor Karen Canfell and her team*
- Dynamic model of HPV vaccination, natural history and cervical screening
- Uses local data to inform modelled assumptions
- Estimates the impact of cervical cancer prevention programs on cervical abnormality rates, cervical cancer incidence and deaths**
- Subsequently used to project the timeframe until cervical cancer elimination in Australia***

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*2017. *Primary HPV testing versus cytology-based cervical screening in women in Australia vaccinated for HPV and unvaccinated: effectiveness and economic assessment for the National Cervical Screening Program.* Lew, Simms et al - The Lancet PH
**2018. *Projected future impact of HPV vaccination and primary HPV screening on cervical cancer rates from 2017-2035: Example from Australia.* Hall, Simms et al – PLoS One
***2018. *The projected timeframe until cervical cancer elimination in Australia: a modelling study.* Hall, Simms et al – The Lancet PH

Primary HPV testing versus cytology-based cervical screening in women in Australia vaccinated for HPV and unvaccinated: effectiveness and economic assessment for the National Cervical Screening Program

Jie-Bin Lew, Kate T Simms*, Megan A Smith, Michaela Hall, Yoon-Jung Kang, Xiang Ming Xu, Michael Caruana, Louiza Sofia Velentzis, Tracey Bessell, Marion Saville, Ian Hammond, Karen Canfell*

Summary

Background Australia's National Cervical Screening Program currently recommends cytological screening every 2 years for women aged 18–69 years. Human papillomavirus (HPV) vaccination was implemented in 2007 with high population coverage, and falls in high-grade lesions in young women have been reported extensively. This decline prompted a major review of the National Cervical Screening Program and new clinical management guidelines, for which we undertook this analysis.

Methods We did effectiveness modelling and an economic assessment of potential new screening strategies, using a model of HPV transmission, vaccination, natural history, and cervical screening. First, we evaluated 132 screening strategies, including those based on cytology and primary HPV testing. Second, after a recommendation was made to adopt primary HPV screening with partial genotyping and direct referral to colposcopy of women positive for HPV16/18, we evaluated the final effect of HPV screening after incorporating new clinical guidelines for women positive for HPV. Both evaluations considered both unvaccinated and vaccinated cohorts.

Findings Strategies entailing HPV testing every 5 years and either partial genotyping for HPV16/18 or cytological co-testing were the most effective. One of the most effective and cost-effective strategies comprised primary HPV screening with referral of women positive for oncogenic HPV16/18 direct to colposcopy, with reflex cytological triage for women with other oncogenic types and direct referral for those in this group with high-grade cytological findings. After incorporating detailed clinical guidelines recommendations, this strategy is predicted to reduce cervical cancer incidence and mortality by 31% and 36%, respectively, in unvaccinated cohorts, and by 24% and 29%, respectively, in cohorts offered vaccination. Furthermore, this strategy is predicted to reduce costs by up to 19% for unvaccinated cohorts and 26% for cohorts offered vaccination, compared with the current programme.

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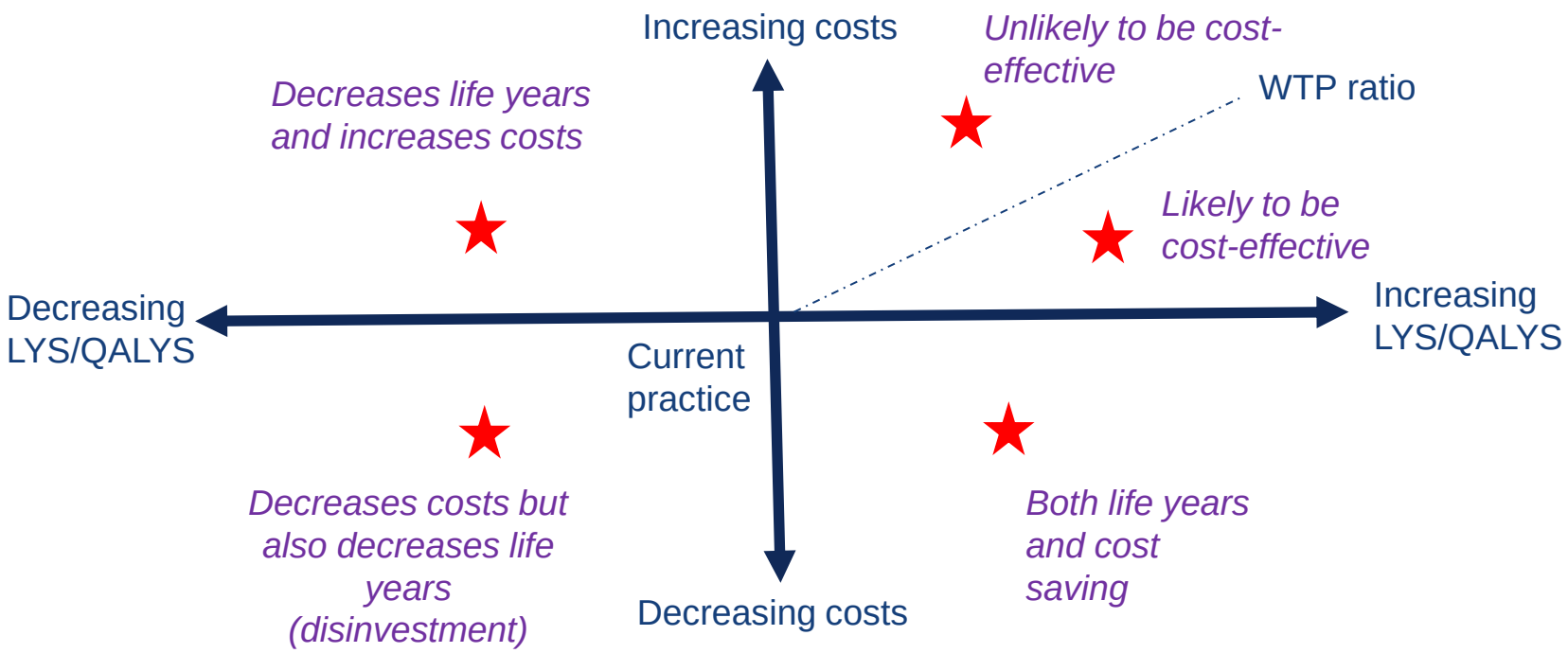
Cost-effectiveness plane

- Comparison of cost-effectiveness of different interventions can be visualised



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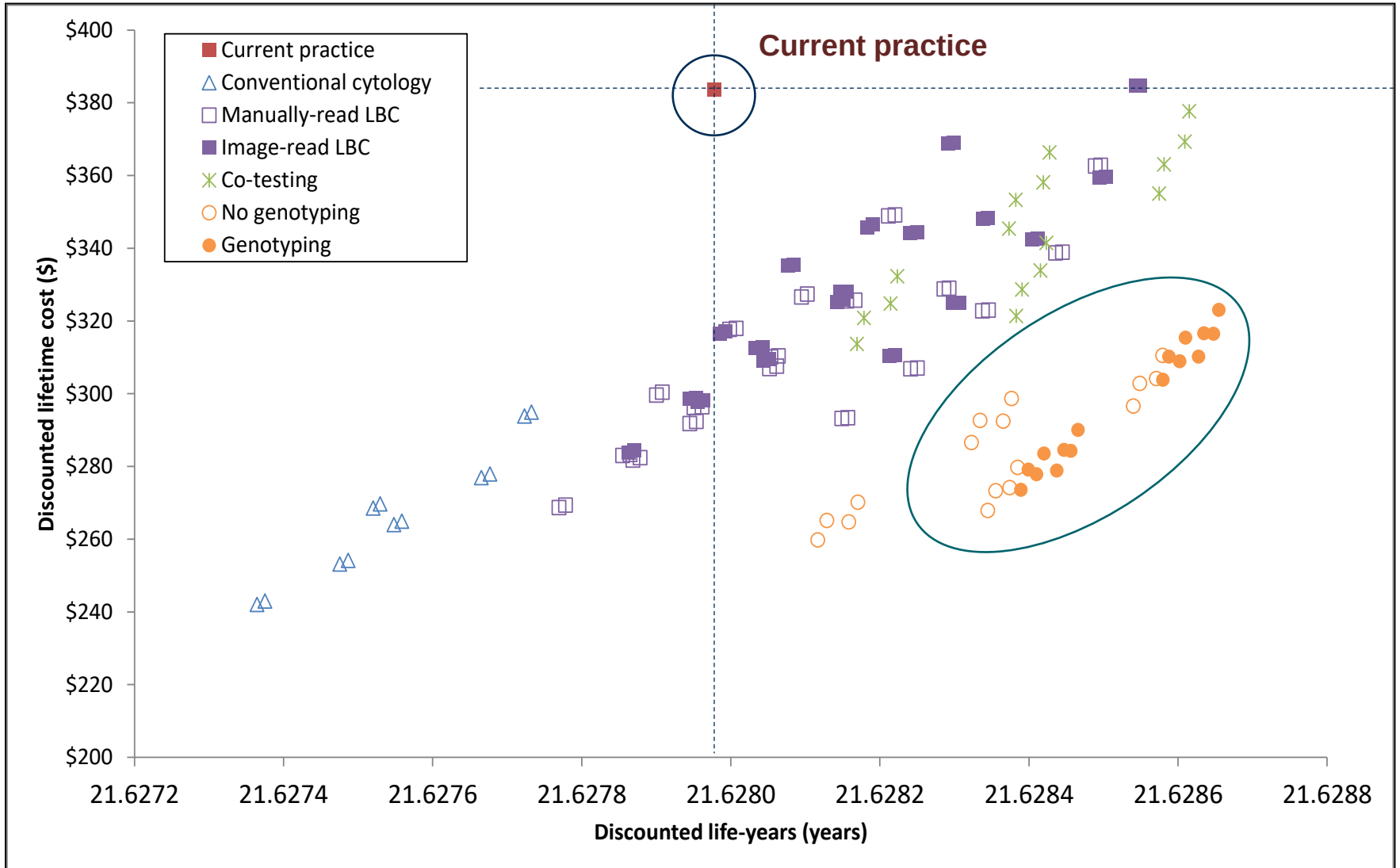
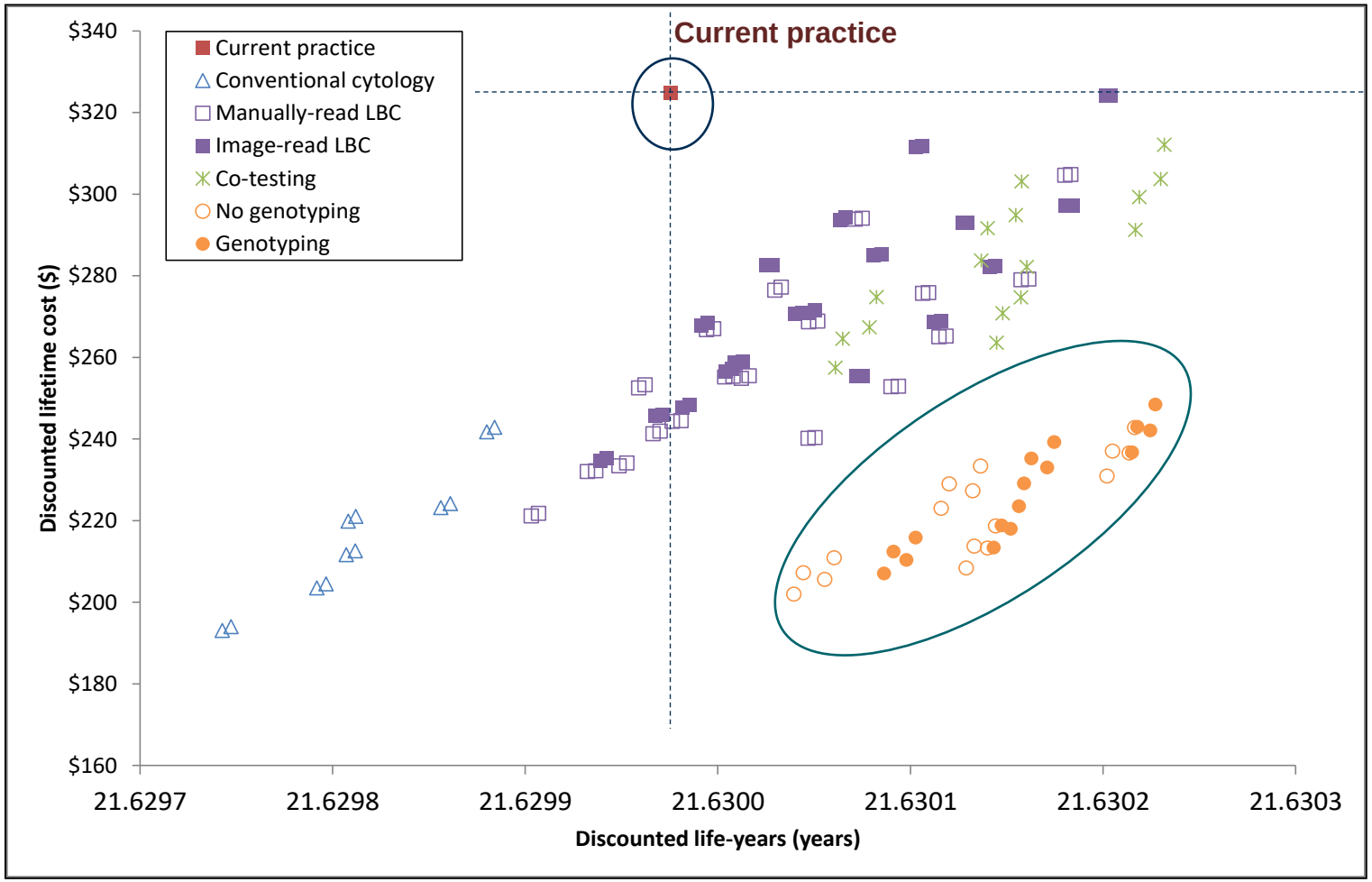
Lew JB, Simms K,* Smith M, Kang YK, Xu X, Caruana M, Walker R and Canfell K. (*Joint first authors)*
National Cervical Screening Program Renewal: Effectiveness modelling and economic evaluation in the Australian setting (Assessment Report). MSAC Application No. 1276. November 2013.

Cost-effectiveness of HPV test - unvaccinated

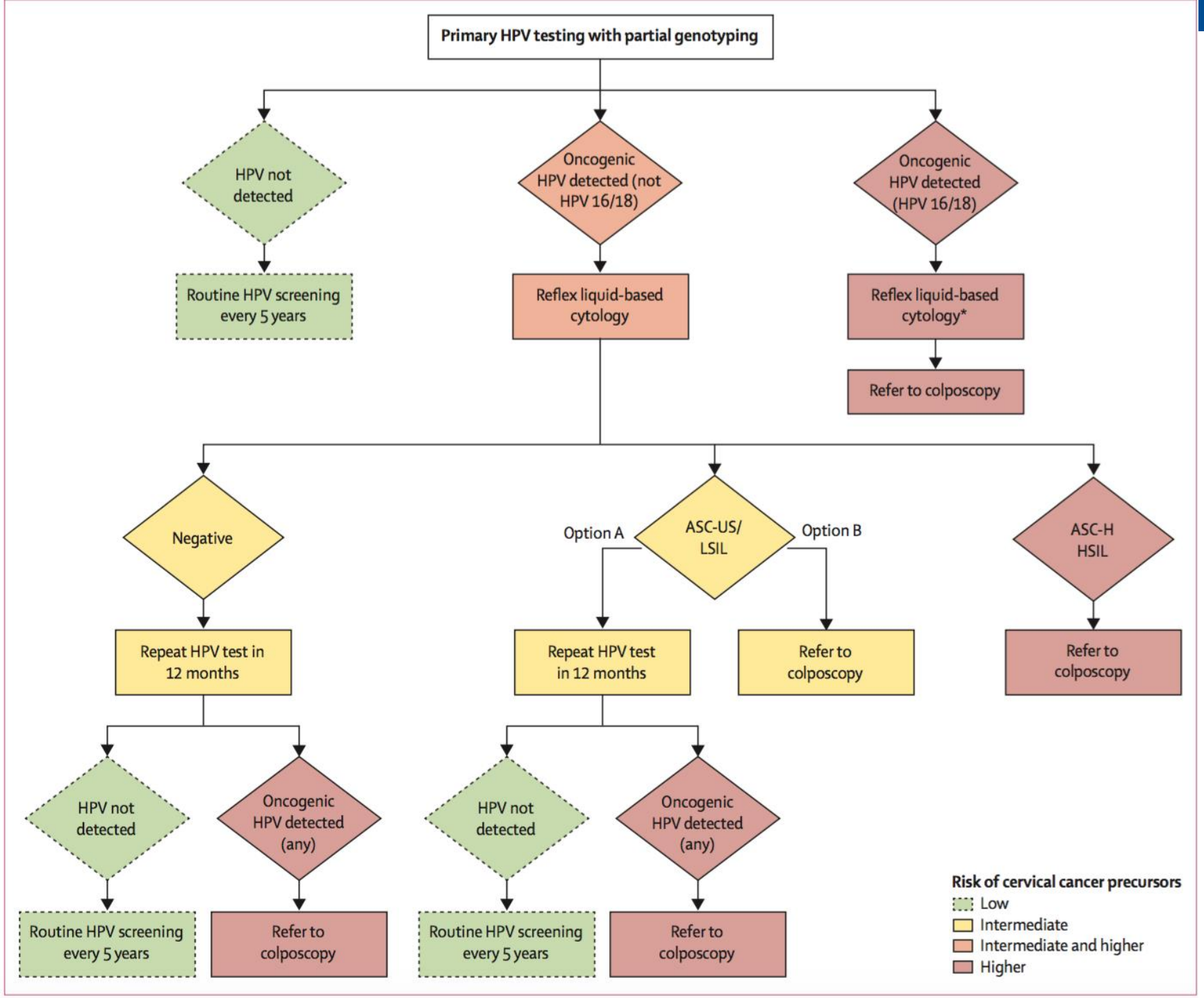


Ref.
Lew et al, 2017 - The Lancet PH

Cost-effectiveness of HPV test - vaccinated



Ref.
Lew et al, 2017 - The Lancet PH



- Partial genotyping
- Screening interval 5 years
- Start age 25
- Exit test 70-74

New guidelines predict a 24-29% reduction in incidence and mortality (with continuation of Vaccination)

New guidelines predict a AU$50 million cost saving (26% reduction)

The projected timeframe until cervical cancer elimination in Australia: a modelling study

Michaela T Hall, Kate T Simms, Jie-Bin Lew, Megan A Smith, Julia ML Brotherton, Marion Saville, Ian H Frazer, Karen Canfell

Summary

Background In 2007, Australia was one of the first countries to introduce a national human papillomavirus (HPV) vaccination programme, and it has since achieved high vaccination coverage across both sexes. In December, 2017, organised cervical screening in Australia transitioned from cytology-based screening every 2 years for women aged from 18–20 years to 69 years, to primary HPV testing every 5 years for women aged 25–69 years and exit testing for women aged 70–74 years. We aimed to identify the earliest years in which the annual age-standardised incidence of cervical cancer in Australia (which is currently seven cases per 100 000 women) could decrease below two annual thresholds that could be considered to be potential elimination thresholds: a rare cancer threshold (six new cases per 100 000 women) or a lower threshold (four new cases per 100 000 women), since Australia is likely to be one of the first countries to reach these benchmarks.

Methods In this modelling study, we used Policy1-Cervix—an extensively validated dynamic model of HPV vaccination, natural history, and cervical screening—to estimate the age-standardised incidence of cervical cancer in Australia from 2015 to 2100. We incorporated age-specific coverage of the Australian National HPV Vaccination Program in girls, including the catch-up programme, and the inclusion of boys into the vaccine programme from 2013, and a change from the quadrivalent to the nonavalent vaccine from 2018. We also modelled the effects of the transition to primary HPV screening. We considered two scenarios for future screening recommendations regarding the cohorts who will be and who have been offered the nonavalent vaccine: either that HPV screening every 5 years continues, or that no screening would be offered to these women.

Findings We estimate that, in Australia, the age-standardised annual incidence of cervical cancer will decrease to fewer than six new cases per 100 000 women by 2020 (range 2018–22), and to fewer than four new cases per 100 000 women by 2028 (2021–35). The precise year of attaining these rates is dependent on the population used for age-standardisation, HPV screening behaviour and test characteristics, the incremental effects of vaccination of men on herd immunity in women, and assumptions about the future frequency of benign hysterectomies. By 2066

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Elimination predictions from modelling

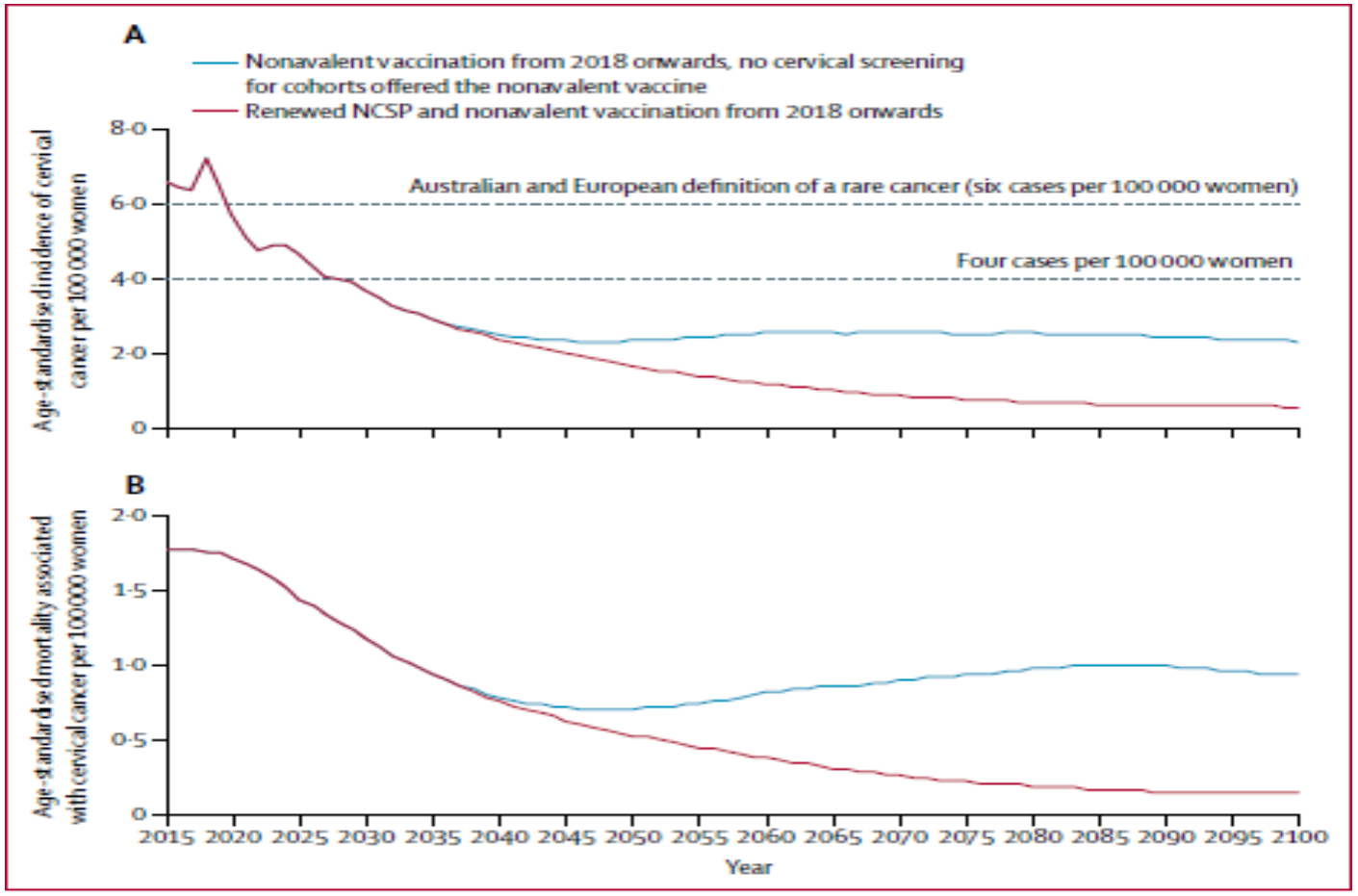

Figure 1: **The (A) age-standardised annual incidence of invasive cervical cancer and (B) associated mortality**
Data are the model predictions for rates from 2015 to 2100, accounting for the transition to primary human papillomavirus screening in 2017 (the renewed NCSP) and the switch to nonavalent vaccine in 2018.
NCSP=National Cervical Screening Programme.

If high-coverage vaccination and screening is maintained, at an elimination threshold of 4 new cases per 100 000 women annually, cervical cancer could be considered to be eliminated as a public health problem in Australia within the next 20 years.

Ref: 2018. Hall, Simms et al – The Lancet PH

A new evaluation of the impact of HPV vaccination

- With the introduction of Gardasil 9, it is timely to undertake another evaluation of the impact of the HPV vaccination program in Australia.
- Undertaken by the National Centre for Immunisation Research and Surveillance (NCIRS).
- To focus on the impact of the program since the 2014 evaluation including: immunisation coverage, Adverse Events Following Immunisation, disease burden and stakeholder perspectives on the impact of the program.
- Aims to inform recommendations to further enhance the program.
- Commenced August 2019.
- Final Report anticipated in mid-2020.

Acknowledgement: Alison Lang for assistance with slides

- Further information:

National Immunisation Program

https://www.health.gov.au/initiatives-and-programs/national-immunisation-program

Australian Immunisation Register

https://www.humanservices.gov.au/individuals/services/medicare/australian-immunisation-register

National Cervical Screening Program

www.cancerscreening.gov.au

National Cancer Screening Register

https://www.ncsr.gov.au/