

IMPACT

National HPV
Monitoring Program

Human papillomavirus and vaccination for cervical cancer

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VIRUSES AND CANCER

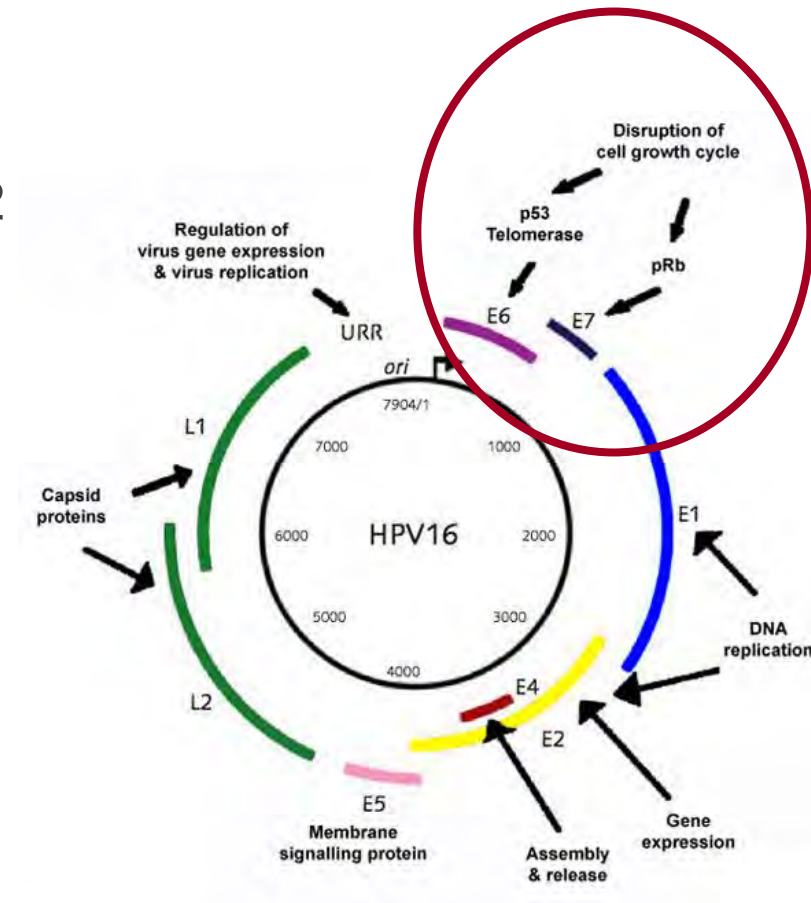
- **Responsible for around 15% of the global burden of cancer**
 - Hepatitis B and C with liver cancer
 - Epstein-Barr virus with Burkitt's lymphoma
 - The human T-cell lymphotropic virus (HTLV1) with adult T-cell leukaemia
 - Human herpesvirus type 8 (HHV-8) with Kaposi's sarcoma
 - **Human papillomavirus (HPV) with cervical and other anogenital cancers (1982)**



Harald zur
Hausen

HUMAN PAPILLOMAVIRUSES

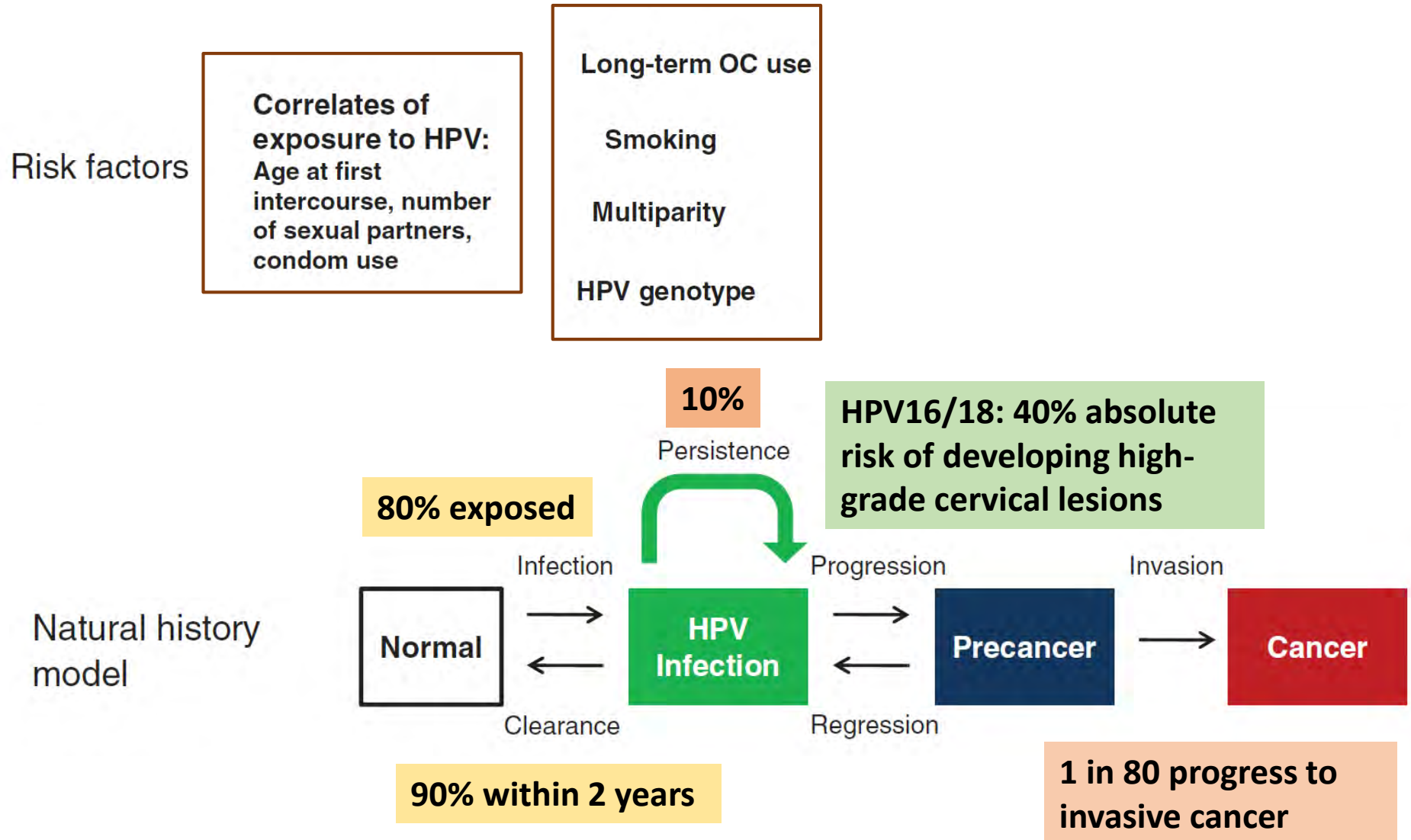
- **8000-base pair, double-stranded, circular DNA viruses**
 - 8 genes: 6 early (viral replication) & 2 late (capsid formation)
- **~150 related types, of those ~40 infect the genital mucosa**
 - 15 classified as oncogenic or high-risk (HR) associated with cancer
 - Low-risk (LR) associated with benign genital warts
- **Varying carcinogenicity related to expression of E6 and E7 oncoproteins**
 - HPV16 and HPV18 are the most oncogenic



HPV IS A COMMON VIRUS

- HPV is the most common sexually transmitted agent worldwide
- Easily transmitted through skin-to-skin contact; mostly through genital contact/intercourse
 - Estimated 20-40% probability of male to female transmission per coital act
 - Higher than other viral STIs (i.e. HSV-2; 1 in 1000) but similar to bacterial STIs such as chlamydia (20%) and gonorrhea (50%)
- Infections are mostly asymptomatic and clears on their own

NATURAL HISTORY



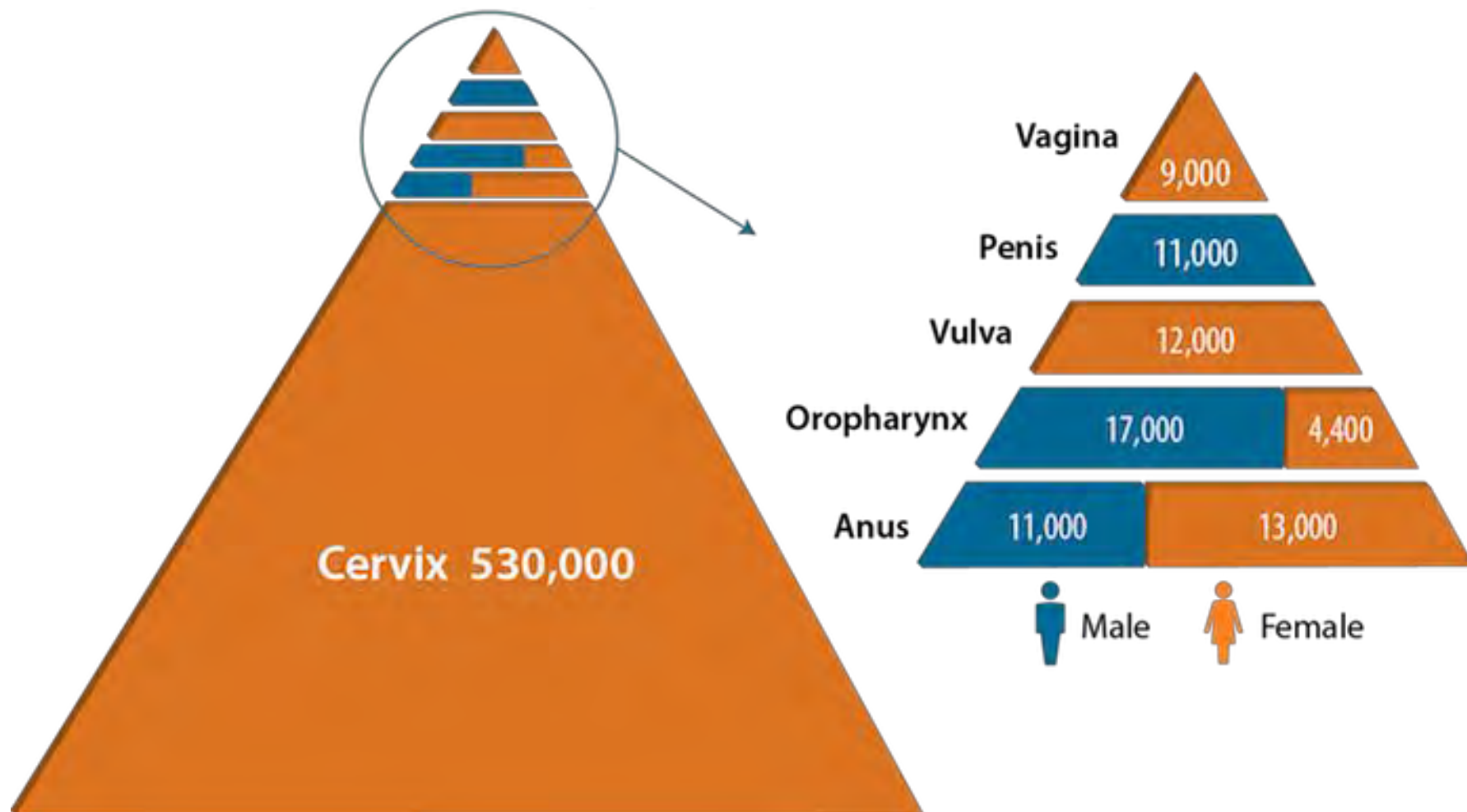
HPV AND CANCER

- Persistent infection with HR-HPV plays a central role in a number of malignancies

Cancer site	Proportion HPV-Associated	Proportion of HPV-Associated Attributable to HPV16/18
Cervix	100%	70%
Oropharynx	35%	89%
Anus	90%	92%
Vulva	40%	80%
Vagina	40%	80%
Penis	40%	63%

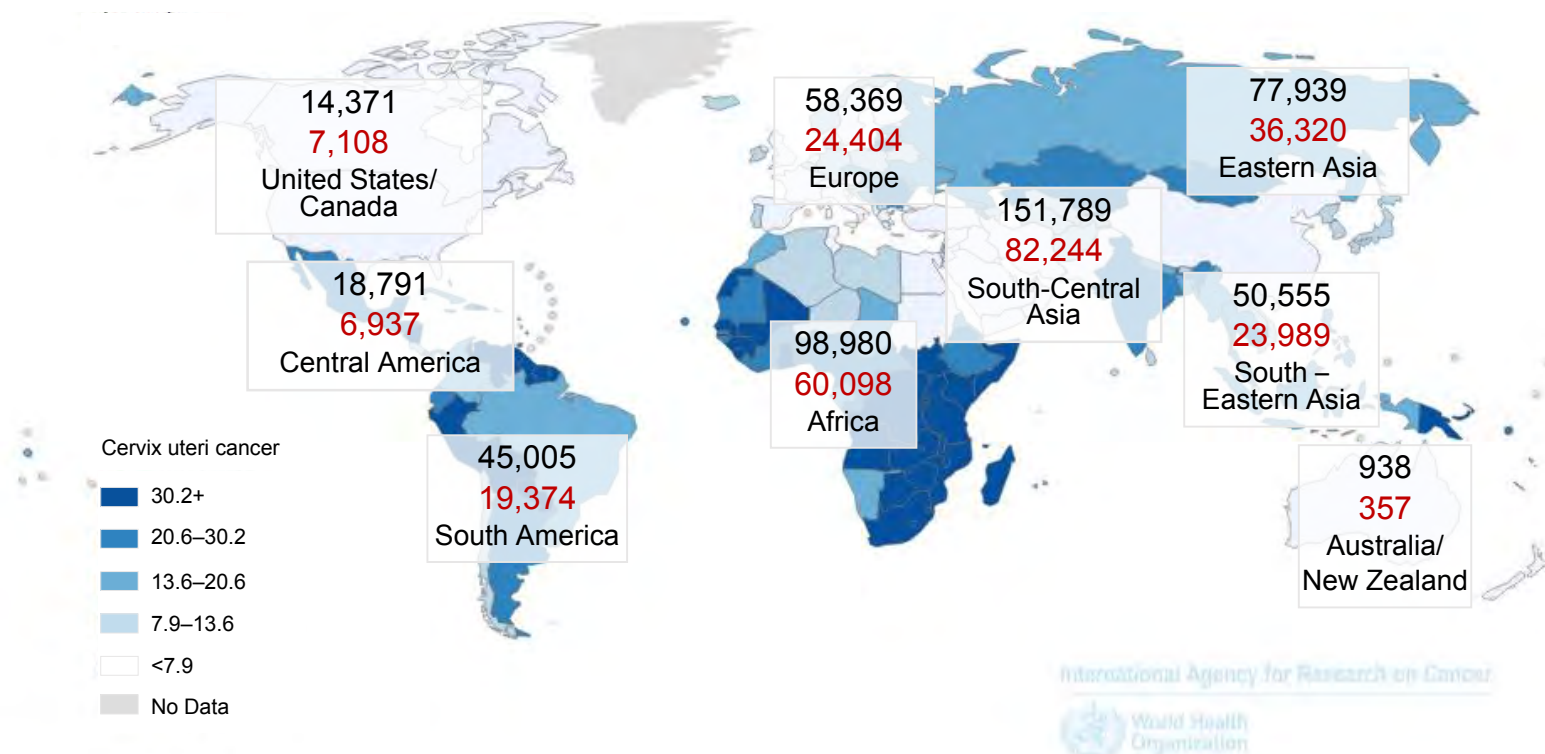
BURDEN OF DISEASE

Annual number of cancers caused by HPV worldwide



GLOBAL ESTIMATES OF CERVICAL CANCER INCIDENCE AND MORTALITY (2012)

- Preventable disease related to disparities, mostly socioeconomic, in access to adequate healthcare
- ~84% of cases occur in less developed regions of the world



^aNumber of cases shown in black text; number of deaths shown in red text.

NATIONAL CERVICAL CANCER SCREENING PROGRAM

- Organised cervical screening program since 1991
- The Papanicolaou test (Pap test or smear) used to detect potentially pre-cancerous and cancerous HPV related changes
- Biennial Pap test for 18-69 year olds
 - 2-year participation at 58%
 - 5-year participation at 83%



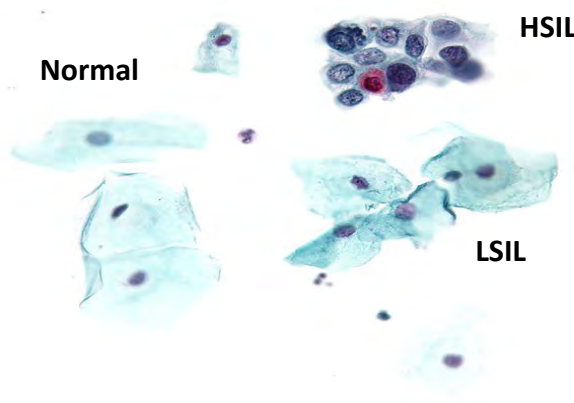
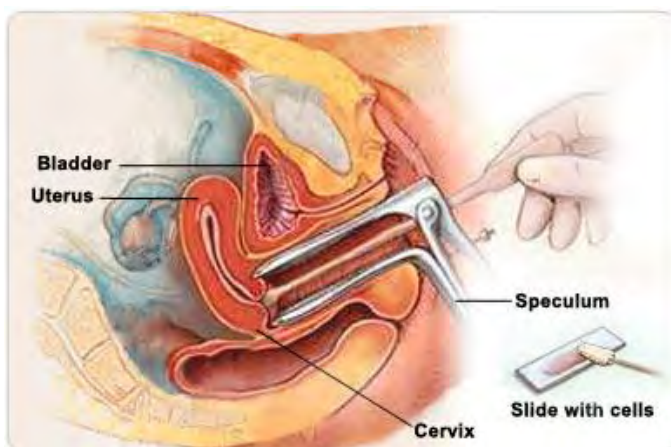
**When did
you last have
a Pap smear?**

Most cancer of the cervix could be prevented if each woman had a Pap smear every two years

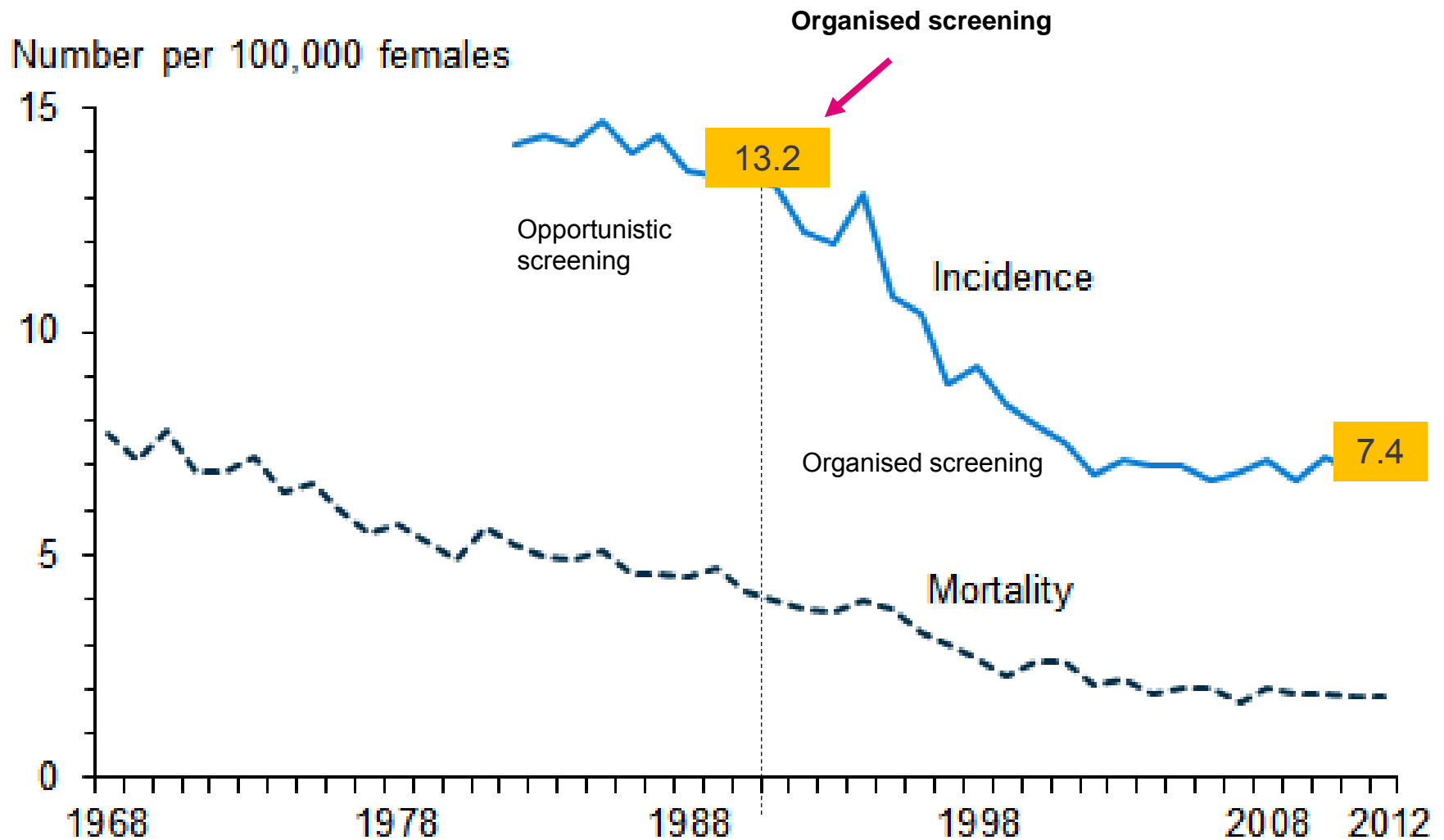
**National Cervical
Screening Program**

A joint Australian, State and Territory Government initiative

DON'T MAKE EXCUSES. MAKE AN APPOINTMENT



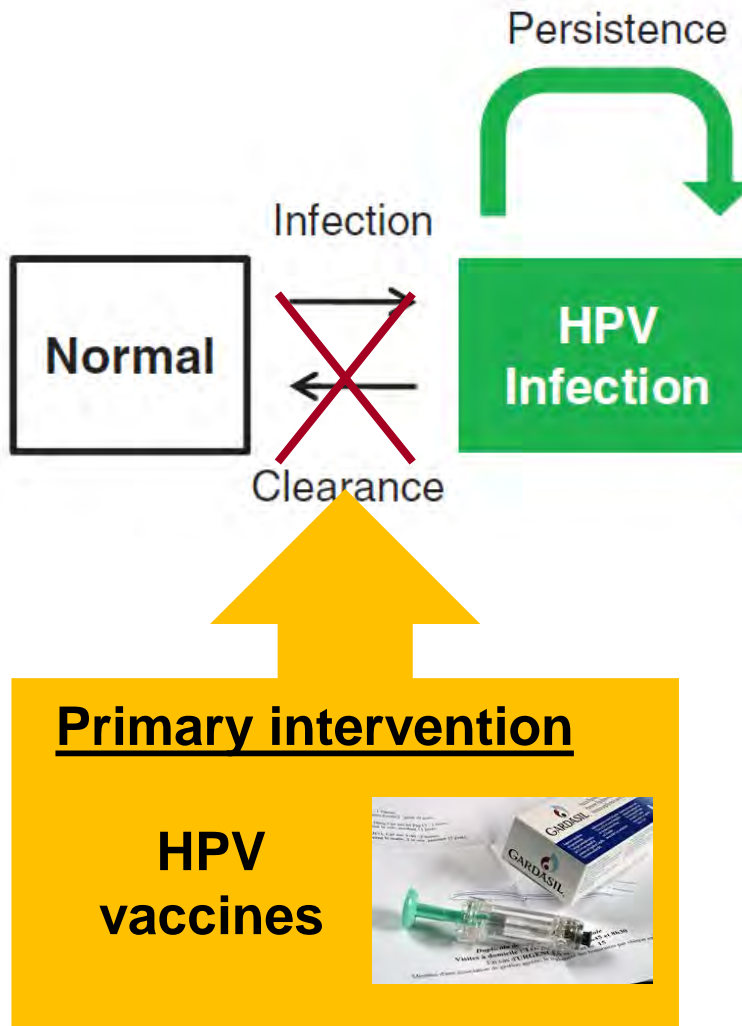
IMPACT OF ORGANISED SCREENING IN AUSTRALIA



CERVICAL CANCER IN AUSTRALIA

- 14th most common cancer in women
- **Populations at highest risk:**
 - New migrants from countries with no organised screening
 - Lapsed screeners or women who never screen
 - 80% of new cervical cancer cases
 - Aboriginal and Torres Strait Islander women
 - 2X higher incidence
 - 4X higher mortality

PROPHYLACTIC HPV VACCINES



Ian Frazer AC

- 1991-2005 Developed the first vaccine for HPV (Gardasil)



“God’s gift to women”
(Weekend Australian, March 2006)

PROPHYLACTIC HPV VACCINES

Gardasil
Quadrivalent
(HPV6/11/16/18)



70% of cervical and 90% other HPV-related cancers + 90% of genital warts
(Gardasil)

Cervarix:
Bivalent (HPV16/18)



Gardasil-9:
9-valent
(HPV6/11/16/18/31/33/45/52/58)

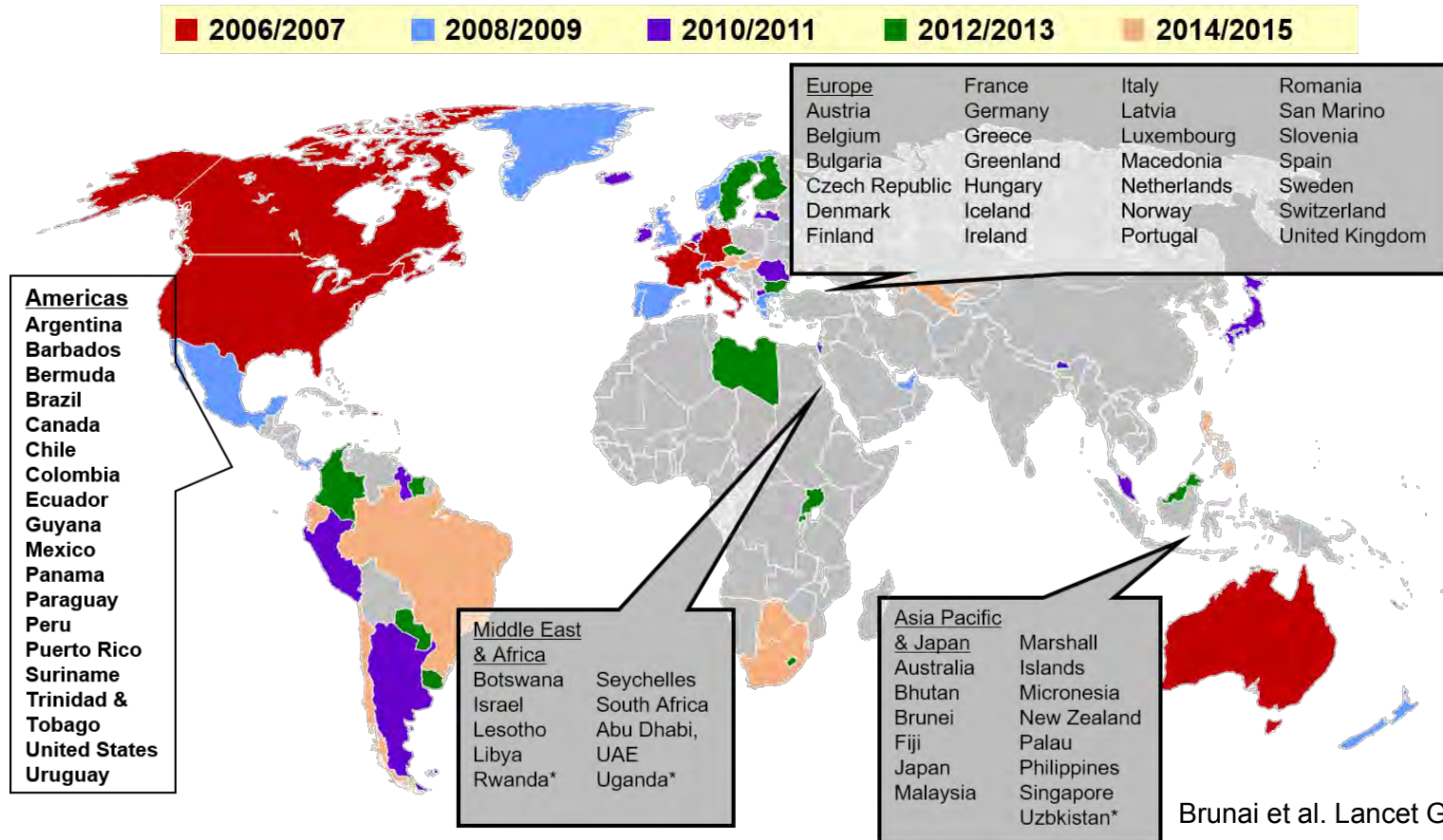


90% of cervical and other HPV-related cancers + genital warts

PROPHYLACTIC HPV VACCINES

Prophylactic HPV vaccine programs constitute major worldwide public-health initiatives

- Implemented in >60 countries; School/clinic based delivery models



NATIONAL HPV VACCINATION PROGRAM

- First country to implement national funded HPV vaccination program - April 2007
- Routine school based vaccination, with initial two year catch-up phase
 - 1st year of high school, usual age 12-13
- Quadrivalent HPV vaccine
 - Three doses: 0, 2 and 6 months



National cervical cancer vaccinations begin April 2007.

Cervical cancer is the second most common cancer in women worldwide which is almost always caused by the human papillomavirus (HPV).

The good news is that a new vaccine, developed in Australia, can protect against HPV, the cause of up to 70% of cervical cancers.

The other good news is that the Australian Government is making the cervical cancer vaccine available free to all females aged 12 to 26 under the National HPV Vaccination Program.

For girls at school, the program starts in April 2007. A consent form will be sent home shortly for parents to fill in and return.

For women who have left school, and are under 27, the free vaccine will be available from your GP or community immunisation clinic from July.

The vaccine doesn't prevent all cervical cancers, so regular Pap smears are still essential.

But a free cervical cancer vaccine is still very good news for women.

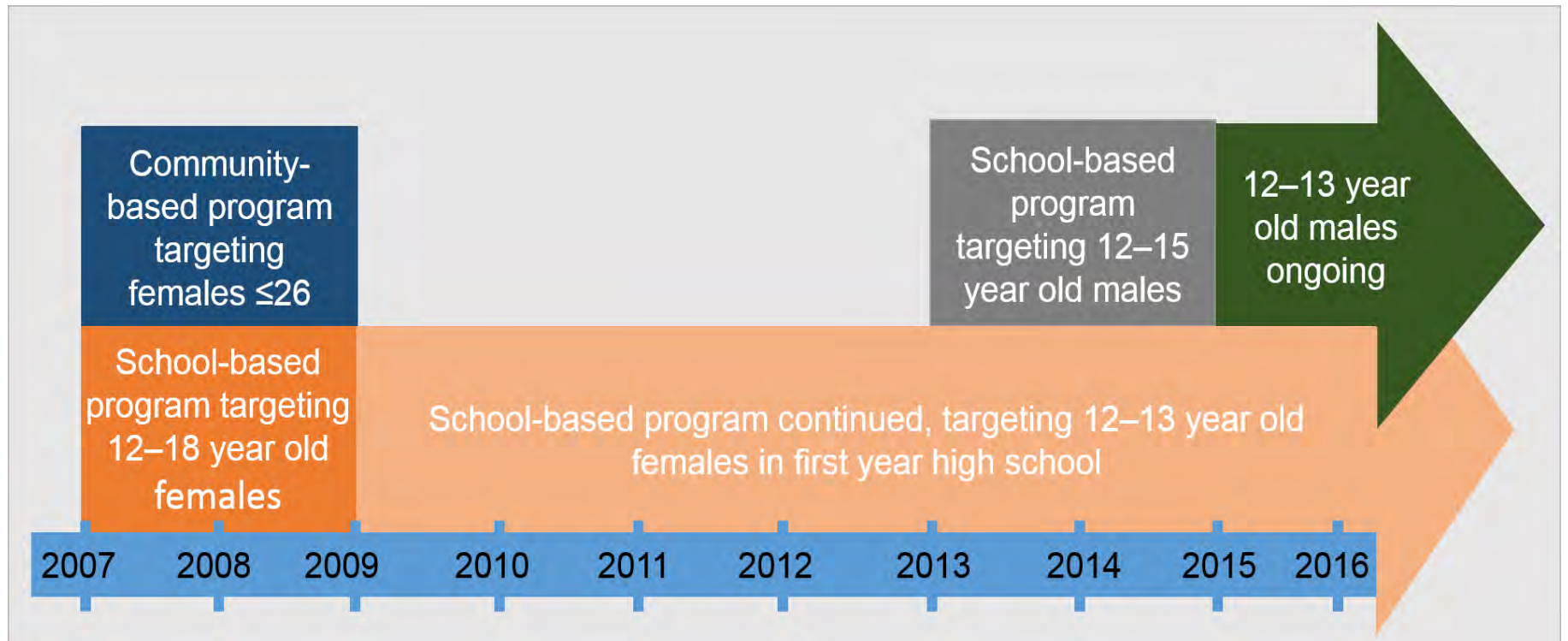
Help protect your daughter from cervical cancer. Sign the consent form.

For more information:
National Immunisation Hotline 1800 671 811
australia.gov.au/cervicalcancer

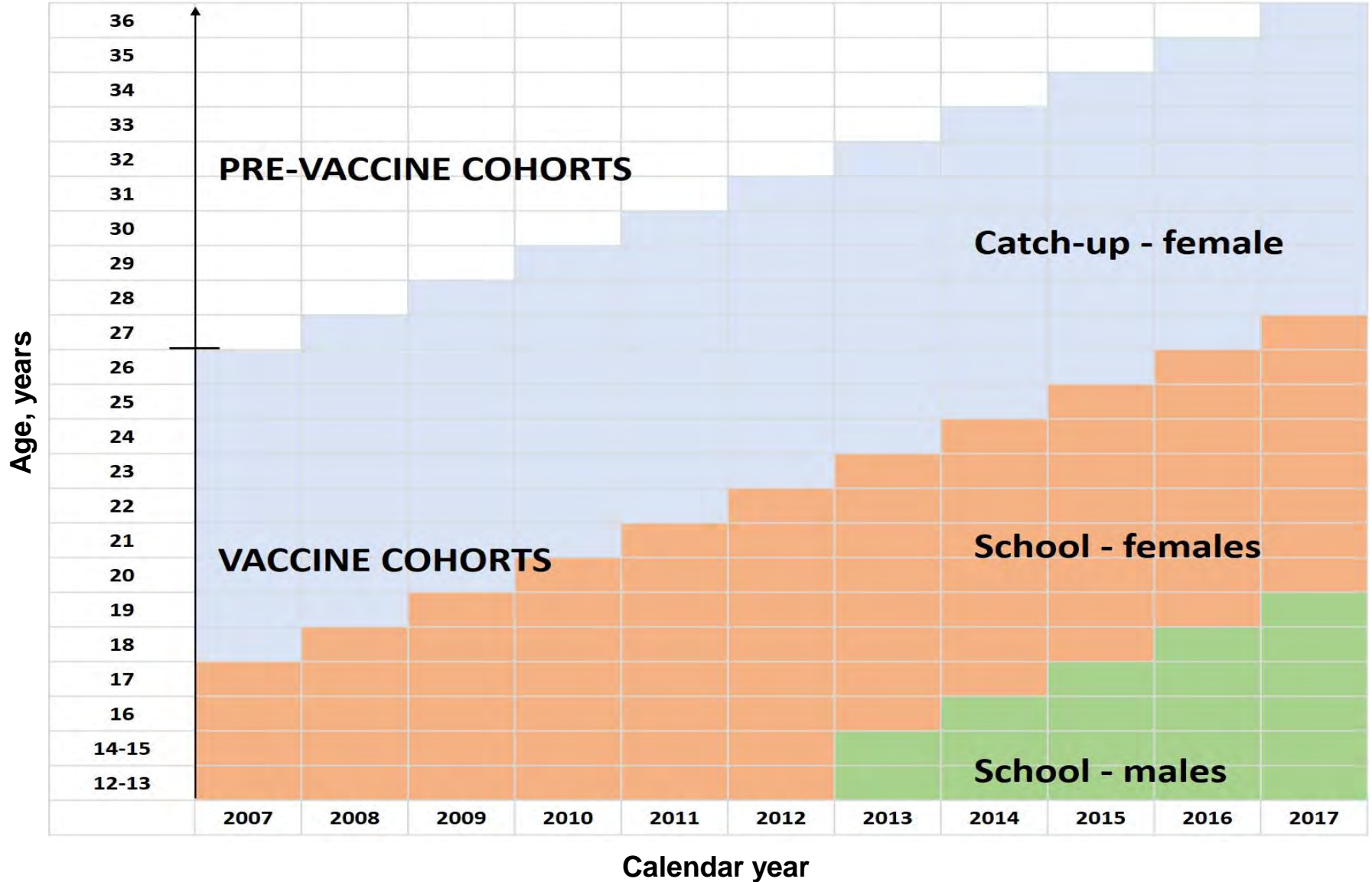


Australian Government

TIMELINE



VACCINE COHORTS TO 2017



THE REGISTER

- Established to support the HPV vaccination program
- Records information about HPV vaccine doses administered in Australia
 - Mandatory reporting of doses administered in schools
 - Voluntary reporting of doses administered in the community



National HPV Vaccination
Program Register

COVERAGE DATA

National vaccination coverage for females, by age in years and dose, in mid 2009



COVERAGE DATA

National three dose vaccination coverage (%) for girls 15 years of age in 2011 through 2014, and males age 15 years in 2014, by state/territory

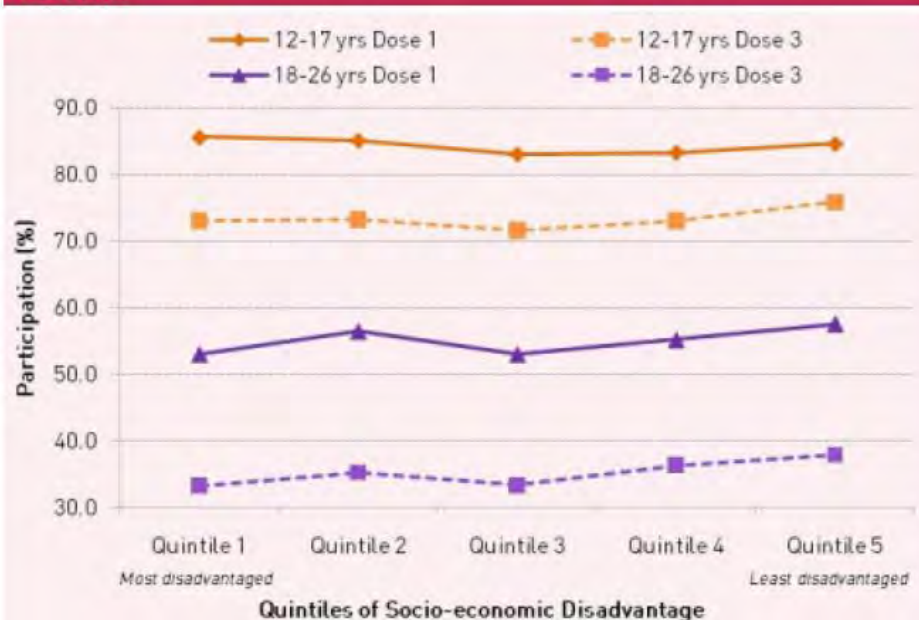
- Relatively stable coverage (>70%) is being achieved over time.
- Some variation in coverage by jurisdiction suggesting more effective delivery in some states/territories than others

	State or territory								Aust.
	ACT	NSW	NT	Qld	SA	Tas.	Vic.	WA	
2011	74.2	74.5	87.0	72.4	68.0	66.5	76.5	64.6	72.9
2012	74.4	71.0	84.5	69.4	71.0	64.7	74.2	70.1	71.4
2013	74.0	68.6	81.4	71.0	72.4	64.1	75.2	71.2	71.4
2014	70.0	69.8	77.3	73.5	73.1	67.7	77.4	76.0	73.4
2014 males*	64.2	56.9	55.4	61.1	63.3	55.1	67.8	61.0	61.4

COVERAGE DATA

Equity in vaccination versus screening

National HPV Vaccination Program by socioeconomic status, Victoria

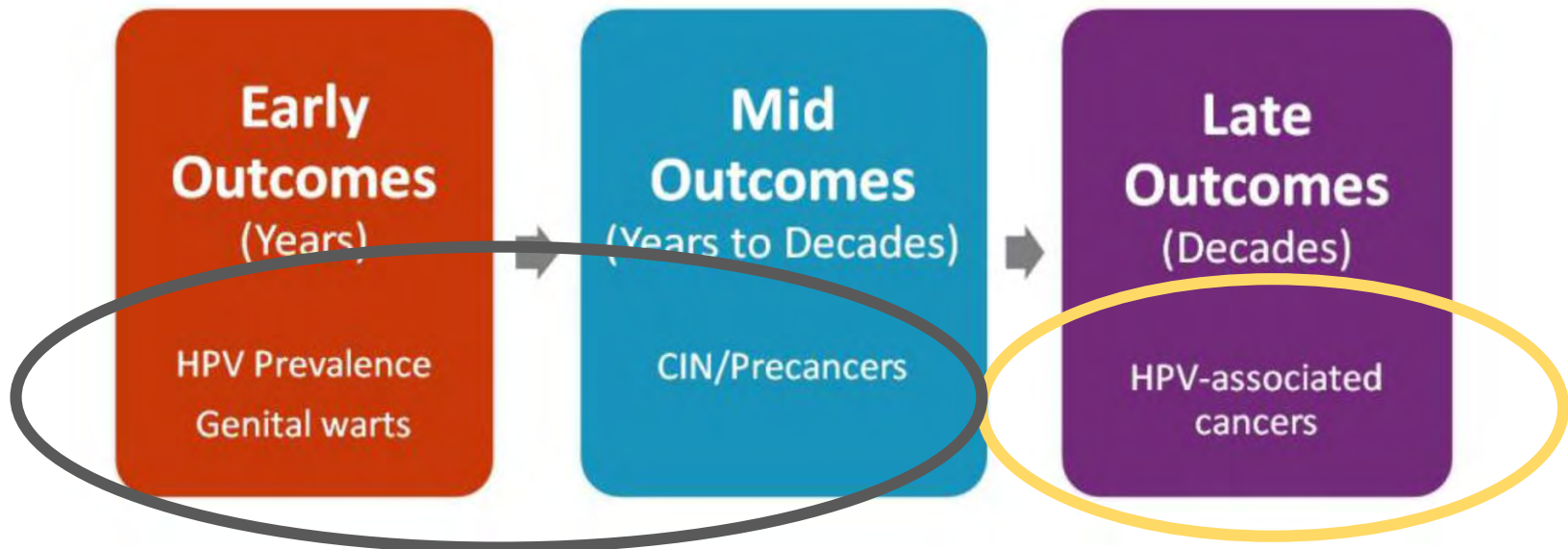


National Cervical Screening Program by socioeconomic status, Victoria



REAL WORLD IMPACT OF VACCINATION

- Program currently in its 11th year
- Impact monitoring is challenging because expected reductions in cancer will take decades to be realised
- Important to monitor changes in early endpoints



IMPACT MONITORING

**Early
Outcomes**
(Years)

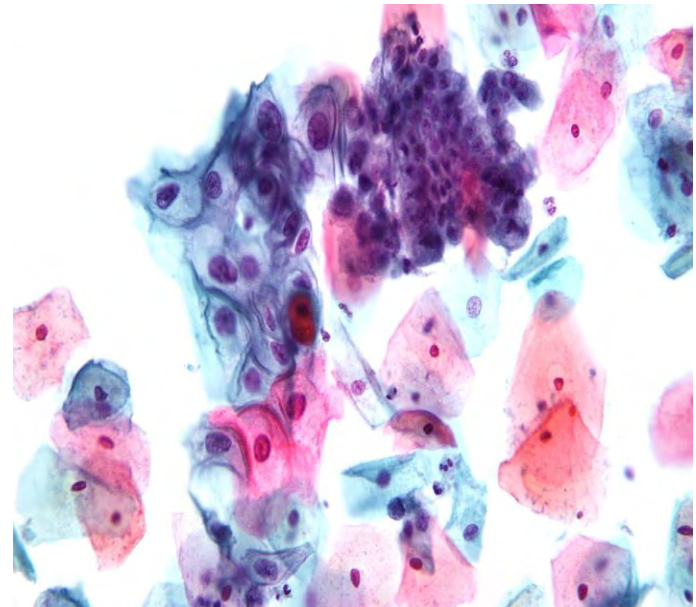
HPV Prevalence
Genital warts

Impact on HPV infection in young women shortly after sexual debut

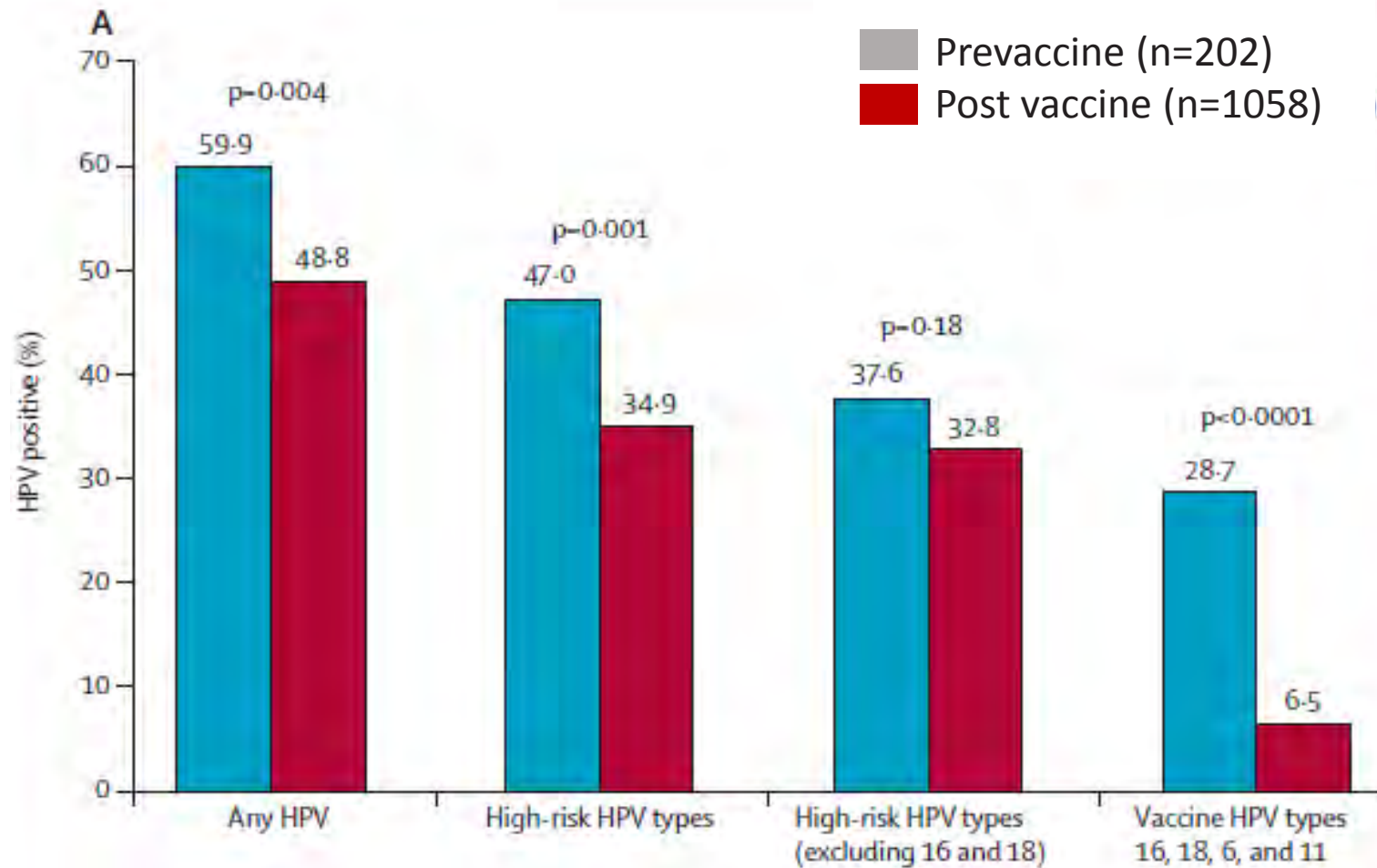
- Before and after HPV prevalence surveys
- Young women presenting for cervical cancer screening
- Baseline survey conducted in pre-vaccine cohorts
- Subsequent surveys conducted in vaccine-eligible cohorts using same recruitment and testing methodologies
- Extent of impact can be quantified

HPV INFECTIONS AMONG 18-24 YEAR OLD WOMEN ATTENDING CERVICAL SCREENING

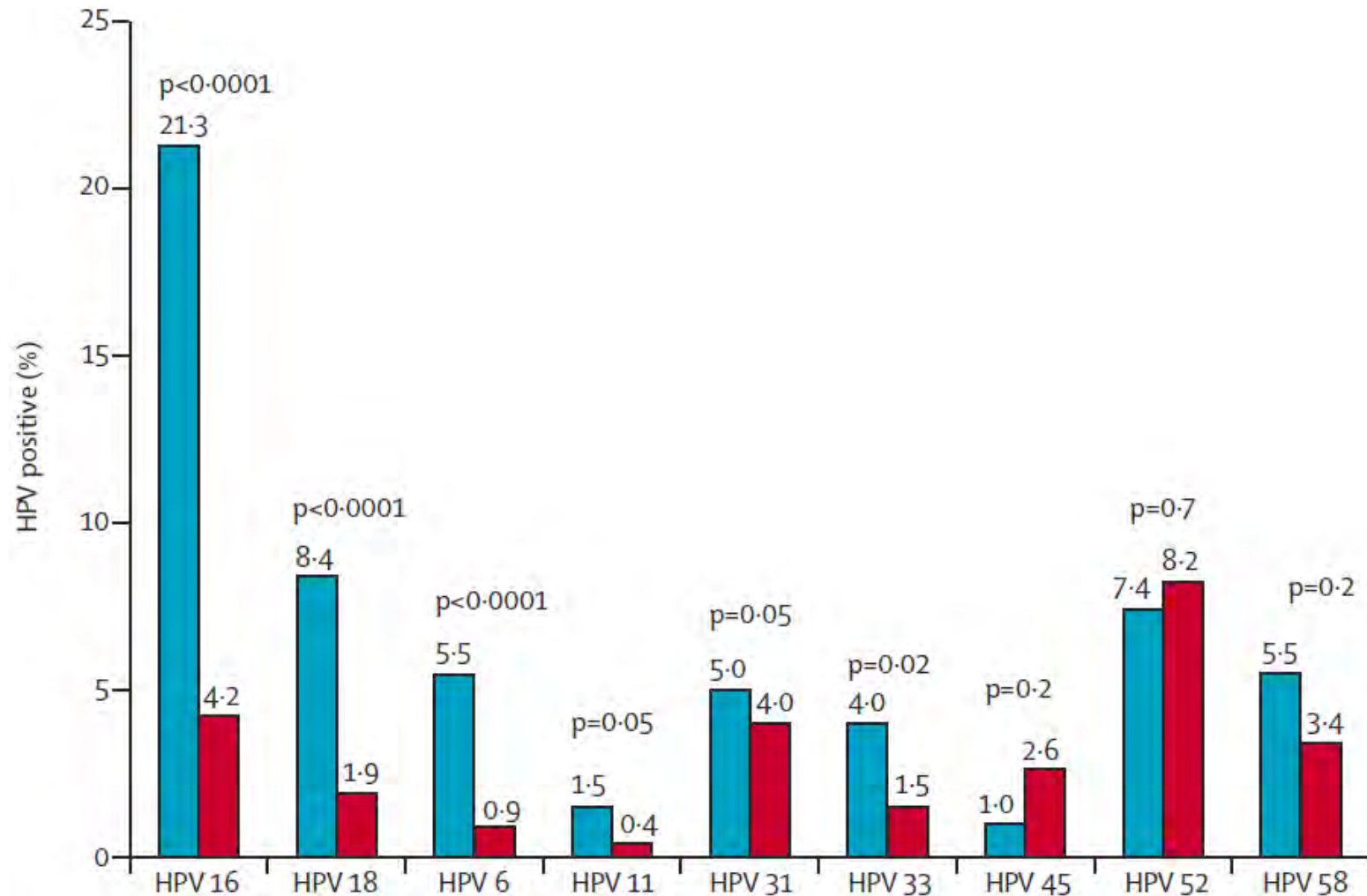
- Cervical HPV prevalence in Australia
 - Two cross-sectional studies, 1 before (2005-2007) and 1 after (2010-2012) vaccine introduction
 - Women age 18-24 years at public family clinics undergoing routine Pap test
 - HPV detection by Pap test specimens



HPV INFECTIONS AMONG 18-24 YEAR OLD WOMEN ATTENDING CERVICAL SCREENING



HPV INFECTIONS AMONG 18-24 YEAR OLD WOMEN ATTENDING CERVICAL SCREENING



HPV INFECTIONS AMONG 18-24 YEAR OLD WOMEN ATTENDING CERVICAL SCREENING

	Crude Rate of HPV Prevalence	
	Ratio	<i>P</i> value
Vaccine-target HPV types 6, 11,16, 18		
Prevaccine implementation	1.0	--
Postvaccine implementation	0.23 (0.17-0.31)	<.0001
Unvaccinated	0.65 (0.44-0.97)	0.0370
Partial or unconfirmed	0.26 (0.17-0.39)	<.0001
Vaccinated	0.08 (0.04-0.15)	<.0001

IMPACT MONITORING

**Early
Outcomes**
(Years)

HPV Prevalence

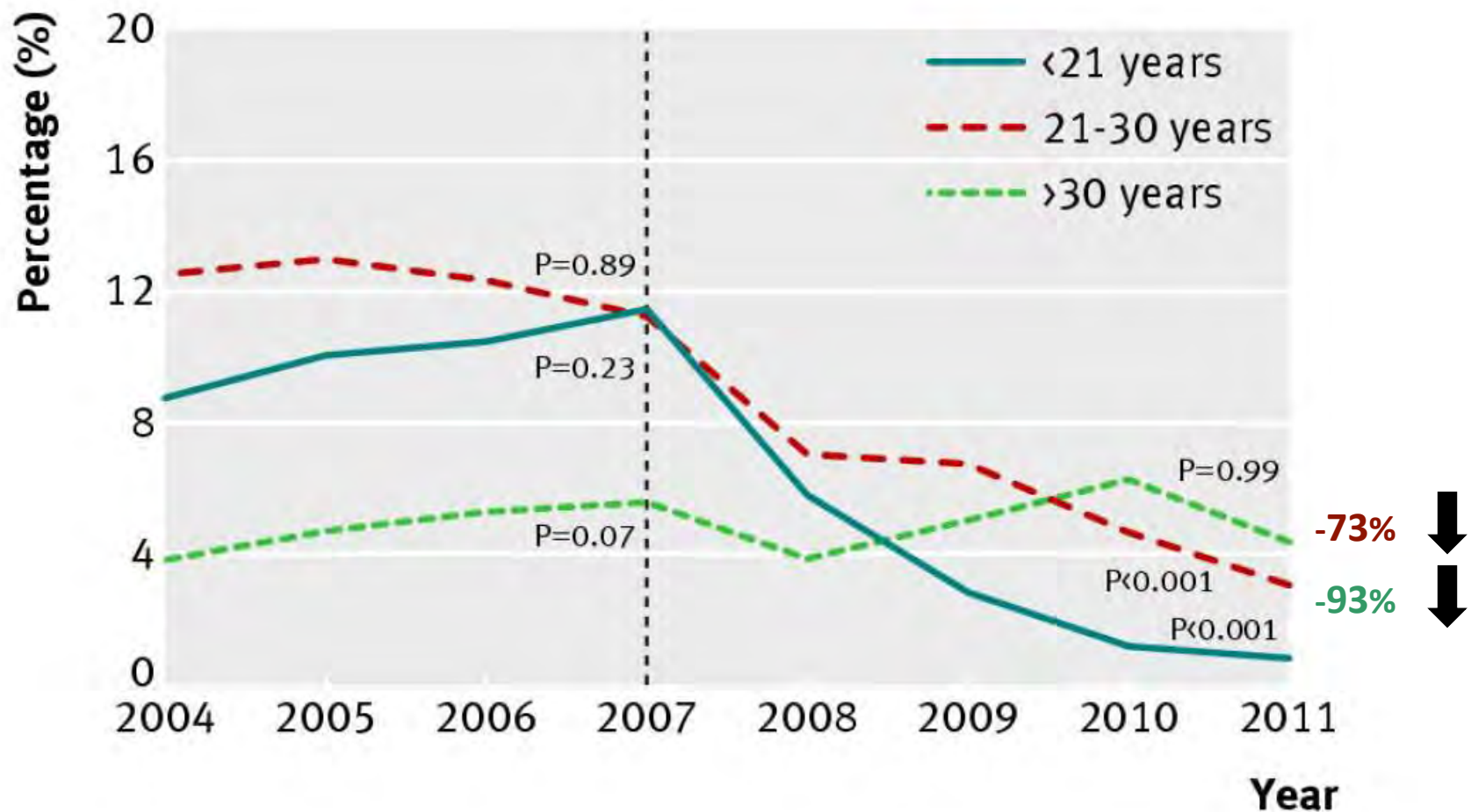
Genital warts

Impact on genital warts

- Ecological trends over time
- Routinely collected hospital admissions data and sexual health sentinel surveillance networks

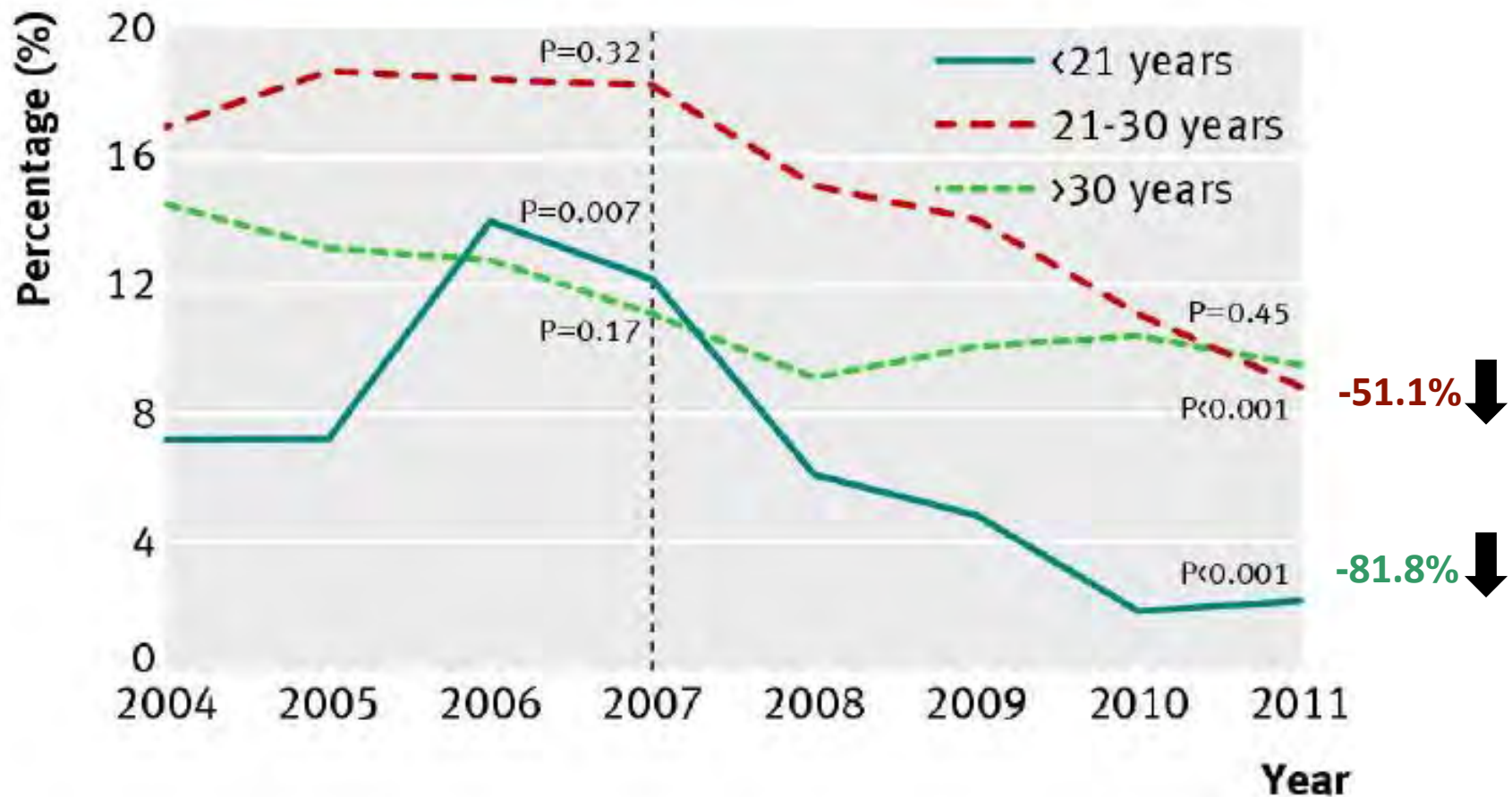
TRENDS IN GENITAL WARTS

Proportion of Australian-born women diagnosed with genital warts at sexual health clinics



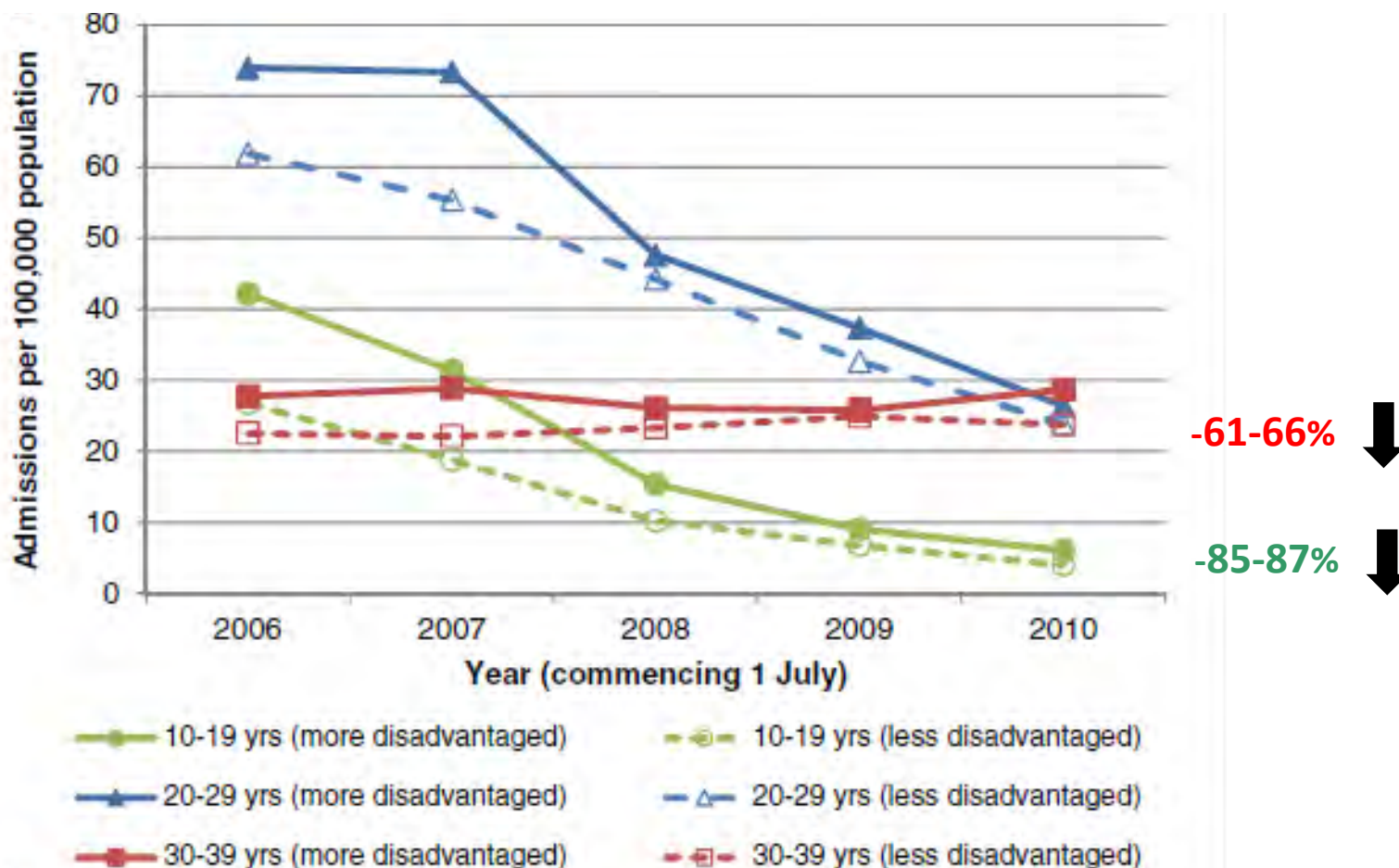
TRENDS IN GENITAL WARTS

Proportion of Australian-born heterosexual men diagnosed with genital warts at sexual health clinics



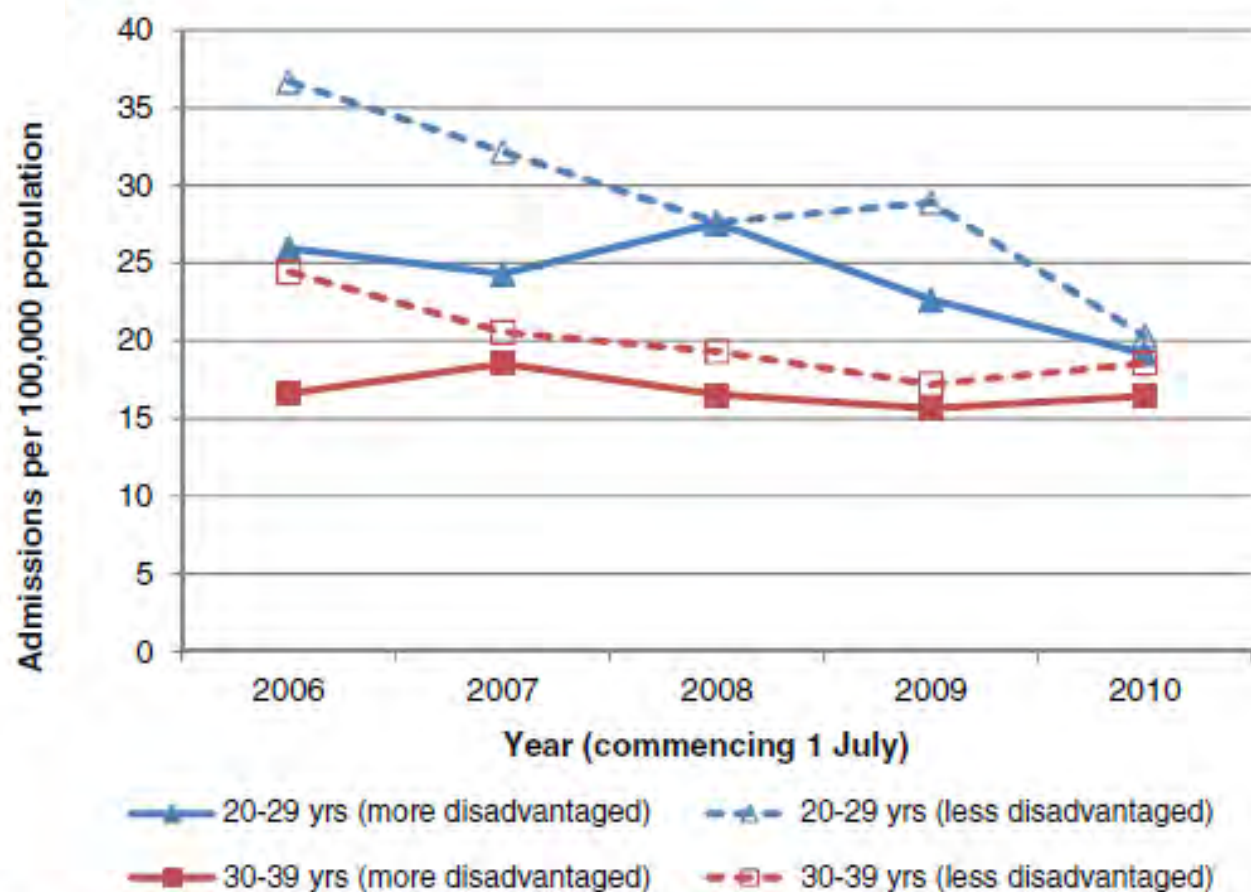
TRENDS IN GENITAL WARTS

Admissions involving diagnosis of genital warts per 100,000 population by socioeconomic status and age group, in females



TRENDS IN GENITAL WARTS

Admissions involving diagnosis of genital warts per 100,000 population by socioeconomic status and age group, in males

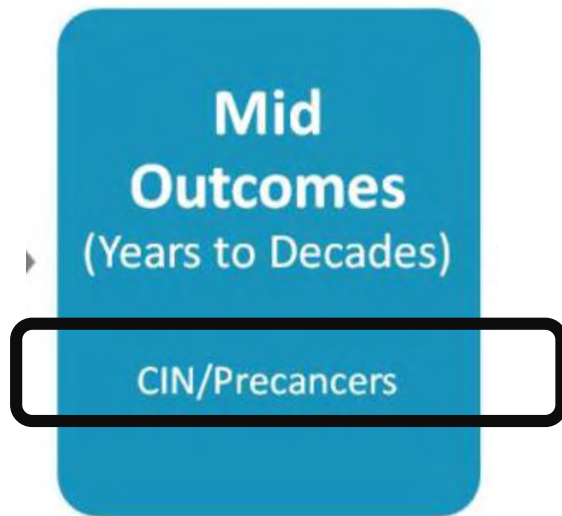


23-40%



Males aged 10–19 years were excluded due to the small number of admissions

IMPACT MONITORING

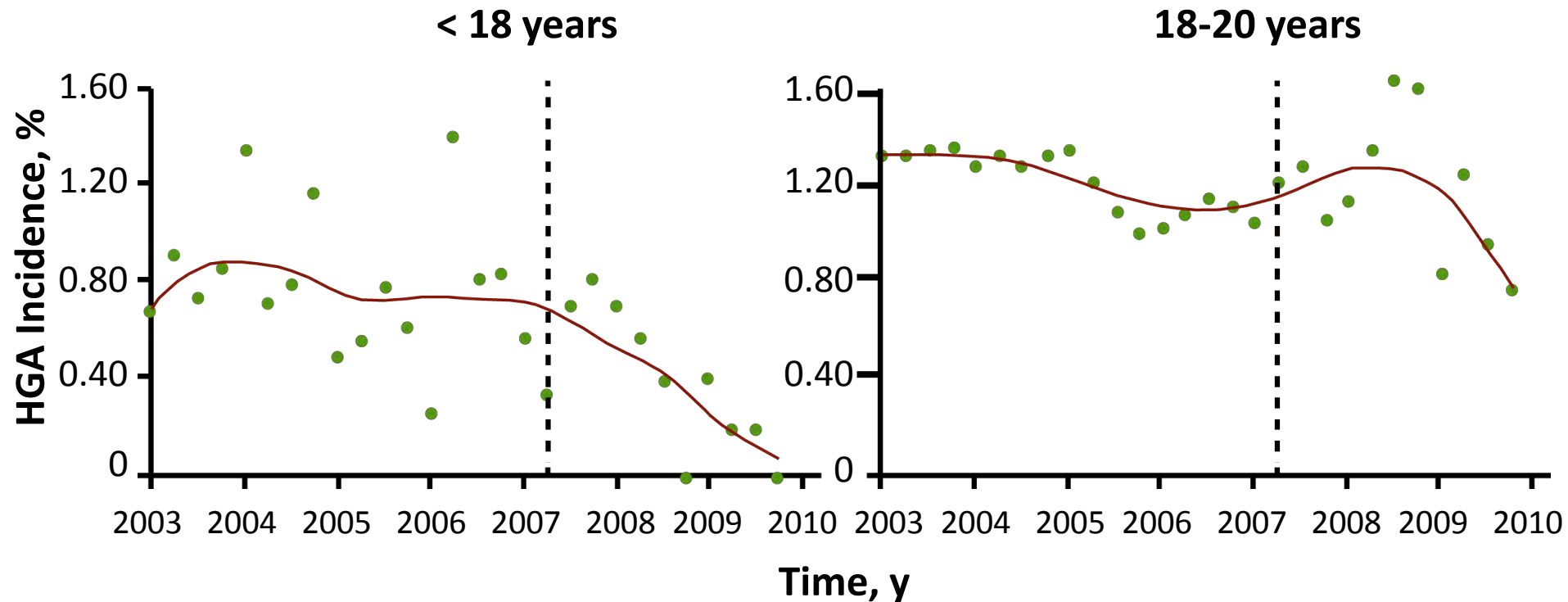


Impact on cervical pre-cancerous abnormalities

- Ecological trends over time
- Routinely collected data on screen detected abnormalities reported to State/territory based Pap registries

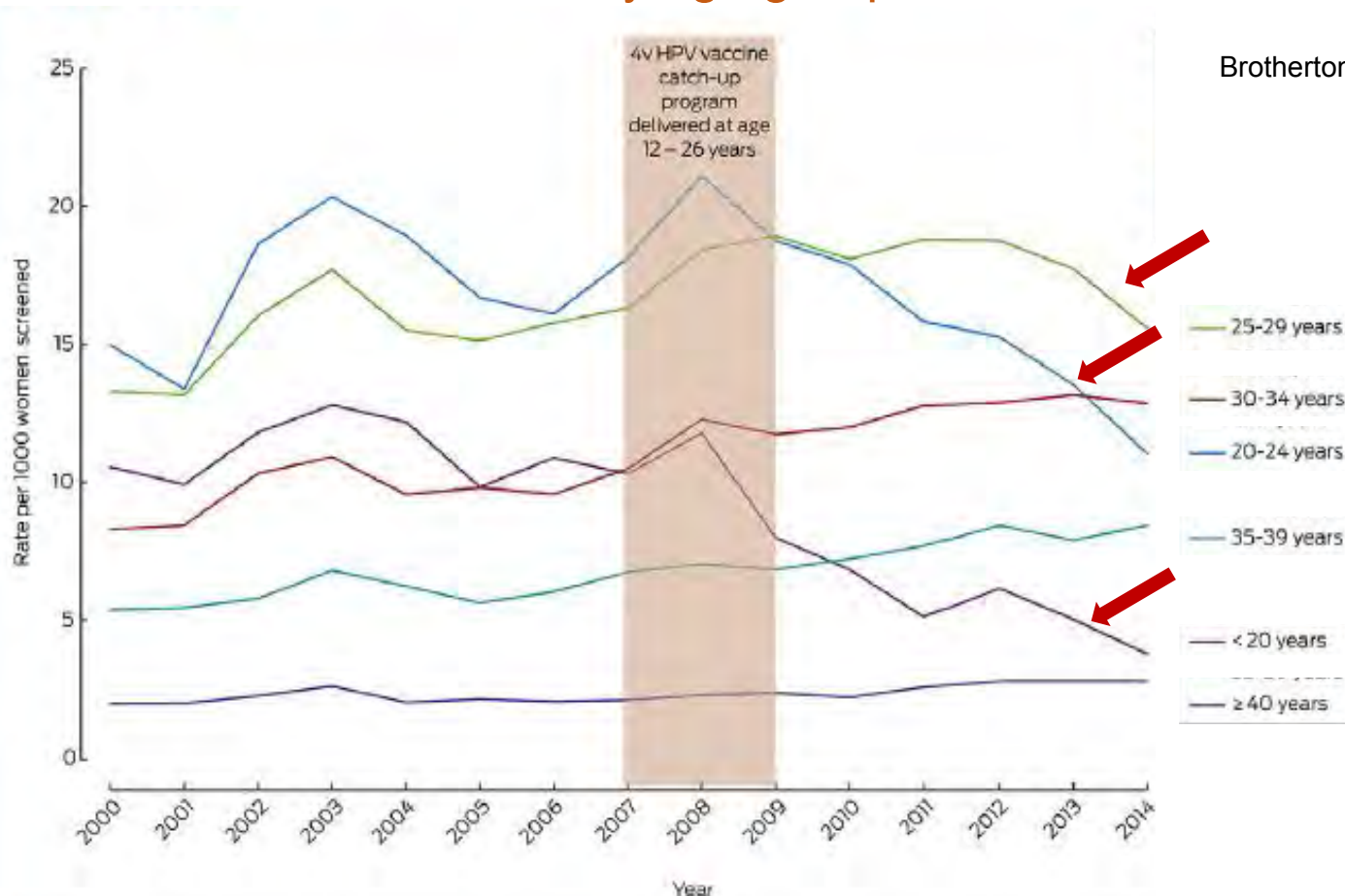
TRENDS IN SCREEN DETECTED ABNORMALITIES

Early effects on cervical abnormalities in Victoria, Australia



TRENDS IN SCREEN DETECTED ABNORMALITIES

Trends in prevalence rates of high-grade cervical abnormalities diagnosed in Victorian women, by age group, 2000-2014



Brotherton JM, et al. MJA. 2016

Future linkage to the vaccination register will allow for determination of association between receipt of vaccine and disease status

WHAT ABOUT INDIGENOUS POPULATIONS?

- High rates of STIs among Aboriginal and Torres Strait Islander populations
- Continue to experience health disadvantage and have poorer outcomes
- Lower participation rates in screening programs
- **Vaccination program has the potential to substantially improve health outcomes**
- **Lack of national data on HPV vaccine uptake**
 - **Estimated 15% lower completion rates in Indigenous adolescents based on limited data***

TRENDS IN GENITAL WARTS

Genital warts admission rates per 100,000 population among Indigenous females

Sex, Age Group, Subanalysis	Admission Rate, No./100 000, Mean		Overall Reduction From Jul 2006–Jun 2007 to Jul 2010–Jun 2011	Rate Ratio (95% CI)	
	Before NHVP ^a	After NHVP ^b	Percentage (95% CI)	After NHVP Mean ^b vs Before NHVP Mean ^a	Jul 2010–Jun 2011 vs Before NHVP Mean ^a
Female					
15–24 y					
Indigenous	82.7	22.7	86.7 (76.0–92.7)	0.27 (.19–.4)	0.22 (.12–.42)
Non-Indigenous ^c	73.8	24.9	76.1 (71.6–79.9)	0.34 (.31–.36)	0.21 (.18–.24)
18–26 y					
All	84.8	32.1	72.7 (67.0–77.5)	0.38 (.36–.4)	0.26 (.23–.29)
Unrelated to cervical screening follow-up	64.9	24.3	75.7 (69.6–80.6)	0.37 (.35–.40)	0.22 (.19–.26)

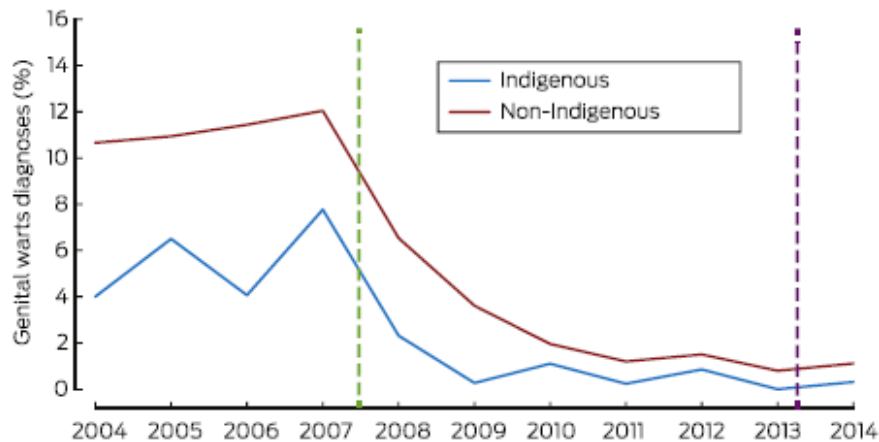
-73% ↓

Fall in genital warts admissions has been comparable for Indigenous and non-Indigenous females

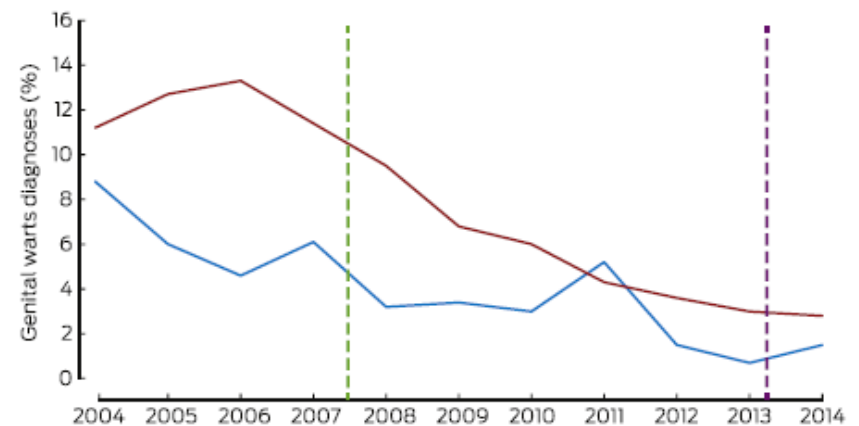
TRENDS IN GENITAL WARTS

Proportion of women diagnosed with genital warts at sexual health clinics, by Indigenous status

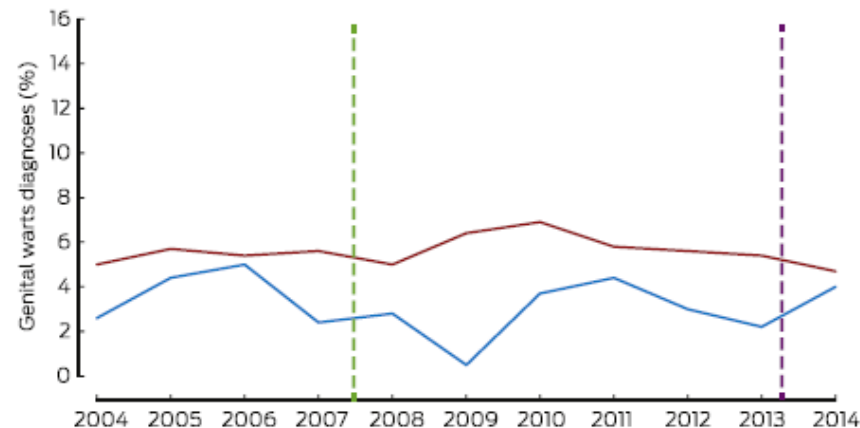
A. Under 21 years of age



B. 21–30 years of age



C. Over 30 years of age



SUMMARY

- HPV vaccination has been a great success for Australia
- Substantial fall in early disease endpoints in vaccine eligible cohorts, where the real-world data closely replicates clinical trial findings
- Very substantial reductions also evident among young Indigenous women
 - Potential benefit even greater than for non-Indigenous
- Likely to translate to significant reductions in HPV associated cancers in the future
- **Need to address the global inequalities in cervical cancer burden**

WHAT IS NEXT FOR THE VACCINE PROGRAM?

- A two dose 9-valent HPV vaccination schedule is effective and will likely replace the three dose quadrivalent schedule in the near future
- Ongoing surveillance will be critical

SURVEILLANCE STRATEGY

- **Program monitoring:** vaccine safety, coverage
- **Infection monitoring:** prevalence in the general male and female populations (genotype/antibody)
- **Monitoring of non-cancer disease endpoints:** GW, RRP, cervical abnormalities (prevalence and genotype)
- **Monitoring cancer endpoints:** incidence, mortality, cancer (anogenital and oropharyngeal)

***Human Papillomavirus (HPV)
Surveillance Plan – an integrated
approach to monitoring the impact of
HPV vaccine in Australia***



December 2013

Prepared by the HPV Surveillance Working Group of the
Communicable Diseases Network Australia (CDNA)

VACCINE IMPACT GLOBALLY

Table 1. Summary of Publications Reporting the Impact and Effectiveness of Quadrivalent Human Papillomavirus Vaccination Programs in 9 Countries

Country (No. of Included Publications) and HPV Vaccination Program	Publications (No.) per Endpoint ^a			
	Genital Warts	HPV Infection	Cervical Cytological Abnormalities	Cervical Histological Abnormalities
Australia (18 publications)	10	3	5	5
<ul style="list-style-type: none"> Since April 2007: ongoing publicly funded school-based national program, girls aged 12–13 y Up to December 2009: school-based catch-up for females aged 12–17 y and community-based catch-up for women aged 18–26 y Since February 2013: ongoing school-based national program for boys aged 12–13 y, with catch-up 14–15 y in 2013–2014^b 	Fairley 2009 [A29] Donovan 2011 [A28] Read 2011 [A37] Ali 2013 [A23, A24] Liu 2014 [A34] Harrison 2014 [A31] Chow 2015 [A27] Smith 2015 [A39], 2016 [A43]	Tabrizi 2012 [A4], 2014 [A5] Chow 2015 [A8]	Brotherton 2011 [A53] Gertig 2013 [A46] Crowe 2014 [A45] Brotherton 2015 [A44, A54]	Brotherton 2011 [A53] Gertig 2013 [A46] Crowe 2014 [A45] Brotherton 2015 [A44, A54]
Belgium (2 publications)	1	1
<ul style="list-style-type: none"> November 2007: females 12–15 y reimbursed End of 2008: reimbursement extended to age 18 y Since 2010/2011: school-based, girls aged 12–13 y 	Dominiak-Felden 2015 [A17]	Merckx 2014 [A14]		
Canada (3 publications)	1	...	2	1
<ul style="list-style-type: none"> Since 2007–2009: school-based, targeting girls grades 4–8 in all provinces/territories 	Smith 2015 [A20]		Mahmud 2014 [A47] Smith 2015 [A20]	Ogilvie 2015 [A58]
Denmark (8 publications)	5	...	2	3
<ul style="list-style-type: none"> 2006: licensed October 2008: 1st catch-up, females aged 13–15 y, free Since 2009: females aged 12 y, free August 2012: 2nd catch-up, females aged ≤27 y old 	Baandrup 2013 [A25] Blomberg 2013 [A21] Sando 2014 [A38] Blomberg 2015 [A16] Bollerup 2016 [A42]		Baldur-Felskov 2014 [A48, A51]	Baldur-Felskov 2014 [A48, A51], 2015 [A52]
France (1 publication)	1
<ul style="list-style-type: none"> Initially: recommended for females ≥14 y old with no prior sexual intercourse or within 1st year following sexual debut Since September 2012: recommended in females aged 11–14 y, with catch-up for females 15–19 y 	Judlin 2015 [A32]			
Germany (2 publications)	1	1
<ul style="list-style-type: none"> Since 2007: females aged 13–17, free 	Mikolajczyk 2013 [A35]	Delere 2014 [A2]		
New Zealand (2 publications)	2
<ul style="list-style-type: none"> September 2008: vaccine available February 2009: school program for females aged 12–13 y, with catch-up until 2010 for females <20 y 	Oliphant 2011 [A36] Wilson 2014 [A40]			
Sweden (5 publications)	3	1	...	1
<ul style="list-style-type: none"> 2006–2011: public subsidy for on-demand vaccination, females aged 13–17 y Since 2012: organized, publicly funded school-based vaccination of females aged 10–12 y with catch-up for females 13–18 y 	Leval 2012 [A33], 2013 [A19] Herweijer 2014 [A18]	Soderlund-Strand 2014 [A13]		Herweijer 2016 [A50]
United States (17 publications)	4	9	...	4
<ul style="list-style-type: none"> Since 2006: US Advisory Committee on Immunization Practices recommended routine vaccination for females aged ≥11 y 	Bauer 2012 [A26] Swedish 2012 [A22] Flagg 2013 [A30] Nsouli-Maktabi 2013 [A41]	Cummings 2012 [A1] Kahn 2012 [A11] Powell 2012 [A6] ^c Schlecht 2012 [A3] Markowitz 2013 [A12] Wilson 2014 [A15] Dickson 2015 [A9] Dunne 2015 [A10] Markowitz 2016 [A7]		Jamal 2013 [A56] Niccolai 2013 [A57] Hariri 2015 [A49, A55]

IMPACT

National HPV
Monitoring Program

THANK YOU!

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