Developing a Resource Strategy for Your National Cancer Control Plan: Cost-effectiveness and value

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Disclosures: I am co-PI of an investigator-initiated trial of primary HPV screening in Australia ('Compass') conducted by the Victorian Cytology Service, which has received a funding contribution from Roche Molecular Systems and Ventana Inc., USA. My modelling work is funded via grants from NHMRC)Australia, National Cancer Institute USA, government contracts in a number of countries, and funding from a number of other non-commercial agencies including Cancer Council NSW,. I receive salary support (Career Development Fellowship) from NHMRC.

HOW DO WE PRIORITISE INTERVENTIONS ACROSS THE CANCER CONTROL SPECTRUM?

Primary prevention | Secondary prevention | Treatment |Survivorship | Palliative care

Overview

- The role of cost-effectiveness studies in planning
- Country-specific data considerations
- What can be learned from other countries:
  - Cost-effectiveness of HPV vaccination
  - Cost-effectiveness of cervical screening
  - Impact of combined interventions

Today's focus is on cervical cancer prevention as a key component of national cancer control plans…but the same principles apply to other elements of such plans.

The role of cost-effectiveness studies in planning

Cost-effectiveness analysis

- The principle behind cost-effectiveness analyses (CEA) is to provide the decision maker with information on the ***best value investments*** or **"best buys".**
- Results provided as $/LYS, $/QALY saved (or $/DALY averted)
  - i.e. how much does it cost per life year saved or quality-adjusted life year saved?
- Evaluated in relation to other feasible interventions (incremental analysis) and compared to a "willingness-to-pay" threshold
- Estimates are done by modelling both ***future impact of intervention*** on disease and ***future costs of intervention***
  - Both are discounted into the future
  - Taking into account country-specific conventions about what is an acceptable threshold.

Example cost-effectiveness plane

- Example evaluation of alternate cervical screening options (varying by technology, interval, age range and triaging and surveillance strategies), in unvaccinated women and cohorts offered vaccination: Australia

- Predictive modelling informed by observational and trial data on test accuracy & local data on screening and vaccination uptake.

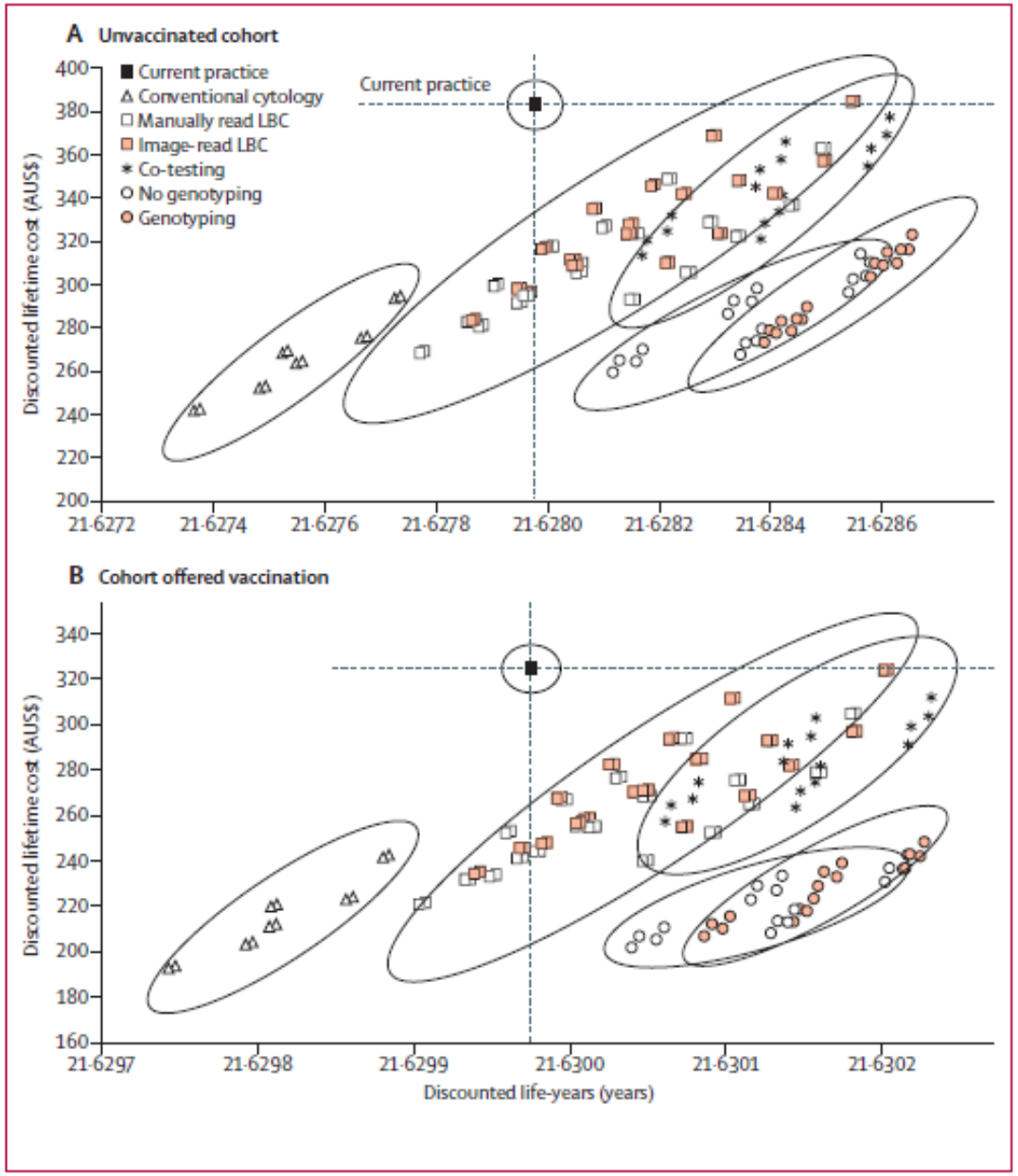


Figure 3: **Cost-effectiveness of screening strategies compared with current practice with screening ending at age 64 years**
The ovals represent clusters of strategies with the same, or very similar, primary screening approaches.
LBC=liquid-based cytology.

Lew/Simms et al., Lancet PH 2017

Cost-effectiveness analysis

- Importantly, cost-effectiveness *per se* says nothing about ***affordability*** (which depends on the absolute costs incurred, not cost per life year saved)
- Budget impact analysis is a separate tools to estimate actual aggregated costs, and goes hand in hand with cost-effectiveness analysis.
- Effectiveness (and strength of evidence base for effectiveness), cost-effectiveness, budget impact, safety, feasibility of service delivery, acceptability and equity are ***all*** considerations.

WORLD BANK DISEASE CONTROL PRIORITIES, 2015

Deaths in 2012, <70 years		Interventions
All cancers	3,230,000	Education on tobacco hazards, HPV/HBV vaccination, early treatment for common cancers, palliative care
Tobacco-related cancer (lung, oral, oesophagus)	900,000	Taxation, warning labels or plain packaging, bans on public smoking, advertising, monitoring, cessation advice & services
Liver cancer	380,000	HBV vaccination including birth dose
Breast cancer	280,000	Treat early-stage cancer
Colorectal cancer	210,000	Emergency surgery for obstruction
Cervical cancer	180,000	School based HPV vaccination & opportunistic screening, treat precancer and cancer
Childhood cancer	80,000	Treat selected cancers

Gelbrand et al., Lancet 2015

Of the 500,000+ women diagnosed with cervical cancer each year, 85% are in low and middle income countries


Photo credit: Travel Stock / Shutterstock.com

Globocan 2012, International Agency for Research on Cancer, Lyon

Cervical cancer prevention modalities

- **Primary prevention** with prophylactic HPV vaccination is highly effective and cost-effective *for HPV-naïve females and males prior to HPV exposure*
  - Optimal effectiveness if administered to pre-adolescents (12-13 years)
  - Three vaccine types:
    1. *Cervarix* (GSK) bivalent (2v) vaccine: HPV 16,18
    2. *Gardasil* (Merck) quadrivalent (4v) vaccine: +HPV 6,11 (warts)
    3. *Gardasil 9* (Merck) nonavalent vaccine includes the HPV types in the quadrivalent vaccine and 5 additional oncogenic types (31, 33, 45, 52, and 58).
- **Secondary prevention** with cervical screening is highly effective and cost-effective for older cohorts already exposed to HPV
  - Traditionally, cervical cytology (Pap smears) have been used
  - Screening with HPV DNA is more effective, and improves protection against invasive cervical cancer by up to 70% compared to cytology.[1]

Optimal results are achieved in all settings when combining HPV vaccination initiatives with cervical screening using HPV testing

[1]Ronco et al., Lancet 2014.

HPV vaccination

75 countries with national programs

47 million females received full course

34% of females in target population vaccinated in more developed regions

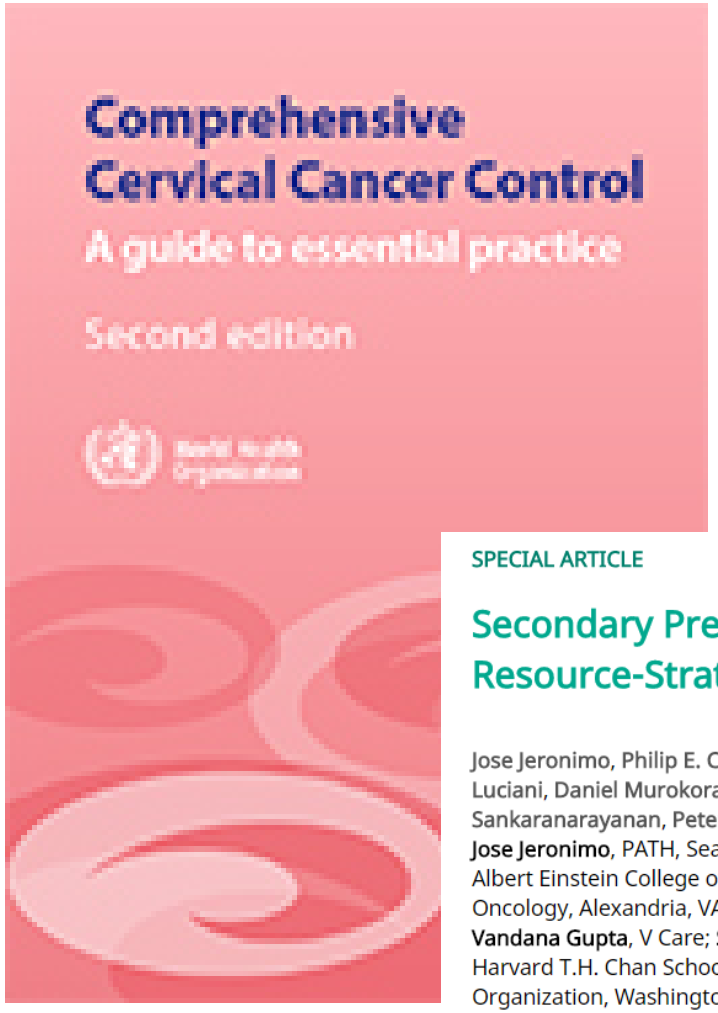
…but only…

2.7% vaccinated in less developed countries.

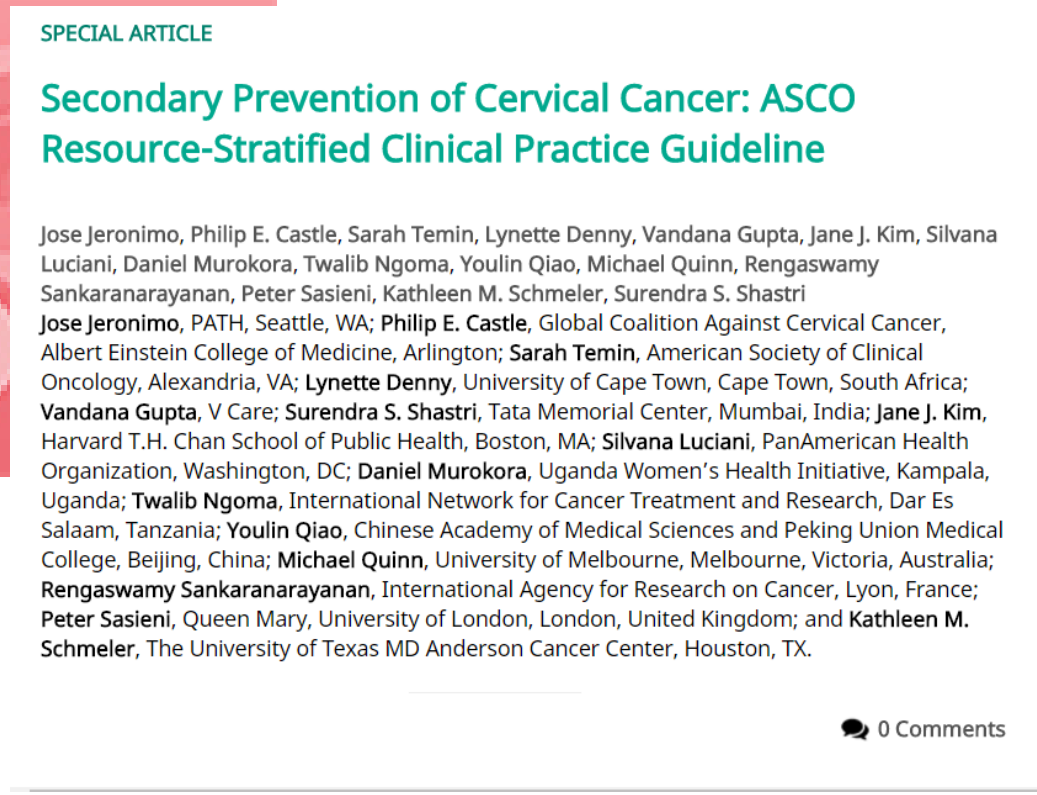
Bruni L et al., Lancet Global Health 2016

Cervical screening

- 2014 WHO guidelines include provision for HPV, cytology or VIA testing, conducted at least once per lifetime, targeting women aged 30-49 years.
- 2016 ASCO resource-stratified guidelines focus on HPV screening.



World Health Organisation 2014



SPECIAL ARTICLE

Secondary Prevention of Cervical Cancer: ASCO Resource-Stratified Clinical Practice Guideline

Jose Jeronimo, Philip E. Castle, Sarah Temin, Lynette Denny, Vandana Gupta, Jane J. Kim, Silvana Luciani, Daniel Murokora, Twalib Ngoma, Youlin Qiao, Michael Quinn, Rengaswamy Sankaranarayanan, Peter Sasieni, Kathleen M. Schmeler, Surendra S. Shastri

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0 Comments

ASCO 2016

Country-specific data considerations

What data do we need (ideally) to evaluate the cost-effectiveness of alternate cervical cancer prevention strategies in a country?

- Burden of disease – cervical and other HPV-related cancers:
  - HPV infection prevalence
  - Cervical precancerous abnormalities (if screening is done)
  - Cancer incidence and mortality rates (by age)
- Uptake of interventions:
  - Coverage rates (or expected rates) for vaccination and/or cervical screening, follow-up adherence
  - Acceptable age range for vaccination, vaccine type
- Costs:
  - Vaccination administration & per-dose costs
  - Screening tests and administration costs
  - Costs of diagnostic evaluation, stage-specific cancer treatment costs
  - Infrastructure costs (e.g. capital investment in HPV screening technologies, screening/vaccination registers)
- Health economic parameters (discount rate, WTP)

These data are country-specific and can influence cost-effectiveness of different options

Immunization, Vaccines and Biologicals

Vaccines and diseases

Global Vaccine Action Plan

WHO policy recommendations

National programmes and systems

Monitoring and surveillance

Quality, safety and standards

Research and development

Resource materials

Newsroom

WHO Cervical Cancer Prevention and Control Costing Tool (C4P)

Background

Demo User guide
pdf, 1.47Mb

C4P Demo Tool
xlsx, 1.26Mb

C4P 5-Year Scale-Up User Guide
pdf, 1.82Mb

C4P 5-year Scale-Up Tool
xlsx, 2.33Mb

Guide de l'utilisateur de l'outil C4P - français
pdf, 4.41Mb

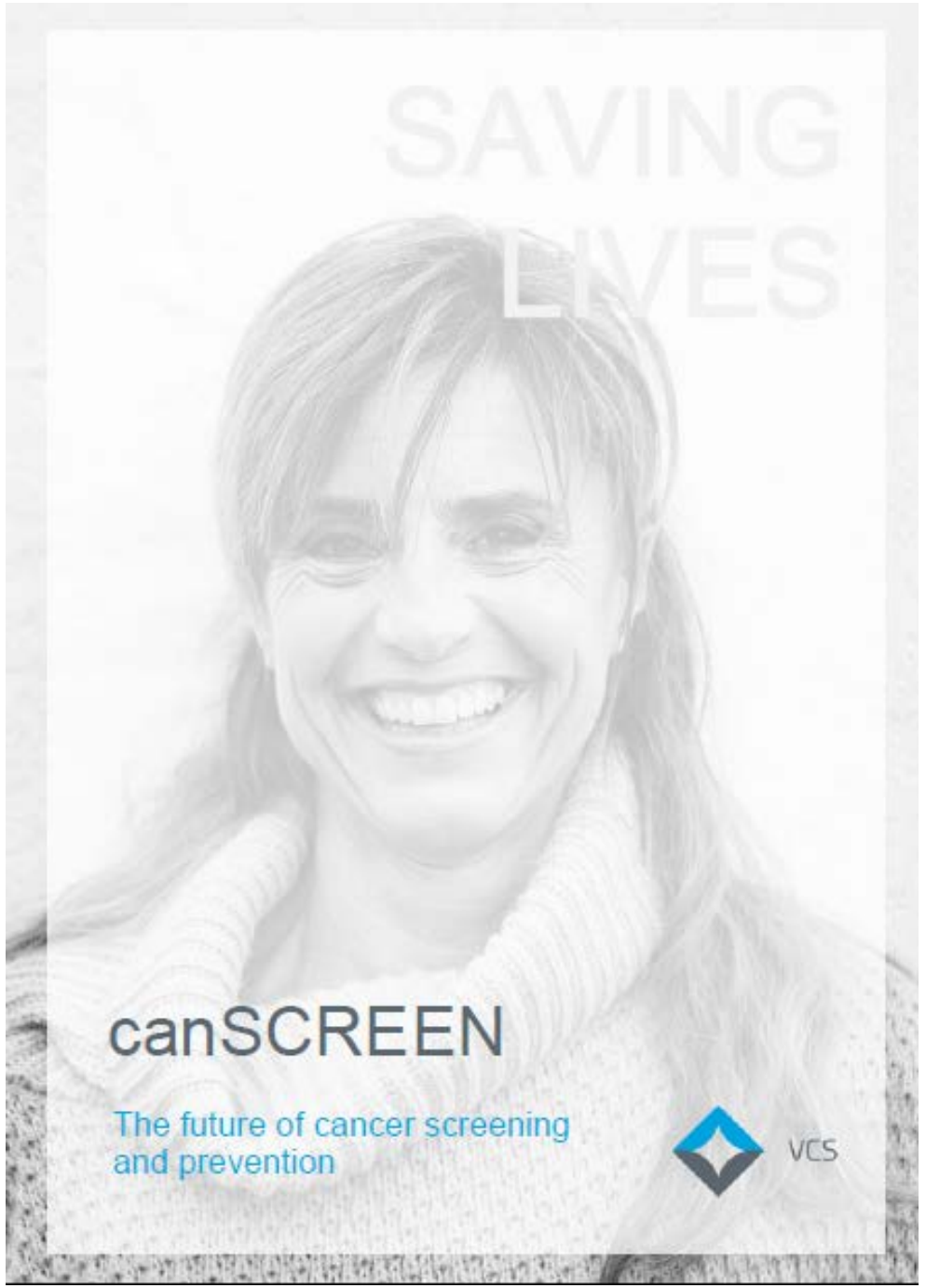
WHO IVB has developed a generic costing and planning tool for cervical cancer prevention and control. The WHO Cervical Cancer Prevention and Costing (C4P) tool has been developed specifically to assist low and middle income countries (LMICs) in planning cervical cancer control strategies. The tool has been built in MS Excel and consists of two independent modules:

1. HPV (human papillomavirus) vaccination of 9-13 year old girls.
2. Cervical cancer screening and treatment for women.

Last update:
13 January 2017 16:06 CET

Registry infrastructure will be critical to evaluate ongoing impact of prevention initiatives

- Underpin quality and integrity of data
- Provide data to maximise participation in under-screened and/or under-vaccinated groups
- Inform effectiveness of new programs via routine data monitoring
- Support critical research
- Provide a framework for clinical trials



What can be learned from other countries?

High income countries:
Cost-effectiveness of HPV vaccination

- At least 55 countries (mainly high resource) have established national HPV vaccination programs
- By 2012, over 40 cost-effectiveness evaluations of HPV vaccination in girls had been conducted in developed countries[1]
  - Consistently found that vaccination of pre-adolescent females is cost-effective, even at initial vaccine list prices of ~US$100 per dose (@3-doses).
  - Vaccinating older females is less cost-effective, but analyses generally supported catch-up programs to age ~18-26 years.
  - Boys also receive benefits from female vaccination due to herd immunity (especially when high coverage in females is attained).
- A few evaluations of the cost-effectiveness of next generation nonavalent (9v) vaccines have been performed (USA, Canada, Australia)[2-4]
  - These can be cost-effective compared to first generation vaccines if the incremental cost-per-dose is <~US$13-30.

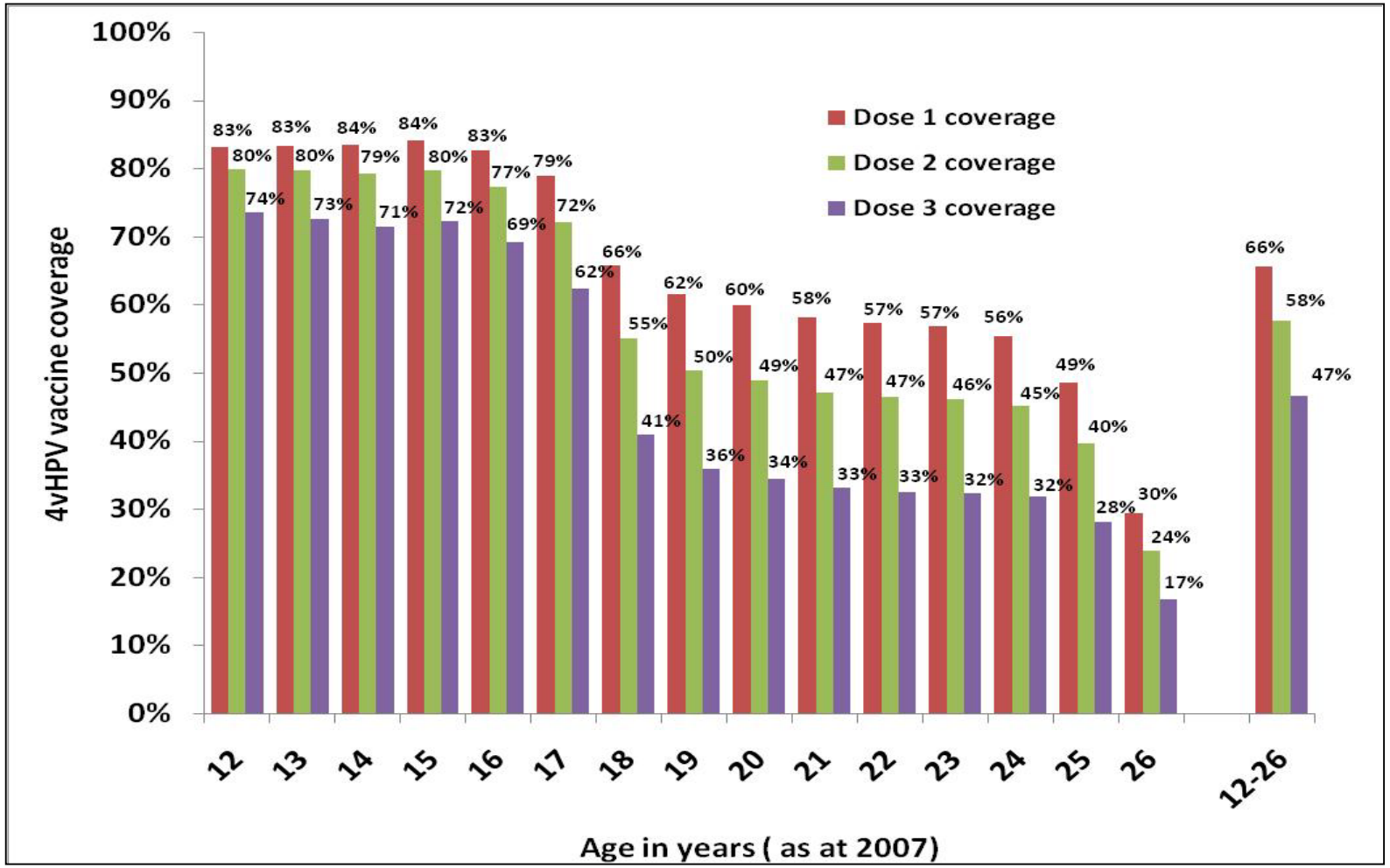
[1]Canfell et al., Vaccine (WHO/ICO Special Supplement on HPV Prevention), 2012.
[2]Drolet M et al, Int J Cancer 2014, [3]Brisson M et al, JNCI 2016 [4]Simms K et al., Lancet PH 2016

The Australian example:

HPV vaccine impact

Australia was the first country in the world to implement a publicly-funded HPV vaccination program in 2007.

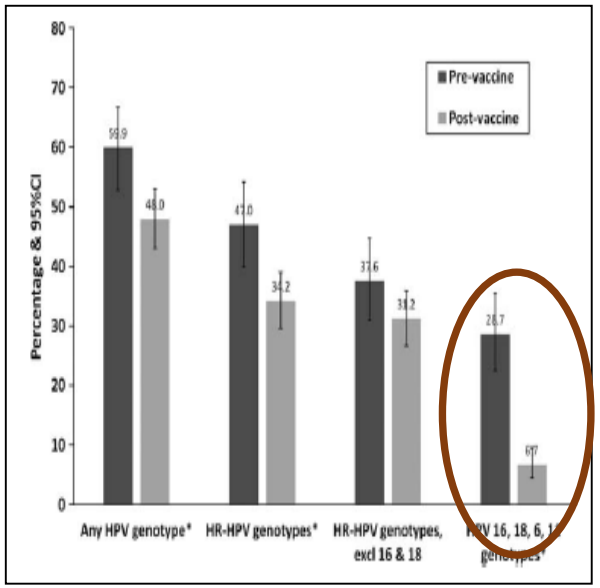
- Routine vaccination of 12-13 year old girls
- A two year catch up in females ages 12-26 years
- In 2013, young boys were included in the National HPV Vaccination Program.



Data extracted from the National HPV Vaccination Register as at Sept 2011 (excludes people who have opted off)

Vaccine impact in Australia

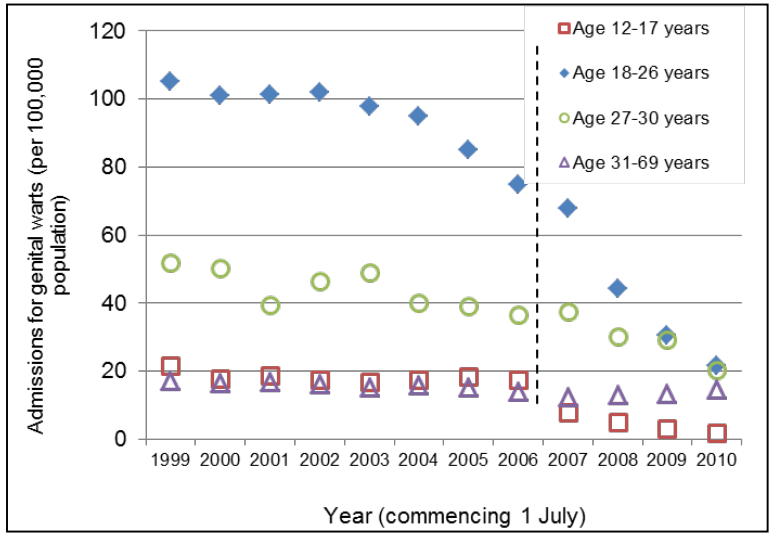
Females, early twenties, to 2011-14



HPV infections

77%↓

Tabrizi S/Brotherton J et al JID 2012



Warts

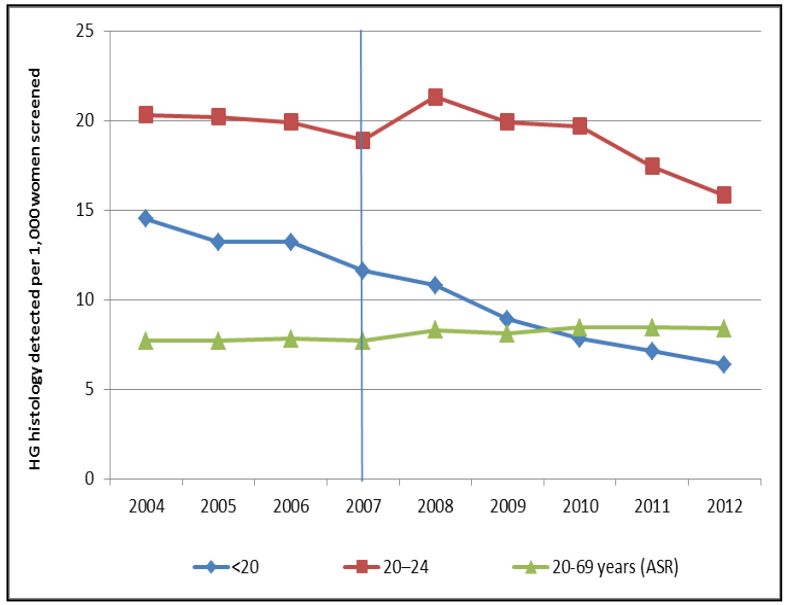
73%↓

Smith M et al JID 2014

Confirmed HSIL

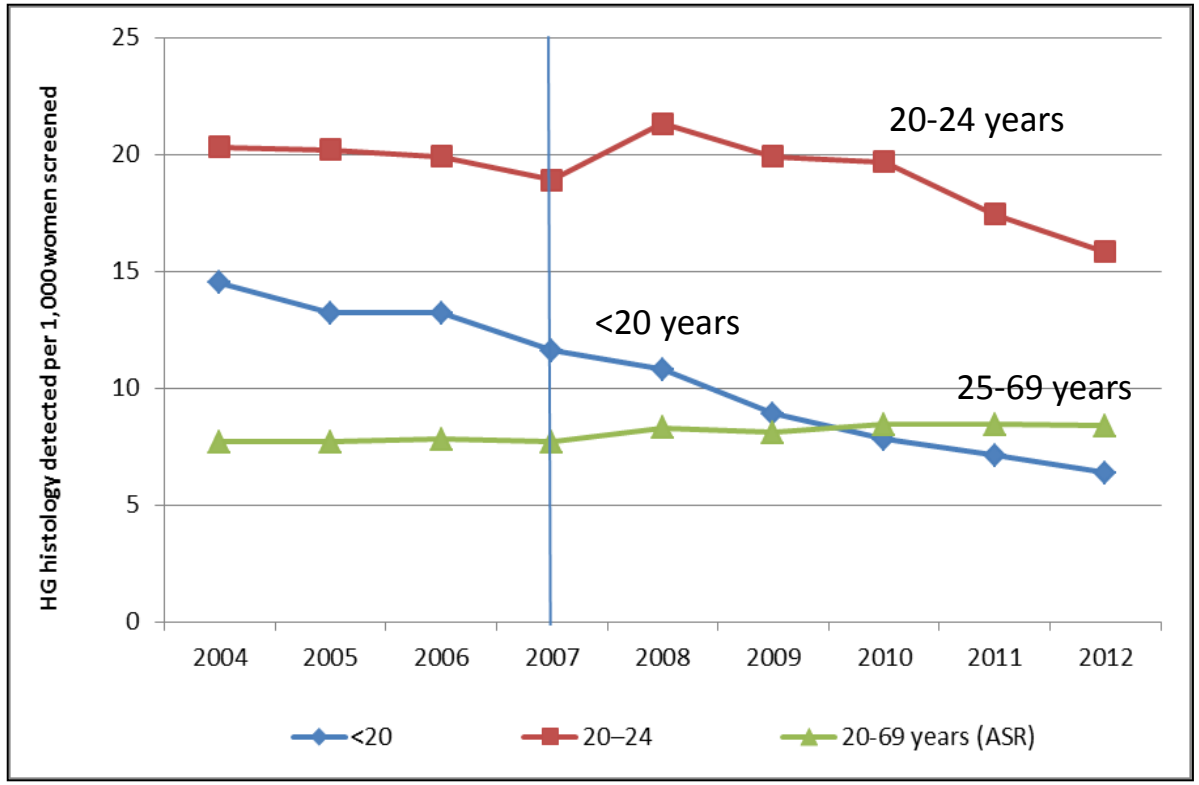
21%↓

Australian Institute of Health and Welfare 2014, 2011-2012.

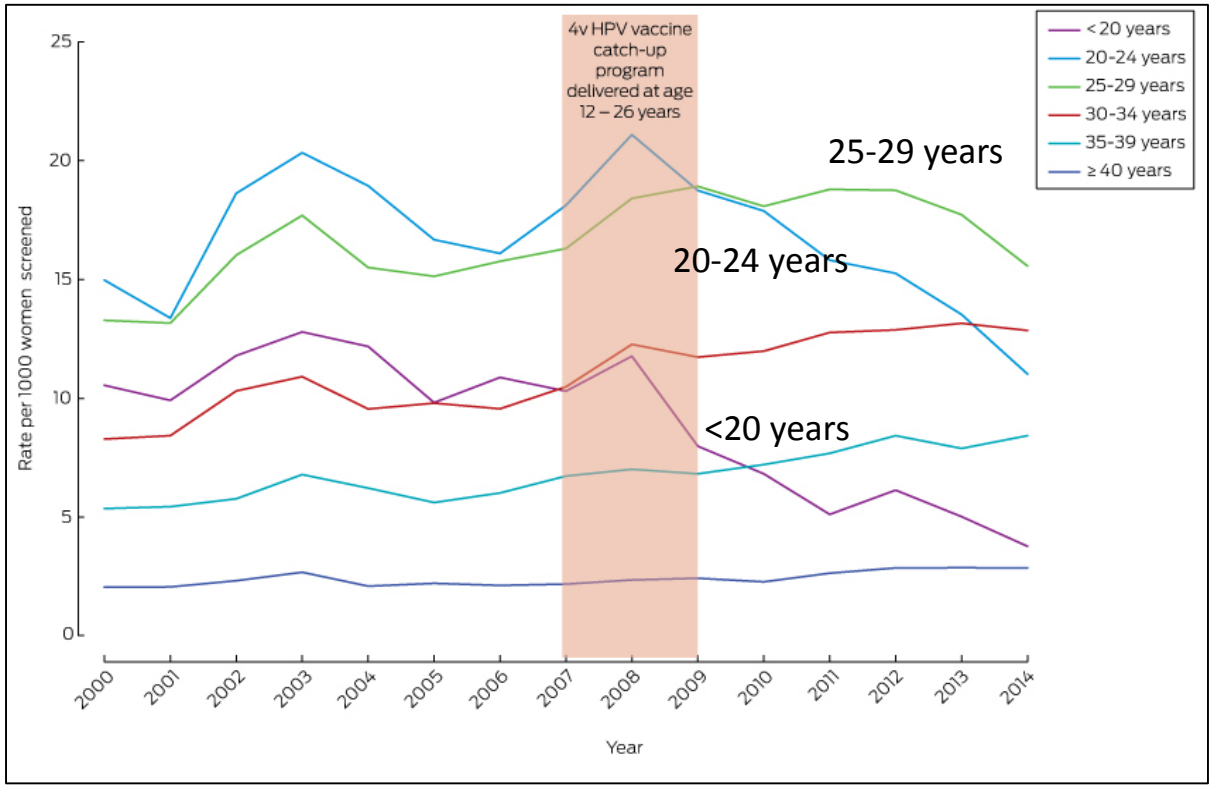


Vaccine impact in Australia:

High grade cervical precancerous lesions



Australian Institute of Health and Welfare 2014, 2011-2012.



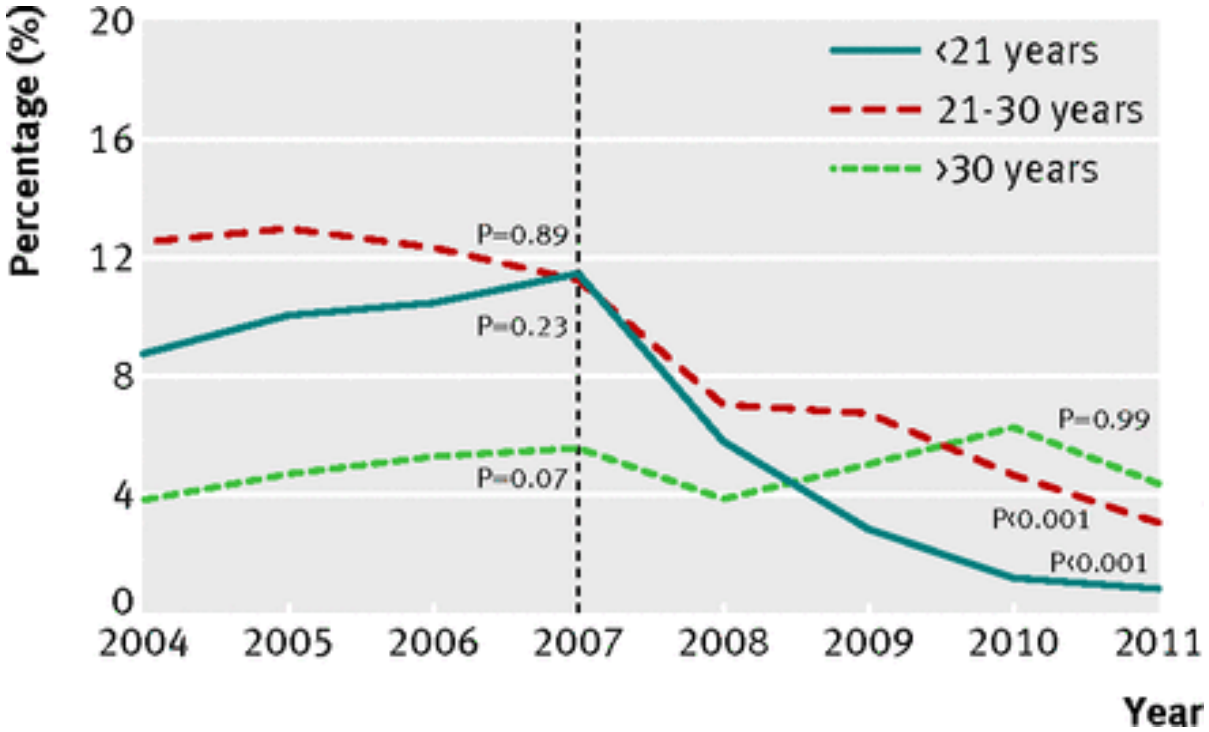
Brotherton et al., MJA 2016.

21%↓ in 20-24 year olds nationally to 2012

17%↓ in 25-29 year olds in Victoria to 2014

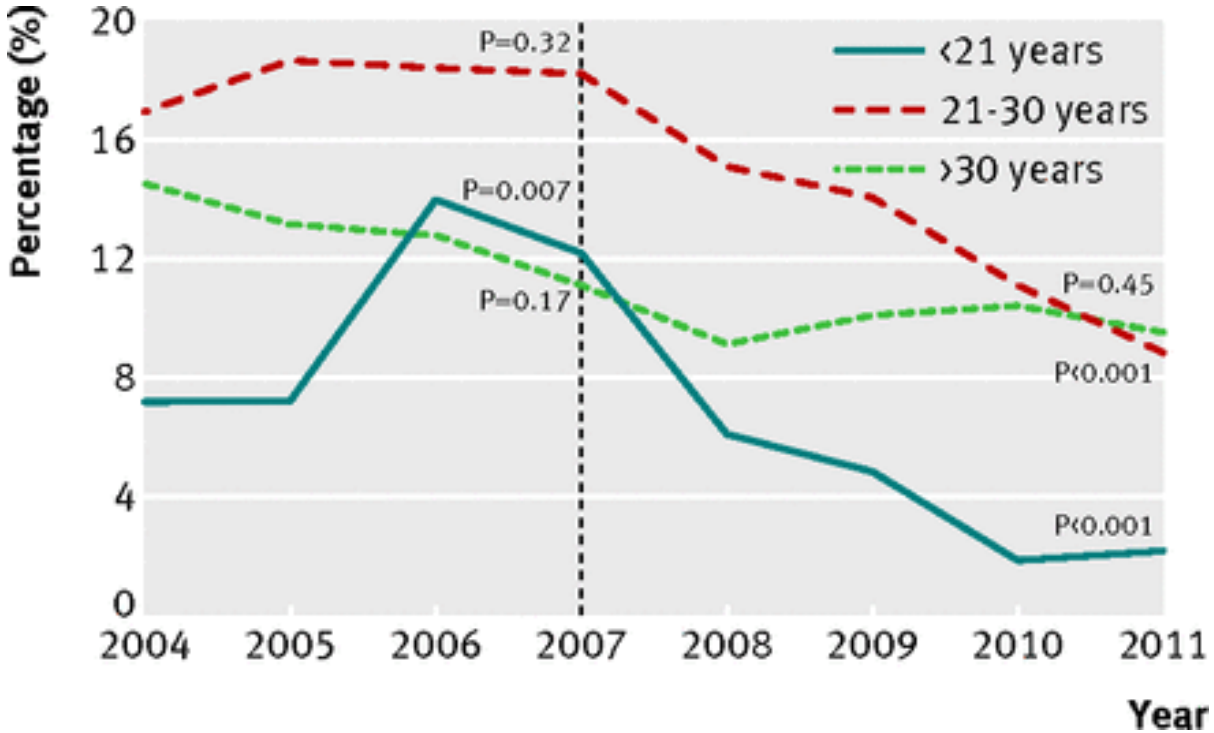
Vaccine impact in Australia:

Anogenital warts



Proportion of Australian born women diagnosed as having genital warts at first visit, by age group, 2004-11

93% reduction in <21 years
73% reduction in 21-30 years
No reduction in 30+ years



Proportion of Australian born heterosexual men diagnosed as having genital warts at first visit, by age group, 2004-11

82% reduction in <21 years
51% reduction in 21-30 years
No reduction in 30+ years

"Large declines in diagnoses of genital warts in heterosexual men are probably due to herd immunity."

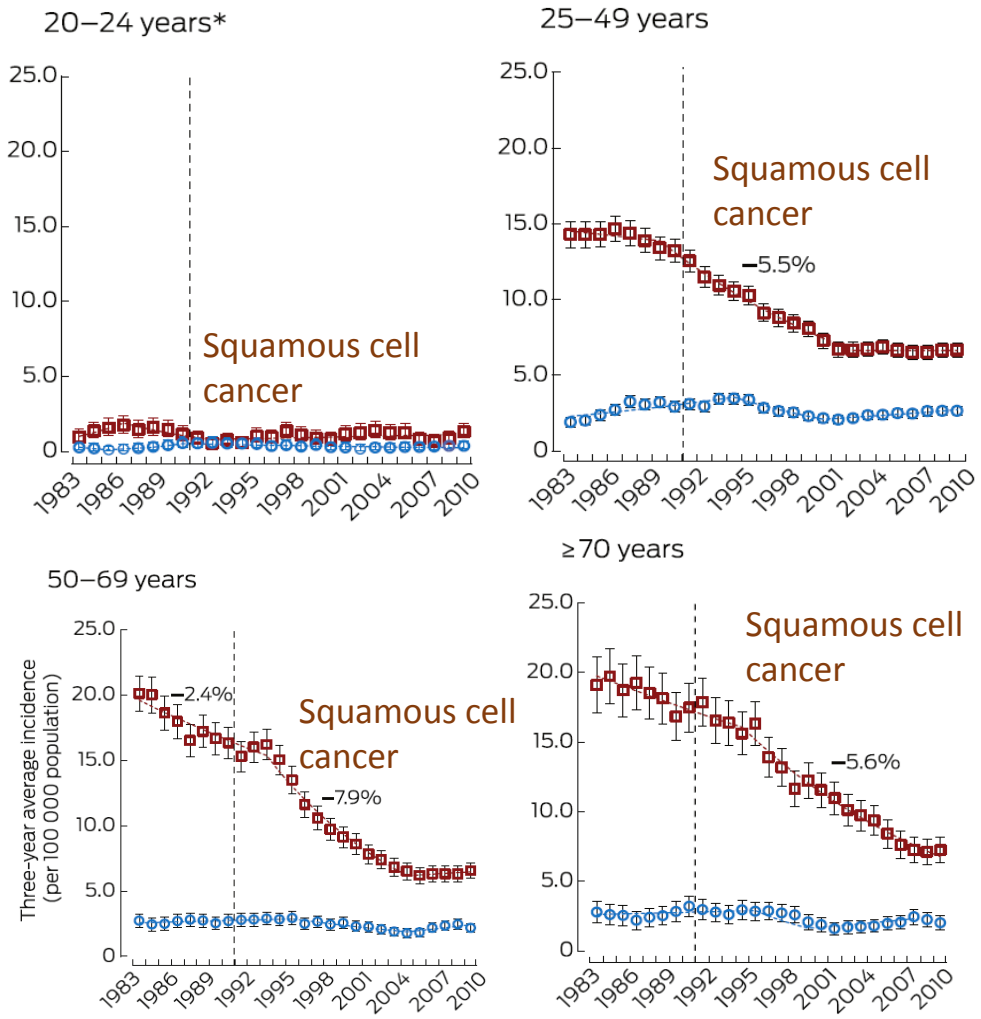
Ali H et al. BMJ 2013.

Cervical screening impact in Australia:

Invasive cervical cancer

National Cervical Screening Program
A joint Australian, State and Territory Government initiative

Australian Government
Department of Health



In 1991 Australia introduced an organised program of 2-yearly Pap smears in women aged 18-69 years.

Between 1988–1990 and 2008–2010, falls in cervical cancer incidence of:

- 45% in women 25–49
- 54% in women 50–69
- 50% in women 70+ years

Smith M and Canfell K, MJA 2016

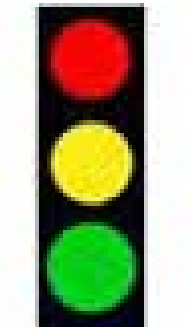
The new, integrated approach to screening and vaccination in Australia

Australian Government
Department of Health and Ageing

- The success of vaccination prompted a major review of screening in 2011
- Decision to implement primary HPV screening in 2017
  - 5-yearly screening in women aged 25-74 years
- This was based on cost-effectiveness evaluation, showing that HPV screening is:
  - *More effective than Pap smears* – reduce cervical cancer incidence and mortality by a further 30%
  - *Less costly* – reduce screening costs by 30-40%.

Lew/Simms et al., Lancet PH 2017

Integrated HPV prevention



HPV screening

Negative

Routine screening in 5 years

Other oncogenic HPV

Cytology negative or low grade

12 month HPV FU

Refer to colposcopy if any HPV +ve
Otherwise return to routine screening

Cytology high grade

HPV16/18
(Vaccine included types)

Colposcopy (diagnostic referral)

Use the same strategy, whether or not a woman has been offered vaccination against HPV 16,18

Low and middle income countries:
Cost-effectiveness of HPV vaccination

- A global analysis suggests HPV vaccination is likely to be cost-effective in almost every country:
  - Very cost-effective (cost per DALY averted <GDP per capita) in 160 of 179 countries
  - Cost-effective (cost per DALY averted <3xGDP per capita) in a further 17 countries.
- Conservative:
  - Assumes 3-dose schedules, but more recently WHO and EMA have recommended 2-dose schedules.
  - Does not take into account herd immunity, impact on boys, non-cervical cancers.
- >70% of the prevented cases/deaths in low or low-middle-income countries.

	Vaccine cost (US$, millions)	Net cost (US$, millions)	Cancers prevented (thousands)	Deaths prevented (thousands)	Not cost effective (n)	Cost effective (n)	Very cost effective (n)
Base case	4500	4100	690	420	6	17	160

Lifetime impact of vaccination of a full cohort of 12 year old girls (full coverage in all 179 countries); Costs in 2011 USD.

[1]Jit et al. Lancet Global Health 2014.

Low and middle income countries:
Cost-effectiveness of cervical screening

- A study in rural China concluded that at a cost per vaccinated girl (CVG) of ≤US$50, and if an HPV screening test can be supplied at ≤$5, it is cost-effective to vaccinate at 12-15 years *and* to screen older women with HPV testing once or twice in a lifetime.[1]
- The best age to screen is 35-49 years.[2]
- HPV-based screening delivers the greatest health benefits, compared to other screening modalities.[2]

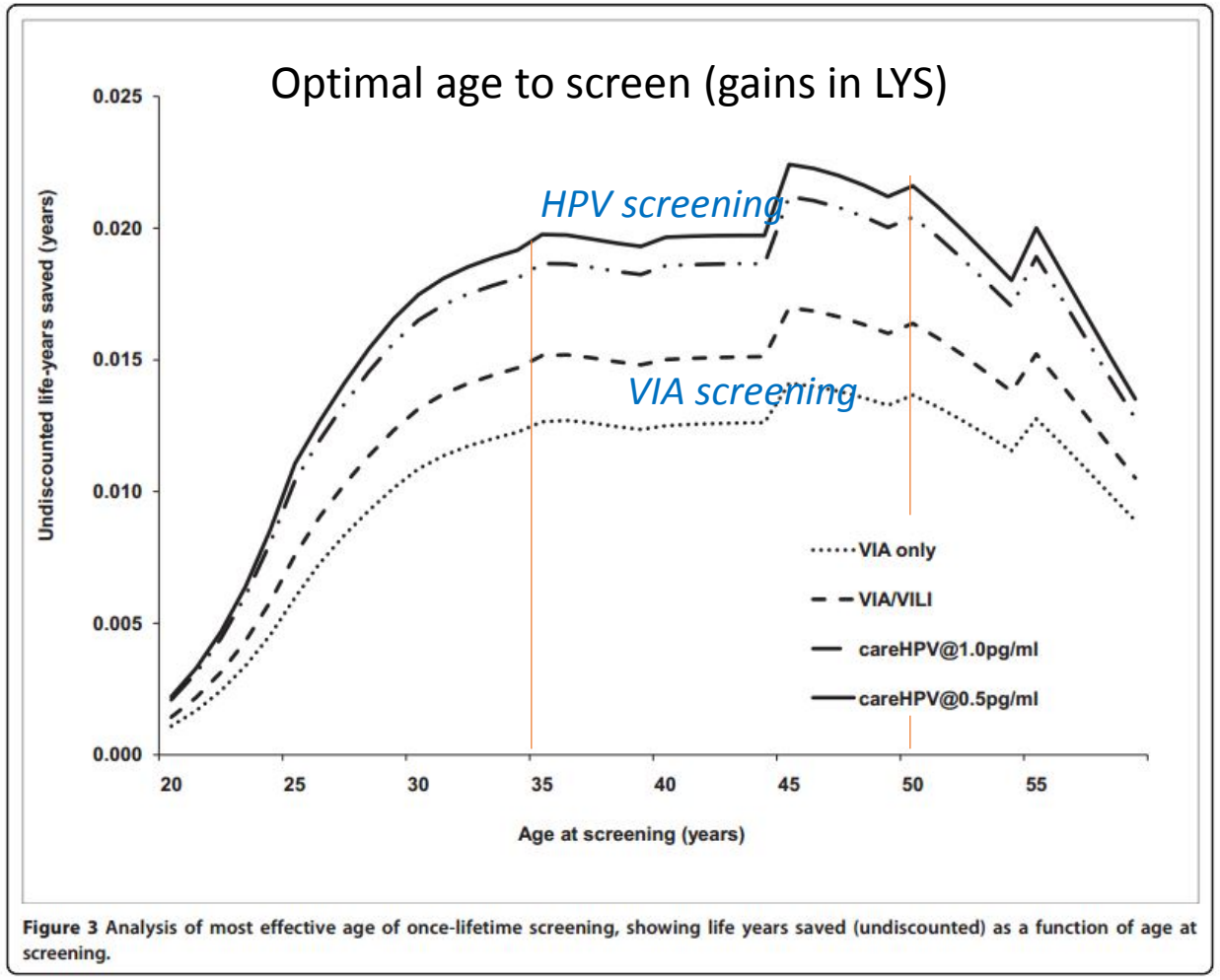
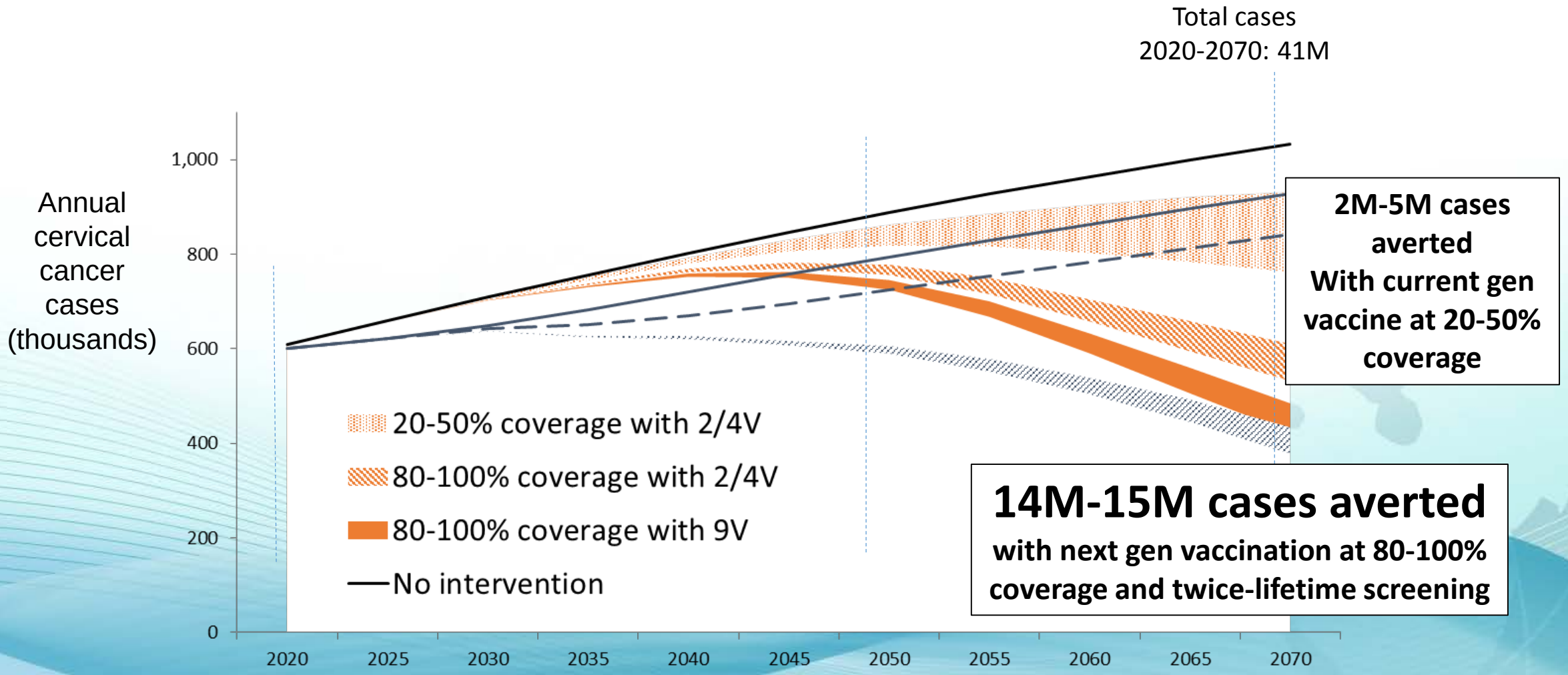


Figure 3 Analysis of most effective age of once-lifetime screening, showing life years saved (undiscounted) as a function of age at screening.

[1]Canfell et al. Vaccine 2011; [2]Shi et al. BMC Cancer, 2011.

Global burden of disease:
Predicted impact of combined interventions



Simms K et al., Presented at HPV 2017, Cape Town

Conclusions

- High income countries:
  - HPV vaccination in pre-adolescent females is highly cost-effective.
  - The Australian example shows that well-coordinated immunization programs achieving coverage ~70-80% have a rapid and dramatic impact.
  - However, it is still necessary and still cost-effective to screen older women regularly, with the best results achieved with primary HPV-based screening.
  - Vaccination enables more efficient screening strategies.
- Low and middle income countries:
  - HPV vaccination is cost-effective in virtually all countries.
  - The China example shows vaccinating + screening once or twice a lifetime can be cost-effective.
  - Combined interventions have the greatest impact.

Optimal results are achieved in all settings when combining HPV vaccination initiatives with cervical screening using HPV testing

“This is a transformational moment for the health of women and girls across the world”

Seth Berkley, CEO GAVI Alliance

Photo credit: Travel Stock / Shutterstock.com

Thank-you

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