

# DEVELOPMENT OF THE HPV VACCINE:

## TRANSFORMING DISCOVERY INTO DISEASE ERADICATION

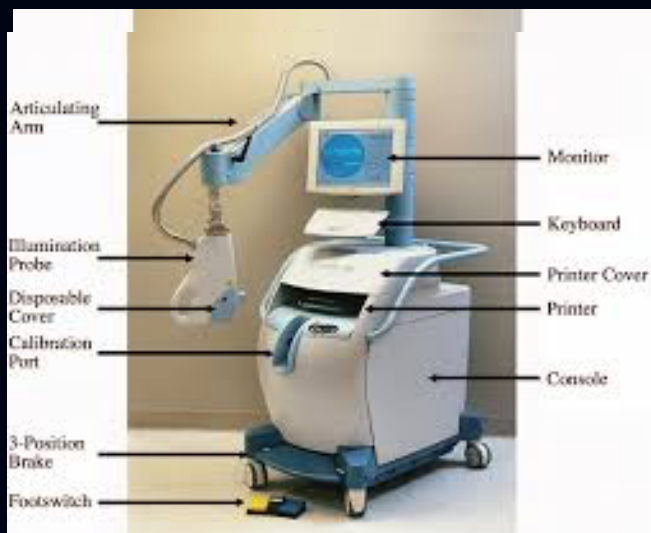
Warner K. Huh, MD, FACOG, FACS  
University of Alabama at Birmingham  
Birmingham, Alabama USA

**O'NEAL** COMPREHENSIVE  
CANCER CENTER



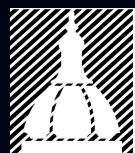
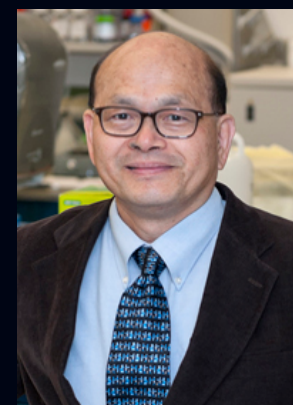
THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

# University of Alabama at Birmingham (UAB): Cervical Cancer Screening, Prevention, And Treatment Research





# Johns Hopkins-UAB-University of Colorado Cervical Cancer Specialized Programs in Research Excellence (SPORE)



THE SIDNEY KIMMEL  
COMPREHENSIVE CANCER CENTER  
AT JOHNS HOPKINS



THE UNIVERSITY OF  
ALABAMA AT BIRMINGHAM

NATIONAL  
CANCER  
INSTITUTE

# Smallpox

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- The great scourge of mankind
- Has crippled, disfigured and/or killed one quarter of all humanity
- In the 20th Century alone, nearly 200 million deaths





# The Impact of Vaccines

Disease	Average Annual Reported Cases Pre-vaccine*	Cases in U.S. 2013**	Provisional Cases in U.S. 2014***	Provisional % Reduction In U.S. 2014
Smallpox	48,164	Eradicated worldwide in 1980		
Diphtheria	175,885	0	1	>99.9%
Measles	503,282	187	628	>99.9%
Mumps	152,209	584	1,151	99.2%
Pertussis	147,271	28,639	28,660	80.6%
Polio (paralytic)	16,316	1	0	100%
Rubella	47,745	9	8	>99.9%
Congenital Rubella Syndrome	823	1	0	100%
Tetanus	1,314	26	21	98.4%
<i>H. Influenzae</i> Type b Age<5 years	20,000	31	27	99.9%

\*MMWR 48(12);243-248 April 2, 1999

\*\*\*MMWR 63(53);733-746 January 9, 2015

\*\* MMWR 63(32);702-715 August 15, 2014

# RESEARCHERS WHO DESERVE OUR CONSIDERABLE GRATITUDE

## PROF. DR. HARALD ZUR HAUSEN

Nationality	Germany
Institution	German Cancer Research Centre Heidelberg
Award	2008
Discipline	Physiology or Medicine
Co-recipients	Profs. Barré-Sinoussi and Montagnier

[Biography](#) on the Official Web Site of the Nobel Prize

### CURRICULUM VITAE

German virologist Harald zur Hausen was awarded half of the 2008 Nobel Prize for his discovery of the role of human papilloma viruses (HPV) in cervical cancer. Ultimately his work led to the introduction in 2006 of a vaccine to combat HPV.

Zur Hausen was born on March 11, 1936 and grew up in the city of Gelsenkirchen-Buer. He earned a place at the University of Bonn where he studied medicine and after passing his preliminary medical examination, continued his studies at Hamburg and the Medical Academy in Düsseldorf, where he completed his MD thesis in 1960. After two years as a medical assistant, during which he developed an interest in gynaecology and obstetrics, he joined the University of Düsseldorf as a laboratory assistant, exploring virus-induced chromosomal modifications. Seeking greater scientific knowledge, zur Hausen moved to the US in 1965 to work at the Philadelphia Children's Hospital with German virologists Werner and Gertrude Henle. The Henles' laboratory was working on the newly discovered Epstein-Barr virus (EBV) and zur Hausen helped demonstrate that a cancer virus (EBV) can transform healthy cells (lymphocytes) into cancerous cells.



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# RESEARCHERS WHO DESERVE OUR CONSIDERABLE GRATITUDE



University of Queensland



Georgetown University



National Cancer Institute



University of Rochester



# Intellectual Property/Patent “Interference”

- 6 individual patent interference actions
- Disputed over 16 years with dozens of judges involved
- On appeal, patent ultimately award to Professor Ian Frazer
- License agreement created with CSL, Merck and MedImmune



# 2017 Lasker-DeBakey Clinical Medical Research Award



**“When we started this work, there was no greater optimism for an HPV vaccine than there was for an HIV vaccine. In fact, there was skepticism that it could work at all.”**

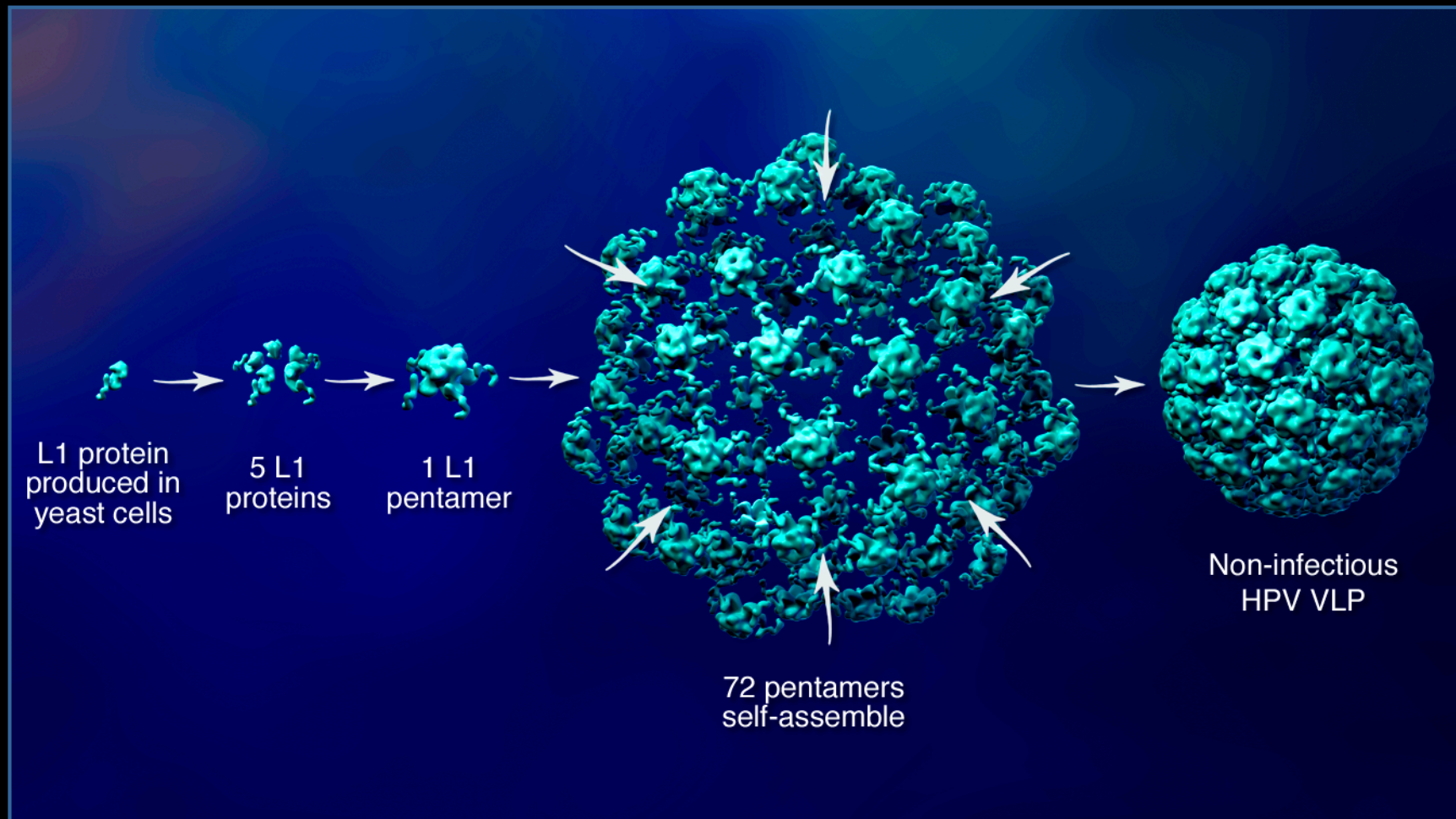
**—Dr. John Schiller, Ph.D.**



John T. Schiller, Ph.D

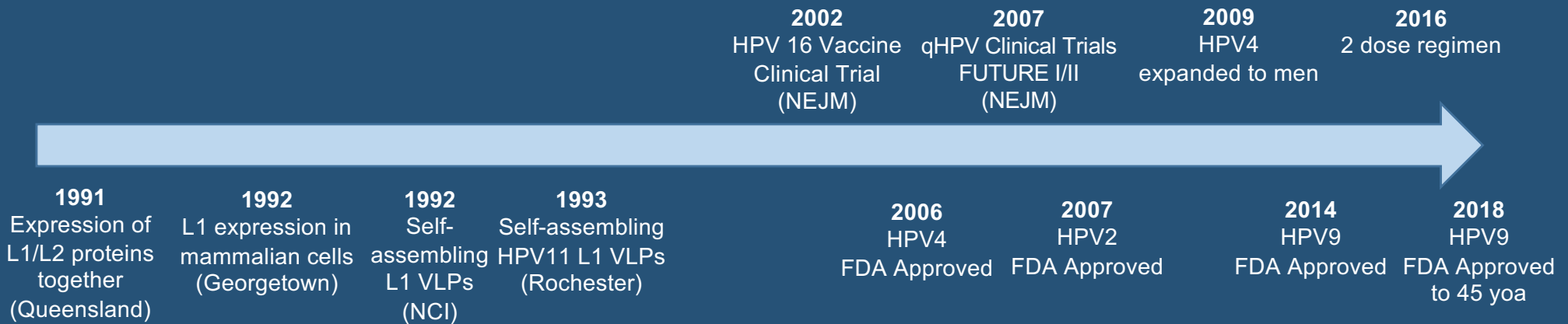
Douglas R. Lowy, M.D

# Assembly of VLPs



1. Berzofsky JA, et al. *J Clin Invest.* 2004;114:450–462.
2. Kirnbauer R, et al. *Proc Natl Acad Sci USA.* 1992;89:12180–12184.
3. Modis Y, et al. *EMBO J.* 2002;21:4754–4762.

# HPV Vaccine Development Timeline



**Vaccines Are Always Political**

# Perfect political storm in 2006

- qHPV vaccine approved by the Therapeutics Goods Administration.
- Australian vaccine with an iconic inventor.
- National Immunization Program initially rejected it.



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- Election year, with a budget surplus.
- Health Minister with a dubious reputation in women's health.

*“I won't be rushing out to get my daughters vaccinated...”*



Tony Abbott



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- **First Lady** with cancer of the cervix



John  
Howard

Janette  
Howard

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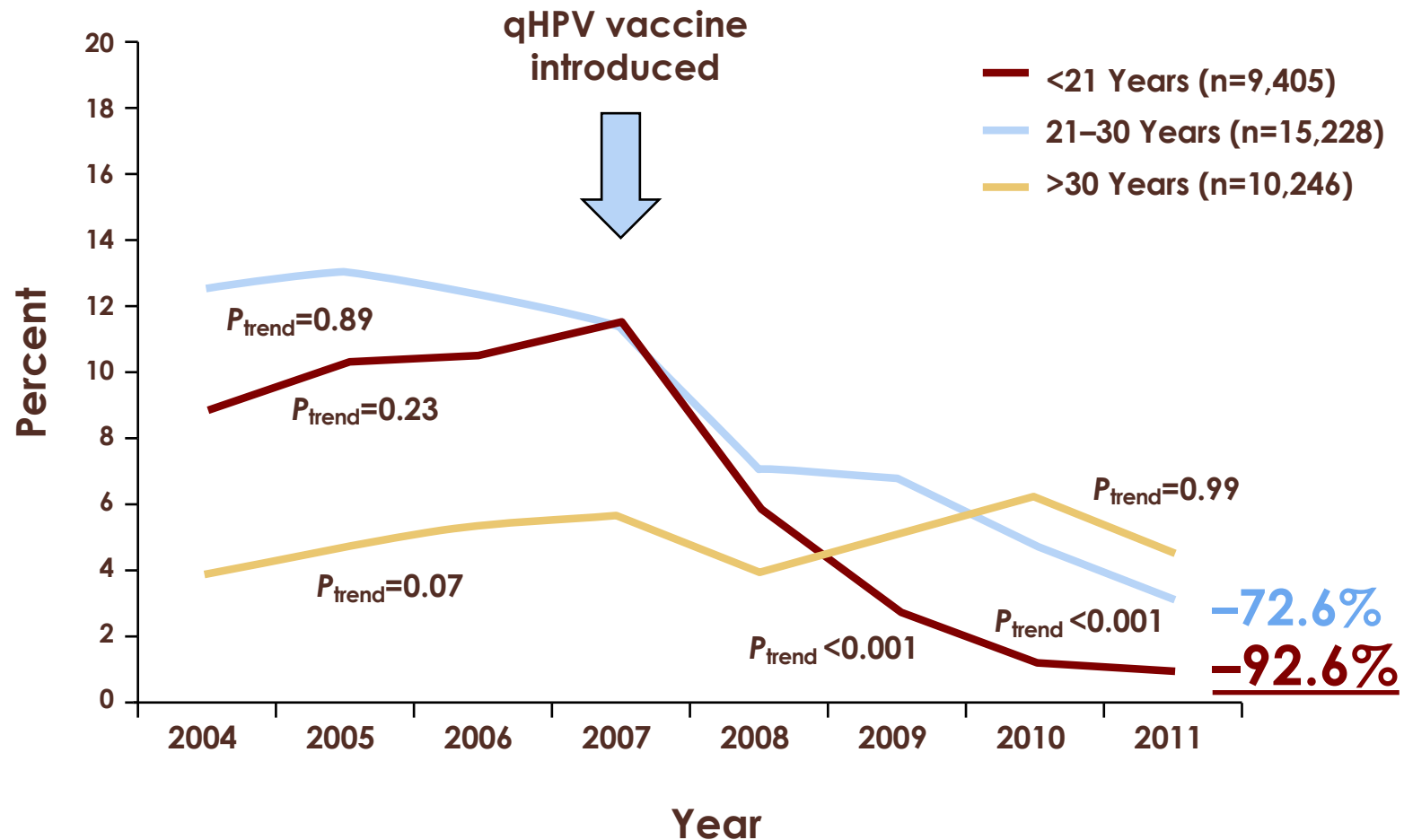
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- Australian vaccine with an iconic inventor.
- National Immunization Program initially rejected the HPV Vaccine
  - Election year, with a budget surplus.
- Health Minister with a dubious reputation in women's health.
- **First Lady** with cancer of the cervix.
  - De-stigmatized the disease
  - Influenced husband



John  
Howard

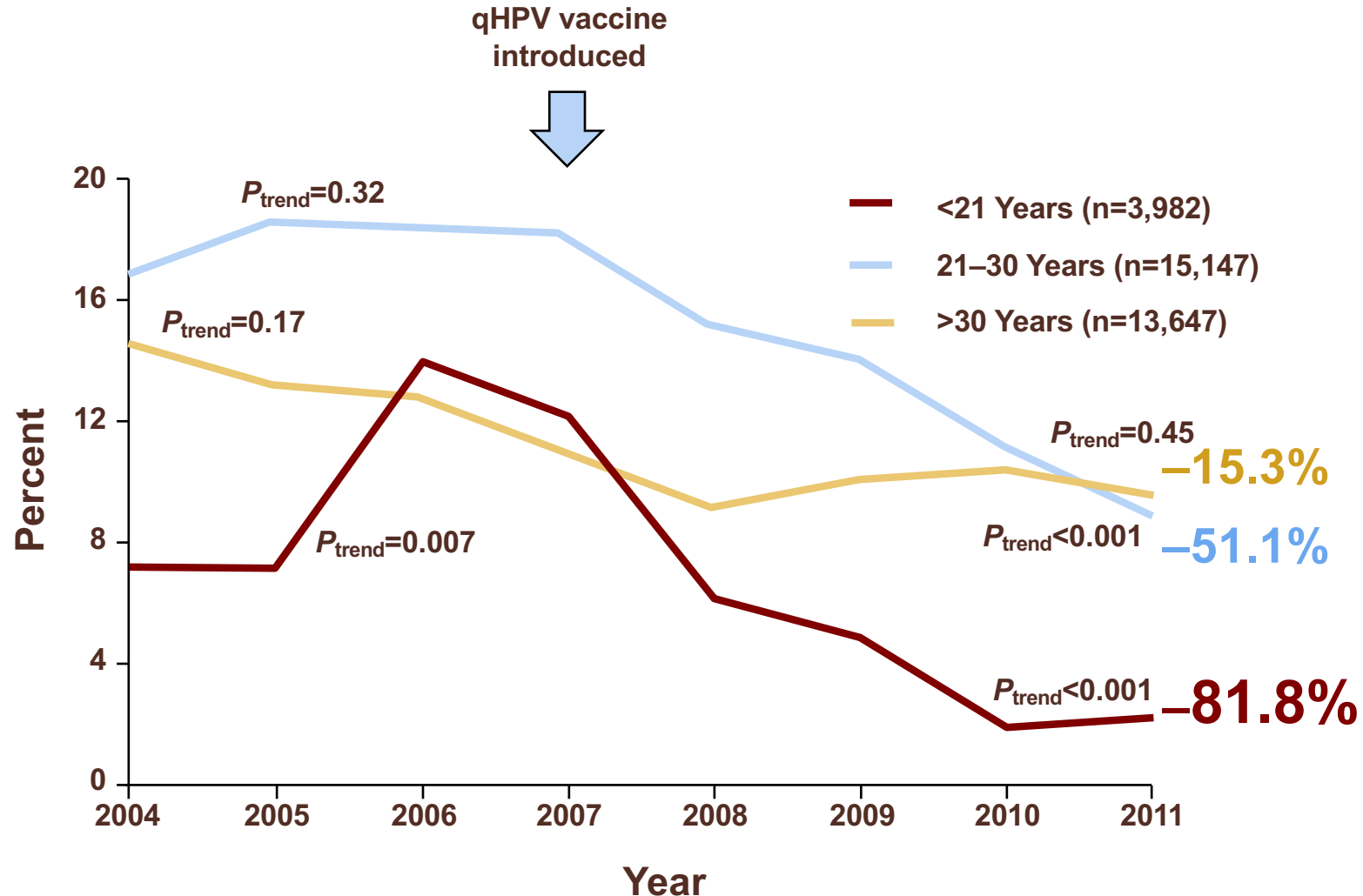
Janette  
Howard

# Proportion of Australian-born females with GW, by age group, 2004–2011



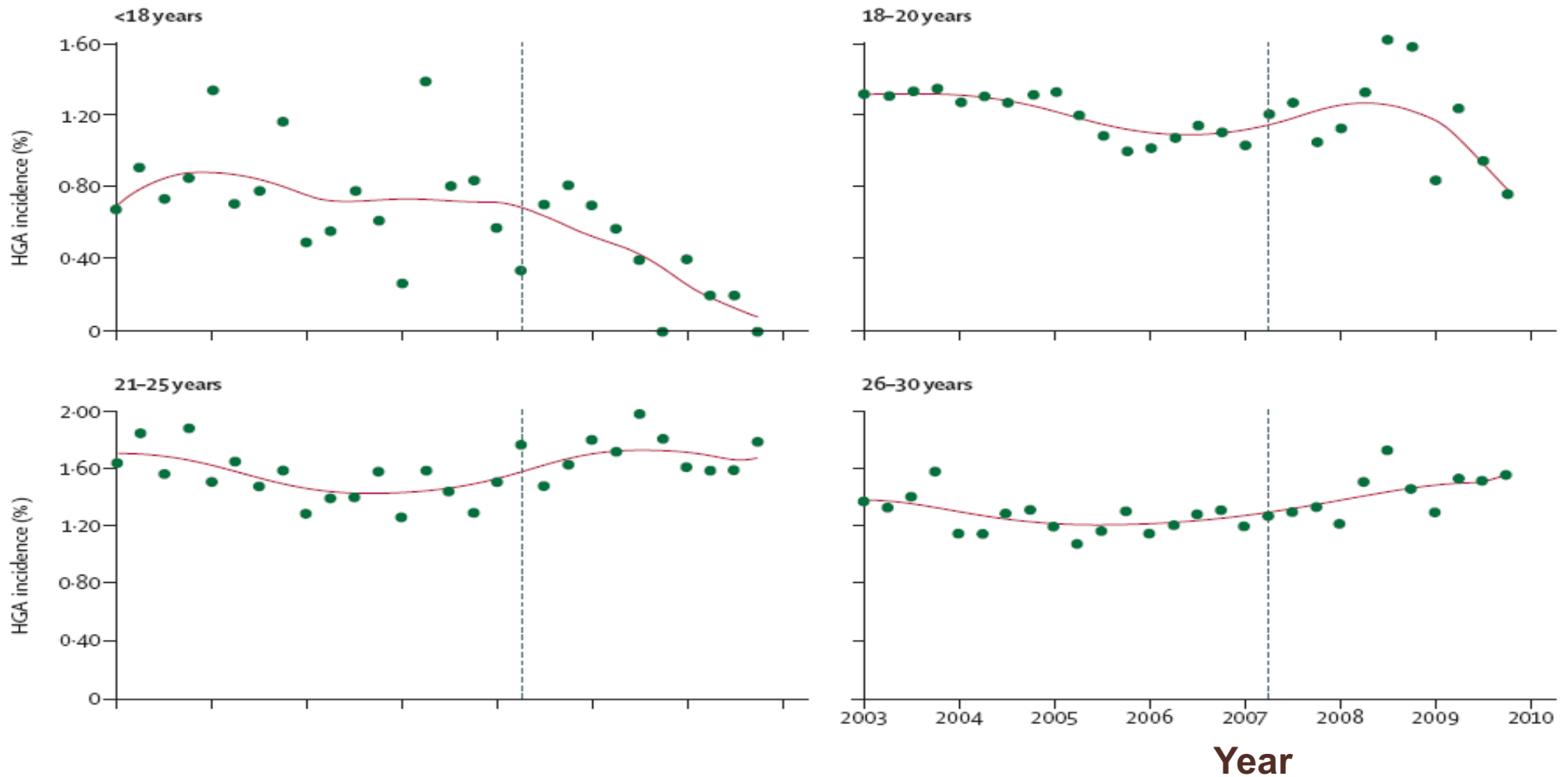
Ali H et al. *BMJ* 2013;346:f2032.

# Proportion of Australian-born heterosexual males with GW by age group, 2004–2011



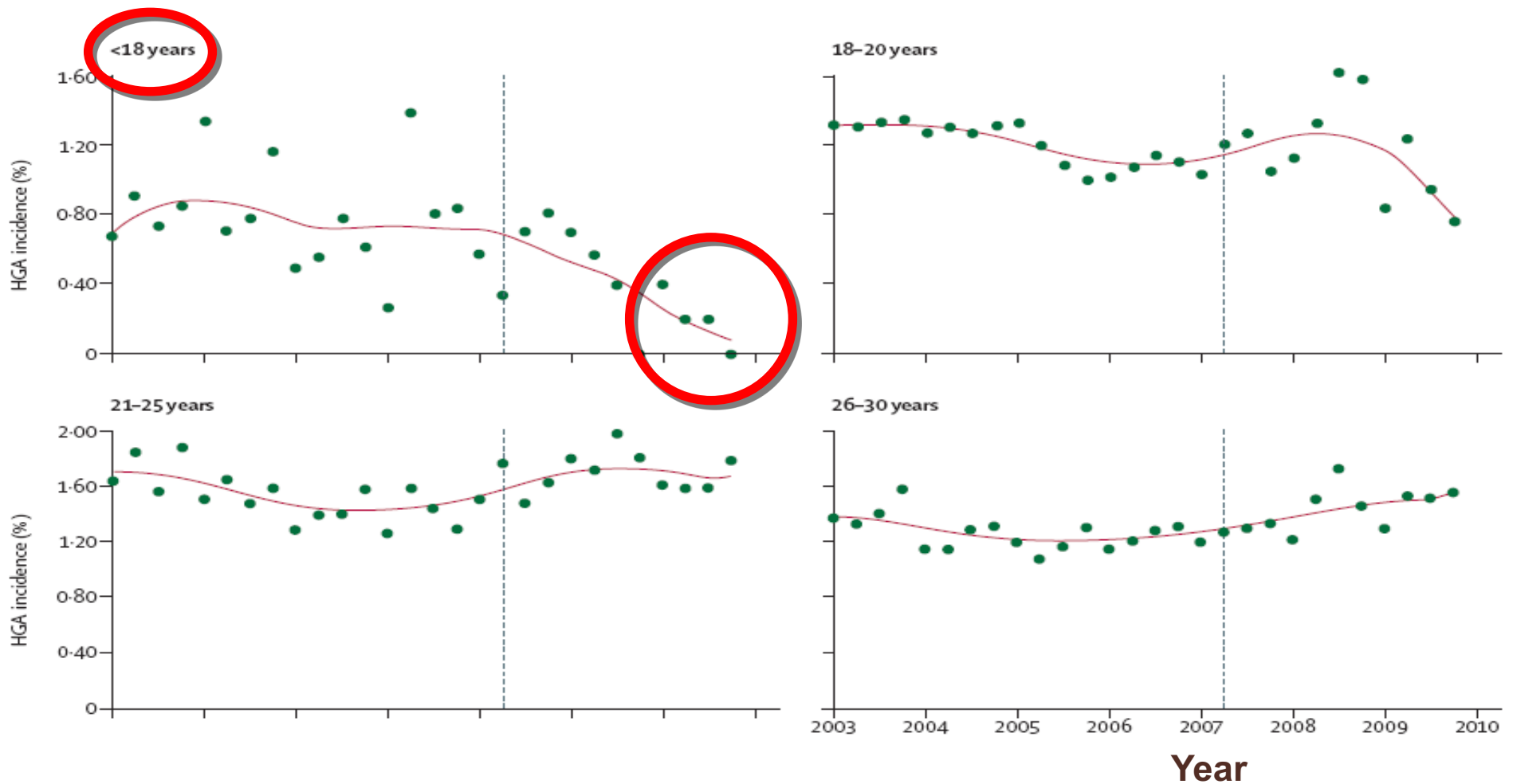
Ali H et al. *BMJ* 2013;346:f2032.

# High-grade cervical abnormalities in young Victorian women, by age group, 2003–2010



Brotherton JM et al. *Lancet* 2011; 377: 2085

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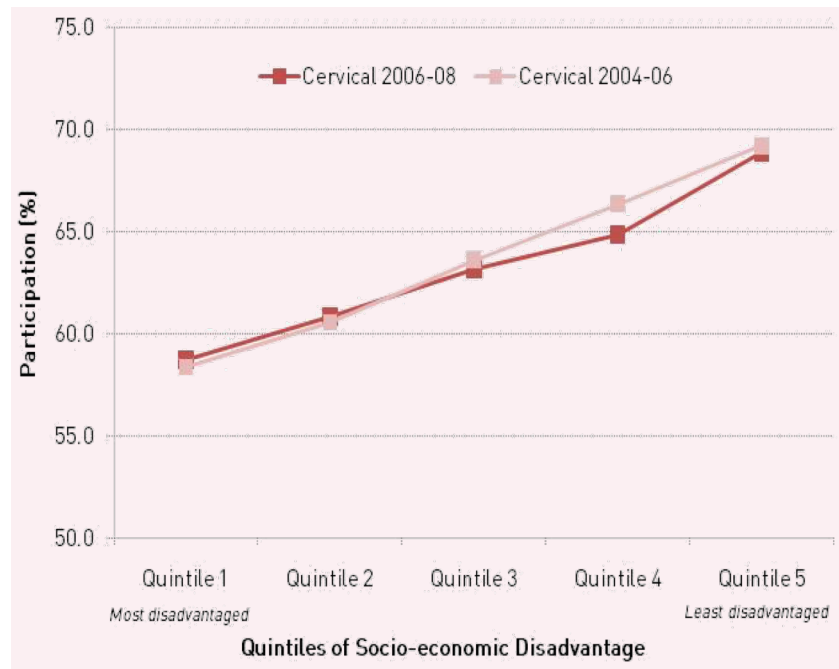


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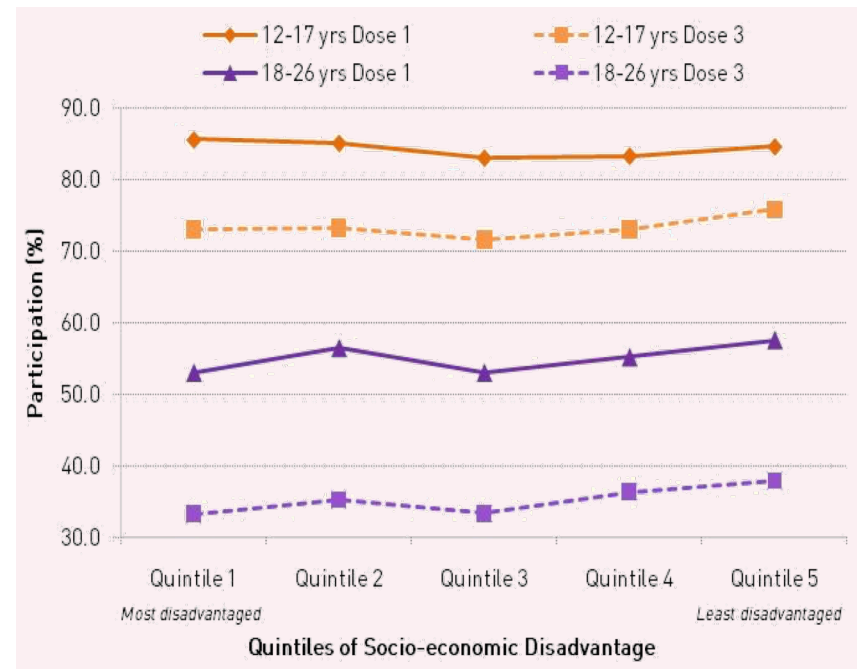


# Equity in cervical screening v HPV vaccination

## National Cervical Screening Program by socioeconomic status, Victoria

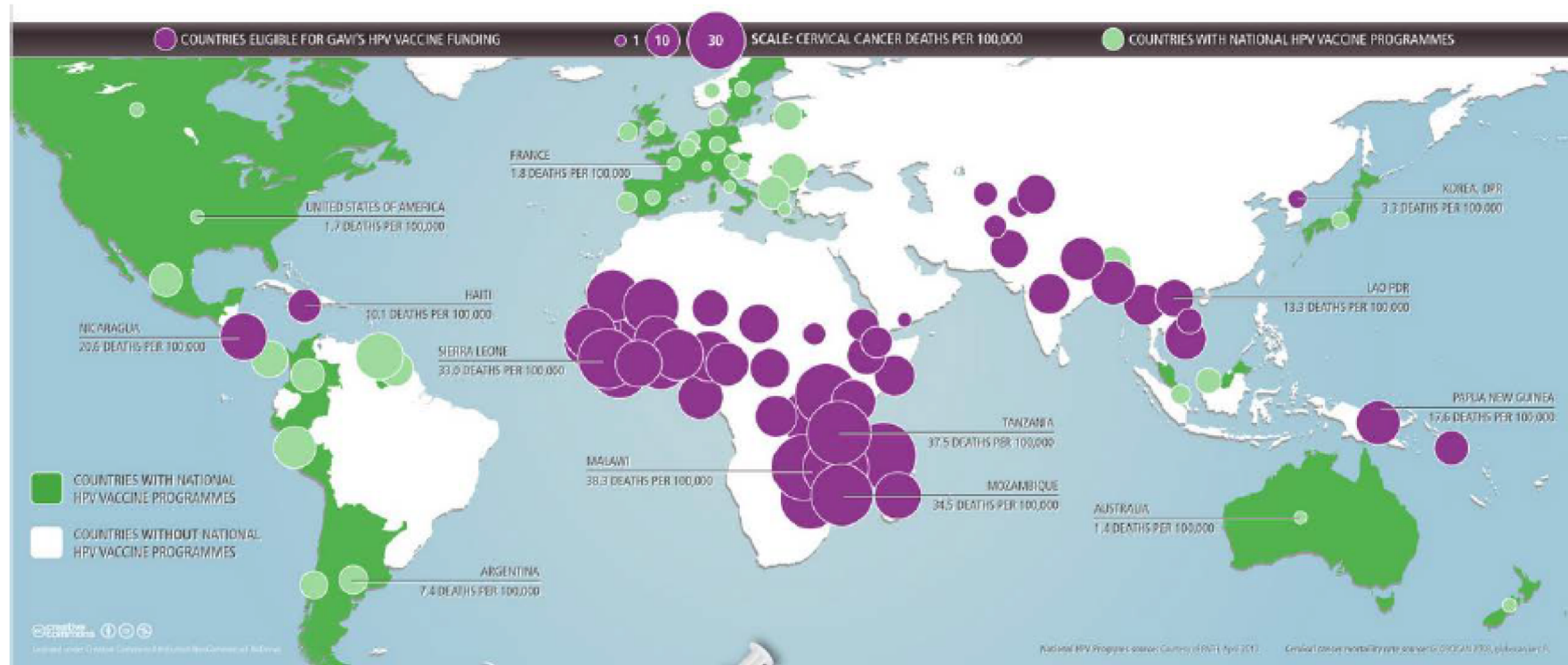


## National HPV Vaccination Program by socioeconomic status, Victoria



Barbaro et al. *Med J Aust* 2012; 196: 445

# Current global vaccination patterns will only have a marginal reduction on cervical cancer



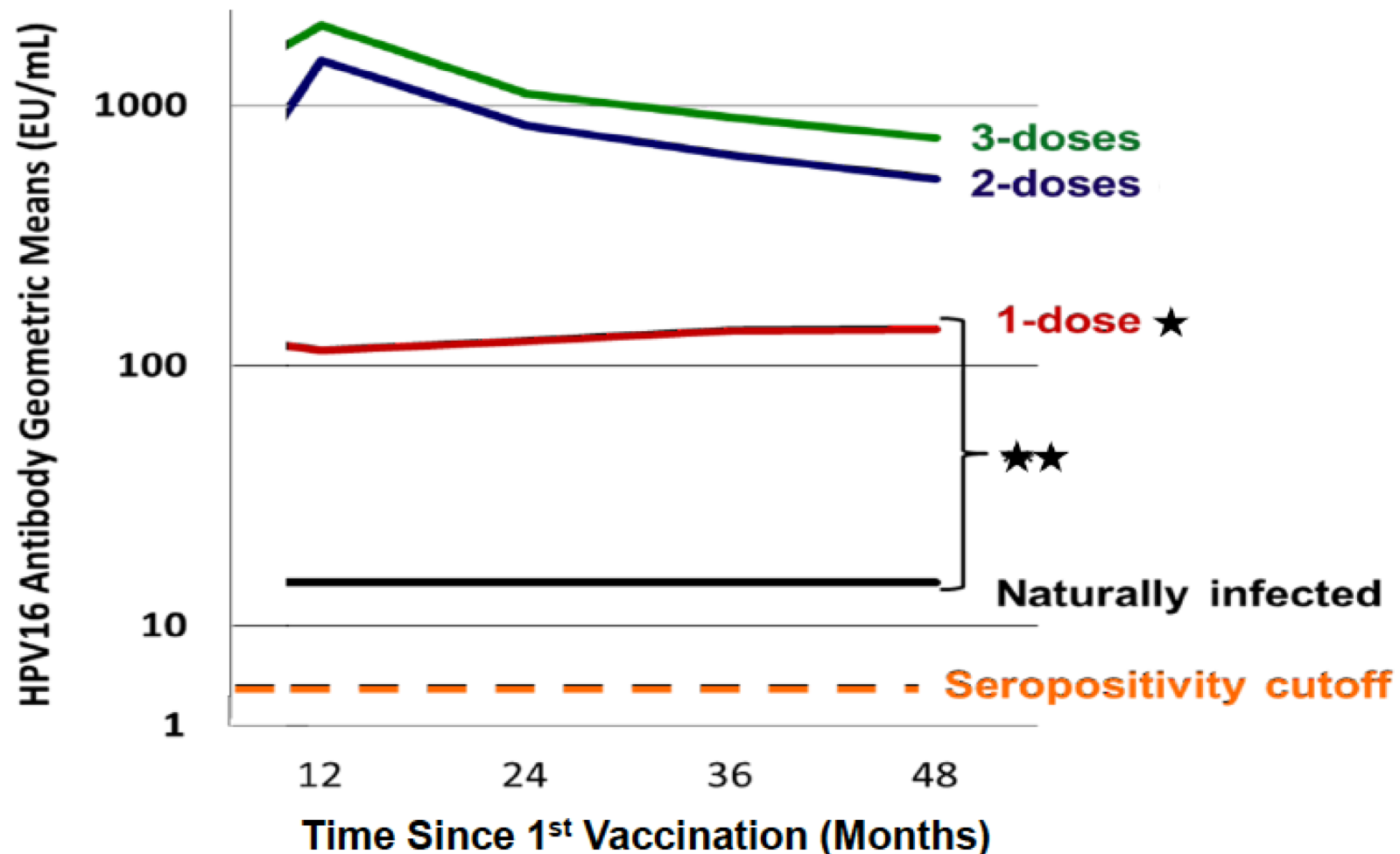
[http://www.gavi.org/uploadedImages/Types\\_of\\_support/NVS/HPV/HPV-vaccine-infographic-1600\\_source.jpg](http://www.gavi.org/uploadedImages/Types_of_support/NVS/HPV/HPV-vaccine-infographic-1600_source.jpg)

**TWO DOSES IS NOW STANDARD OF CARE:  
WHAT ABOUT ONE DOSE? IS THAT ACHIEVABLE?**

# Single-dose immunogenicity

\* 4-fold difference between 1 and 3 dose plateau titers

\*\* ~10-fold difference between 1 dose and natural infection plateau titers



# Single-dose vaccine efficacy

*Post-hoc analysis of bivalent HPV vaccine in Costa Rica HPV Vaccine Trial*

# of Doses	Arm	# Women	HPV16/18 6+ mo Persistence N (%)	HPV16/18 Vaccine Efficacy (95%CI)
3	Control	3010	229 (8%)	84% (77% to 89%)
	HPV	2957	37 (1%)	
2	Control	380	24 (6%)	81% (53% to 94%)
	HPV	422	5 (1%)	
1	Control	188	15 (8%)	100% (79% to 100%)
	HPV	196	0 (0%)	

# **Scientific Evaluation of One or Two Doses of the Bivalent or Nonavalent Prophylactic HPV Vaccines: The ESCUDDO Study**



**Estimated Enrollment: 25,000**

**Location: Costa Rica**

**Estimated Study Start Date: March 6, 2019**

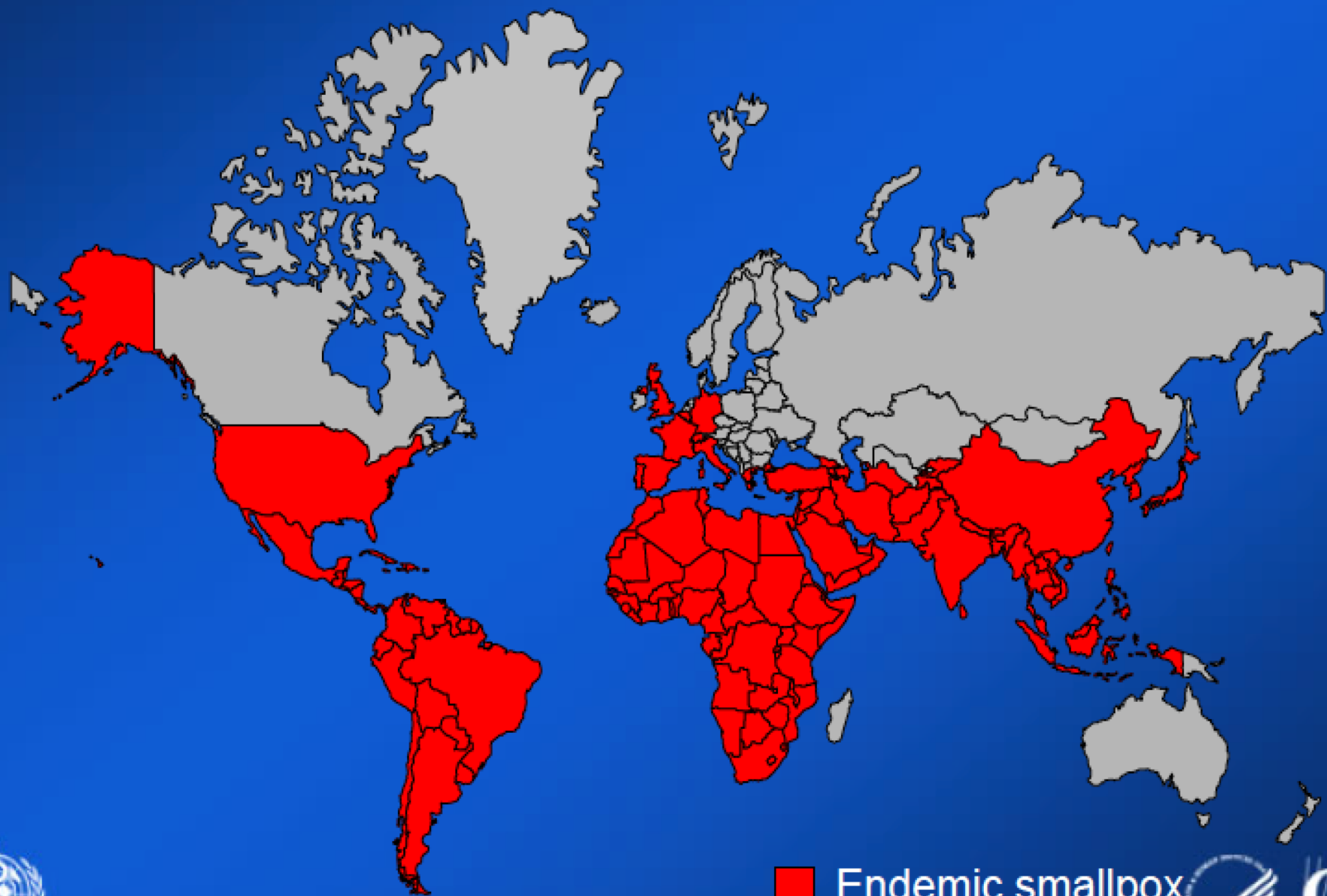
**Estimated Primary Completion Date: December 31, 2022**

**Estimated Study Completion Date: December 31, 2024**

**Aimée R. Kreimer, Ph.D.  
Senior Investigator  
National Cancer Institute**



# Smallpox Endemic Areas 1945

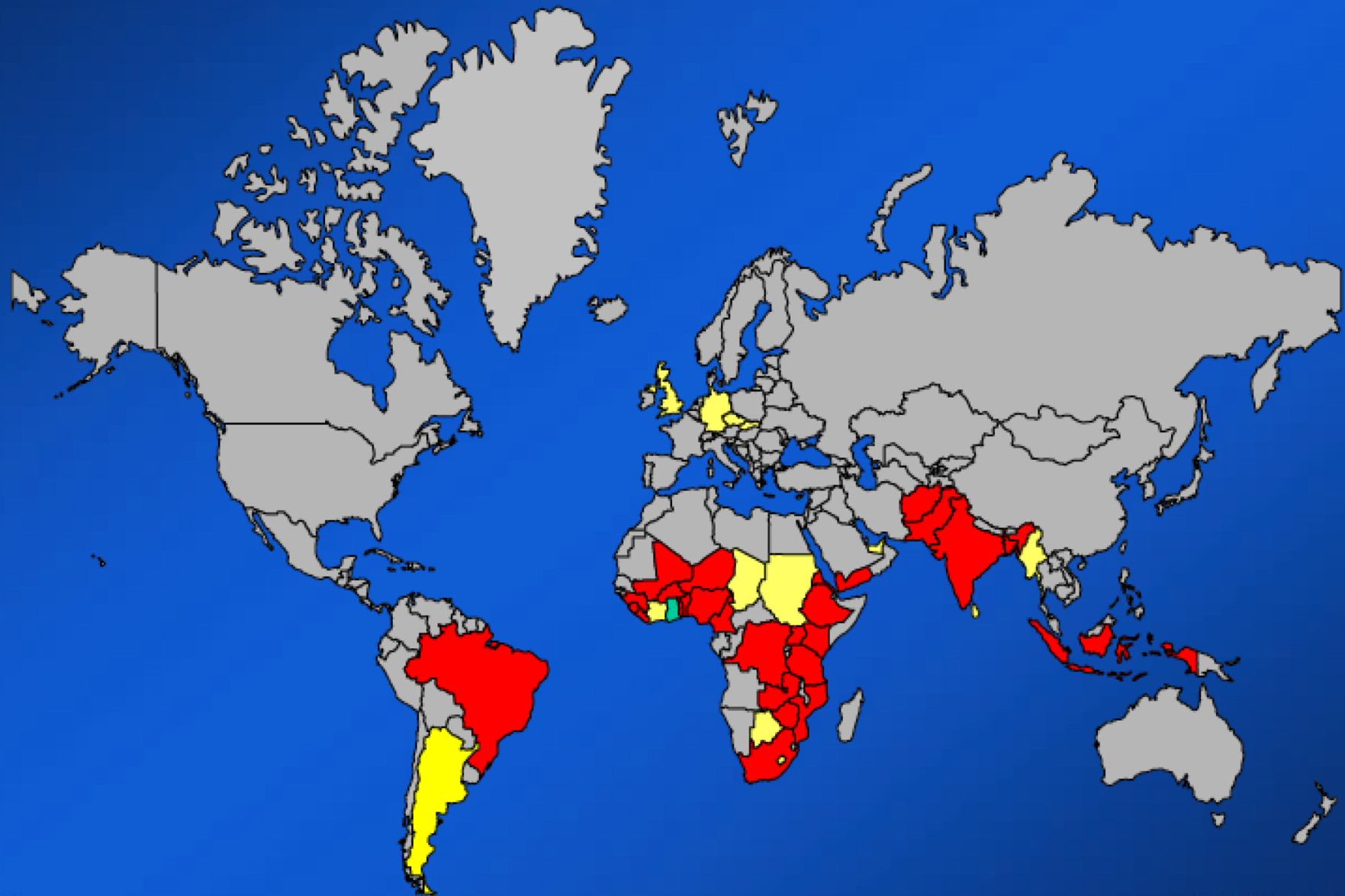


Endemic smallpox



CDC

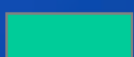
# Smallpox Endemic Areas 1967



Endemic



Importations

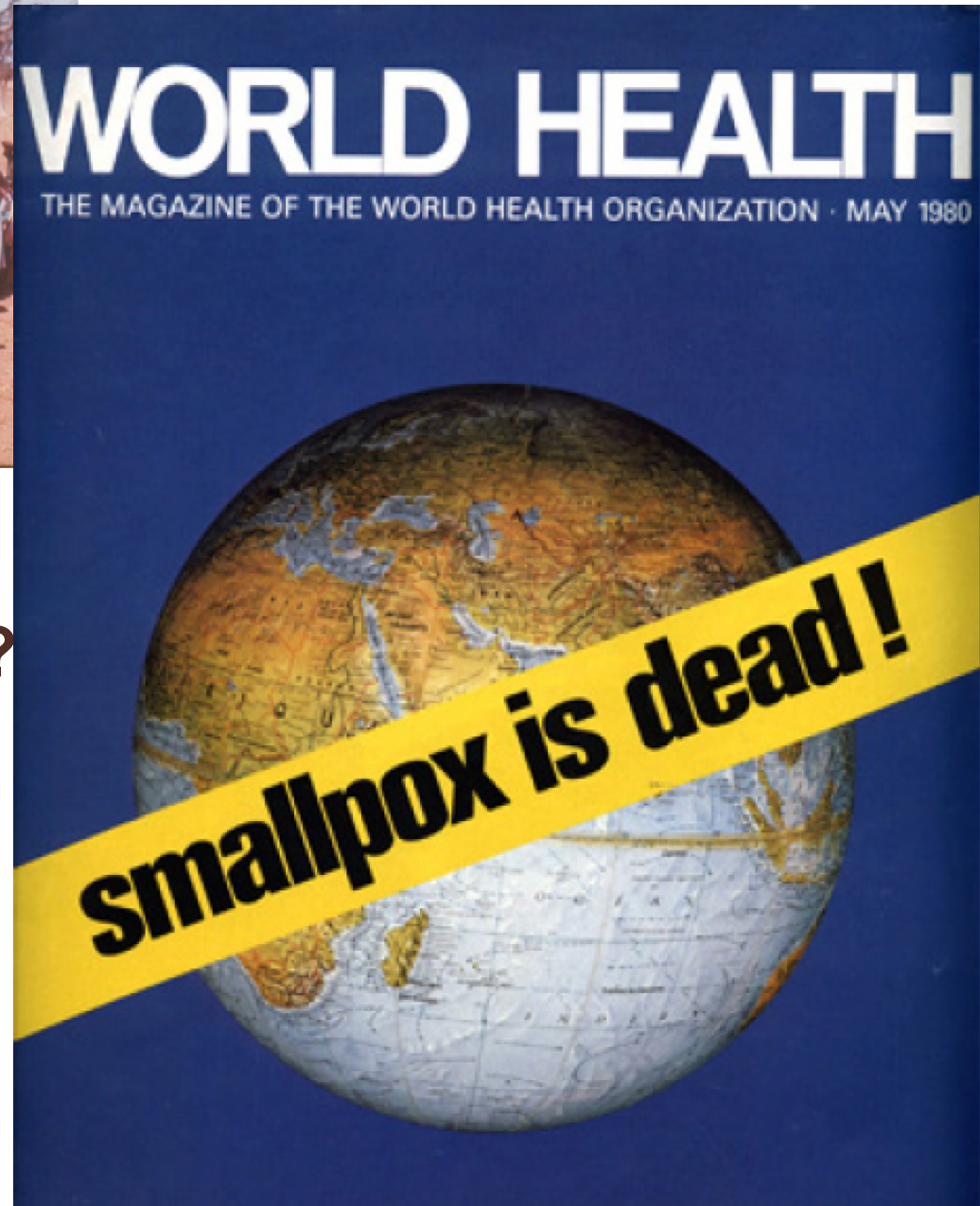


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CDC





Why can't we do the same  
for HPV and cervical cancer?

