National Cancer Institute

Deep Sea, Deep Science

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ACS National HPV Vaccine Roundtable Meeting
Atlanta, Georgia
August 21, 2019

The views expressed are my own and do not necessarily reflect those of NCI/NIH

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health

Disclosures

- National Institutes of Health (NIH) has patents on papillomavirus L1 virus-like particle (VLP) vaccine technology. I am an inventor.
- NIH has licensed L1 VLP technology to Merck and GlaxoSmithKline, the two companies with commercial versions of the vaccine.
- ***I will discuss a potential off-label use of the FDA-approved vaccines: protecting with a single vaccine dose***
- Licensees of other NIH technologies of which I am an inventor: GlaxoSmithKline, Sanofi, Shanta Biotech, Cytos Biotech, Aura Biosciences, Etna Biotech, Acambis, PanVax

Topics for this evening

- **A ”fish story”**
- **HPV vaccination, reducing disparities in the US and globally**
  - Cervical cancer screening can reduce disease burden faster than vaccination
- **A single vaccine dose: a future possibility?**
- **A 2025 goal**

The closest I could get to a fish story

Lopez-Bueno et al, Concurrence of Iridovirus, Polyomavirus, and a unique member of a new group of fish papillomaviruses in lymphocytosis disease-affected gilthead seabream. J Virol 90: 8768-79, 2016.

A "papillomavirus" whose genome is 5,748 bp. No lesions attributable to it have been described.

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Bossart et al, Viral papillomatosis in Florida manatees (Trichechus manatus latirostris). Exp Mol Pathol 72: 37-48, 2002. **"In 1997, seven captive Florida manatees developed multiple, cutaneous, pedunculated papillomas over a period of 6 months. Approximately 3 years later, four of the seven manatees developed multiple, cutaneous, sessile papillomas topically and clinically distinct from the initial lesions, some of which are still present."**

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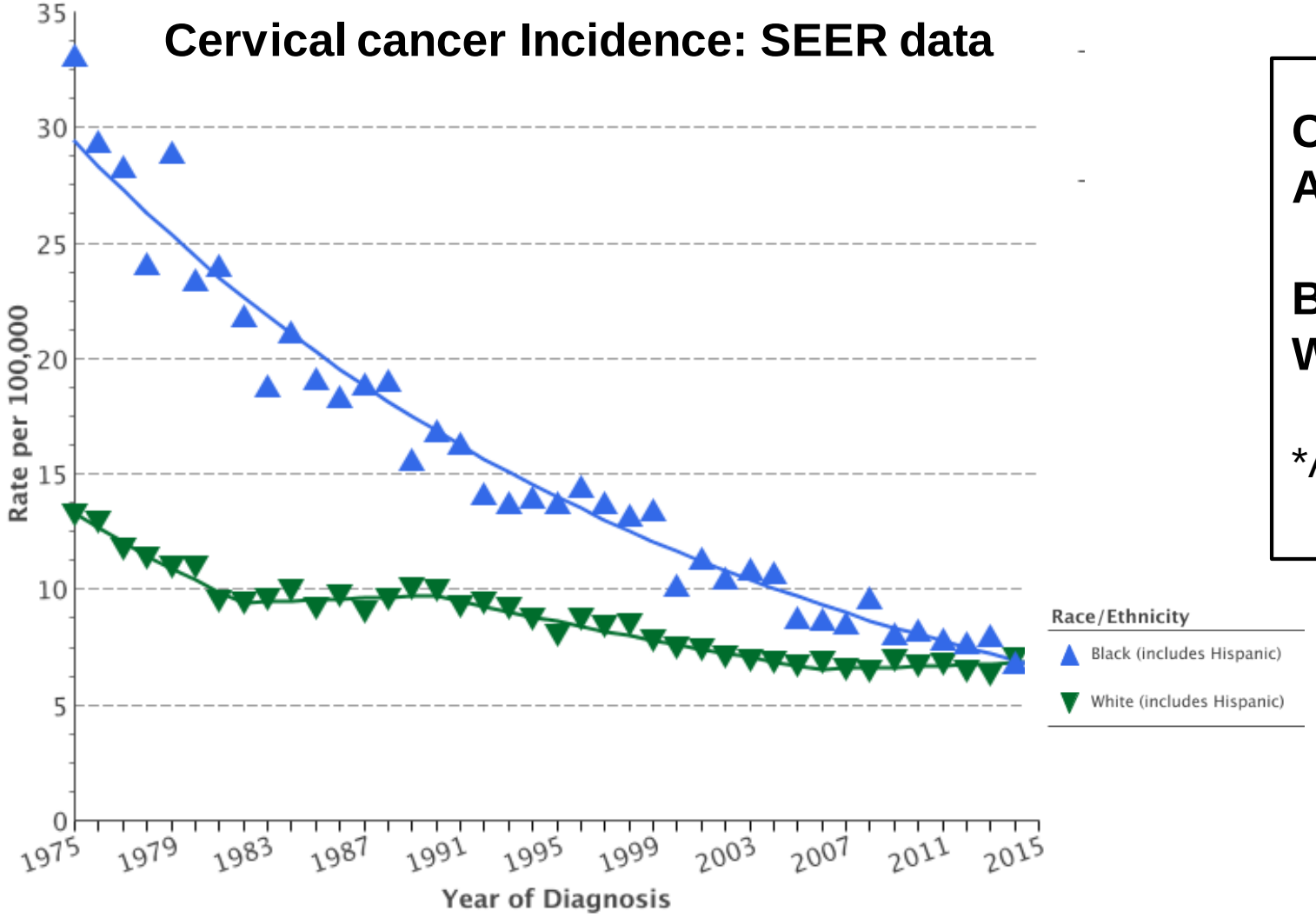
Herman Melville, Chapter 32, Cetology, Moby-Dick, 1851. **"The whale is a fish."**

Cervical cancer in the USA: Incidence in black women is now similar to white women; mortality disparity remains

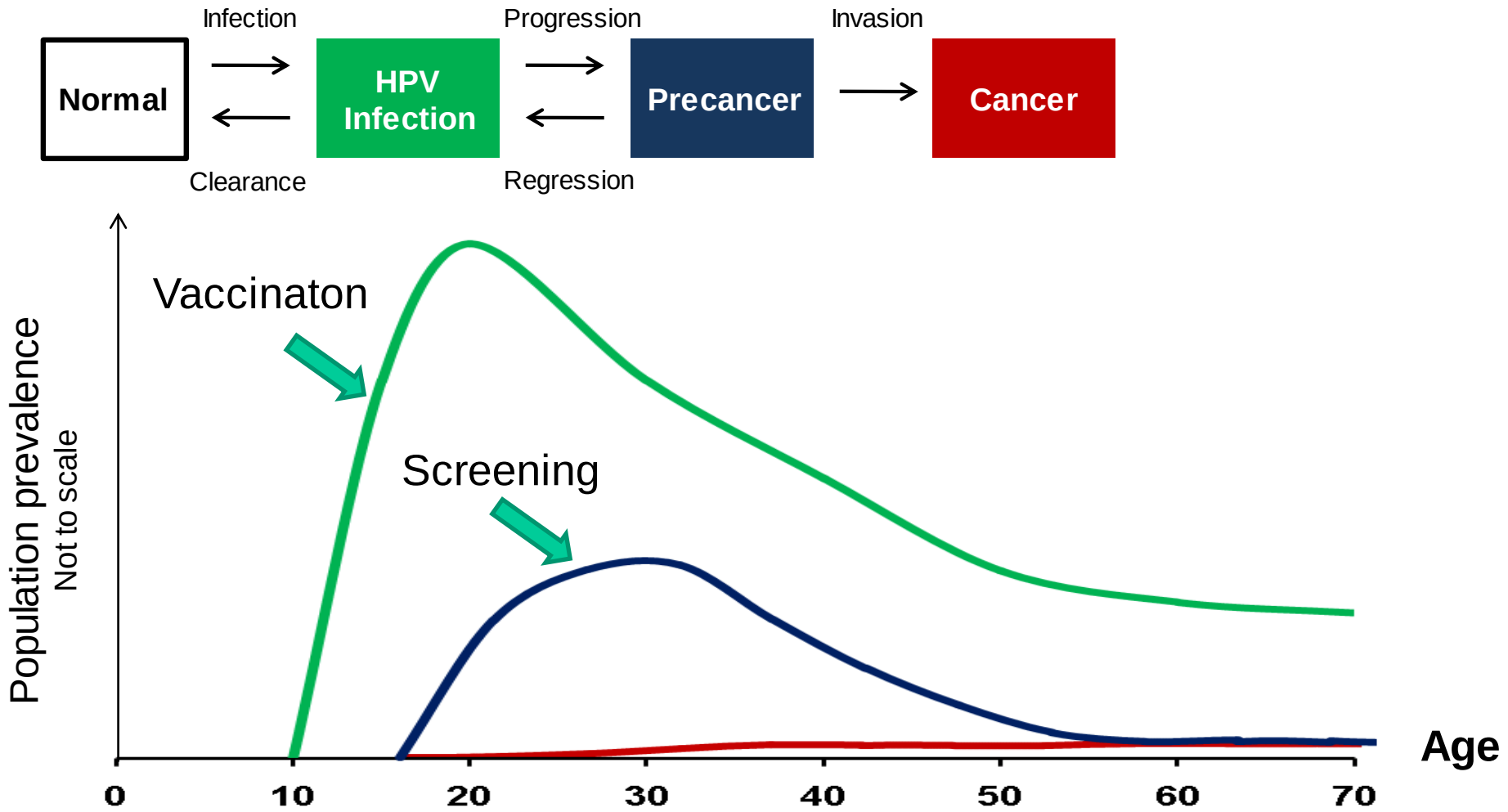


Current mortality rates
ASR* 2012-2016

Black women: 3.5
White women. 2.2

*ASR=Annual Standardized Rate

Cervical cancer screening can reduce cancer faster than vaccination



Natural history is universal: Same in high- and low-resource settings

Wentzensen and Schiffman Lancet Public Health 2017

Collaborators

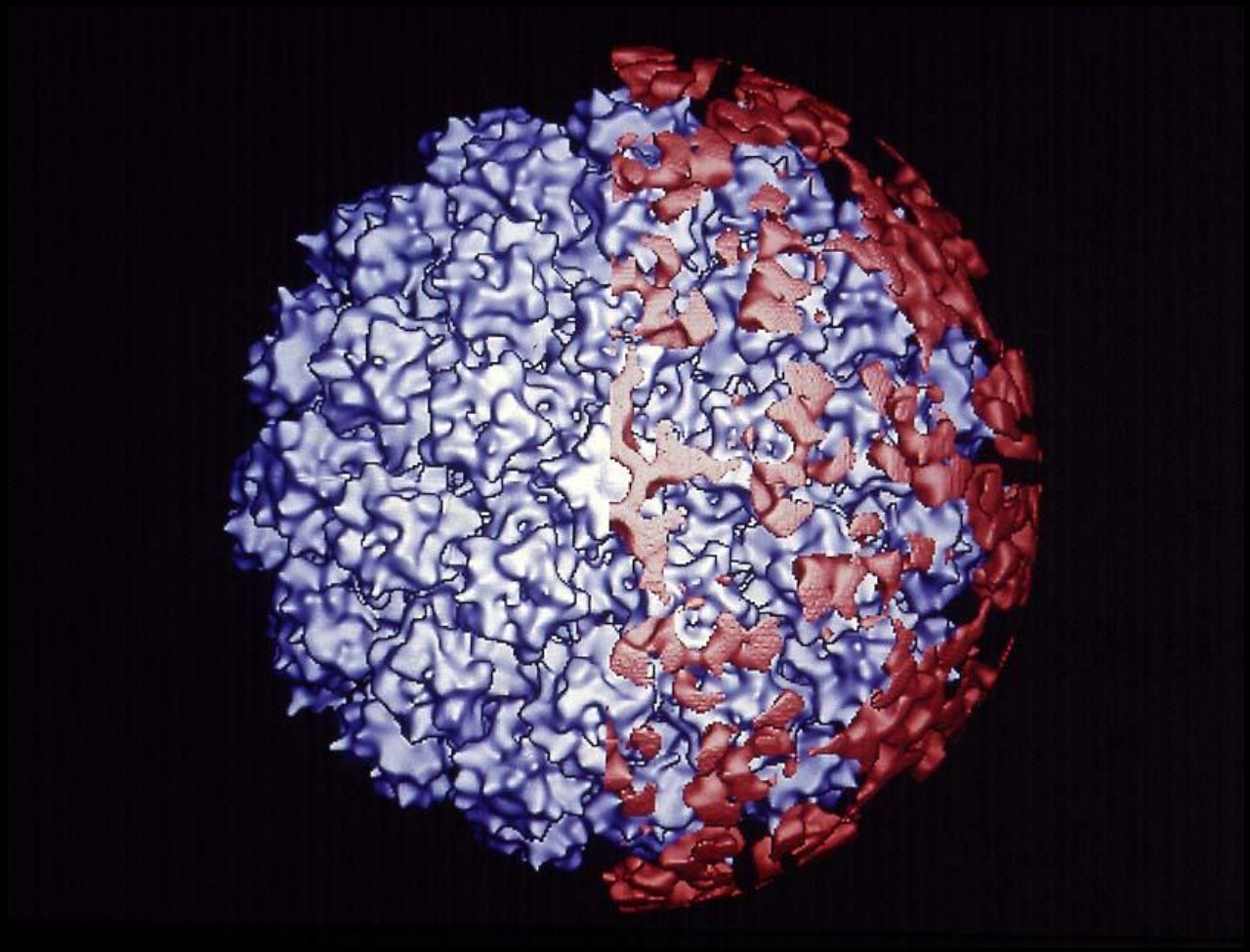
Laboratory of Cellular Oncology, CCR, NCI

John Schiller

- Patricia Day
- Nicolas Cuburu
- Rhonda Kines
- Susana Pang
- Cynthia Thompson
- Alessandra Handisurya
- Lukas Bialkowski
- Alex Bell

- Chris Buck, Diana Pastrana
  – **LCO, CCR, NCI, Bethesda**
- Aimee Kreimer, Allan Hildesheim, Mark Schiffman, Mahboobeh Safaeian, Ligia Pinto
  – **DCEG, NCI, Bethesda**
- Peter Choyke, Marcelino Bernardo
  – **Molecular Imaging, CCR, NCI, Bethesda**
- Jeffrey Roberts – **FDA, Rockville**
- Rolando Herrero – **IARC, Lyon, France**
- Bryce Chackerian – **University of New Mexico**
- Reinhard Kirnbauer – **University of Vienna, Austria**

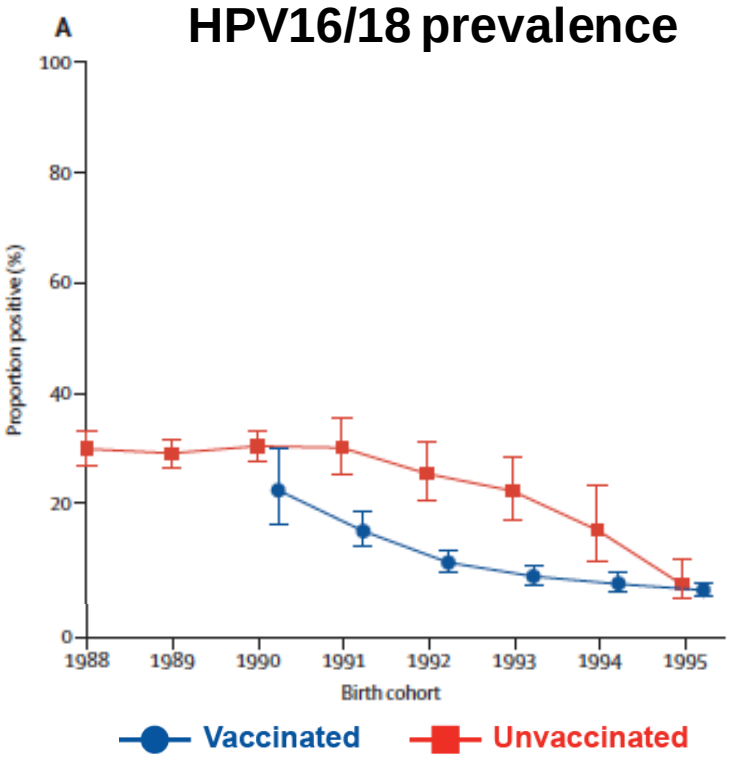
Neutralizing L1 Antibodies (in red) Bound to Papillomavirus Particle



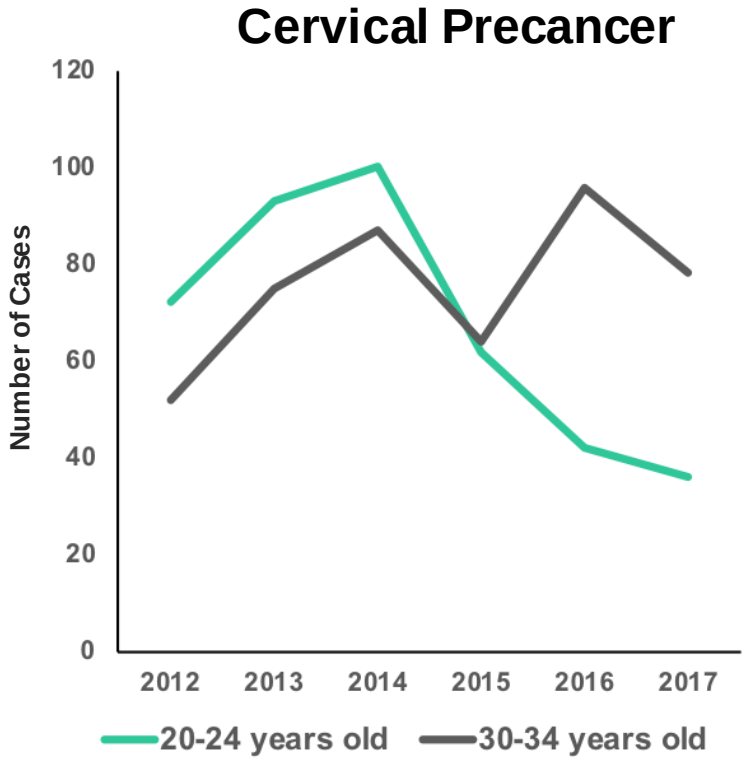
Disease prevention goals of HPV vaccination: in less developed countries vs. more developed countries

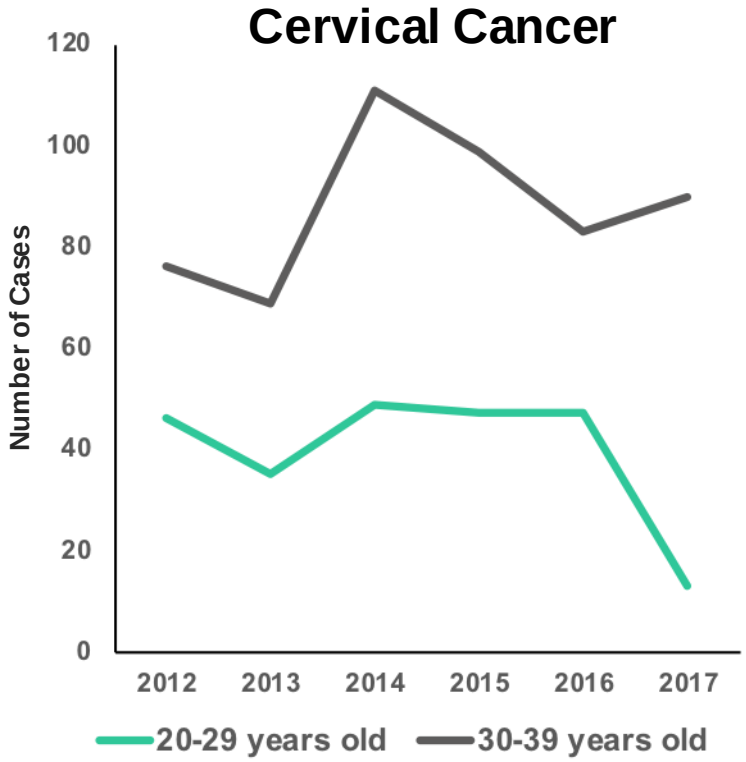
- **Less developed countries:** mainly to protect against cervical cancer
  - Female vaccination most cost-effective
- **More developed countries:** to protect both males and females against a range of HPV-associated cancers
  - Female vaccination with high uptake is most cost-effective, but adding male vaccination can confer even greater protection for vaccinees than can herd immunity alone
  - Male vaccination is the fastest way to reduce HPV prevalence in MSM

Impact of bivalent HPV vaccine on young women in Scotland: herd immunity and reductions in cervical precancer and cervical cancer



Kavanaugh et al, Lancet Infect Dis 17:1293-1302, 2017





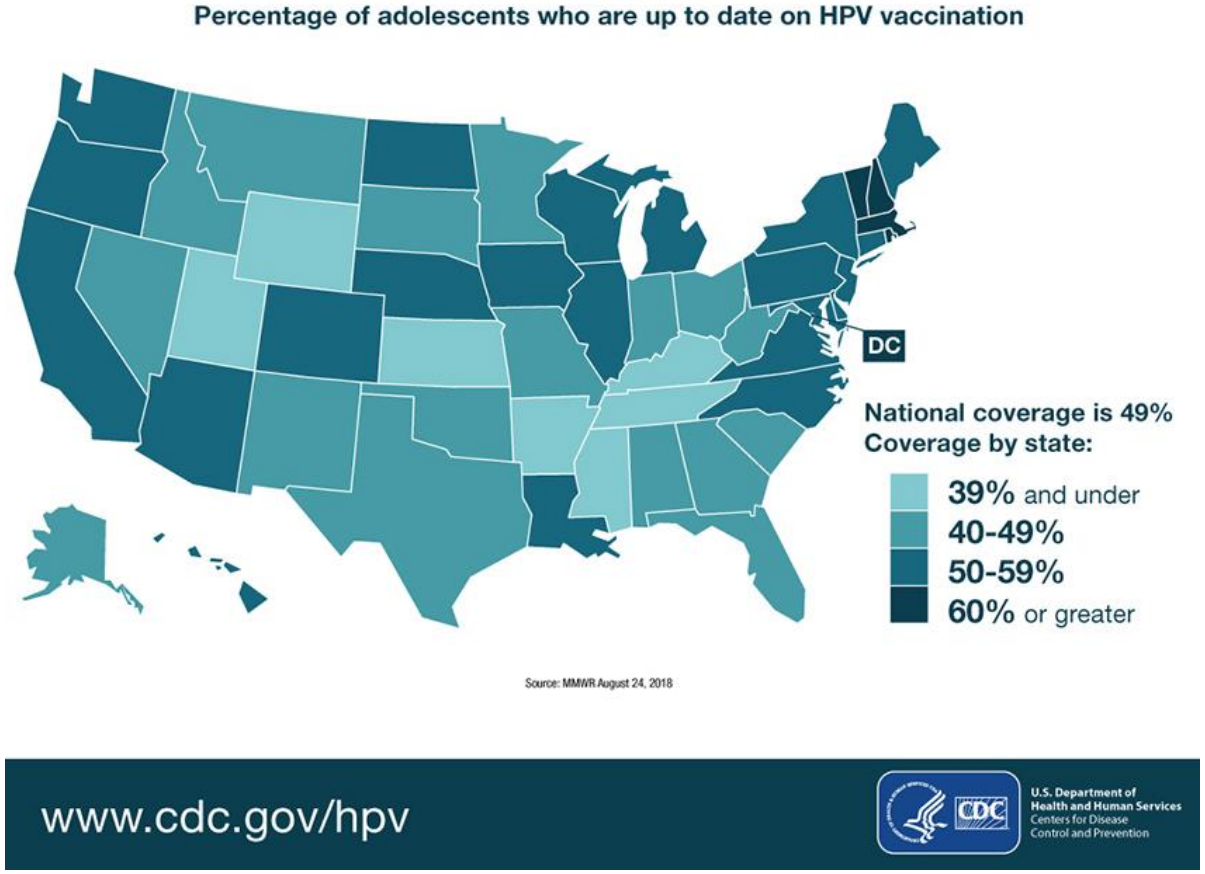
From Scotland cancer statistics web site: *https://www.isdscotland.org/Health-Topics/Cancer/Cancer-Statistics/Female-Genital-Organ/#cervix*

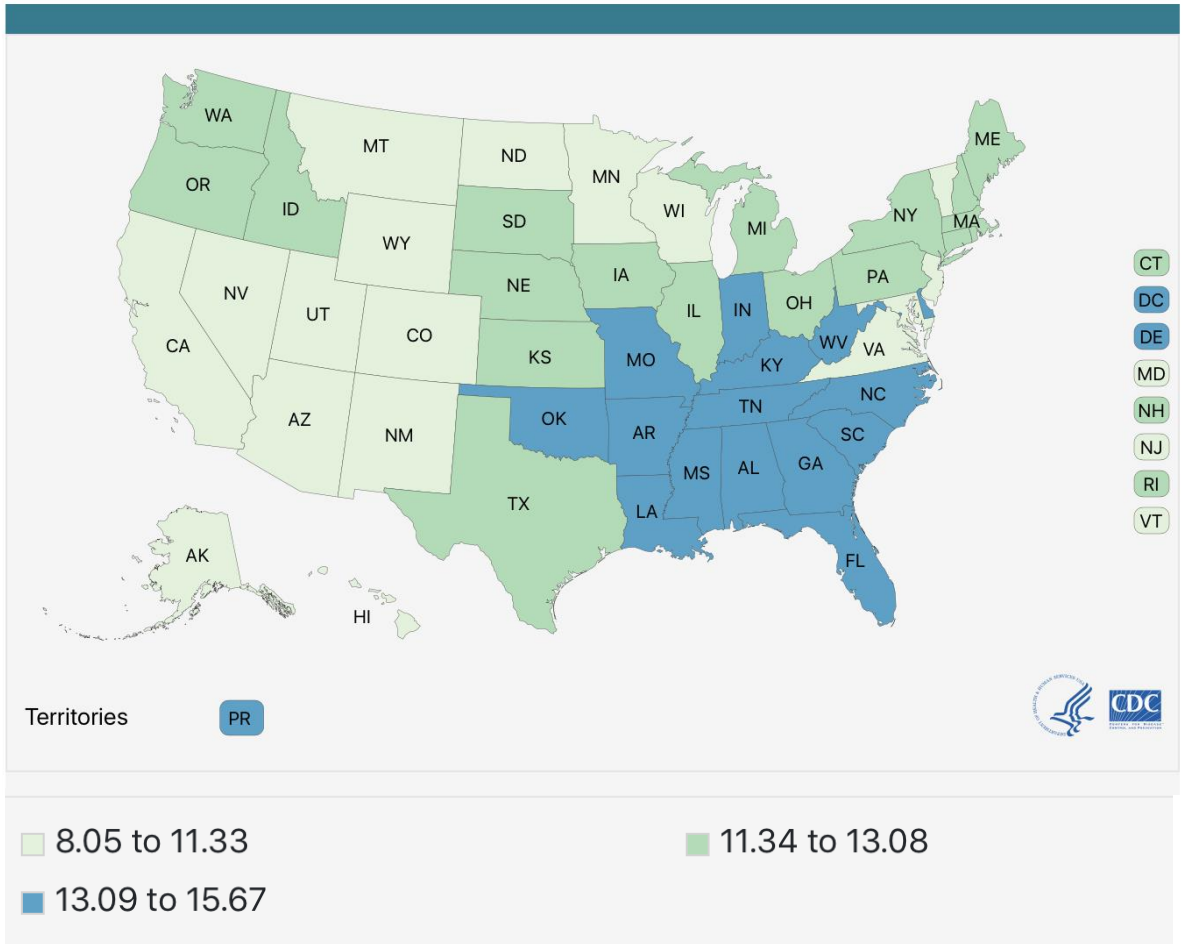
In Black and Hispanic women, 9-valent HPV vaccine may be especially useful for preventing more precancers

	White	Black	Hispanic
Cervical cancer			
HPV16/18	67%	68%	64%
HPV31/33/45/52/58	12%	15%	18%
Total	79%	83%	82%
In situ cervical cancer			
HPV16/18	67%	27%	50%
HPV31/33/45/52/58	16%	37%	26%
Total	83%	64%	76%

From Saraiya et al, JNCI, 2015

Lower HPV vaccine uptake in many states with higher incidence of HPV-associated cancer





2017 HPV and Meningococcal Vaccination Rates for 13-17 year olds

	HPV vaccine (≥1 dose)	Meningococcal vaccine (≥1 dose)
United States	**65%**	**85%**
Below poverty	**73%**	**86%**
At or above poverty	**63%**	**85%**
Illinois	**66%**	**89%**
Chicago	82%	91%
Rest of state	63%	89%
Indiana	**59%**	**93%**

From MMWR August 24, 2018

One more complication: A worldwide HPV vaccine shortage

- In 2018, UNICEF and the World Health Organization called attention to a worldwide shortage of the HPV vaccine.
  - https://www.unicef.org/supply/files/HPV_2_Status_Update.pdf
  - https://www.who.int/immunization/programmes_systems/procurement/v3p/platform/module2/WHO_HPV_market_study_public_summary.pdf
- Secondary to increased vaccine demand
- The shortage is projected to last several years.

Question: During this period, should there be policy implications in the industrialized world when considering **adding** gender-neutral vaccination or **increasing** the age range for recommending vaccination?

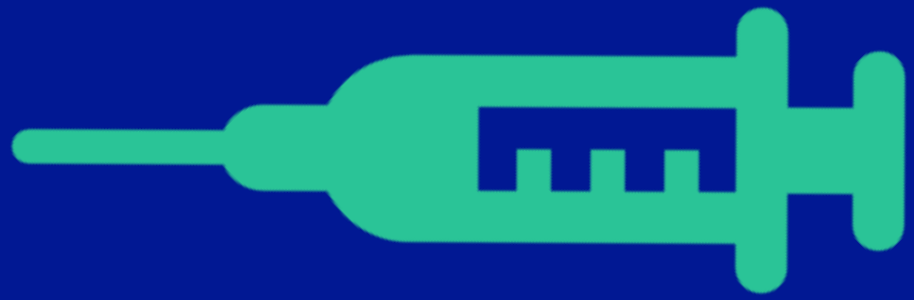
The challenge to global HPV vaccination

107 million girls 10-14 years old have received at least one dose of the HPV vaccine (2006-2017)

- However, <5% of eligible girls have been vaccinated in Low- and Middle-Income Countries (LMICs), where ~90% of cervical cancer deaths occur
- Worldwide >60 million girls are now born annually

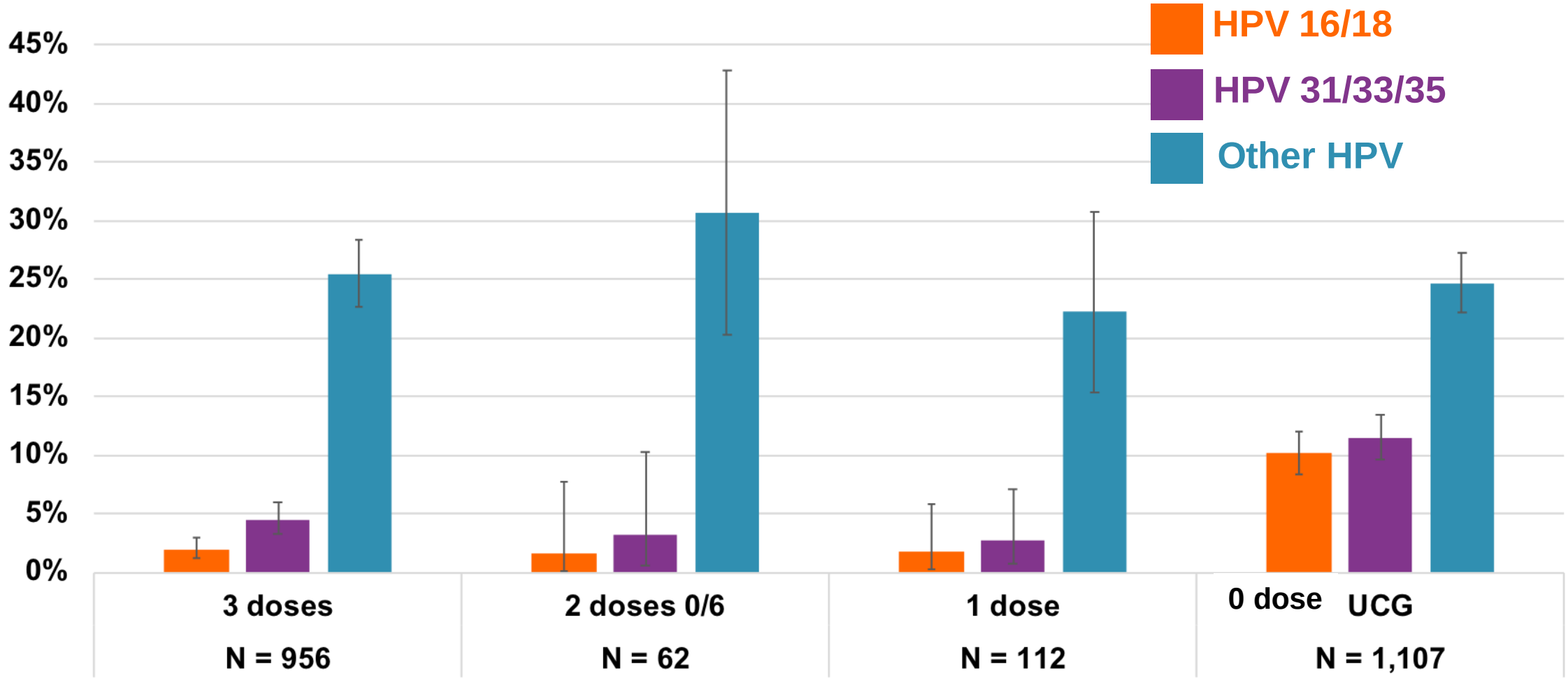
To control of cervical cancer worldwide, should vaccinate 40-50 million girls in each birth cohort

Might a single HPV vaccine dose confer years of protection?



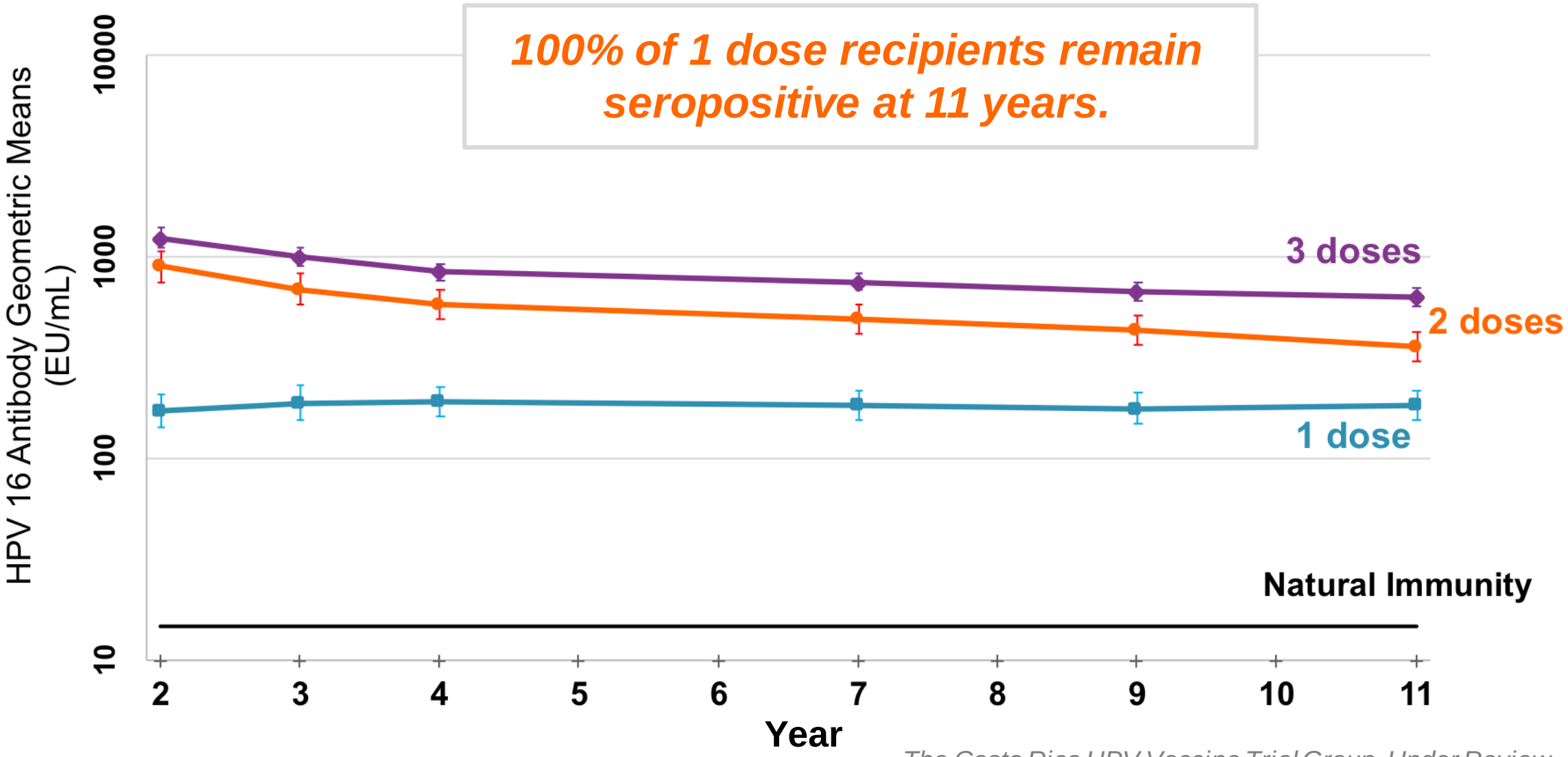
The Costa Rica Vaccine Trial: Prevalent HPV infection 11 years after bivalent HPV vaccination:

One dose is not inferior to three doses (post-hoc analysis)



The Costa Rica HPV Vaccine Trial Group, Under Review

Stable HPV16 serum antibodies 11 years after one dose of the bivalent HPV vaccine (post-hoc analysis)



The Costa Rica HPV Vaccine Trial Group, Under Review

Randomized controlled trial in Costa Rica to test efficacy of 1 dose vs. 2 doses (NCI & Gates Foundation)

- 4-arm: 1 vs. 2 dose Cervarix
  1 vs. 2 dose Gardasil9
- 5000 12-16 year old females per arm
- Survey of HPV prevalence in region
- 4 year primary trial, longer term follow-up

For more information

- **clinicaltrials.gov:** Identifier NCT03180034
- Aimee Kreimer et al, *Vaccine 2018*

Potential impact of demonstrating 1 dose can confer strong protection

- Could change standard of care in US & globally
  - Could save US > $300 million each year in vaccine costs
- Could make it feasible to control the worldwide public health problem of cervical cancer and other HPV-associated cancers

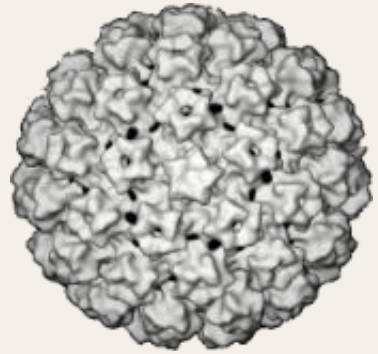



A 2025 Goal: HPV16 will replace the bald eagle on the endangered species list!

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

Endangered Species Act

Out



In