



# New Horizons






# What's New? Elimination

---

Susan T. Vadaparampil, PhD, MPH  
Moffitt Cancer Center



The image features a teal-to-green gradient background with a subtle geometric pattern of overlapping triangles. In the top-left corner, there are white floral silhouettes, including a hibiscus-like flower and a five-petaled flower. In the bottom-right corner, there are more white floral silhouettes, including a large hibiscus-like flower and several smaller five-petaled flowers.

November 2020  
was a moment in history  
when the world  
made a commitment  
to eliminating cancer.

# Cervical Cancer is the 4<sup>th</sup> Most Common Cancer Worldwide

Globally

>600,000

women are diagnosed every year

>300,000

women die from cervical cancer every year

- These numbers are expected to increase by 2030.
- Cervical cancer is **preventable**, and it can be **eliminated**.



# Global Targets by 2030



90% of girls fully vaccinated with the HPV vaccine by the age of 15



70% of women screened using a high-performance test by the age of 35, and again by the age of 45



90% of women with pre-cancer treated and 90% of women with invasive cancer managed



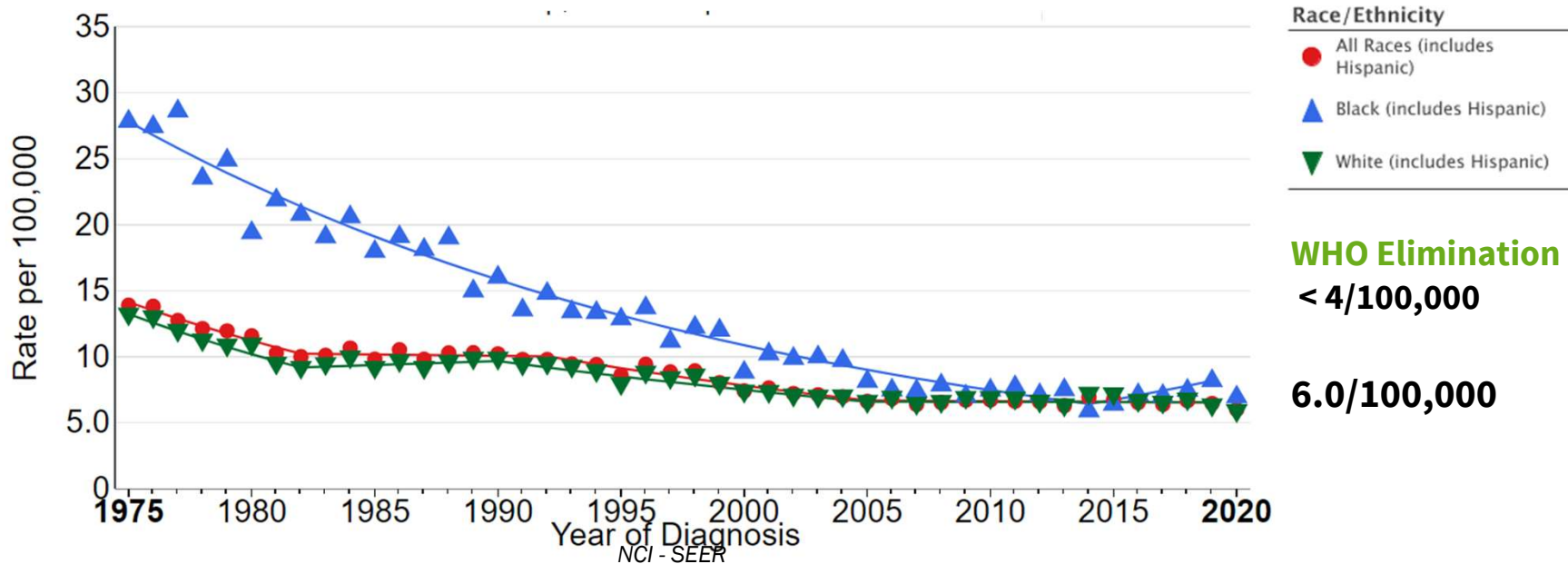


# U.S. Targets by 2030

	<u>Target</u>	<u>As of 2021</u>
Increase the proportion of females, aged 21-65, who get screened for cervical cancer – C-09.	79.2%	73.9%
Increase the proportion of adolescents who get recommended doses of the HPV vaccine – IID-08.	80%	58.5%
Reduce infections of HPV types prevented by the vaccine in young adults – IID-07.	8.7%	15.1%



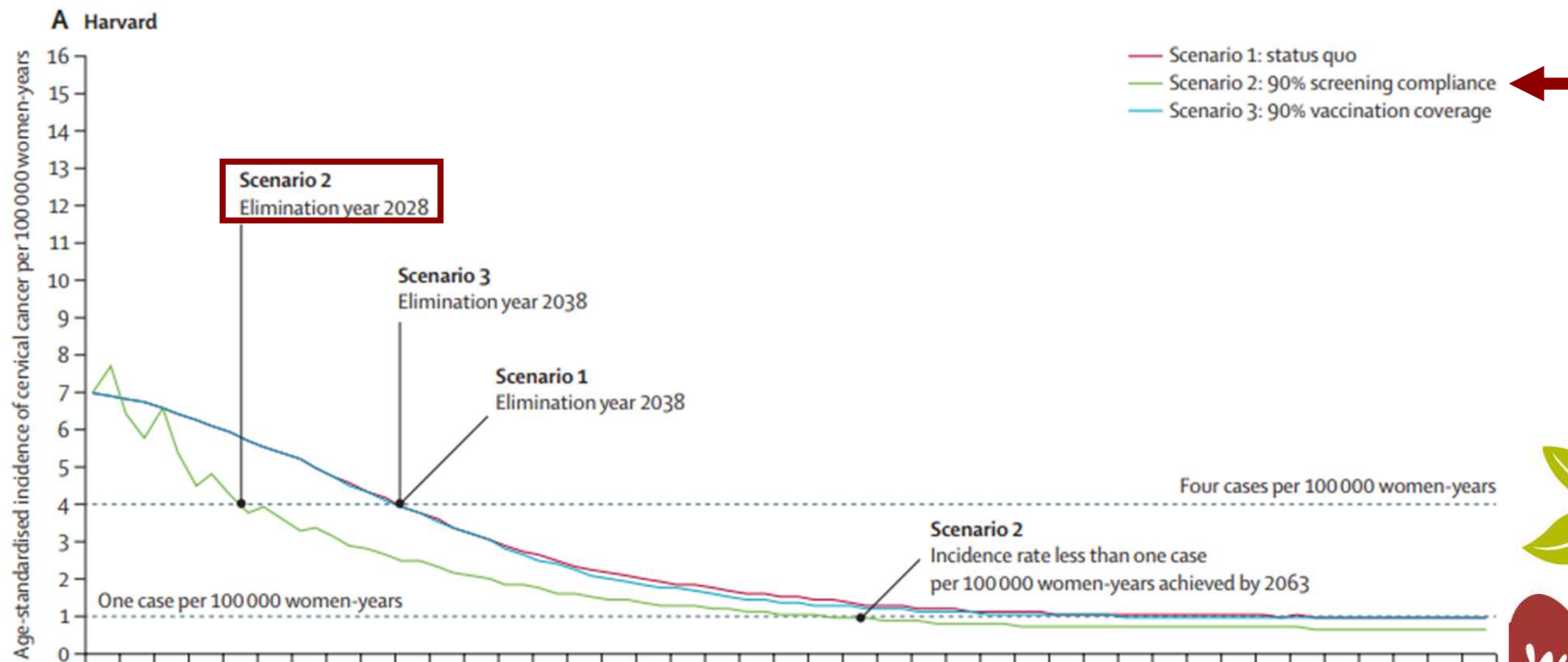
# Cervical Cancer Elimination in the United States is Within Sight



Slide courtesy of Dr. Anna Giuliano

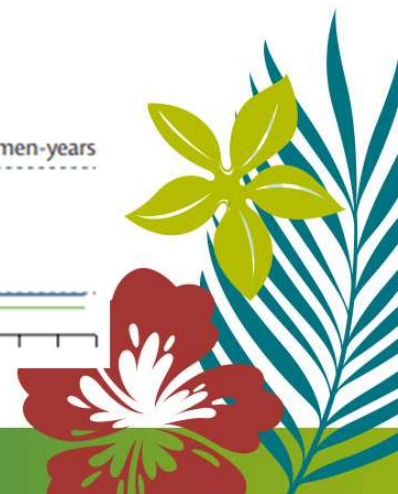


# Predicted Time to Cervical Cancer Elimination in the United States



Burger et al. The Lancet Public Health. 2020.

Slide courtesy of Dr. Anna Giuliano





# Monitoring and Tracking Goals

## Primary prevention

## Secondary prevention

## Tertiary prevention

Population based data

HPV and HIV prevalence; Tobacco and condom use

Screening coverage; pre-cancer incidence

Survival; mortality-to-incidence ratio

Program monitoring

HPV vaccination coverage

Screening positivity rates; treatment coverage for pre-cancers; ablative and excision treatment rates

Guideline-based management of women with cervical disease; stage at diagnosis; treatment coverage; palliative care

Policies and health system capacities

HPV vaccine in National Immunization Programs; vaccine supply and availability; vaccine cost

Availability of national screening programs; availability of pre-cancer treatments; HPV test availability

Availability of guidelines for management of cervical disease, including high-risk groups; availability of treatment; availability of specialized medical staff; Availability of palliative care medications

Cross-cutting incidence and mortality

Cumulative risk of cervical cancer

Cervical cancer incidence and mortality

Premature mortality



# We Have Tools to Eliminate Cervical Cancer



**HPV Vaccine**



**Screening**



**Treatment**



# Unity of Effort





The world is ready to  
eliminate cervical cancer.

Are we?



# Thank You!

## Contact information:

Susan T. Vadaparampil, PhD MPH  
Moffitt Cancer Center

[Susan.Vadaparampil@moffitt.org](mailto:Susan.Vadaparampil@moffitt.org)







# Self-Collection for Primary HPV Screening: Essential Strategy for Cervical Cancer Elimination

---

Dr. Francisco García

Deputy County Administrator &

Chief Medical Officer, Pima County

Professor Emeritus of Public Health, University of Arizona

# Disclosures

---

- No financial or intellectual conflicts of interest



# Learning Objectives

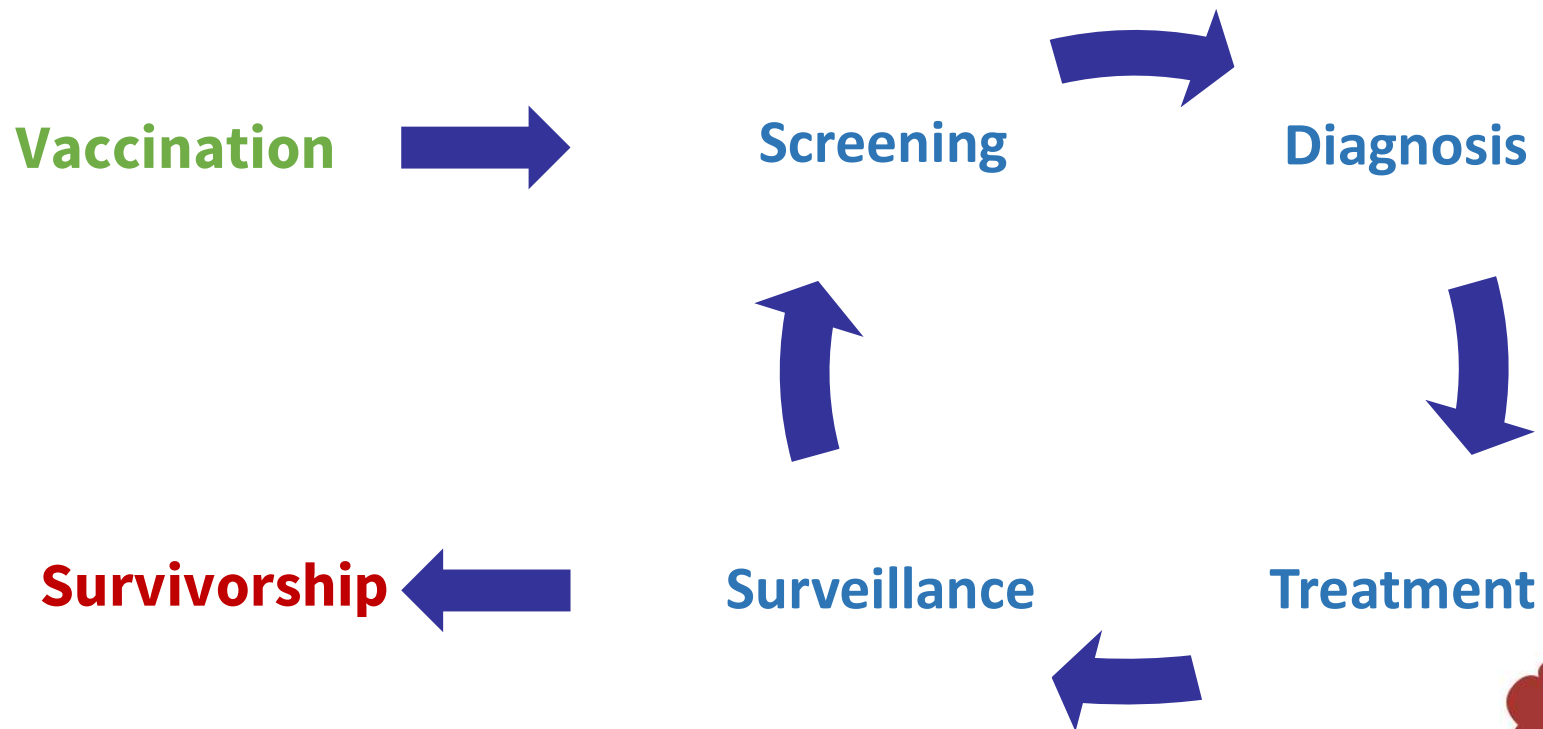
---

- Envision the impact of self-collection for primary HPV screening as a strategy for cervical cancer elimination.
- Understand how primary HPV screening/self-collection may be used to address critical gaps across vulnerable populations.

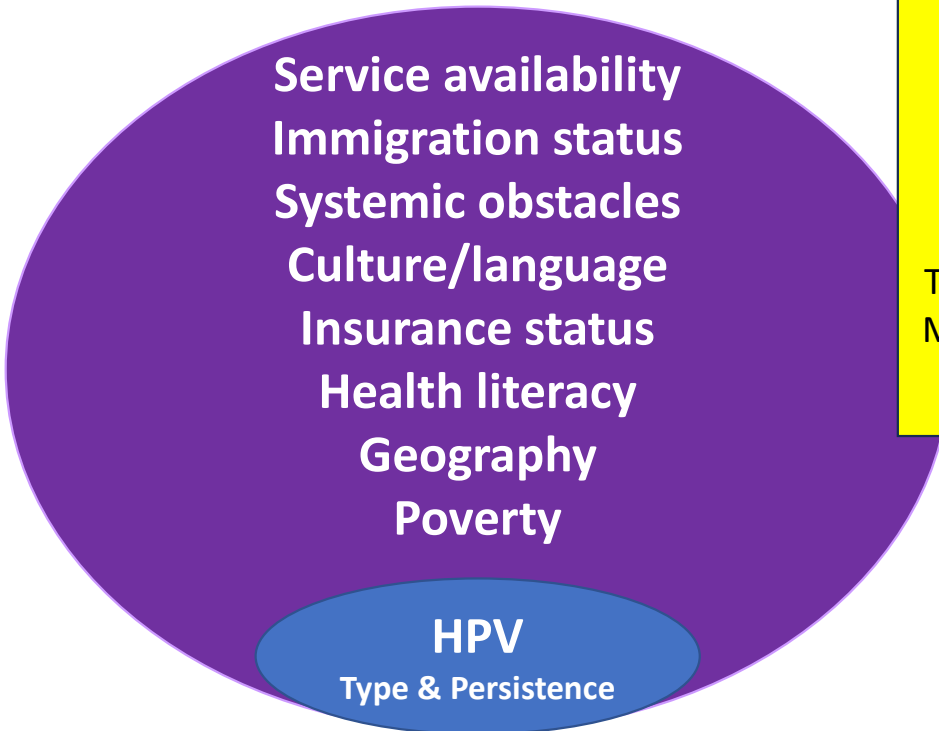


# Comprehensive Cervical Cancer Prevention

---



# The Burden of Cervical Cancer Morbidity and Mortality, and Why it is Borne by Low-Income and Communities of Color?



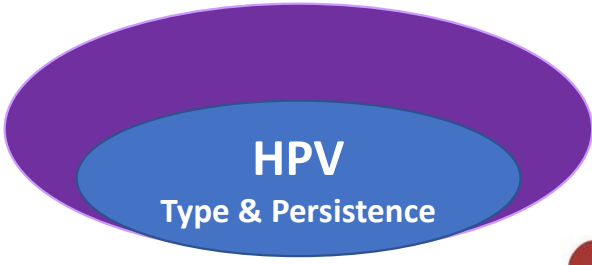
**Vulnerable Population**

Should there be a ? after color? The title seems to be more like a statement.

Suggested:

The Burden of Cervical Cancer Morbidity and Mortality and Why it is Borne by Low-Income Communities and Communities of Color

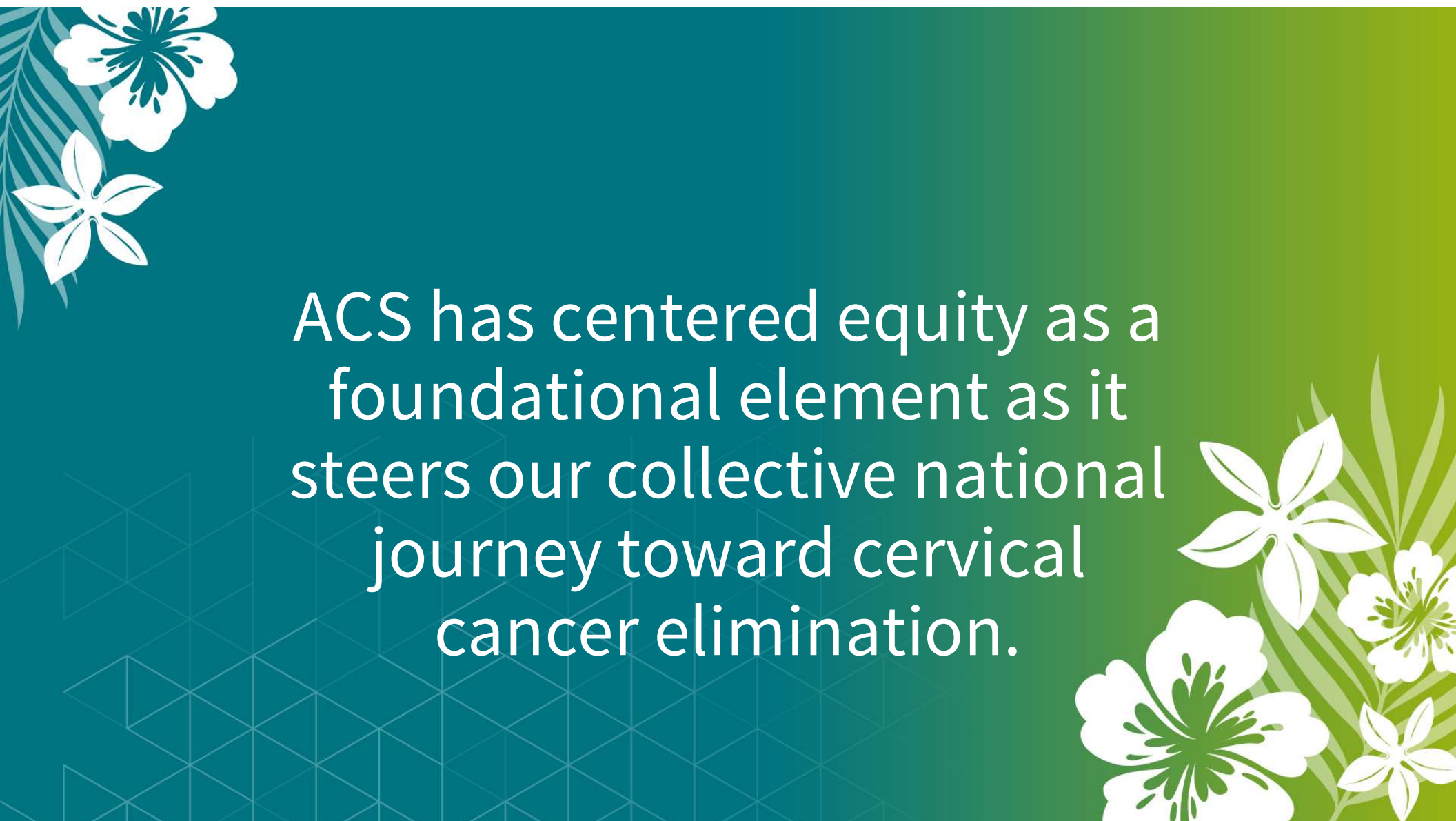
Low-Income – People? Communities?



**Resilient Population**





The slide features a teal-to-green gradient background with a subtle geometric pattern of overlapping triangles. In the top-left corner, there are white floral silhouettes, including a hibiscus and a five-petaled flower. In the bottom-right corner, there is a cluster of white floral silhouettes, including a hibiscus and several five-petaled flowers.

ACS has centered equity as a foundational element as it steers our collective national journey toward cervical cancer elimination.

# The COVID Pandemic Changes the Context for Primary HPV Screening Using Self-Collection

---

- ✓ Low-barrier
- ✓ On demand
- ✓ Free to consumer?
- ✓ No appointment necessary
- ✓ No referral needed
- ✓ Delivered in community
- ✓ At home testing
- ✓ Non-clinical settings
- ✓ Results directly to patient
- ✓ Streamlined fast-track regulatory process?
- ✓ Rapid dissemination of technology



# Self-Collection: Where & When?

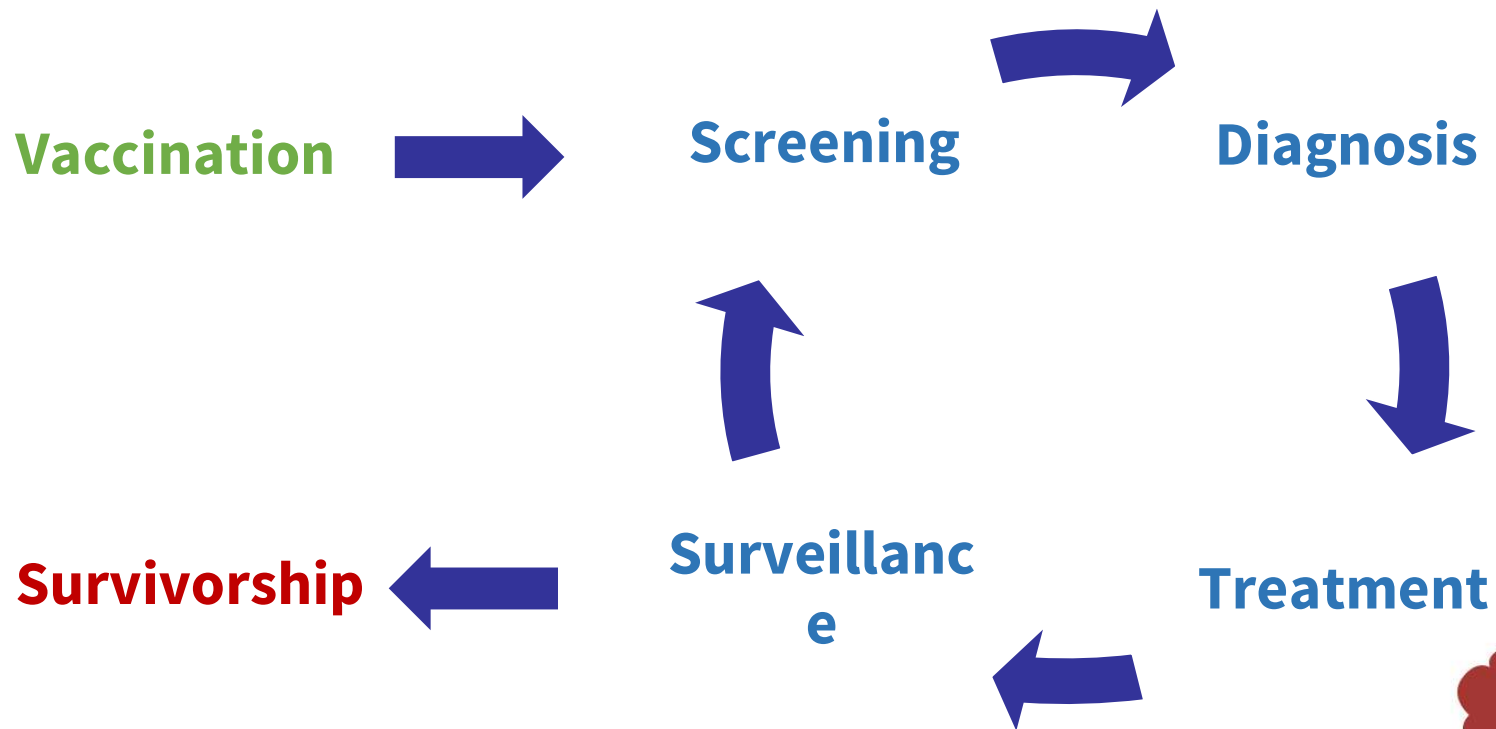
---

- Setting where self-collection should be considered:
  - Remote and frontier communities
  - Detention and other congregate housing
  - Mobile clinics
  - Community Health Worker campaigns
  - Over-the-counter purchase and mail back
- Anywhere
  - Unwilling/unable to undergo speculum examination



# Comprehensive Cervical Cancer ELIMINATION!

---





Gracias/Thank You

Francisco.Garcia@pima.gov







# One Dose

---

Dr. Aimée Kreimer  
NCI



# State of evidence: Single-dose HPV vaccination

Aimée R. Kreimer, PhD  
October 2023

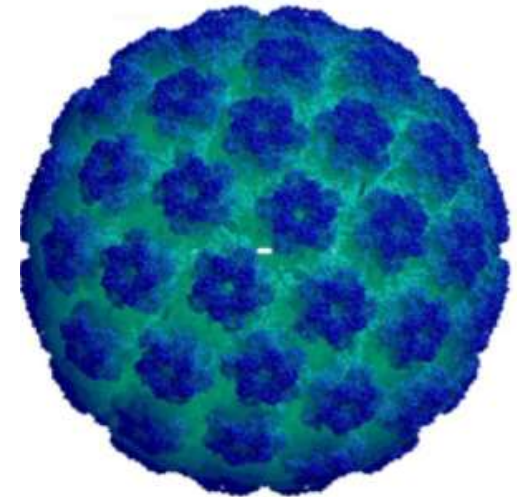
# Talking points

1. Biologic plausibility underpinning single-dose HPV vaccine protection
2. Single-dose HPV vaccine data
3. Changes to global policy
4. Modeling
5. Gaps in knowledge and ongoing trials



## Biologic Plausibility of a single-dose of the HPV vaccines

- Antibodies are the prime mediators of protection for L1 HPV VLP vaccines.
- Particle size (50-55 nm) and geometry (repetitive epitopes) of the VLPs are optimal for stimulating the immune system, including efficient generation of long-lived, antigen-specific antibody-producing cells.
- Durable (>10 years) and stable antibody levels are indicative of induction of long-lived plasma cells.
- HPV virus is exceptionally susceptible to antibody-inhibition at the site of infection.
- A minimum antibody level required for protection has not been established yet.
- Low level of antibodies are protective *in vivo* (animal models).



# KENYA Single-dose HPV-vaccine Efficacy (KEN SHE)

- Randomized trial of 1 dose of 9vHPV, 2vHPV or meningococcal vaccine
  - 2250 Kenyan women aged 15–20 years; 1-5 lifetime partners; HIV negative
- 1458 girls evaluated for efficacy at month 18 in mITT HPV 16/18 cohort

Table 2. Incidence of Persistent HPV 16/18 Infection and Vaccine Efficacy by Month 18 (mITT Cohort).											
Arm	Enrolled (n)	HPV 16/18 Naive (mITT) (n)*	Incident Persistent HPV 16/18 (n)	Woman-yr of Follow-Up†	Incidence of Persistent HPV 16/18 per 100 Woman-yr	95% CI‡		Statistical Comparisons§			
						Lower Bound	Upper Bound	Comparison	VE (%)	95% CI (%)	P Value (Log-Rank)
Nonavalent HPV	758	496	1	596.27	0.17	0.00	0.93	Nonavalent vs. meningococcal	97.5	81.7–99.7	<0.0001
Bivalent HPV	760	489	1	589.38	0.17	0.00	0.95	Bivalent vs. meningococcal	97.5	81.6–99.7	<0.0001
Meningococcal	757	473	36	527.35	6.83	4.78	9.45				

Enrollment between December 2018 and June 2021

mITT, modified intention to treat: HPV 16/18 HPV DNA negative (external genital and cervical swabs) at enrollment and month 3 (self-collected vaginal swab) and HPV antibody negative at enrollment

Barnabas, et al. NEJM Evid 2022; 1 (5)

Results based on 18 months; 36 month data presented at IPVC in Washington DC

# India IARC Trial: Protection after 1, 2 or 3 doses of 4vHPV through 10 years

	Unvaccinated cohort	Single-dose default cohort	Two-dose cohort	Three-dose cohort
<b>Persistent HPV</b>				
Women assessed	1260	2135	1452	1460
<b>Persistent HPV 16 and 18 infections</b>				
Observed events	32	1	1	1
Crude attack rates	2.54%	0.05%	0.07%	0.07%
Adjusted vaccine efficacy* (95% CI)	..	95.4% (85.0 to 99.9)	93.1% (77.3 to 99.8)	93.3% (77.5 to 99.7)
Difference in vaccine efficacy† (95% CI)	..	..	-2.0% (-20.2 to 11.3)	-1.9% (-19.4 to 12.4)

Post-hoc analysis; women vaccinated at age 10-18 years, randomized to receive 3 or 2 4vHPV doses

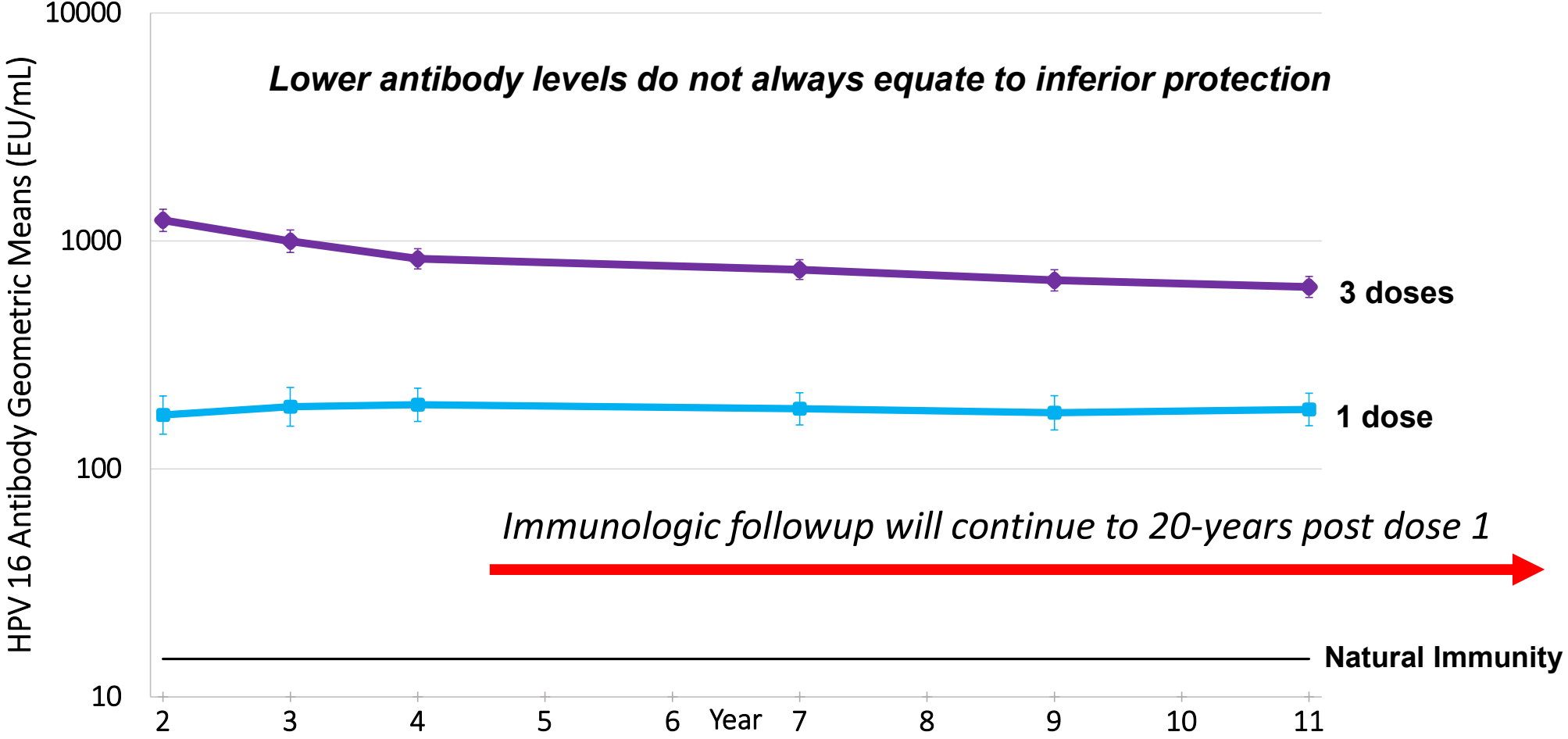
Unvaccinated women age-matched to married vaccinated participants recruited as controls

Persistent infection defined as the same HPV type detected in consecutive samples at least 10 months apart

VE adjusted for background HPV infection frequency, time between date of marriage and first cervical specimen collection, and number of cervical specimens per participant



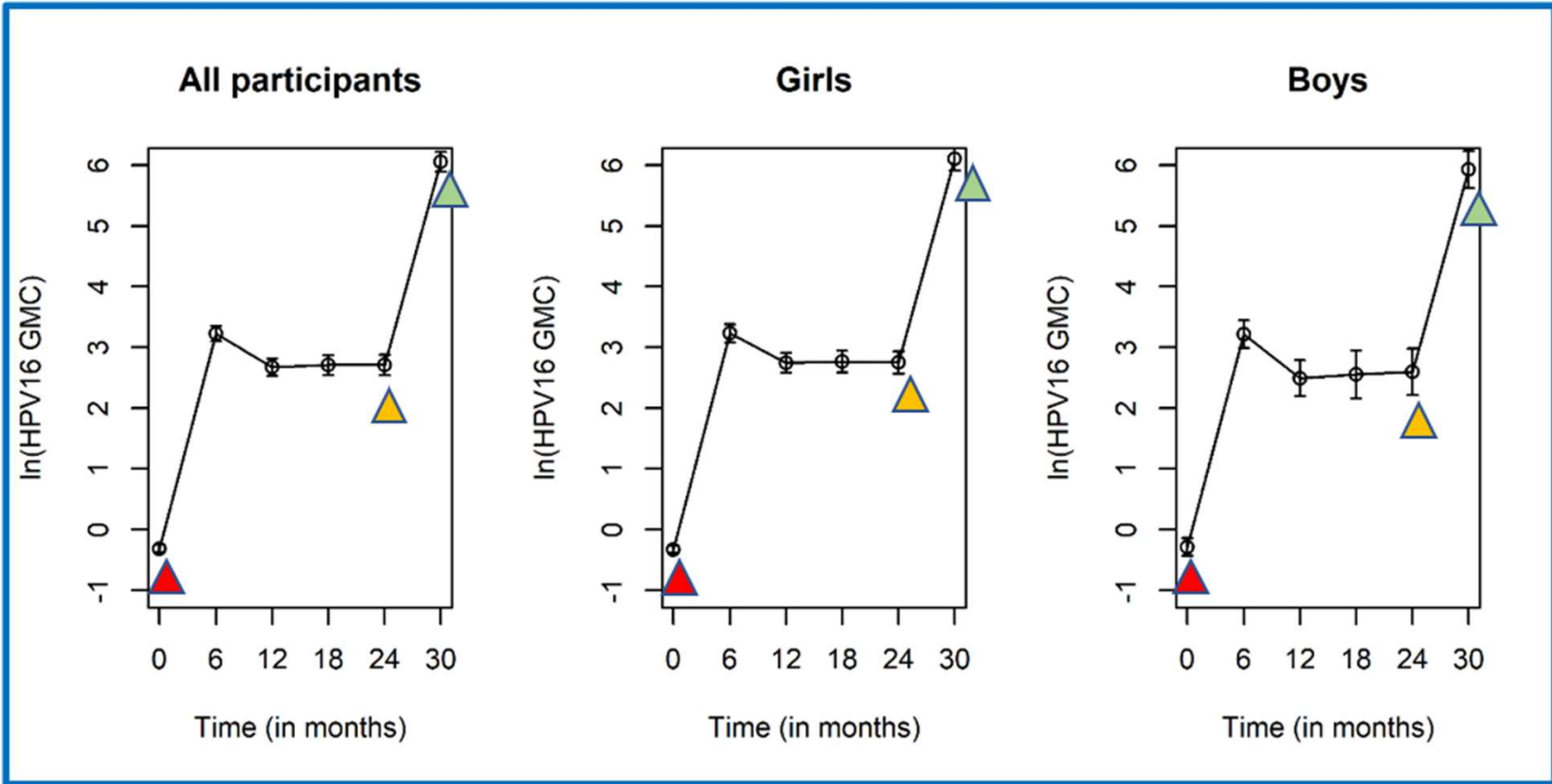
# Costa Rica: One dose of bivalent HPV vaccination induces stable HPV16 serum antibodies for >10 years



Kreimer AR JNCI 2020

# HPV 9-valent Vaccine Delayed Booster Immunogenicity Study (DEBS)

Plot of HPV16 antibody GMC levels by study visit for all participants, girls and boys



Slide courtesy of Dr Vik Sahasrabudde

ClinicalTrials.gov registration NCT02568566

# Single-dose HPV vaccine **impact** among 17- to 18-year-old women with HIV in South Africa: the HOPE study

HPV type	Crude prevalence		Prevalence ratio (PR) (95% CI)
	Pre-vaccine sample N=157 n (%)	Post-vaccine sample N=117 n (%)	
HPV 16/18	52 (33)	24 (21)	0.62 (0.41-0.94)

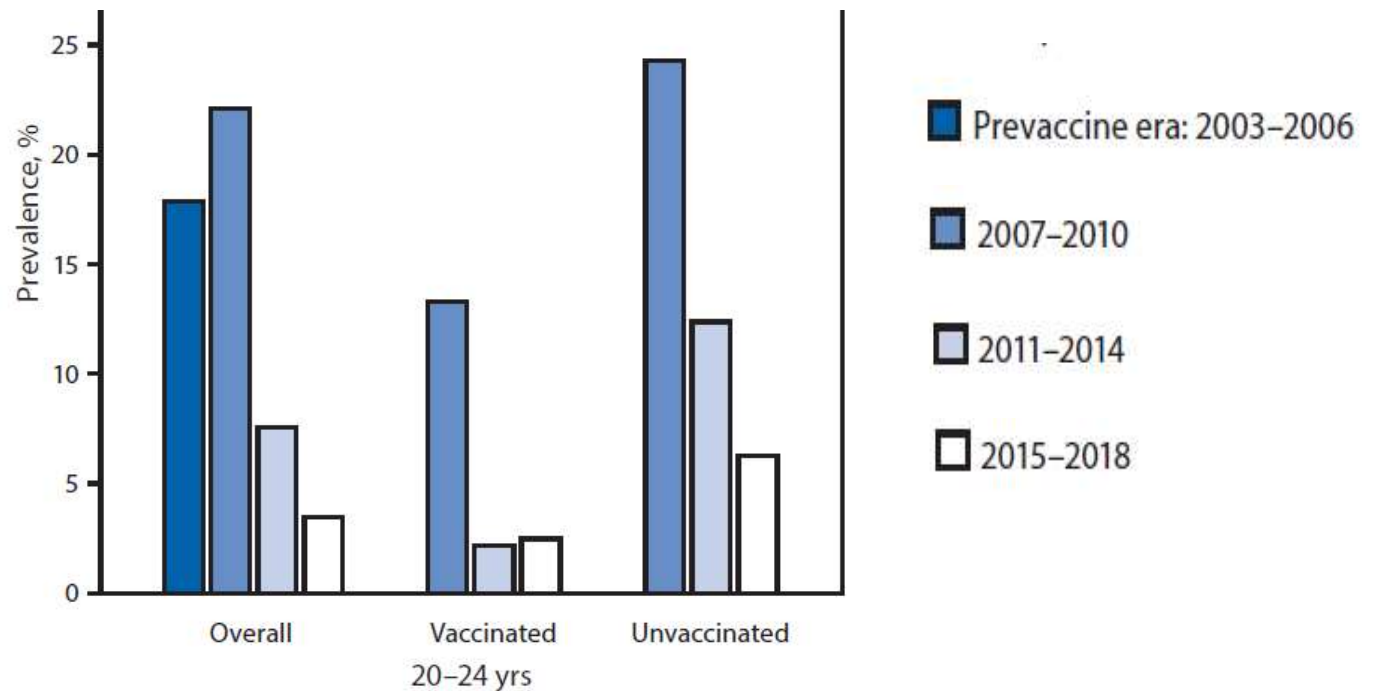
Sinead Delany-Moretlwe, Dorothy Machalek, Richard Munthali, Danielle Travill, Kathy Petoumenos, Helen Rees, John Kaldor on behalf of the HOPE study group

IPVC, April 2023

# Herd immunity is greater than expected

## US 2018: Herd immunity for 4v HPV vaccine types among 20–24-year-old women, NHANES

FIGURE. Quadrivalent vaccine-type (4vHPV-type) prevalence among sexually experienced females aged 14–34 years, by age group, vaccination history,\* and survey years — National Health and Nutrition Examination Survey, United States, 2003–2018<sup>†,§</sup>



NHANES is an ongoing cross-sectional survey conducted by CDC's National Center for Health Statistics designed to monitor the health and nutrition of the U.S. non-institutionalized civilian population.

## WHO SAGE recommends updating HPV vaccination dose schedules as follows

- **One or two-dose schedule** for the primary target of girls aged **9-14**.
- **One or two-dose schedule** for young women aged **15-20**.
- Two doses with a 6-month interval for women **older than 21**.
- Immunocompromised individuals, including those with HIV, should receive three doses if feasible, and if not at least two doses.



World Health  
Organization

Organisation mondiale de la Santé

Weekly epidemiological record  
Relevé épidémiologique hebdomadaire

16 DECEMBER 2022, 97th YEAR / 16 DÉCEMBRE 2022, 97<sup>e</sup> ANNÉE

No 50, 2022, 97, 645–672

<http://www.who.int/wer>

# Countries that switched to 1-dose HPV schedule as of April 2023

Region	Country (intro year)	WB group	Policy change
AFR	<ul style="list-style-type: none"> <li>Cap Verde (2021)</li> </ul>	LMIC	<ul style="list-style-type: none"> <li>Switch to 1-dose, <b>extended MAC to 14 yr old girls</b></li> </ul>
AMR	<ul style="list-style-type: none"> <li>Bolivia (2017)</li> <li>Guatemala (2018)</li> <li>Guyana (2011)</li> <li>Jamaica (2017)</li> <li>Mexico (2008)</li> <li>Peru (2015)</li> </ul>	<ul style="list-style-type: none"> <li>LMIC</li> <li>UMIC</li> <li>UMIC</li> <li>UMIC</li> <li>UMIC</li> <li>UMIC</li> </ul>	<ul style="list-style-type: none"> <li>Switch to 1-dose in routine programme</li> <li>Switch to 1-dose in routine programme</li> <li>Switch to 1-dose in routine programme ♀</li> <li>Switch to 1-dose in routine programme ♀</li> <li>Switch to 1-dose in routine programme ♀</li> <li>Switch to 1-dose in routine programme</li> </ul>
EUR	<ul style="list-style-type: none"> <li>UK (2008)</li> <li>Ireland (2009)</li> <li>Albania(2022)</li> <li>Netherlands (2008)</li> <li>Sweden (2010)</li> </ul>	<ul style="list-style-type: none"> <li>HIC</li> <li>HIC</li> <li>LMIC</li> <li>HIC</li> <li>HIC</li> </ul>	<ul style="list-style-type: none"> <li>Switch to 1-dose, 9 - 25 year old ♀ ; <b>MSM&gt;25yr: 2 doses</b></li> <li>Switch to 1-dose, 9 - 25 year old ♀ ; <b>MSM&gt;25yr: 2 doses</b></li> <li>Introduction with 1-dose in 13-year-old girls</li> <li><b>15-26 year ♀ in catch-up 2-doses</b></li> <li><b>15 year and older females in catch-up 2-doses</b></li> </ul>
WPR	<ul style="list-style-type: none"> <li>Tonga (2022)</li> <li>Australia (2007)</li> </ul>	<ul style="list-style-type: none"> <li>LMIC</li> <li>HIC</li> </ul>	<ul style="list-style-type: none"> <li>Introduction with 1-dose in girls, <b>extended MAC to 14 year</b></li> <li>Switch to 1-dose dose in routine programme ♀</li> </ul>
<b>GAVI Countries</b>	<p><i>NITAGs in several GAVI-supported countries (LMICs) have recommended 1-dose HPV schedule</i></p>		<ul style="list-style-type: none"> <li>Bangladesh (2023/24)</li> <li>Nigeria (2023/24) + 8 more</li> <li>India (2023/24)</li> </ul>

Slide courtesy of Dr Paul Bloem, WHO

Black: Primary target, switch from 2 (or 3) to 1-dose  
 Blue: Secondary target, switch from 3 to 2 doses



# Gaps in Knowledge

- Impact of HIV infection on existing HPV-vaccine-induced antibodies from a single dose
- Males (DEBS trial suggests similar immune response to 1 dose)
- Adults
- Protection at non-cervical sites (i.e.: oral and anal)
- Protection at non-mucosal sites (i.e.: genital warts)
- 1 dose for DCVM HPV vaccines (Innovax, Walvax, Serum Institute)
- Programmatically- how to monitor for breakthrough/signs of waning

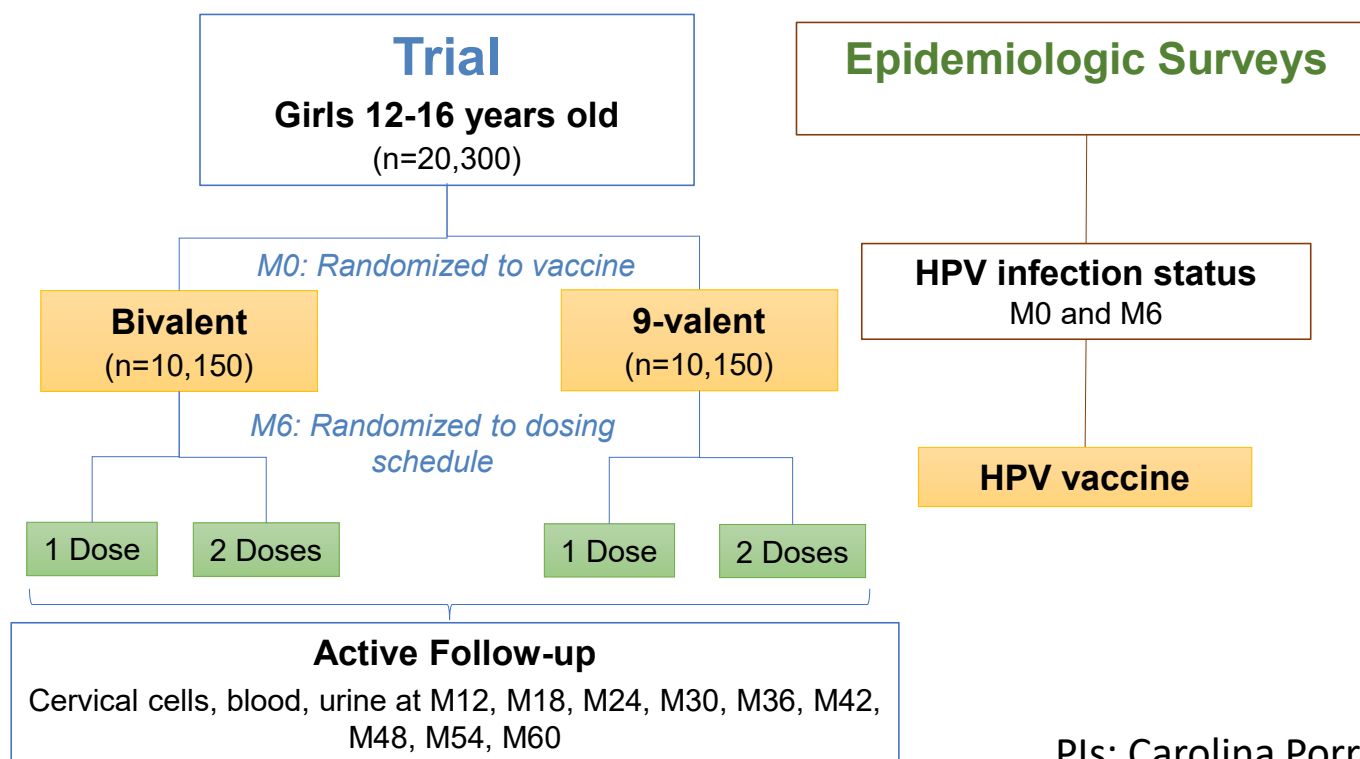
# More data coming: evidence into 2025

**BOLD indicates randomization to 1 dose**

- Durability
  - Costa Rica- followup to 20 years for immunologic endpoints
  - India- followup to 15 years with histologic endpoints
  - **Tanzania- followup to 9 years immunologic endpoints**
  - **Kenya- followup beyond 3 years virologic endpoints**
- Vaccine effectiveness (examples)
  - Thailand
  - South Africa
- Additional population subsets (examples)
  - Women with HIV- South Africa (HOPE)
  - Younger age at vaccination- Gambia- 4 to 8 yr olds (HANDS)
  - **Older age at vaccination- Costa Rica, 18 to 30 (PRISMA)**
- **Non-cervical sites- Costa Rica, anal and oral endpoints (PRISMA)**
- **Non-inferiority of 1 to 2 doses- Costa Rica (ESCUDDO)**

# ESCUDDO, Costa Rica- Primary data available in 2024/2025

- RCT to evaluate non-inferiority of one versus two doses of bivalent and 9-valent vaccines for prevention of new cervical HPV16/18 infections that persist 6+ months
- Evaluate one dose compared to zero doses



PIs: Carolina Porras and Aimée Kreimer

# THANK YOU



**NATIONAL CANCER INSTITUTE**  
Division of Cancer  
Epidemiology & Genetics

Contact: [kreimera@nih.gov](mailto:kreimera@nih.gov)