What’s New?
Elimination

Susan T. Vadaparampil, PhD, MPH
Moffitt Cancer Center
November 2020 was a moment in history when the world made a commitment to eliminating cancer.
Cervical Cancer is the 4\textsuperscript{th} 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 \textit{preventable}, and it can be \textit{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

<table>
<thead>
<tr>
<th>Target</th>
<th>Target</th>
<th>As of 2021</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increase the proportion of females, aged 21-65, who get screened for</td>
<td>79.2%</td>
<td>73.9%</td>
</tr>
<tr>
<td>cervical cancer – C-09.</td>
<td></td>
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<tr>
<td>Increase the proportion of adolescents who get recommended doses of</td>
<td>80%</td>
<td>58.5%</td>
</tr>
<tr>
<td>the HPV vaccine – IID-08.</td>
<td></td>
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<tr>
<td>Reduce infections of HPV types prevented by the vaccine in young</td>
<td>8.7%</td>
<td>15.1%</td>
</tr>
<tr>
<td>adults – IID-07.</td>
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</table>
Cervical Cancer Elimination in the United States is Within Sight

WHO Elimination Goal:
< 4/100,000

6.0/100,000

Slide courtesy of Dr. Anna Giuliano
Predicted Time to Cervical Cancer Elimination in the United States


Slide courtesy of Dr. Anna Giuliani
<table>
<thead>
<tr>
<th>Monitoring and Tracking Goals</th>
<th>Primary prevention</th>
<th>Secondary prevention</th>
<th>Tertiary prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population based data</td>
<td>HPV and HIV prevalence; Tobacco and condom use</td>
<td>Screening coverage; pre-cancer incidence</td>
<td>Survival; mortality-to-incidence ratio</td>
</tr>
<tr>
<td>Program monitoring</td>
<td>HPV vaccination coverage</td>
<td>Screening positivity rates; treatment coverage for pre-cancers; ablative and excision treatment rates</td>
<td>Guideline-based management of women with cervical disease; stage at diagnosis; treatment coverage; palliative care</td>
</tr>
<tr>
<td>Policies and health system capacities</td>
<td>HPV vaccine in National Immunization Programs; vaccine supply and availability; vaccine cost</td>
<td>Availability of national screening programs; availability of pre-cancer treatments; HPV test availability</td>
<td>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</td>
</tr>
<tr>
<td>Cross-cutting incidence and mortality</td>
<td>Cumulative risk of cervical cancer</td>
<td>Cervical cancer incidence and mortality</td>
<td>Premature mortality</td>
</tr>
</tbody>
</table>
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:

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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

Vaccination  Screening  Diagnosis

Survivorship  Surveillance  Treatment
The Burden of Cervical Cancer Morbidity and Mortality, and Why it is Borne by Low-Income and Communities of Color?
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
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>
<thead>
<tr>
<th>Arm</th>
<th>Enrolled (n)</th>
<th>HPV 16/18 Naive (mITT) (n)</th>
<th>Incident Persistent HPV 16/18 (n)</th>
<th>Woman-yr of Follow-Up †</th>
<th>Incidence of Persistent HPV 16/18 per 100 Woman-yr</th>
<th>95% CI ‡</th>
<th>Statistical Comparisons ‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonavalent HPV</td>
<td>758</td>
<td>496</td>
<td>1</td>
<td>596.27</td>
<td>0.17</td>
<td>0.00</td>
<td>0.93</td>
</tr>
<tr>
<td>Bivalent HPV</td>
<td>760</td>
<td>489</td>
<td>1</td>
<td>589.38</td>
<td>0.17</td>
<td>0.00</td>
<td>0.95</td>
</tr>
<tr>
<td>Meningococcal</td>
<td>757</td>
<td>473</td>
<td>36</td>
<td>527.35</td>
<td>6.83</td>
<td>4.78</td>
<td>9.45</td>
</tr>
</tbody>
</table>

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

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

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

Lower antibody levels do not always equate to inferior protection

Immunologic followup will continue to 20-years post dose 1

Natural Immunity

Kreimer AR JNCI 2020
Plot of HPV16 antibody GMC levels by study visit for all participants, girls and boys

Slide courtesy of Dr Vik Sahasrabuddhe

ClinicalTrials.gov registration NCT02568566
Single-dose HPV vaccine impact among 17- to 18-year-old women with HIV in South Africa: the HOPE study

<table>
<thead>
<tr>
<th>HPV type</th>
<th>Crude prevalence</th>
<th>Prevalence ratio (PR) (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-vaccine</td>
<td>Post-vaccine</td>
</tr>
<tr>
<td></td>
<td>sample N=157</td>
<td>sample N=117</td>
</tr>
<tr>
<td>HPV 16/18</td>
<td>52 (33)</td>
<td>24 (21)</td>
</tr>
</tbody>
</table>

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 (4v HPV-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.

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.

Rosenblum et al MMWR 70: 415-420, 2021
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.
## Countries that switched to 1-dose HPV schedule as of April 2023

<table>
<thead>
<tr>
<th>Region</th>
<th>Country (intro year)</th>
<th>WB group</th>
<th>Policy change</th>
</tr>
</thead>
<tbody>
<tr>
<td>AFR</td>
<td>• Cap Verde (2021)</td>
<td>LMIC</td>
<td>Switch to 1-dose, extended MAC to 14 yr old girls</td>
</tr>
<tr>
<td></td>
<td>• Bolivia (2017)</td>
<td>LMIC</td>
<td>Switch to 1-dose in routine programme</td>
</tr>
<tr>
<td></td>
<td>• Guatemala (2018)</td>
<td>UMIC</td>
<td>Switch to 1-dose in routine programme</td>
</tr>
<tr>
<td></td>
<td>• Guyana (2011)</td>
<td>UMIC</td>
<td>Switch to 1-dose in routine programme ♀</td>
</tr>
<tr>
<td></td>
<td>• Jamaica (2017)</td>
<td>UMIC</td>
<td>Switch to 1-dose in routine programme ♀</td>
</tr>
<tr>
<td></td>
<td>• Mexico (2008)</td>
<td>UMIC</td>
<td>Switch to 1-dose in routine programme</td>
</tr>
<tr>
<td></td>
<td>• Peru (2015)</td>
<td>UMIC</td>
<td></td>
</tr>
<tr>
<td>AMR</td>
<td>• Bolivia (2017)</td>
<td>LMIC</td>
<td>Switch to 1-dose, 9 – 25 year old ♀ ; MSM&gt;25yr: 2 doses</td>
</tr>
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<td></td>
<td>• Guatemala (2018)</td>
<td>UMIC</td>
<td>Switch to 1-dose, 9 – 25 year old ♀ ; MSM&gt;25yr: 2 doses</td>
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<tr>
<td></td>
<td>• Guyana (2011)</td>
<td>UMIC</td>
<td>Introduction with 1-dose in 13-year-old girls</td>
</tr>
<tr>
<td></td>
<td>• Jamaica (2017)</td>
<td>UMIC</td>
<td>15–26 year ♀ in catch-up 2-doses</td>
</tr>
<tr>
<td></td>
<td>• Mexico (2008)</td>
<td>UMIC</td>
<td>15 year and older females in catch-up 2-doses</td>
</tr>
<tr>
<td></td>
<td>• Peru (2015)</td>
<td>UMIC</td>
<td></td>
</tr>
<tr>
<td>EUR</td>
<td>• UK (2008)</td>
<td>HIC</td>
<td>Switch to 1-dose in girls, extended MAC to 14 year</td>
</tr>
<tr>
<td></td>
<td>• Ireland (2009)</td>
<td>HIC</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Albania (2022)</td>
<td>LMIC</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Netherlands (2008)</td>
<td>HIC</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Sweden (2010)</td>
<td>HIC</td>
<td></td>
</tr>
<tr>
<td>WPR</td>
<td>• Tonga (2022)</td>
<td>LMIC</td>
<td>Switch to 1-dose dose in routine programme ♀</td>
</tr>
<tr>
<td></td>
<td>• Australia (2007)</td>
<td>HIC</td>
<td></td>
</tr>
</tbody>
</table>

### GAVI Countries
- NITAGs in several GAVI–supported countries (LMICs) have recommended 1-dose HPV schedule
  - Bangladesh (2023/24)
  - Nigeria (2023/24) + 8 more
  - India (2023/24)

*Slide courtesy of Dr Paul Bloem, WHO*
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

**Trial**

Girls 12-16 years old  
(n=20,300)

- M0: Randomized to vaccine
- M6: Randomized to dosing schedule

**Bivalent**  
(n=10,150)
- 1 Dose
- 2 Doses

**9-valent**  
(n=10,150)
- 1 Dose
- 2 Doses

**Epidemiologic Surveys**

HPV infection status  
M0 and M6

HPV vaccine

**Active Follow-up**

Cervical cells, blood, urine at M12, M18, M24, M30, M36, M42, M48, M54, M60

PIs: Carolina Porras and Aimée Kreimer
THANK YOU

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