

# **Evolving landscape on HPV vaccination tools and strategies**

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*on behalf of the Single-dose HPV Vaccine  
Evaluation Consortium*

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# HPV infection can progress to cervical cancer and untimely death, especially in lower-income countries

HPV is a common viral infection to which **almost all cervical cancers can be attributed; most of the burden lies in LMICs\***



2<sup>nd</sup>

most common cancer in Africa and 4th among women worldwide<sup>1</sup>



~350K

annual deaths caused by cervical cancer<sup>2</sup>



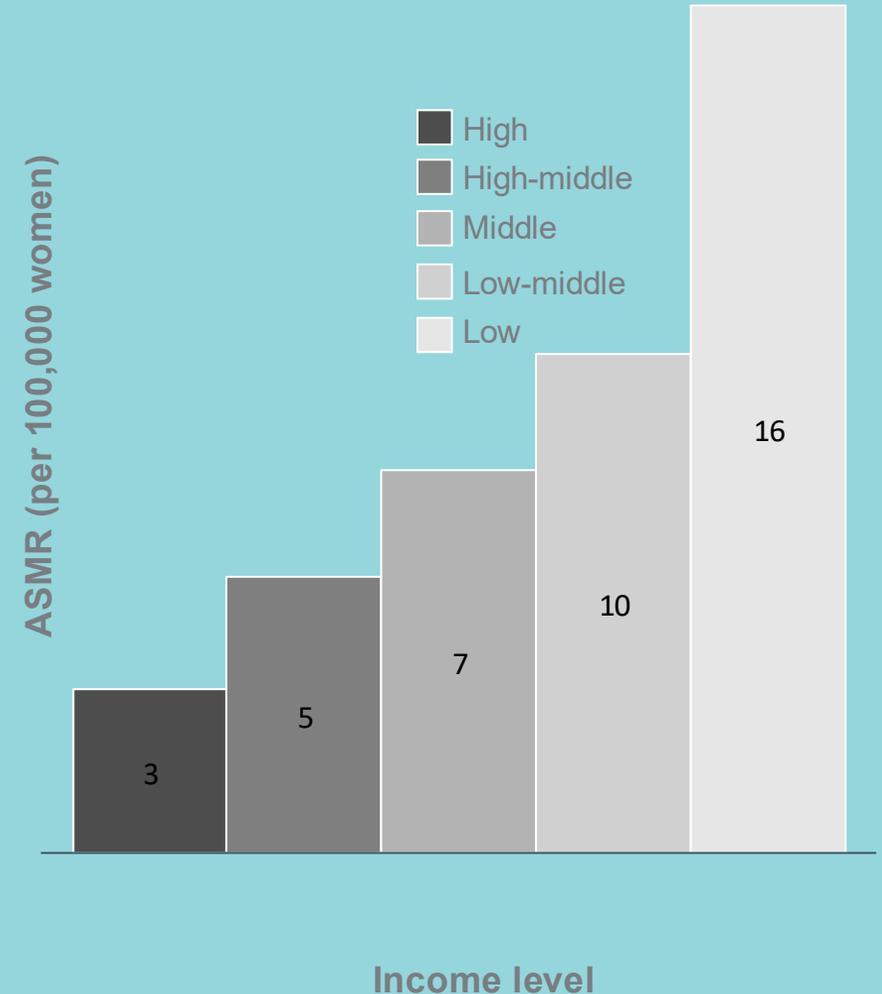
~90%

of those deaths happen in LMICs<sup>2</sup>

\*HPV types 16 and 18 are responsible for over 70% of cases

1. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA: A Cancer Journal for Clinicians*. 2021;71(3):209-249. doi:10.3322/caac.21660. 2. Global Cancer Observatory. Cervix uteri. Accessed January 2025. <https://gco.iarc.who.int/media/globocan/factsheets/cancers/23-cervix-uteri-factsheet.pdf>. 3. Cheng L, Zhao J, Zou T, Xu Z, Lv Y. Cervical cancer burden and attributable risk factors across different age and regions from 1990 to 2021 and future burden prediction: Results from the Global Burden of Disease study 2021. *Frontiers in Oncology*. 2025;15:1541452. doi:10.3389/fonc.2025.1541452.

2021 age-standardized mortality rate (ASMR) for cervical cancer by socio-demographic index areas<sup>3</sup>



# HPV vaccines

- **HPV vaccines were first introduced in 2006 on a three-dose schedule, based on safety and efficacy data**
- In 2014, WHO reduced the schedule from three doses to two in pre-adolescents/adolescents, following an evidence review by SAGE
- Evidence today shows comparable efficacy and effectiveness between single- and multi-dose schedules in preventing HPV-16/18 infections, lasting at least to 12 years following vaccination<sup>1</sup>
- In December 2022, WHO recommended a single dose vaccine schedule as an alternative to the two-dose schedule



1. Malvi SG et al. A prospective cohort study comparing efficacy of 1 dose of quadrivalent human papillomavirus vaccine to 2 and 3 doses at an average follow-up of 12 years postvaccination. *Journal of the National Cancer Institute. Monographs.* 2024;2024(67):317–328. doi:10.1093/jncimonographs/lgae042

# Five safe and highly efficacious HPV vaccines are WHO-prequalified

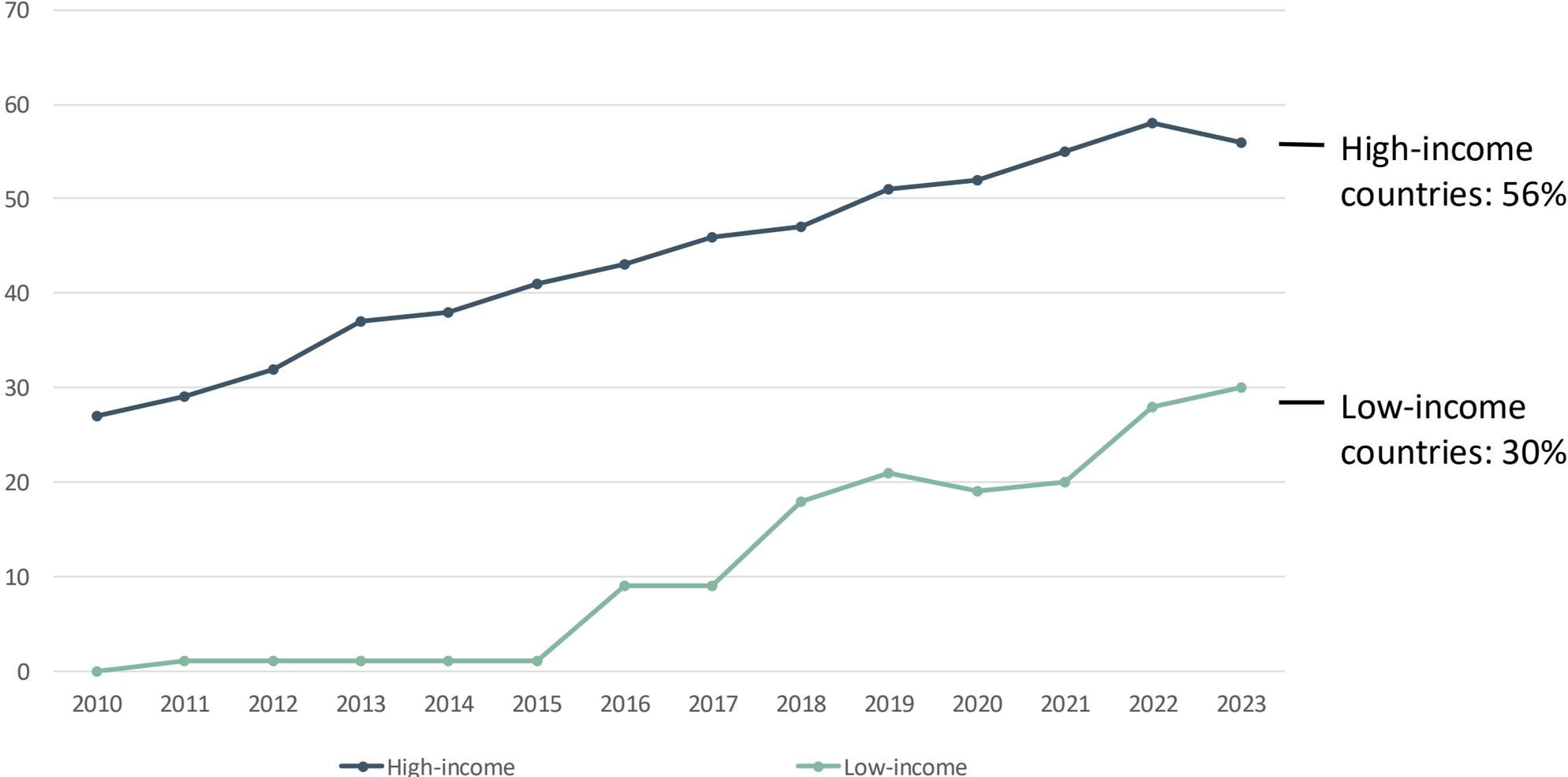
	WHO-prequalified HPV vaccines <sup>1,2</sup>				
	Quadrivalent (4vHPV, Gardasil®)	Bivalent (2vHPV, Cervarix®)	Nonavalent (9vHPV, Gardasil®9)	Bivalent (2vHPV, Cecolin®)	Bivalent (2vHPV, Walrinvax®)
 HPV types covered	6, 11, 16, 18	16, 18	6, 11, 16, 18, 31, 33, 45, 52, 58	16, 18	16, 18
 WHO-recommended dose	1 or 2	1 or 2	1 or 2	1 or 2	2
 Year of initial registration	2006	2007	2014	2019	2022
 WHO prequalification	2009	2009	2018	2021	2024
 Distributed by Gavi	✓	✓	Contingent on having an appropriately priced product	✓	TBD

*Products covered in several meetings of the HPV Prevention and Control Board*

1. List of WHO prequalified vaccines. <https://extranet.who.int/prequal/vaccines/prequalified-vaccines>.

2. World Health Organization. *Considerations for Human Papillomavirus (HPV) Vaccine Product Choice, Second Edition*. Geneva: WHO; 2024. Licence: CC BY-NC-SA 3.0 IGO.

# HPV vaccine coverage remains low and varies by national income level



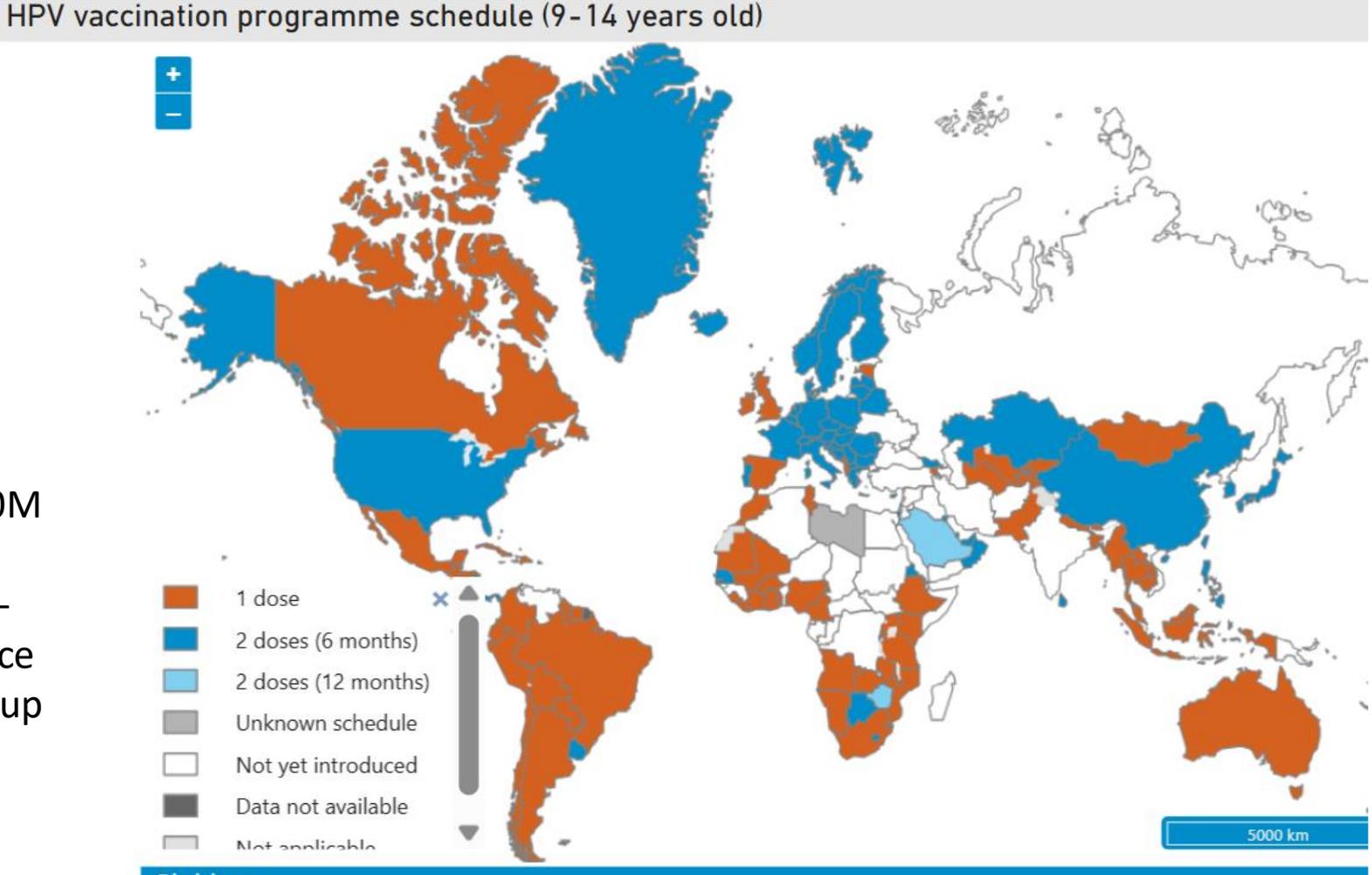
Source: WHO and UNICEF estimates of national immunization coverage (WUENIC) 2024. <https://www.who.int/teams/immunization-vaccines-and-biologicals/immunization-analysis-and-insights/global-monitoring/immunization-coverage/who-unicef-estimates-of-national-immunization-coverage>

# More than half of countries that have introduced HPV vaccines have adopted a single-dose regimen

Interval_doses	No. of countries
1 dose	83
2 doses (12 months)	2
2 doses (6 months)	71
Not yet introduced	36
Unknown schedule	2

Last update:  
11/10/2025 8:53:59...

Between 2023–2025, an estimated >30M additional girls have/will receive HPV vaccine due to the adoption of a single-dose schedule, which increased the pace of introductions and allowed for catch-up vaccinations



World Health Organization. HPV vaccine dashboard: Schedule (interval between doses). Assessed Nov 17, 2026.  
<https://app.powerbi.com/view?r=eyJrIjoiNDIxZTFkZGUtMDQ1Ny00MDZkLThiZDktYWFhYTkxOGU2NDcwIiwidCI6ImY2MTBjMG13LWJkMjQ0NGIzOS04MTBiLTNkYzI4MGFmYjU5MCIslmMIOjh9>

# Current evidence supporting single-dose HPV vaccination

*Covered in a technical meeting of the HPV Prevention and Control Board in 2021*

# Key topics & questions for single-dose HPV vaccination

## Biological plausibility

Single-dose level of protection

Is single-dose protection similar to multi-dose regimens?

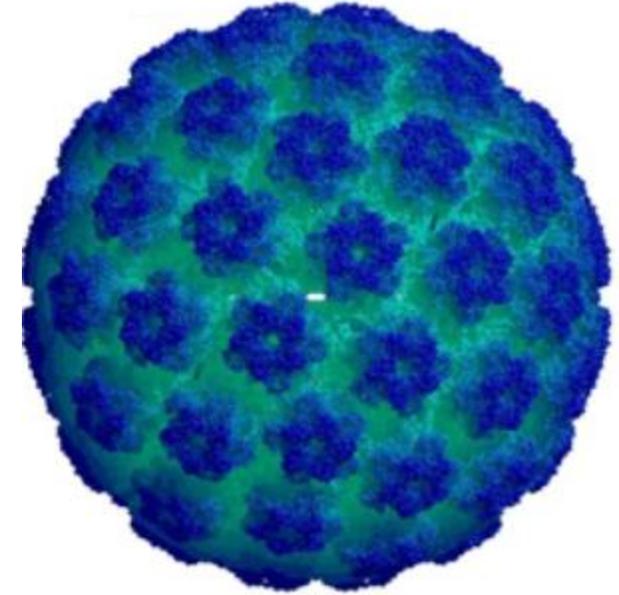
Durability of protection after a single dose

Would a single-dose regimen be applicable to different populations?

- Across geographies (data generated in different continents)
- Across age groups
- Males
- People with HIV

# High potency of HPV vaccines

- Antibodies are the prime mediators of protection for L1 HPV virus-like particle (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 (>16 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).



Schiller J, Lowy D. Explanations for the high potency of HPV prophylactic vaccines. *Vaccine*. 2018;36(32 Pt A):4768-4773. doi:10.1016/j.vaccine.2017.12.079

Befano B, Campos NG, Egemen D, et.al. Estimating human papillomavirus vaccine efficacy from a single-arm trial: Proof-of-principle in the Costa Rica vaccine trial. *Journal of the National Cancer Institute*. 2023;115(7):788-795. doi:10.1093/jnci/djad064

# Key topics & questions for single-dose HPV vaccination

Biological plausibility

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# Data from clinical studies across multiple geographies suggest a single-dose regimen provides significant protection against HPV

A single dose delivers high levels of protection similar in magnitude to multi-dose regimens



Study*	KENya Single-dose HPV-vaccine Efficacy (KEN SHE) <sup>1</sup>	Dose Reduction Immunobridging and Safety (DoRIS) <sup>2,3</sup>	International Agency for Research on Cancer (IARC) <sup>4</sup>	Costa Rica HPV Vaccine Trial (CVT) <sup>5</sup>
Start year	2018	2017	2009	2004
Location	Kenya	Tanzania	India	Costa Rica
Key findings	Single-dose vaccination with Gardasil <sup>®</sup> 9 or Cervarix <sup>®</sup> was <b>&gt;95% effective in preventing new-onset persistent HPV 16/18 infection among African adolescent girls and young women up to 54 months post-vaccination.</b>	<b>Antibody levels among girls receiving a single dose of Gardasil<sup>®</sup>9 or Cervarix<sup>®</sup> were at least as high as those in women from the KEN SHE, CVT, or IARC studies where single-dose efficacy was shown.</b>  Data suggest the efficacy of a single dose of HPV vaccine <b>can be inferred to the targeted 9–14-year-old age group.</b>	Single dose showed <b>92% efficacy with Gardasil<sup>®</sup></b> against persistent HPV 16/18 infection <b>for at least 12 years.</b>  <b>Comparable vaccine efficacy regardless of the dose regimen</b> with Gardasil <sup>®</sup> (1, 2 or 3 doses).	<b>Comparable efficacy from 1 and 3 doses of Cervarix<sup>®</sup></b> in protecting against HPV 16/18 infection up to after 10 years post-vaccination. <sup>4</sup>  <b>10X the level of antibody induced</b> after a single dose, compared to after natural infection <b>up to 16 years post-vaccination.</b> <sup>6</sup>

1. Barnabas RV, Mugo N, Onono M, et al. A randomized crossover trial of single-dose HPV vaccination efficacy among young women: Durability and vaccine efficacy after 54 months. Abstract presented at 36th International Papillomavirus Conference, November 2024; United Kingdom.  
 2. Baisley K, Kemp TJ, Kreimer AR, et al. Comparing one dose of HPV vaccine in girls aged 9-14 years in Tanzania (DoRIS) with one dose of HPV vaccine in historical cohorts: An immunobridging analysis of a randomised controlled trial. *Lancet Global Health.* 2022;10(10):e1485–e1493.  
 3. Baisley K, Kemp TJ, Mugo NR, et al. Comparing one dose of HPV vaccine in girls aged 9-14 years in Tanzania (DoRIS) with one dose in young women aged 15-20 years in Kenya (KEN SHE): An immunobridging analysis of randomised controlled trials. *Lancet Global Health.* 2024;12(3):e491–e499.  
 4. Malvi SG, et al. A prospective cohort study comparing efficacy of 1 dose of quadrivalent human papillomavirus vaccine to 2 and 3 doses at an average follow-up of 12 years postvaccination. *JNCI Mono graphs.* 2024;2024(67):317–328. doi:10.1093/jncimonographs/lgae042  
 5. Kreimer AR, Sampson JN, Porras C, et al. Evaluation of durability of a single dose of the bivalent HPV vaccine: The CVT trial. *Journal of the National Cancer Institute.* 2020;112(10):1038–1046. doi:10.1093/jnci/djaa011  
 6. Porras, C, Romero B, Kemp T, et al. HPV16/18 antibodies 16-years after single dose of bivalent HPV vaccination: Costa Rica HPV vaccine trial. *JNCI Mono graphs.* 2024;2024(67):329–336. doi:10.1093/jncimonographs/lgae032

# KEN SHE: Vaccine efficacy mITT

	Number of participants	Number of events	VE	VE 95% CI
	<b>Month 36</b>			
	<b>Incident persistent HPV 16/18 infections</b>			
Delayed vaccination	473	72	Referent	
Single-dose Cervarix®	489	2	<b>97.5%</b>	90.0; 99.4
Single-dose Gardasil®9	496	1	<b>98.8%</b>	91.3; 99.8
	<b>Incident persistent HPV 16/18/31/33/45/52/58 infections</b>			
Delayed vaccination	290	84	Referent	
Single-dose Gardasil®9	325	5	<b>95.5%</b>	89.0; 98.2

Abbreviations: CI, confidence interval; KEN SHE, KENya Single-dose HPV-vaccine Efficacy; mITT, modified intent-to-treat; VE, vaccine efficacy

mITT: seronegative at baseline and HPV-DNA negative at baseline and month 3 for types considered in analysis.

## VE as function of time (initial + crossover periods)

HPV-16/18: 96.5% (95%CI 92.1–98.5) at month 6 and 99.6% (95%CI 98.0–99.9) at month 54

HPV-16/18/31/33/45/52/58: 93.5% (95%CI 86.2–96.9) at month 6 and 99.1% (95%CI 96.4–99.8) at month 54

Barnabas RV, Brown ER, Onono MA, et al. Durability of single-dose HPV vaccination in young Kenyan women: Randomized controlled trial 3-year results. *Nature Medicine*. 2023;29(12):3224-3232.

Barnabas R, Mugo N, Onono M, et al. A randomized crossover trial of single-dose HPV vaccination efficacy among young women: Durability and vaccine efficacy after 54 months. Abstract presented at International Papillomavirus Society Conference 2024.

# Key topics & questions for single-dose HPV vaccination

Biological plausibility

Single-dose level of protection

**Is single-dose protection similar to multi-dose regimens?**

Durability of protection after a single dose

Would a single-dose regimen be applicable to different populations?

- Across geographies (data generated in different continents)
- Across age groups
- Males
- People with HIV

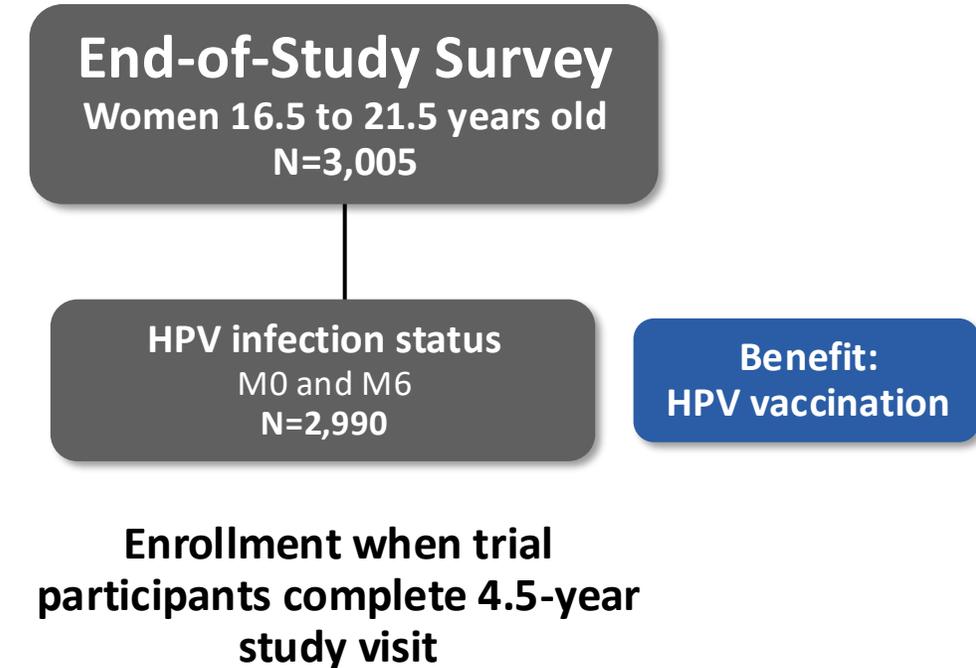
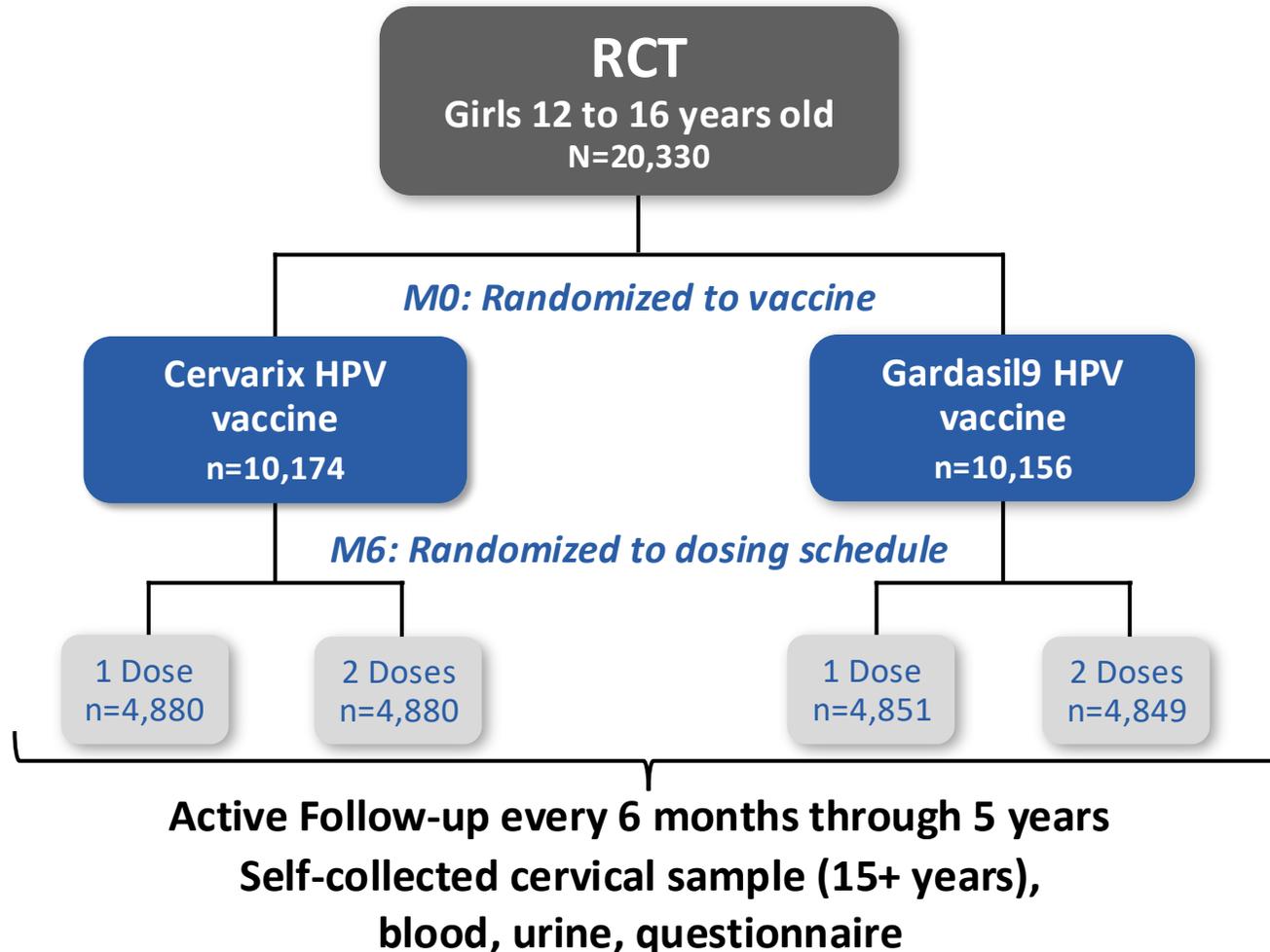
## Co-primary aims. For the Gardasil9 and the Cervarix vaccines:

- Evaluate **non-inferiority** of one compared to two vaccination doses in preventing new HPV16/18 infections that persist 6+ months over five years
- Evaluate one dose HPV **vaccine efficacy** compared to no vaccination in preventing new HPV16/18 infections that persist 6+ months in the fifth year of study followup

Secondary aims: assessment of other virologic endpoints (i.e.: composite and individual HPV genotypes) and immunogenicity (presented next by Dr. Troy Kemp)

# Study Design

**Co-primary aims. For the Gardasil9 and the Cervarix vaccines:** Evaluate **non-inferiority** of one compared to two vaccination doses in preventing new HPV16/18 infections that persist 6+ months over five years and evaluate one dose HPV **vaccine efficacy** compared to no vaccination in preventing new HPV16/18 infections that persist 6+ months in the fifth year of study followup



# Cervarix bivalent HPV Vaccine

One dose provides non-inferior protection against new HPV16/18 persistent infection compared to two doses. One dose and two dose, VE= 98%

Non-inferiority aim				
Study Arm	N	Number of events <sup>1</sup>	Cumulative event rate per 100 participants (95% CI)	Rate Difference <sup>2</sup>
1-dose	4880	14	0.29 (0.15 to 0.52)	-0.13 (-0.45 to 0.15)
2-dose	4880	21	0.42 (0.23 to 0.71)	--
p value <sup>3</sup>				<0.001

Vaccine Efficacy aim				
Study Arm	N	Number of events <sup>1</sup>	Event rate per 100 participants (95% CI)	Vaccine efficacy (95% CI)
Survey	2990	160	5.37 (4.37 to 5.98)	98.2 (96.3 to 99.4)
1-dose	4068	4	0.10 (0.03 to 0.19)	
P value <sup>2</sup>				<0.001
Survey	2990	162	5.43 (4.37 to 6.03)	97.8 (95.6 to 99.2)
2-dose	4040	5	0.12 (0.04 to 0.23)	
P value <sup>2</sup>				<0.001

<sup>1</sup> Incident-persistent HPV infections from month 12 to 60.

<sup>2</sup> Rate difference, event rate in the one-dose arm minus that in the two-dose arm

<sup>3</sup> One-sided p-value below 0.025 is considered statistical significance, i.e., the observed risk difference is significantly lower than the pre-specified non-inferiority margin of 1.25 infections per 100 participants

<sup>1</sup> Incident-persistent infections in the two visits of interest, accounting for missing HPV data. Event counts and rates differ slightly in the survey due to propensity score adjustment to adjust for covariate distribution between survey and trial participants.

<sup>2</sup> One-sided p-value testing for higher than 80% VE.

# Gardasil9 HPV Vaccine

One dose provides non-inferior protection against new HPV16/18 persistent infection compared to two doses. One dose and two dose, VE > 97%

Non-inferiority aim				
Study Arm	N in arm	Number of events <sup>1</sup>	Cumulative event rate per 100 participants (95% CI)	Rate Difference <sup>2</sup>
1-dose	4851	23	0.48 (0.28 to 0.75)	0.21 (-0.09 to 0.51)
2-dose	4849	13	0.27 (0.12 to 0.51)	--
p value <sup>3</sup>				<0.001

<sup>1</sup> Incident-persistent HPV infections from month 12 to 60.

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Vaccine Efficacy aim				
Study Arm	N	Number of events <sup>1</sup>	Event rate per 100 participants (95% CI)	Vaccine efficacy (95% CI)
Survey	2990	159	5.32 (4.31 to 5.94)	97.0 (94.2 to 99.1)
1-dose	4109	7	0.16 (0.05 to 0.29)	
P value <sup>2</sup>				<0.001
Survey	2990	160	5.35 (4.36 to 6.03)	98.5 (96.6 to 99.6)
2-dose	4083	3	0.08 (0.02 to 0.16)	
P value <sup>2</sup>				<0.001

<sup>1</sup> Incident-persistent infections in the two visits of interest, accounting for missing HPV data. Event counts and rates differ slightly in the survey due to propensity score adjustment to adjust for covariate distribution between survey and trial participants.

<sup>2</sup> One-sided p-value testing for higher than 80% VE.

## Gardasil9 HPV Vaccine

One dose provides non-inferior protection against new HPV16/18/31/33/45/52/58 persistent infection compared to two doses. One dose and two dose, VE > 94%

Non-inferiority aim				
Study Arm	N in arm	Number of events <sup>1</sup>	Cumulative event rate per 100 participants (95% CI)	Rate Difference <sup>2</sup>
1-dose	4851	79	1.64 (1.25 to 2.10)	0.56 (0.01 to 1.11)
2-dose	4849	52	1.08 (0.75 to 1.50)	--
p value <sup>3</sup>				<0.001

<sup>1</sup> Incident-persistent HPV infections from month 12 to 60.

<sup>2</sup> Rate difference, event rate in the one-dose arm minus that in the two-dose arm

<sup>3</sup> One-sided p-value below 0.025 is considered statistical significance, i.e., the observed risk difference is significantly lower than the pre-specified non-inferiority margin of 2.25 infections per 100 participants

Vaccine Efficacy aim				
Study Arm	N	Number of events <sup>1</sup>	Event rate per 100 participants (95% CI)	Vaccine efficacy (95% CI)
Survey	2990	389	13.01 (11.00 to 13.67)	94.5 (92.0 to 96.3)
1-dose	4109	29	0.72 (0.45 to 0.97)	
Survey	2990	393	13.16 (11.31 to 13.89)	95.8 (93.5 to 97.2)
2-dose	4083	22	0.55 (0.35 to 0.79)	

<sup>1</sup> Incident-persistent infections in the two visits of interest, accounting for missing HPV data. Event counts and rates differ slightly in the survey due to propensity score adjustment to adjust for covariate distribution between survey and trial participants.

<sup>2</sup> One-sided p-value testing for higher than 80% VE.

# Key topics & questions for single-dose HPV vaccination

Biological plausibility

Single-dose level of protection

Is single-dose protection similar to multi-dose regimens?

Durability of protection after a single dose- antibodies persist to at least 16 years  
*Covered in a meeting of the HPV Prevention and Control Board in 2022*

**Would a single-dose regimen be applicable to different populations?**

- Across geographies (data generated in different continents)
- Across age groups *Touched on in a meeting of the HPV Prevention and Control Board in 2019*
- Males
- People with HIV- *Covered in a meeting of the HPV Prevention and Control Board in 2021*

# HOPE study: HPV one & two-dose population effectiveness study

In a catch-up program in one South African district in adolescent girls 15–16 years of age, the impact of a single dose of GSK’s bivalent vaccine on HPV-16/18 prevalence was assessed using repeat cross-sectional surveys; overall vaccine coverage was 20%.

## HPV-16/18 prevalence

	Cases	Prevalence	aPR (95% CI)	Cases	Prevalence	aPR (95% CI)
	People without HIV			People living with HIV		
Pre- survey	65/349	19%	0.62 (0.46; 0.83)	52/157	33%	0.63 (0.41; 0.95)
Two years post-survey	84/775	11%		24/117	21%	

## Single-dose vaccine effectiveness (HPV-16/18 prevalence)

	N (women)	n (cases)	% (95% CI)	Vaccine effectiveness	95% CI
No vaccination	717	99	14 (12; 17)	64%	30; 81
One dose	175	9	5 (3; 10)		

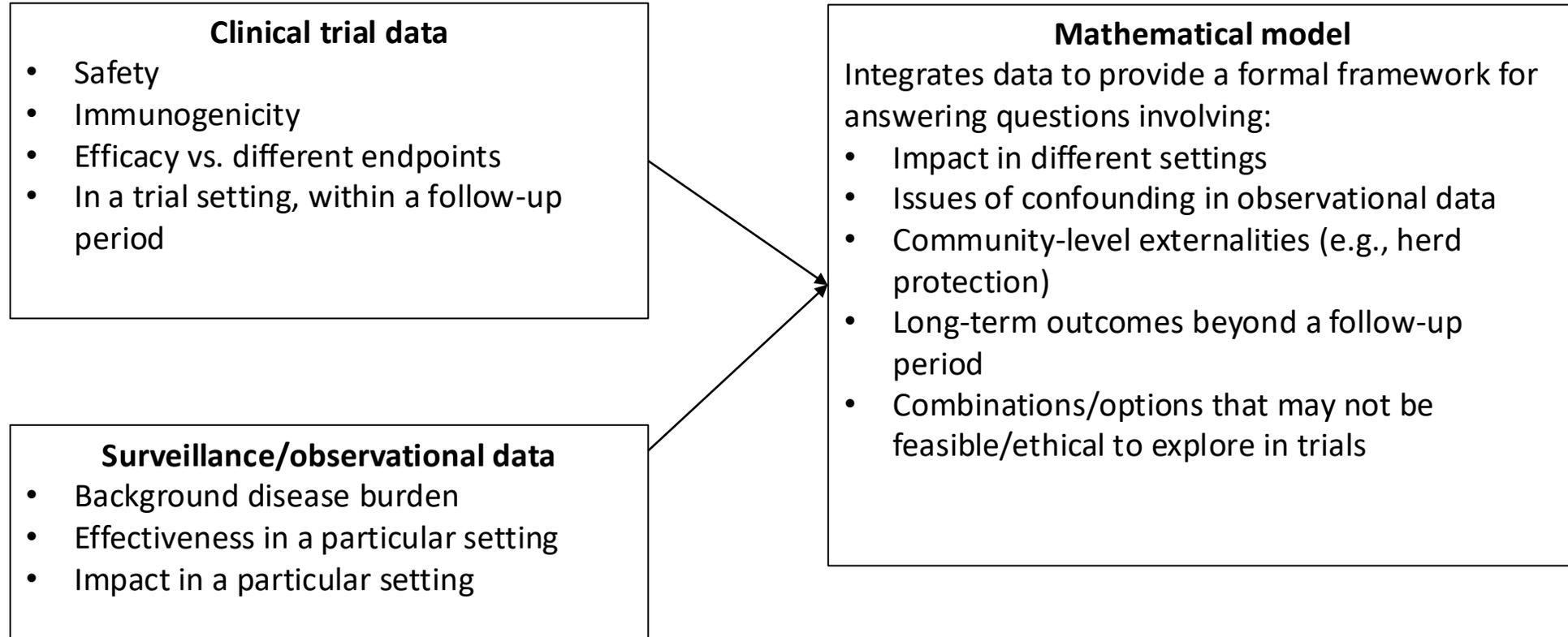
**Evidence of population-level impact of a single-dose HPV vaccine on HPV 16/18 prevalence irrespective of HIV status**

Delany-Moretlwe, S, Machalek DA, Travill D, et al. Impact of single-dose HPV vaccination on HPV 16 and 18 prevalence in South African adolescent girls with and without HIV. *JNCI Monographs*. 2024;2024(67):337–345. doi:10.1093/jncimonographs/lgae041

Abbreviations: aPR, adjusted prevalence ratio; CI: confidence interval

# Supportive evidence from modeling analysis

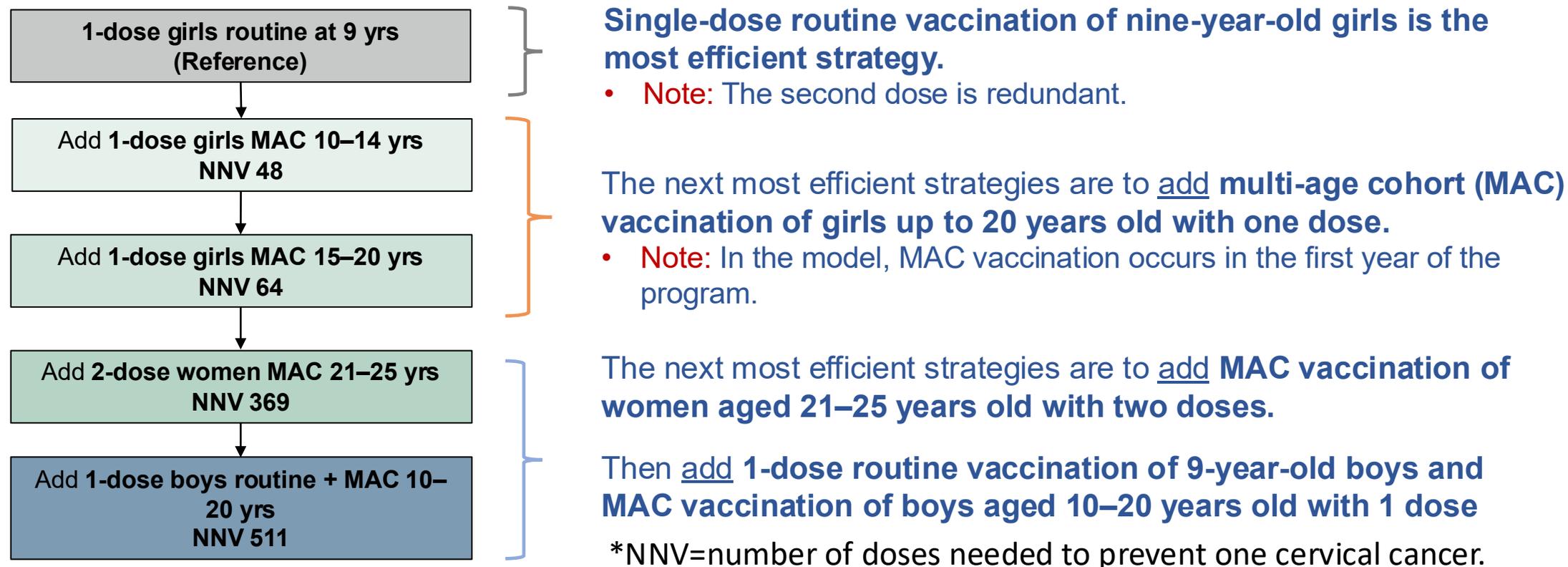
# Why use modeling to understand HPV vaccine impact?



## Scenario: single-dose non-inferiority to two-dose vaccination

Assumes 80% vaccine coverage, 1-dose vaccine effectiveness of 100%, and lifelong duration of protection. All NNVs\* are incremental.

*Note: Same ranking result for a scenario that assumes a 30-year duration of protection.*



# 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)- *covered in a meeting of the HPV Prevention and Control Board in 2025*
- Adults
- Protection at non-cervical sites (i.e.: oral and anal)
- Protection at non-mucosal sites (i.e.: genital warts)
- 1 dose as new vaccine products come online
- Accelerating elimination- *covered in a meeting of the HPV Prevention and Control Board in 2023*
- Therapeutic HPV vaccines for people with HPV-driven precancers

# More data coming: evidence into 2026

**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**
- 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)**

# Costa Rica/NCI HPV vaccine research team

## US National Cancer Institute, NIH

Aimée Kreimer (co-PI), Allan Hildesheim (retired)  
Danping Liu, Douglas Lowy, John Schiller, Casey  
Dagnall, Troy Kemp, Ligia Pinto

## Costa Rica ACIB, FUNIN

Carolina Porras (co-PI), Rolando Herrero,  
Byron Romero, Loretto Carvajal, Rebeca  
Ocampo, Daniella Mora, Carolina Coto



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