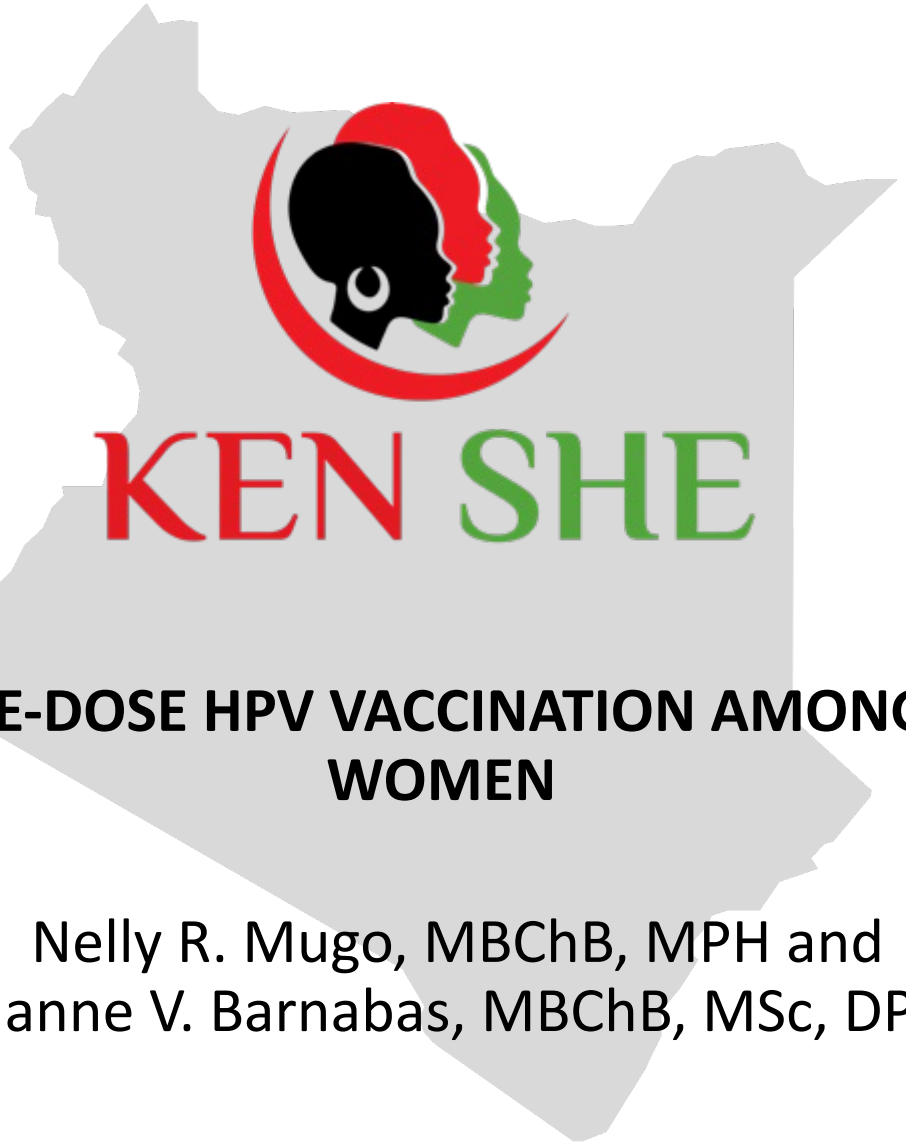


# EFFICACY OF SINGLE-DOSE HPV VACCINATION AMONG YOUNG AFRICAN WOMEN

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Study Partners:

UNIVERSITY OF WASHINGTON
INTERNATIONAL CLINICAL RESEARCH CENTER

BILL & MELINDA GATES foundation

# Study collaborators

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- KEMRI – Center for Clinical Research (CCR)
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- KEMRI – Center for Medical Research (CMR)
  - Prof. Elizabeth Bukusi (Kisumu, co-PI)
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- Fred Hutchinson Cancer Research Center
  - Dr. Elizabeth Brown, Unblinded Study Statistician
  - Prof. Deborah Donnell, Blinded Statistician
  - Prof. Denise Galloway, Immunology, co-Investigator
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- University of Washington Mombasa Lab
  - Dr. Scott McClelland

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# Outline

- Background
- Aim
- Methods
- Results
- Discussion

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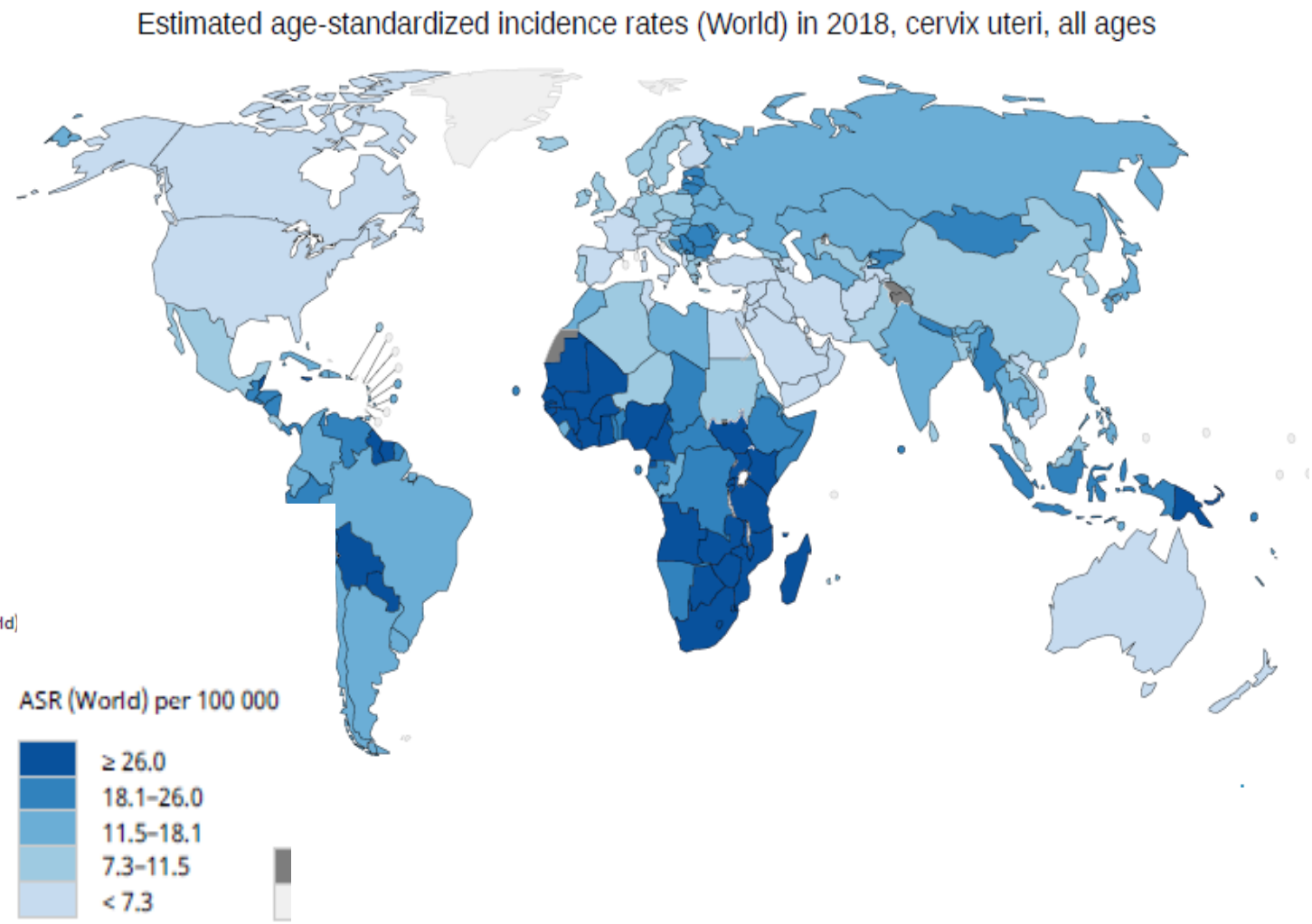
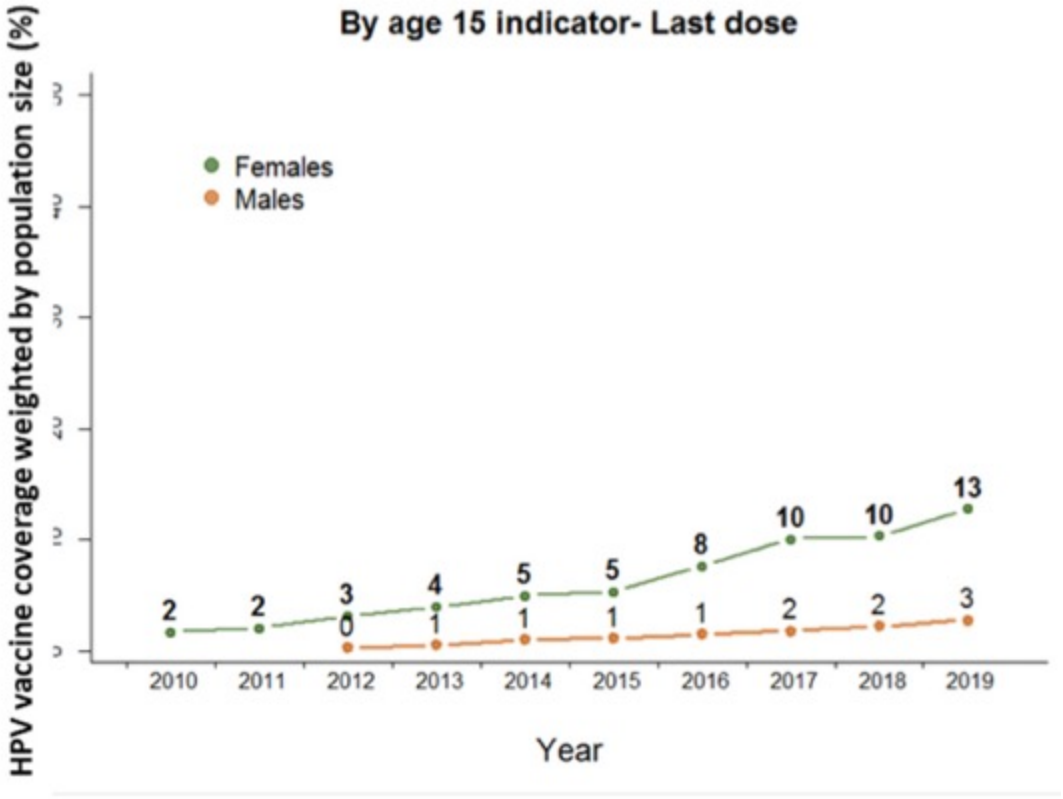
# Global cervical cancer incidence




# Global HPV vaccine coverage (2019)




Bruni, HPV vaccine coverage, Preventive Medicine, 2021

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# Primary objectives

- To test the efficacy of immediate single-dose **nonavalent** or **bivalent** HPV vaccination to prevent incident persistent **HPV 16/18** infection
- To test the efficacy of immediate single-dose **nonavalent** HPV vaccination to prevent incident persistent **HPV 16/18/31/33/45/52/58** infection

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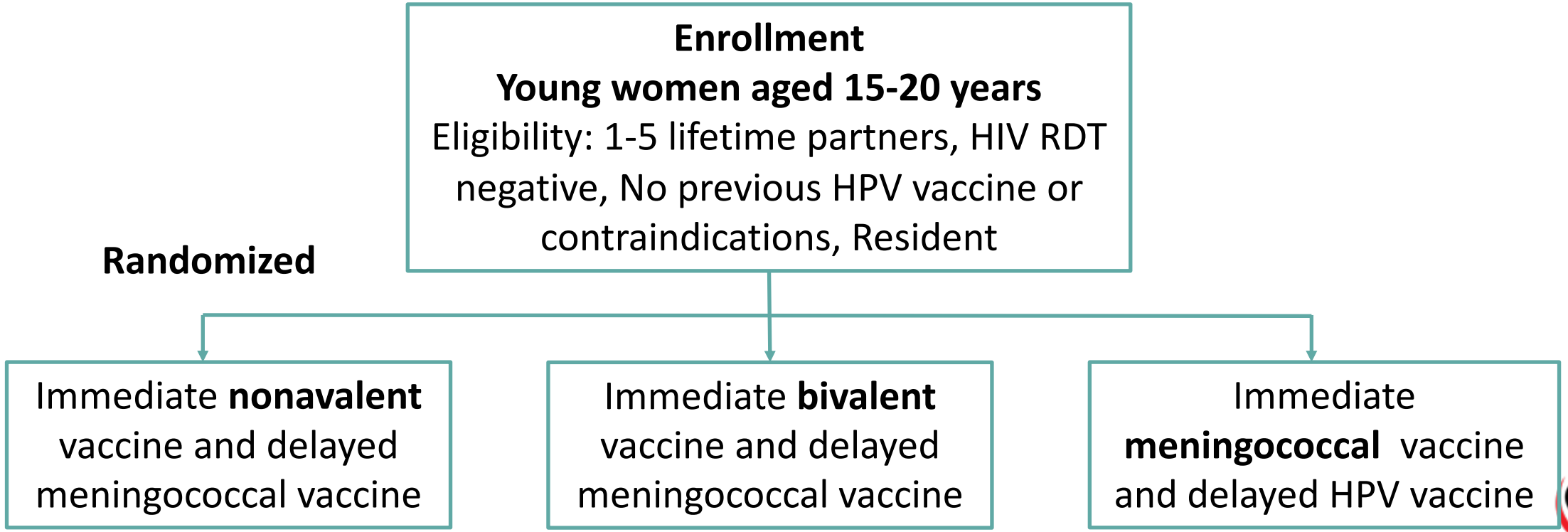
# Study Design

- Individual randomized, double-blind, control, three group trial
- Multi-center: Three KEMRI Center locations in Kenya

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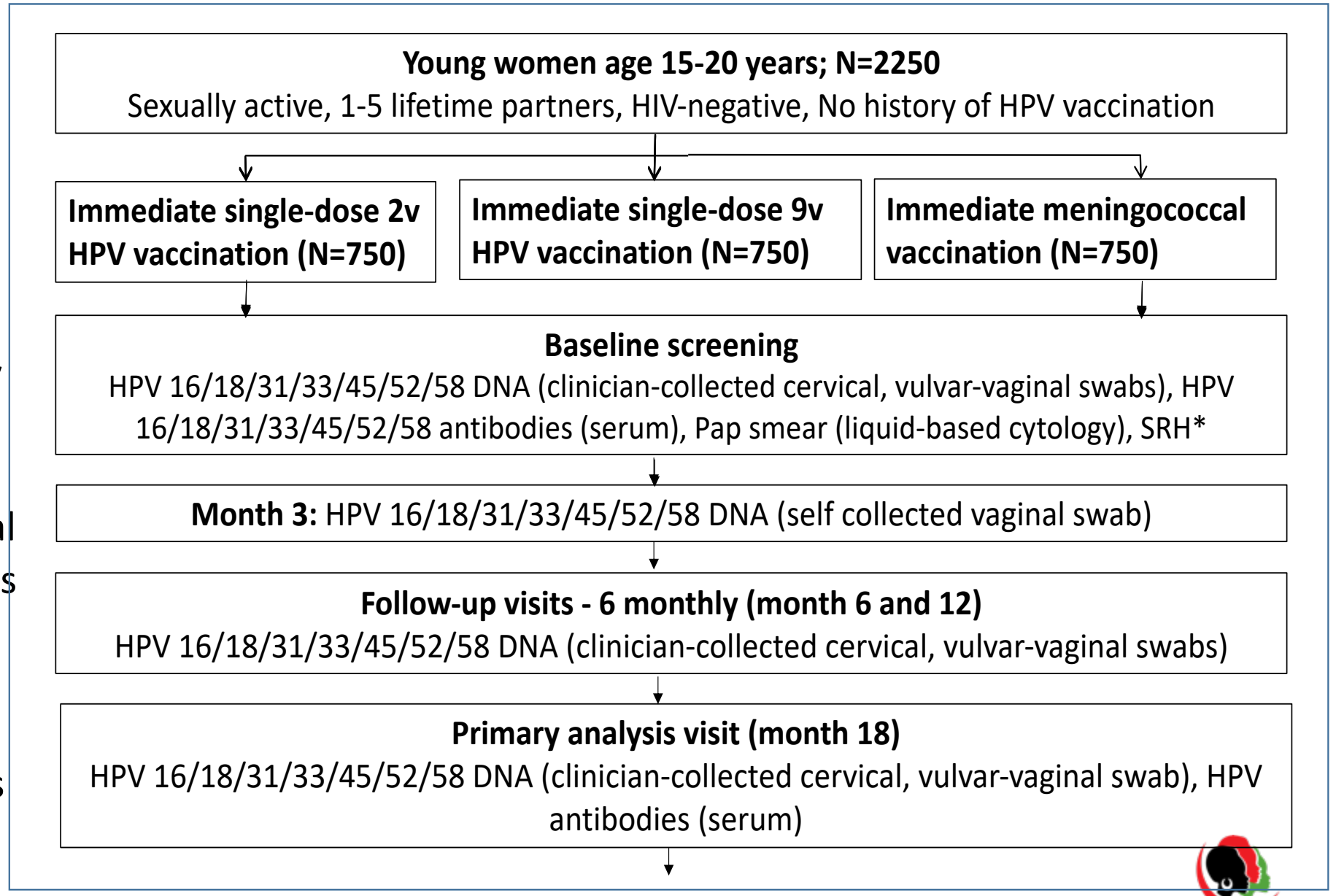
# Study visits & procedures summary

- mITT population: Exclude prevalent infections and/or antibody positive
- Primary endpoint: incident, persistent cervical infection (at least 4 months apart)
- Self-collected vaginal swabs if necessary
- Continue 6 monthly visits for final analysis → all available data

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# Primary Efficacy Outcomes

1. Month 18
   - Report VE
   - mITT cohorts: Test negative for HPV DNA at enrollment and month 3 and antibody negative at enrollment
2. **Pre-planned** sensitivity analyses:
   1. Sensitivity cohort: Include participants who test antibody positive at enrollment
   2. Extended sensitivity cohorts: Exclude participants with HPV DNA at enrollment, month 3, and month 6 and/or antibody positive at enrollment
3. Sensitivity analyses use all available data at the time of the June 24th, 2021, data cut

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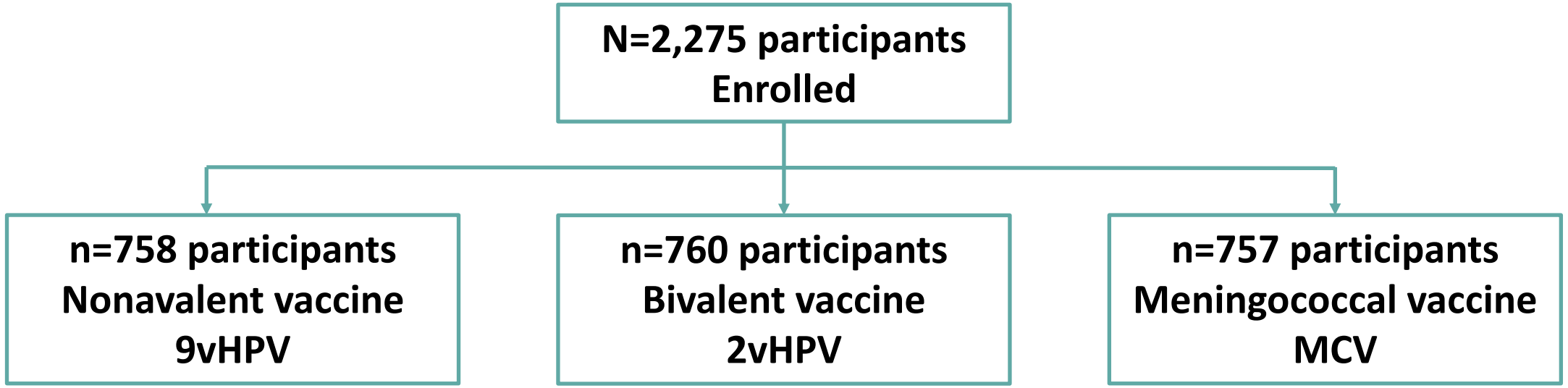
# Results

Enrollment and Baseline Characteristics

# Results: Enrollment

- Enrollment: Dec. 2018 – Nov. 2019
- No difference in enrollment characteristics by group:
  - 57% (n=1,301) were age 15-17 years
  - 61% (n=1,392) reported one lifetime sexual partner

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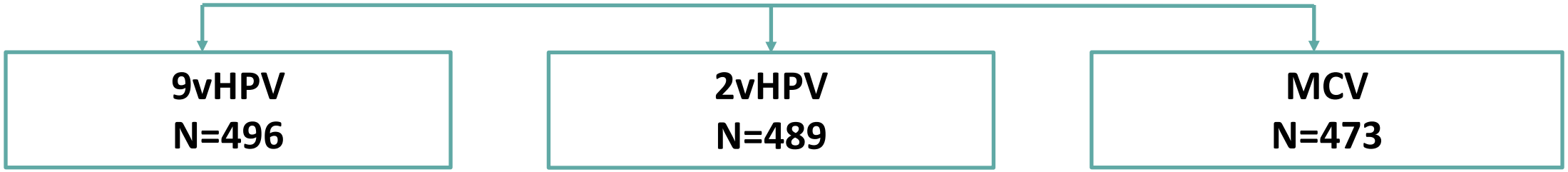
# mITT HPV 16/18 cohort

- 29% (n=661/2,275)* of participants were HPV 16/18 DNA positive at enrollment or month 3 and/or antibody positive at enrollment → excluded
- **1,458** (64%)* of participants are included in the mITT HPV 16/18 cohort:




*156 (7%) did not have complete baseline data (missing data for mITT cohort ascertainment)

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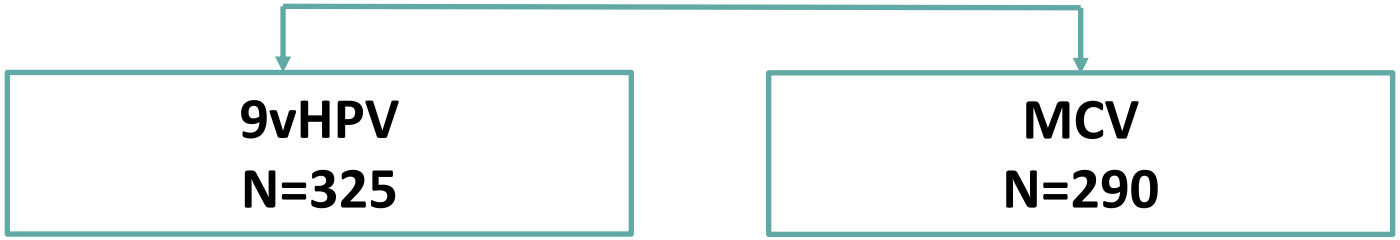
# mITT HPV 16/18/31/33/45/52/58 cohort

- 52% (n=792/1,515)* of participants were HPV 16/18/31/33/45/52/58 DNA positive at enrollment or month 3 and/or antibody positive at enrollment and were excluded
- **615**/1,515 (41%)* of participants are included in the mITT HPV 16/18/31/33/45/52/58 cohort
- Bivalent vaccine group was not included in this analysis




*108 (7%) did not have complete baseline data (missing data for mITT cohort ascertainment).

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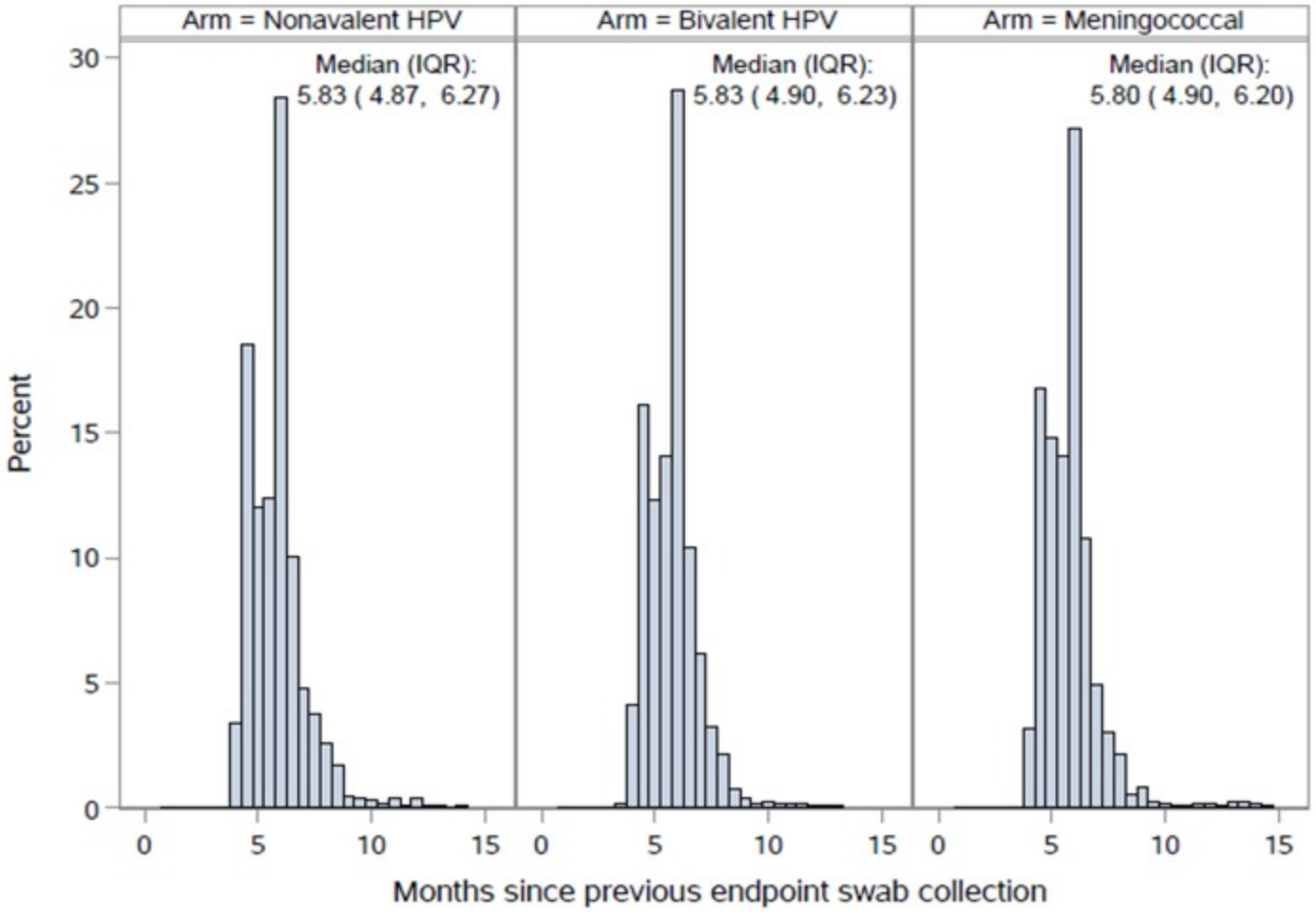
# Retention

- Retention by month 18
  - 2 endpoint swabs: 98%
  - 3 endpoint swabs: 94%
- The median time between swabs was 5.8 months
- 6% of swabs were self-collected vaginal swabs

**Figure 2. Months between Participant Endpoint Swab Collections through Month 18, by Arm (ITT)**

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# Incidence of non-vaccine HPV types

**(26/35/39/40/42/43/44/51/53/54/56/59/60/61/66/68/70/73/82 mITT cohort)**

| Group | 9vHPV | 2vHPV | MCV |
|---|---|---|---|
| Cases | 53 | 55 | 53 |
| Incidence of persistent non-vaccine type HPV per 100 woman-years (95% CI) | 22.2 (16.6-29.0) | 24.5 (18.5-31.9) | 22.6 (17.0-29.6) |

Follow-up time amongst women non-vaccine HPV-type DNA negative at month 0 and month 3 (women are excluded if positive at month 0 or month 3 for any of HPV 26/35/39/40/42/43/44/51/53/54/56/59/60/61/66/68/70/73/82)

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# Primary efficacy results

1. Month 18
    - mITT cohorts (16/18 and 16/18/31/33/45/52/58)

# HPV 16/18 mITT efficacy

| | mITT (n) | Cases (Incident persistent HPV) | Incidence (per 100 woman-years) | VE (%) (95% CI) | p-value (log-rank) |
|---|---|---|---|---|---|
| 9vHPV | 496 | 1 | | | |
| 2vHPV | 489 | 1 | | | |
| MCV | 473 | 36 | | | |

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# HPV 16/18 mITT efficacy

| | mITT (n) | Cases (Incident persistent HPV) | Incidence (per 100 woman-years) | VE (%) (95% CI) | p-value (log-rank) |
|---|---|---|---|---|---|
| 9vHPV | 496 | 1 | 0.17 | 97.5 (81.7-99.7) | <0.0001 |
| 2vHPV | 489 | 1 | 0.17 | 97.5 (81.6-99.7) | <0.0001 |
| MCV | 473 | 36 | 6.83 | | |

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# HPV 16/18/31/33/45/52/58 mITT efficacy

| | mITT (n) | Cases (Incident persistent HPV) | Incidence (per 100 woman-years) | VE (%) (95% CI) | p-value (log-rank) |
|---|---|---|---|---|---|
| 9vHPV | 325 | 4 | 1.03 | 88.9 (68.5-96.1) | <0.0001 |
| MCV | 290 | 29 | 9.42 | | |

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# Pre-planned efficacy sensitivity analyses

Sensitivity cohort

-Include participants with HPV antibodies at enrollment

Extended sensitivity cohort:

-Exclude participants with HPV DNA at month 6

All available data for mITT cohorts

# HPV 16/18 mITT efficacy: Sensitivity analyses (All data)

| | mITT (n) | Cases (Incident persistent HPV) | Incidence (/100 woman-years) | VE (%) (95% CI) | p-value (log-rank) |
|---|---|---|---|---|---|
| **Sensitivity cohort (include participants with HPV antibodies at enrollment)** | | | | | |
| 9vHPV | 569 | 1 | 0.13 | 98.2 (86.6-99.7) | <0.0001 |
| 2vHPV | 561 | 3 | 0.38 | 94.4 (82.1-99.3) | <0.0001 |
| MCV | 543 | 48 | 6.92 | | |
| **Extended sensitivity cohort (exclude participants with HPV DNA detected at month 6)** | | | | | |
| 9vHPV | 429 | 0 | 0.00 | 100 (--)* | <0.0001 |
| 2vHPV | 404 | 0 | 0.00 | 100 (--)* | <0.0001 |
| MCV | 380 | 16 | 3.90 | | |

*VE & 95% CIs computed using incidence rate ratios estimated from an Exact Poisson regression model

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# HPV 16/18/31/33/45/52/58 mITT efficacy: Sensitivity analyses (All data)

| | mITT (n) | Cases (Incident persistent HPV) | Incidence (/100 woman-years) | VE (%) (95% CI) | p-value (log-rank) |
|---|---|---|---|---|---|
| **Sensitivity cohort (include participants with HPV antibodies at enrollment)** | | | | | |
| 9vHPV | 437 | 7 | 1.16 | 89.3 (76.4-95.1) | <0.0001 |
| MCV | 392 | 52 | 10.95 | | |
| **Extended sensitivity cohort (exclude participants with HPV DNA detected at month 6)** | | | | | |
| 9vHPV | 264 | 1 | 0.32 | 95.0 (67.1-99.9) | <0.0001 |
| MCV | 210 | 14 | 6.36 | | |

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# Discussion

- Adolescent girls and young women were effectively protected from HPV infection over the first 18 months post vaccination
- VE 16/18 - >97% - in keeping with licensure trials for three doses
- 9v hr vaccine-type HPV incidence is high (~9/100 woman-years) – 1/3 higher than previous vaccine trials
- Rigorous design, high fidelity to the protocol, high retention, clear ascertainment of outcomes → strong evidence for single-dose HPV vaccine efficacy
- Next step: Proposed blinded crossover vaccination to evaluate durability

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# Thank you


- **Study Participants**
- **Bill and Melinda Gates Foundation** (Peter Dull, Caroline Wendell, Ruha Shadab); **Fred Hutchinson Cancer Research Center** (Elizabeth Brown, Deborah Donnell, Denise Galloway, Jody Carter, Leeya F. Pinder, Marci Wright, Priya Prabhu Robin Smith); **KEMRI Kisumu** (Elizabeth A. Bukusi, Maricianah Onono, Annette A. Opondo, Brian Mata, Byron I. Odhiambo, Catherine W. Mwakio, Charles O. Ochulo, Chrispine O. Abuya, Christine A. Olweny, Consolata A. Opondo, Cynthia Akinyi, David E. Muhoma, Debora A. Odhiambo, Dismas O. Congo, Donnavane A. Ondego, Florence A. Ondiek, Fyrose Makori, George O. Omondi, Gilbert C. Mutai, Hellen A. Olweyo, Imelda N. Imali, Imeldah N. Wakhungu, Irene A. Amada, Irine A. Odongo, Janet A. Okeyo, Joan A. Ongere, Job A. Ouma, Joseph O. Ayoo, Judith A. Osiro, Kevin O. Onyango, Kiplagat Kiptoo, Linet A. Okode, Lizzie N. Kabete, Lyna A. Memo, Maqline A. Achola, Maxwell A. Oluoch, Meldah O. Adipo, Mildred A. Owenga, Millicent A. Oronje, Moses O. Siaji, Nobert B. Walusala, Nollyne A. Okuku, Penina N. Amboka, Prudence A. Amolo, Rebecca A. Otieno, Reina Lenturkana, Renna A. Opere, Robai Mituyi, Sarah G. Obaje, Simon M. Muthusi, Thomas O. Odhul, Tobias O. Odwar, Veronica O. Atogo, Walter W. Otieno, Yuashita E. Hussein); **KEMRI Nairobi** (Betty Njoroge, Andrew Mutinda, Ann I. Namulen, Brenda Amollo, Chrispinus Wanyonyi, Edith W. Mwangi, Edna Nyandiga, Epines K. Chavangi, Esther K. Charles, Hellen W. Kimani, Irene Thuo, Jackline Muthoki, Milkah W. Wambui, Moses M. Mutinda, Peter Mogere, Priscillah Wangeci, Purity Kiwinda, Reginah N. Gichuki, Sahara H. Adan, Snaidah Ongachi, Syovata Kimanthi, Ted Opiyo, Umi W. Mugo, Veronica W. Muchoki, Victoria N. Kyengo, Victoria Oluoch, Vincent Juma); **KEMRI Thika** (Nelly Mugo, Anne Akinyi, Barbara Akinyi, Benedict Muchai, Caren Koli, Catherine Kiptinness, Charlene Biwott, Charles Mwangi, David Chege, Dennis Wafula, Diana Rubia, Edith Kimani, Edwin Mugo, Elizabeth Okwaro, Emily Anyango, Erick Koome, Faith Nyantika, Francis Khaemba, Fridah Nkatha, Gladys Namboka, Grace Muguro, Grace Ndung'u, Irene Njeru, Jacinta Nyokabi, Jelioth Muthoni, John Njoroge, Joshua Omari, Judith Achieng, Linet Makena, Lydiah Wambui, Lynda Oluoch, Margaret Mwangi, Margaret Wairima, Mary Kibatha, Mathew Irungu, Matilda Saina, Moses Musau, Nancy Kiarie, Nina Ouko, Peter Mogere, Peter Mwenda, Peterson Mwaniki, Praxides Pessah, Rosemary Ngacha, Sarah Mbaire, Scholastica Wanjiku, Snaidah Ongachi, Solomon Maina, Stephen Gakuo, Victoria Wambui, Vincent Juma, Zachary Gathu); **University of Washington, Mombasa** (R. Scott McClelland, Emmanuel Kabare, Fatma H. Mwidadi, Juma Shafi, Khamis Mwinyikai, Rukiya Hassan, Salwa Mustafa); **University of Washington, Seattle** (Ruanne Barnabas, Elizabeth Brown, Bobbi Nodell, Cara Bayer, Caroline H. Liou, Clare E. Brown, Connie Celum, Daphne Hamilton, Deborah Donnell, Deidra Montoya, Elena A. Rechkina, Elizabeth Harrington, Gui Lui, Hannah Leingang, Harald Haugen, Jared M. Baeten, Jasper Bleijs, Jack Knauer, Jenell C. Stewart, Jennifer Baugh, Jodi Greathouse, John Lin, Justice Quame-Amaglo, Kate B. Heller, Lara Kidoguchi, Meighan Krows, Rachel Johnson, Rachel L. Winer, Stephen L. Cherne, Susan Morrison, Toni Maddox, Torin Schaafsma); **DF/Net Research, Inc., Seattle** (Angela Williams, Bill Larson, Gavin Robertson, Krissa Gunderson, Lisa Ondrejcek, Rheanna Summers, Tadas Lukosevicius). **The study is dedicated to Kowselia Ramaswami Ramiah, Sarah Kanyi Mugo, Reginalda Auma Onono, Edwina Muga, Mary Nduta, and all our mothers.**


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*ClinicalTrials.gov*: NCT03675256

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