CHIC | COALITION to STRENGTHEN the HPV IMMUNIZATION COMMUNITY

EFFICACY OF SINGLE-DOSE HPV VACCINATION AMONG YOUNG AFRICAN WOMEN (KEN SHE)

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CHIC SPC Symposium

HPV Vaccination Programs: From Pre-introduction Planning to Restoration and Sustainability

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Outline

- Background
- Aim
- Methods
- Results
- Discussion

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Rationale

- High coverage of HPV vaccination is a key intervention in the WHO's Global Cervical Cancer Elimination Strategy
- 15% of girls are immunized* → goal is 90%
- Observational studies:
  - Single-dose efficacy supported by observational studies^
- A single-dose HPV vaccination approach → simplify the logistics and decrease costs of HPV vaccination
- Due to gaps in evidence for single-dose HPV vaccine efficacy and concerns about clinically meaningful lower efficacy → policy makers recommend multi-dose HPV vaccination

*Bruni, Preventive Medicine, 2021; ^Kreimer, Lancet Onc, 2015; Safaeian, JNCI 2018; Whitworth, Vaccine, 2019; Basu, Lancet Onc, 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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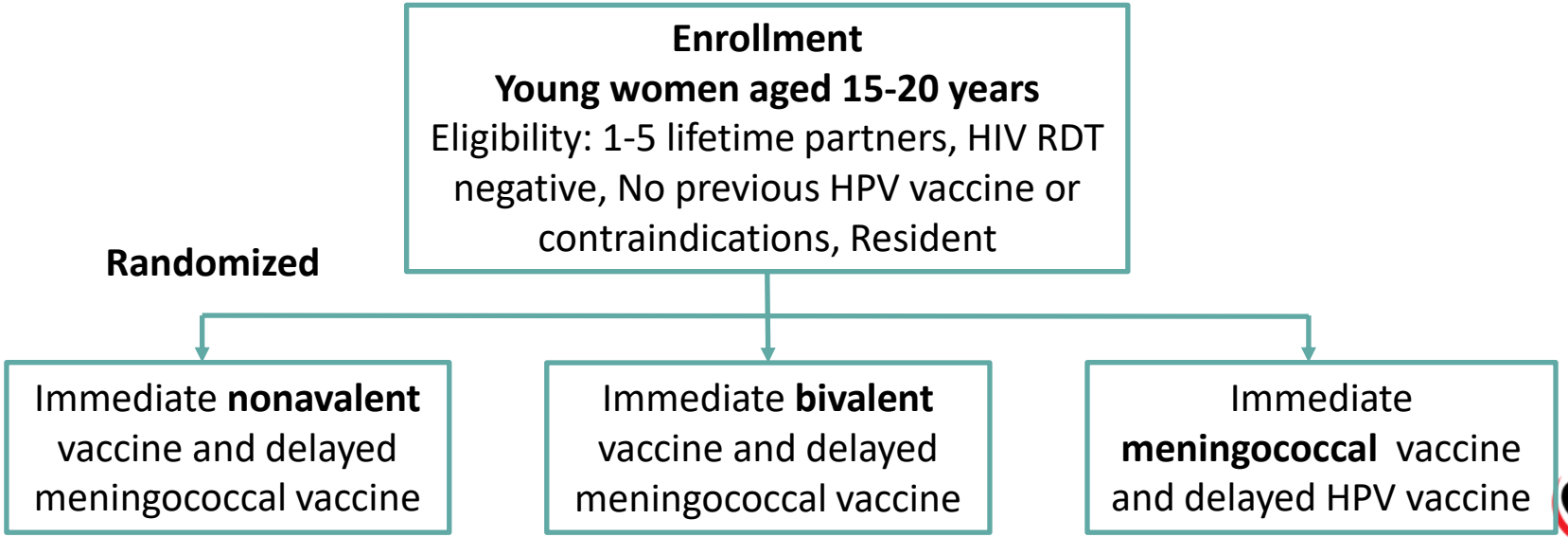
Study Design

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



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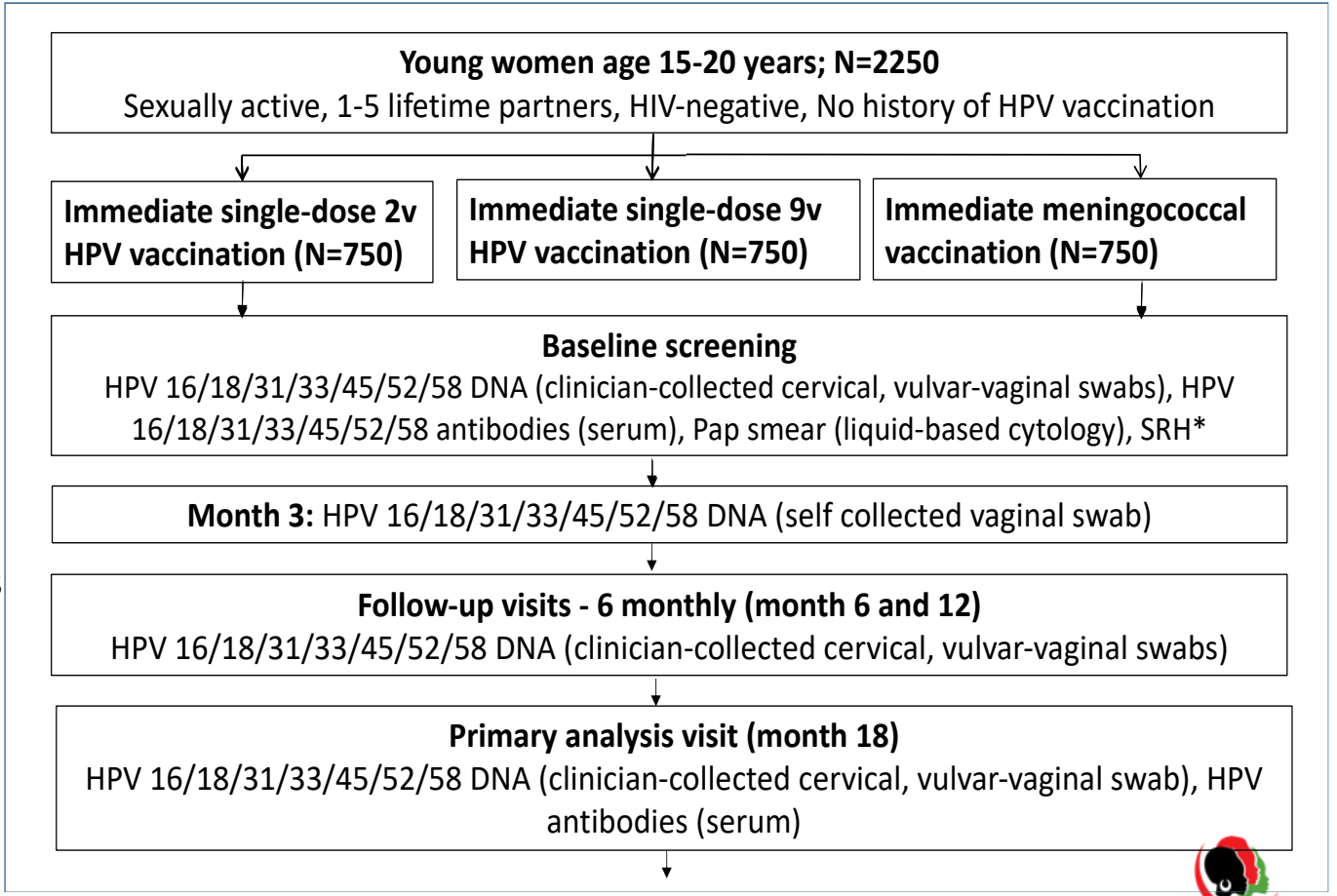
Study visits & procedures summary

- 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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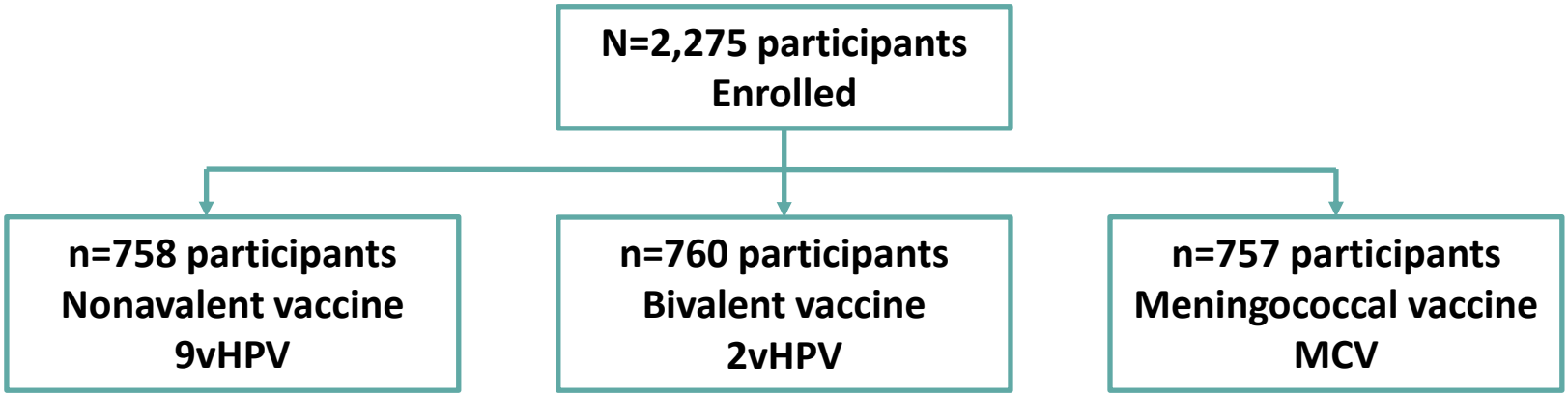
Results

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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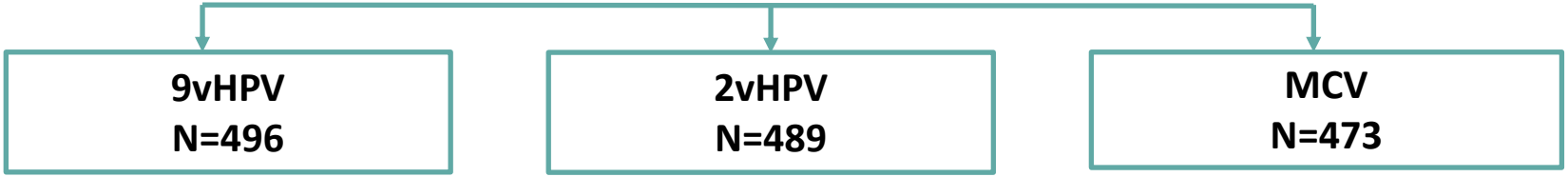
mITT HPV 16/18 cohort

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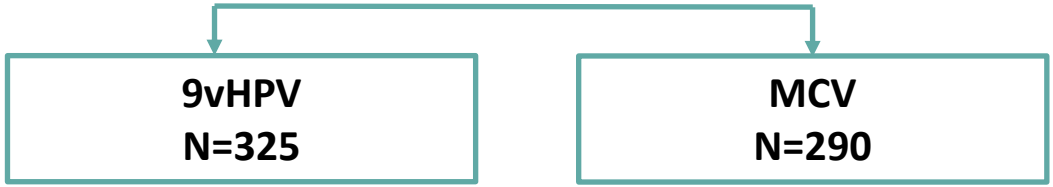
mITT HPV 16/18/31/33/45/52/58 cohort

- 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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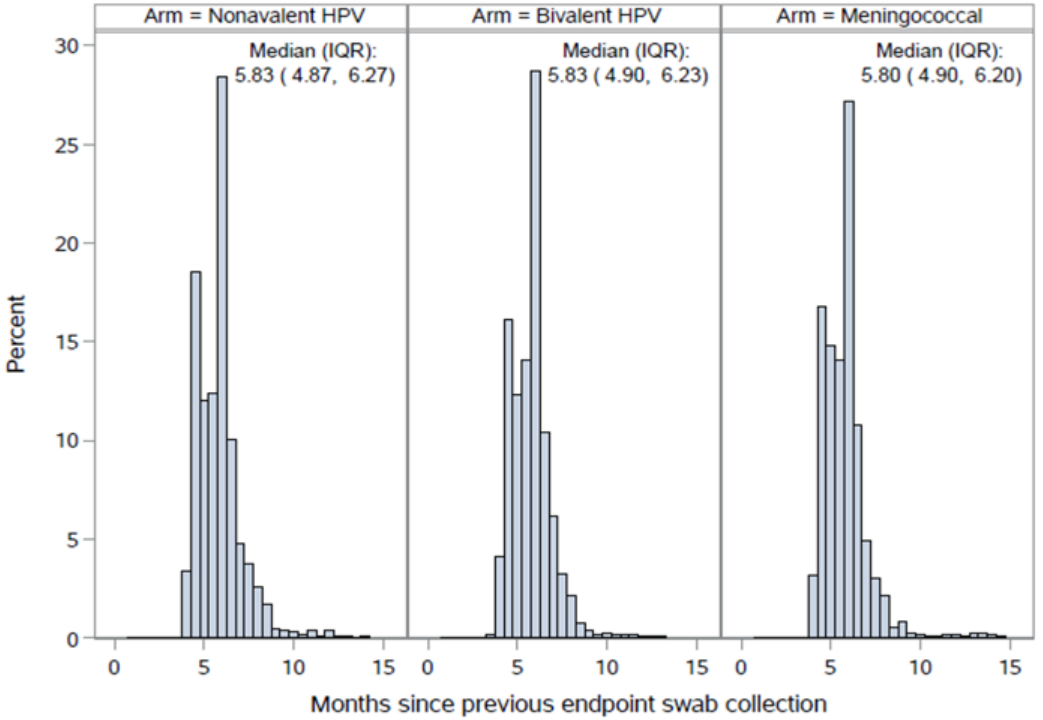
Retention

- 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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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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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: Blinded crossover vaccination to evaluate durability up to month 55

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