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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 partners

- ICRC, University of Washington, Seattle
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- KEMRI – Center for Clinical Research (CCR)
  - Dr. Nelly Mugo, co-PI (Thika PI)
  - Dr. Betty Njoroge (Nairobi PI)
- KEMRI – Center for Medical Research (CMR)
  - Prof. Elizabeth Bukusi (Kisumu, co-PI)
  - Dr. Maricianah Onono (Kisumu, co-PI)
- Country Director: Dr. Maricianah Onono
- Fred Hutchinson Cancer Research Center
  - Dr. Elizabeth Brown, Unblinded Study Statistician
  - Prof. Deborah Donnell, Blinded Statistician
  - Prof. Denise Galloway, Immunology, co-Investigator
  - Dr. Leeya Pinder, UW OBGYN and Immunology;
- University of Washington Mombasa Lab
  - Dr. Scott McClelland

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Outline

- Background
- Aim
- Methods
- Results
- Discussion

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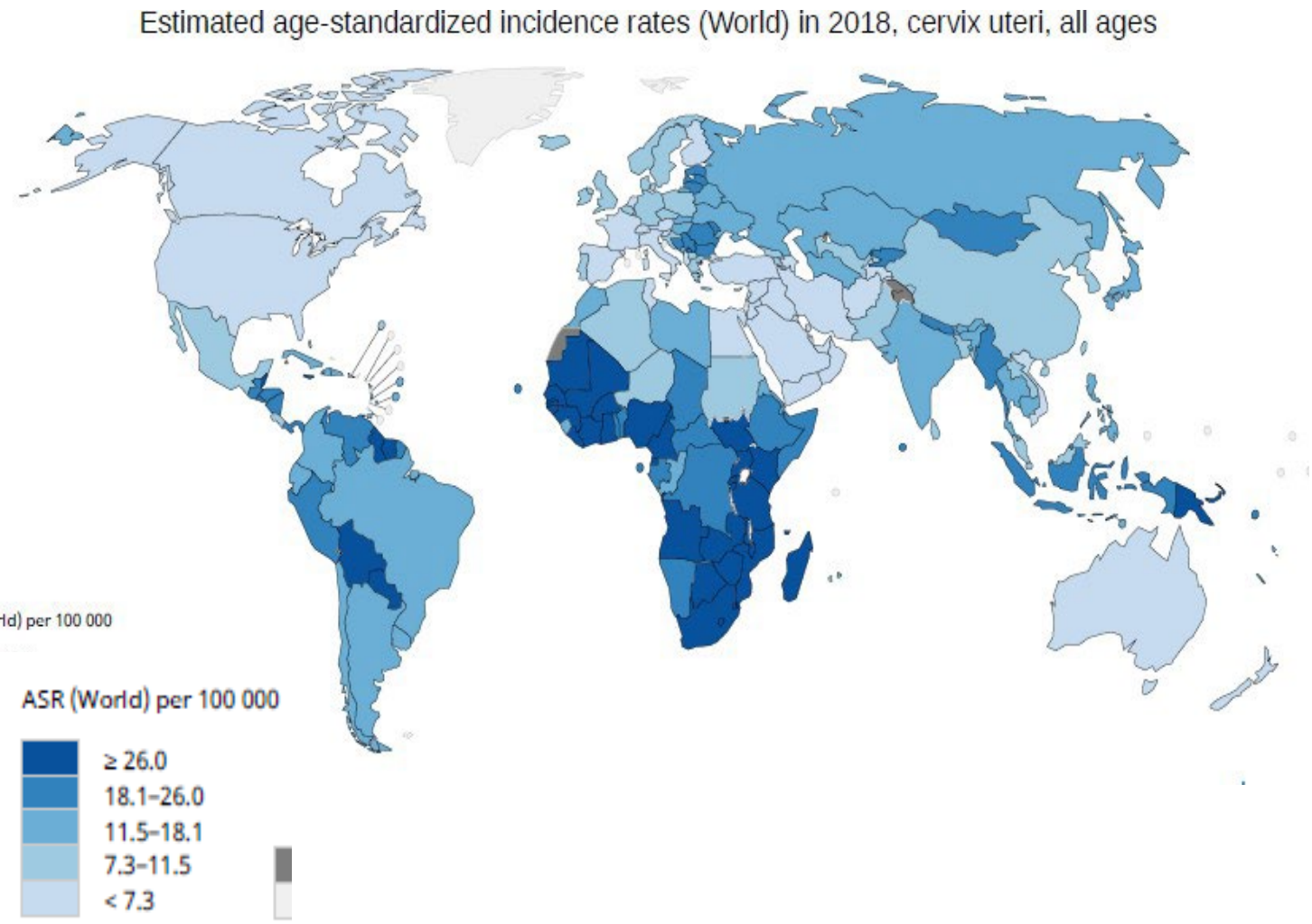
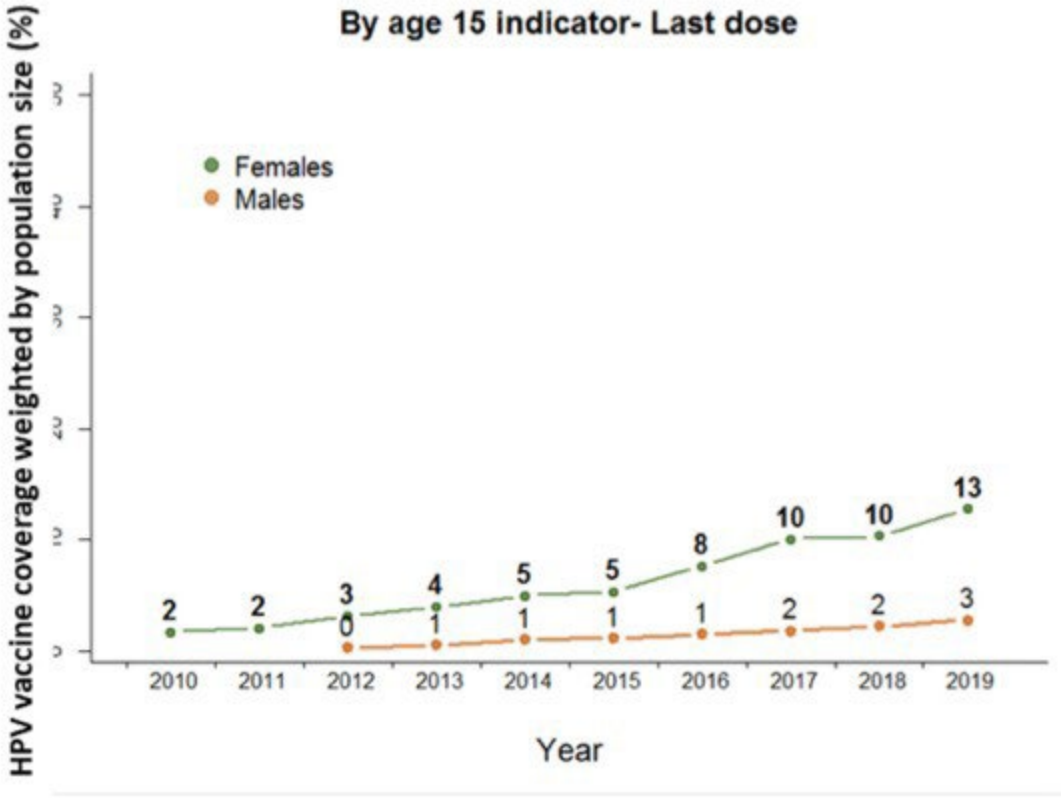
Global cervical cancer incidence



Global HPV vaccine coverage (2019)



Bruni, HPV vaccine coverage, Preventive Medicine, 2021

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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^
  - Multi-age cohort & catch-up vaccination ➔ earlier benefits ➔ approach elimination
- 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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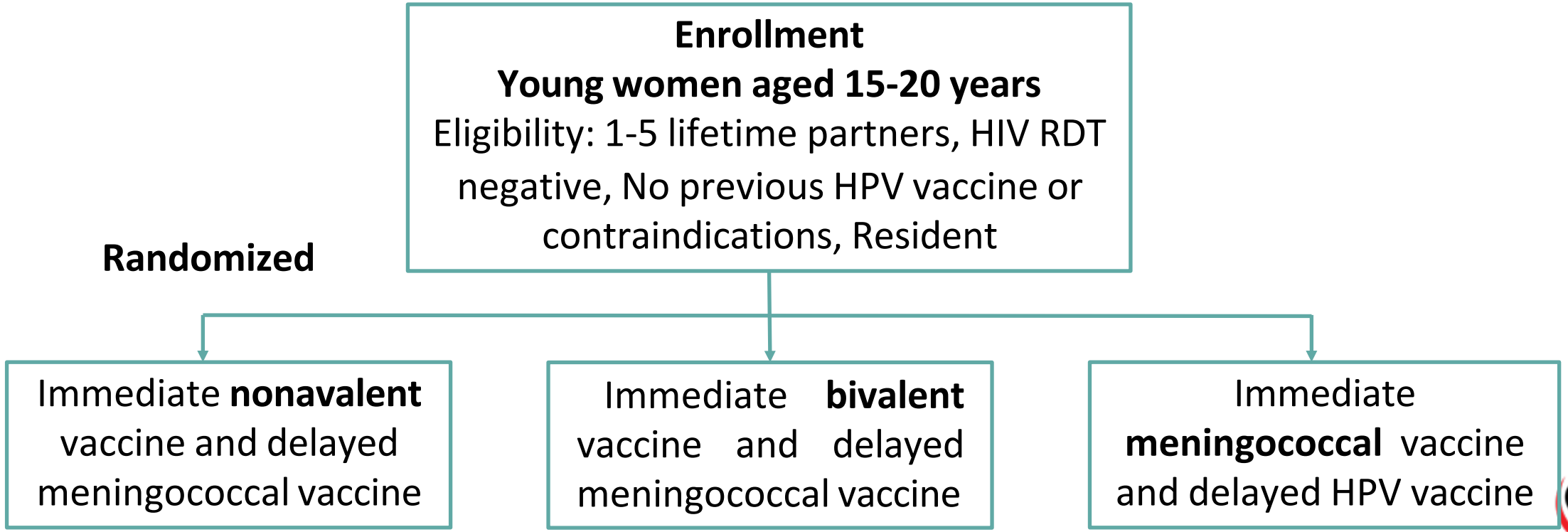
Study Design

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



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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:
   3. Sensitivity cohort: Include participants who test antibody positive at enrollment
   4. Extended sensitivity cohorts: Exclude participants with HPV DNA at enrollment, month 3, and month 6 and/or antibody positive at enrollment

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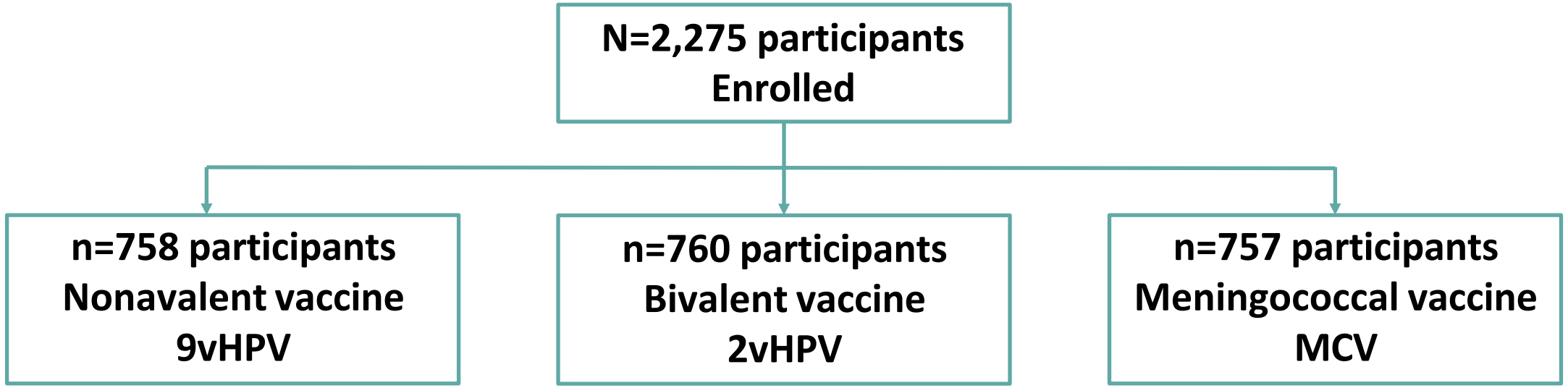
Results

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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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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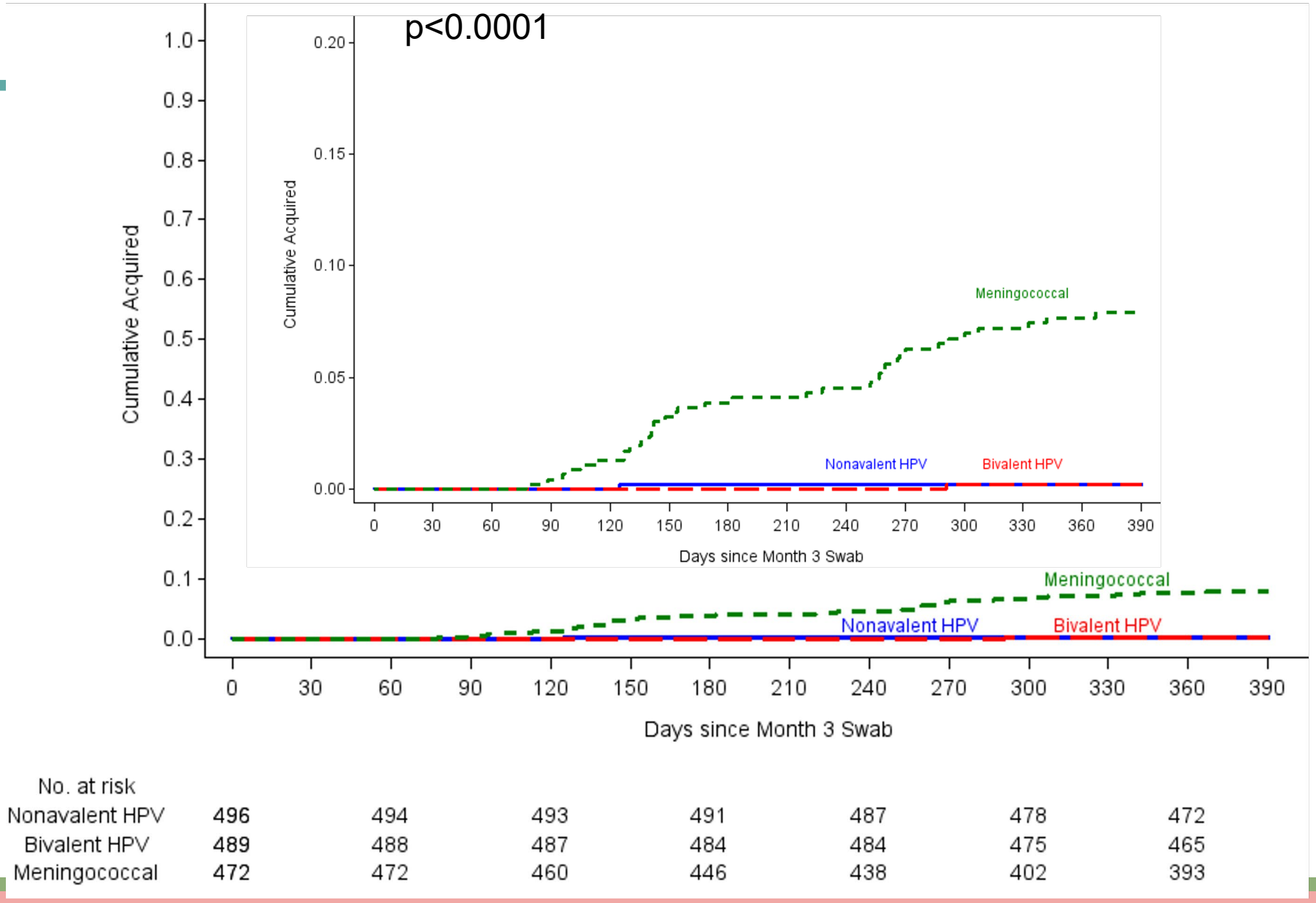
mITT 16/18 VE



No. at risk							
Nonavalent HPV	496	494	493	491	487	478	472
Bivalent HPV	489	488	487	484	484	475	465
Meningococcal	472	472	460	446	438	402	393

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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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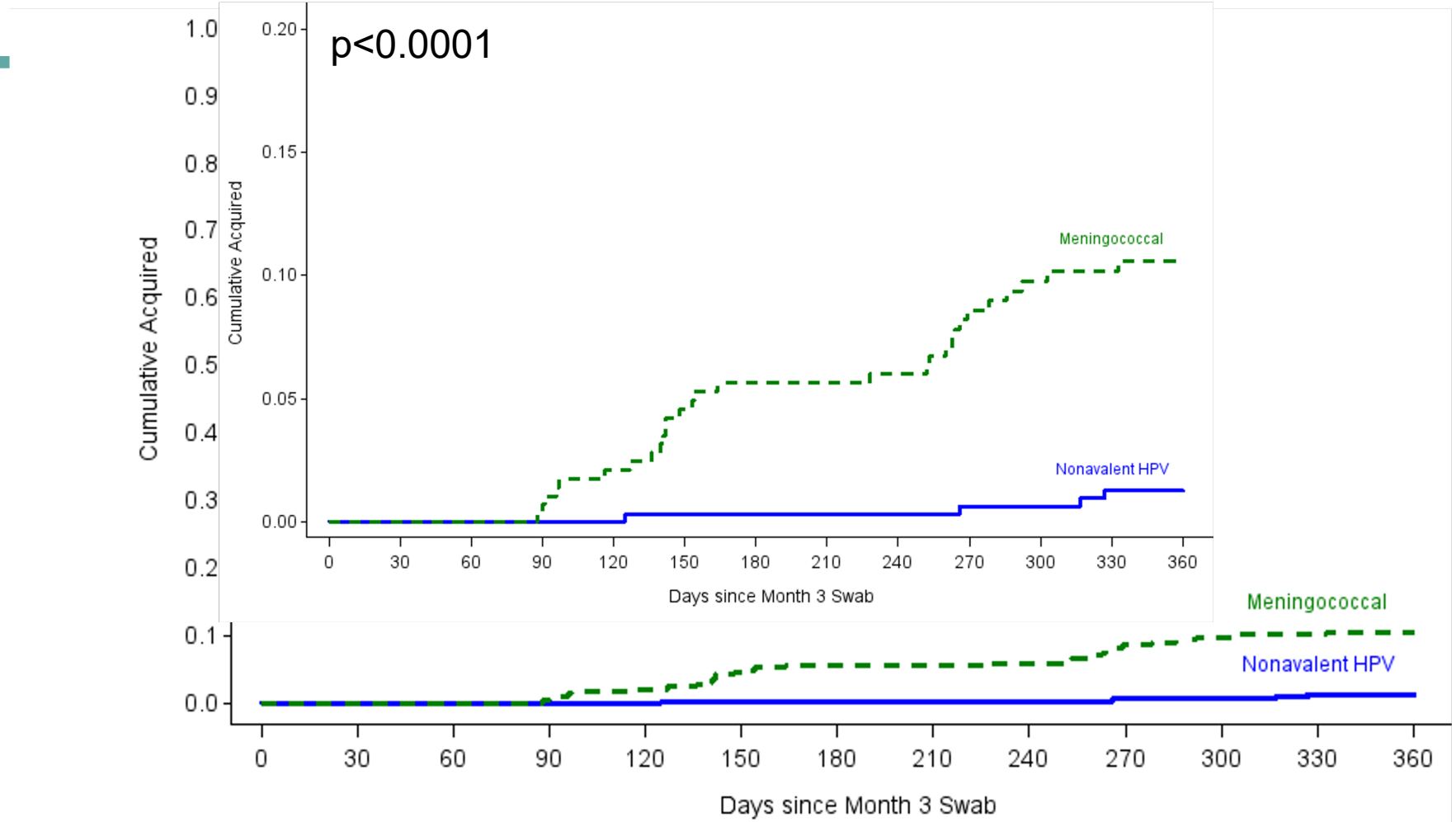
mITT 16/18/31/33/45/52/58



No. at risk							
Nonavalent HPV	325	324	323	321	320	312	306
Meningococcal	289	289	277	266	260	224	212

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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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Safety

SAE: Serious Adverse Events

Safety

	9vHPV	2vHPV	MCV	All
Enrolled, n	758	760	757	2275
Any vaccine related SAE, n(%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Any non-vaccine related SAE, n(%)	34 (4.5%)	39 (5.1%)	39 (5.2%)	112 (4.9%)
Any pregnancy-related, n (%)	24 (3.2%)	19 (2.5%)	14 (1.8%)	57 (2.5%)
Any infection/inflammation, n (%)	9 (1.2%)	16 (2.1%)	21 (2.8%)	46 (2.0%)
Any injury, n (%)	0 (0.0%)	3 (0.4%)	4 (0.5%)	7 (0.3%)
Any mental health, n (%)	2 (0.3%)	1 (0.1%)	2 (0.3%)	5 (0.2%)

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Discussion

- Adolescent girls and young women were effectively protected from HPV infection over the first 18 months post vaccination
- VE was >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

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