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A randomized trial of single-dose HPV vaccination efficacy among young women: Month 54 durability results

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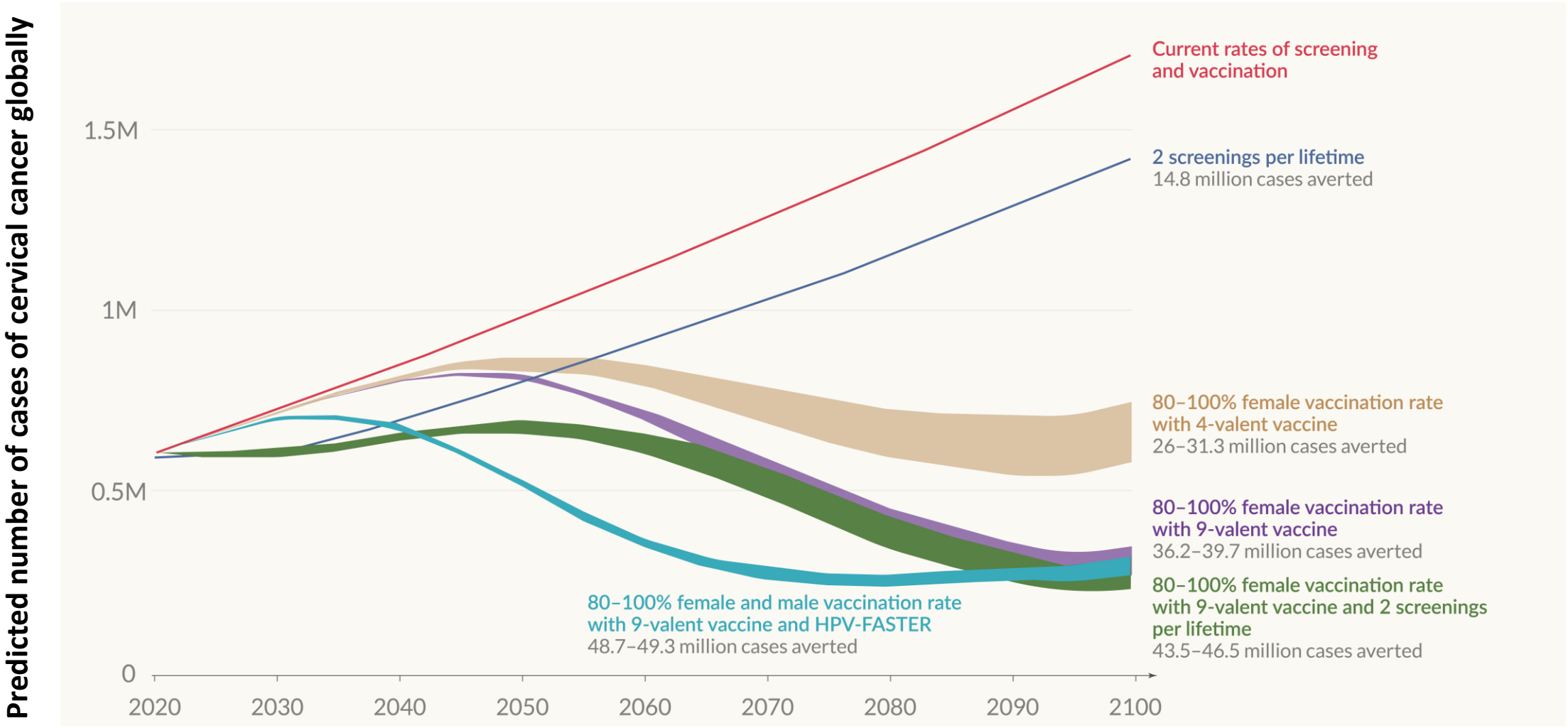
HPV vaccination for all and catch-up vaccination to young adulthood accelerate the timeline to cervical cancer elimination.



Simms, K. T., Steinberg, J., …, & Canfell, K. (2019). Impact of scaled up human papillomavirus vaccination: A modelling study. The Lancet Oncology

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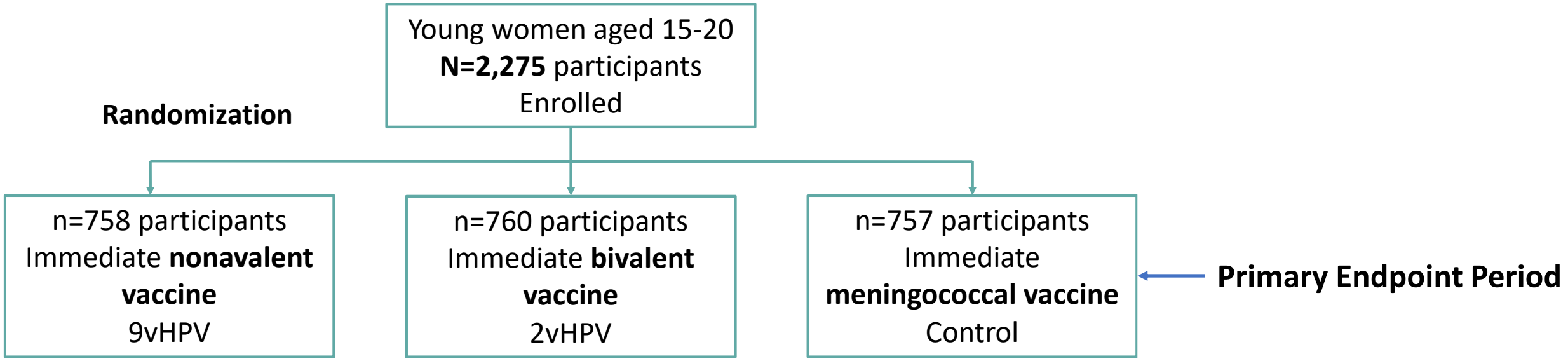
We conducted a rigorous randomized trial (the KEN SHE Study) and found that the single dose HPV vaccination is highly efficacious, with 98% vaccine efficacy for HPV 16/18.



Six monthly follow-up visits: clinician collected cervical swabs

Endpoint: Incident, persistent vaccine type-specific infection among participants HPV naïve at vaccination

Retention was 96% for four or more swab

Duration of follow-up: 36 months

Barnabas, R., Brown, E., and colleagues. KEN SHE Study 36 months VE results. Nature Medicine, Dec. 2023

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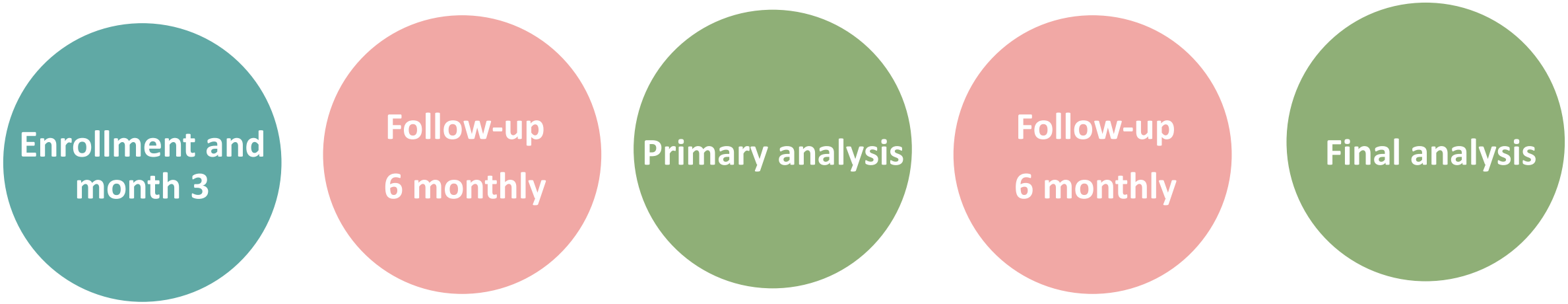
Participants were followed over 36 months.



Exclude prevalent infection

Physician collected cervical swabs for HPV DNA

VE

18 months

Physician collected cervical swabs for HPV DNA

Participants vaccinated

VE

36 months

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Participants with prevalent HPV infections at enrollment were excluded from the per protocol/mITT analysis, because the vaccine is prophylactic only.

mITT HPV 16/18 cohort

- 29% (n=661/2,275) prevalent infections → excluded

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

- 52% (n=792/1,515) prevalent infection → excluded

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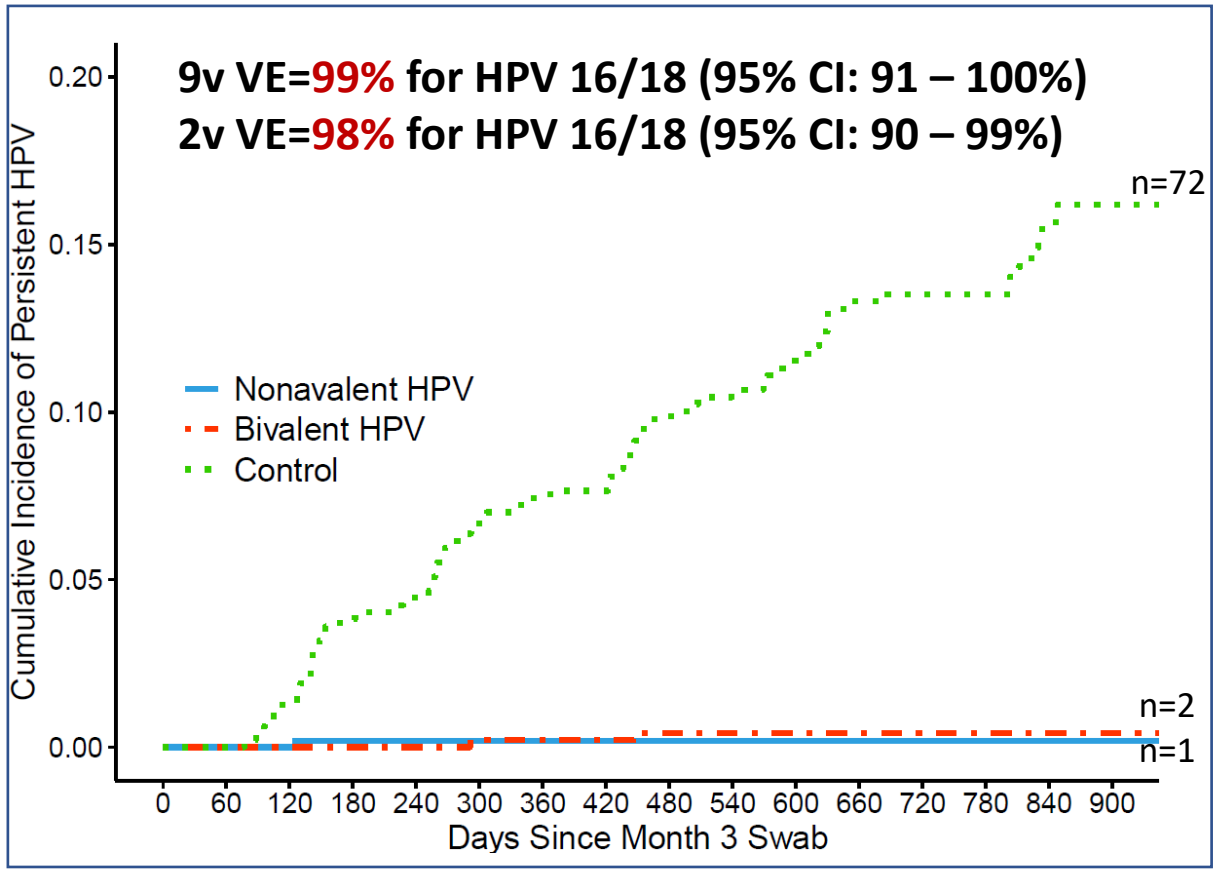
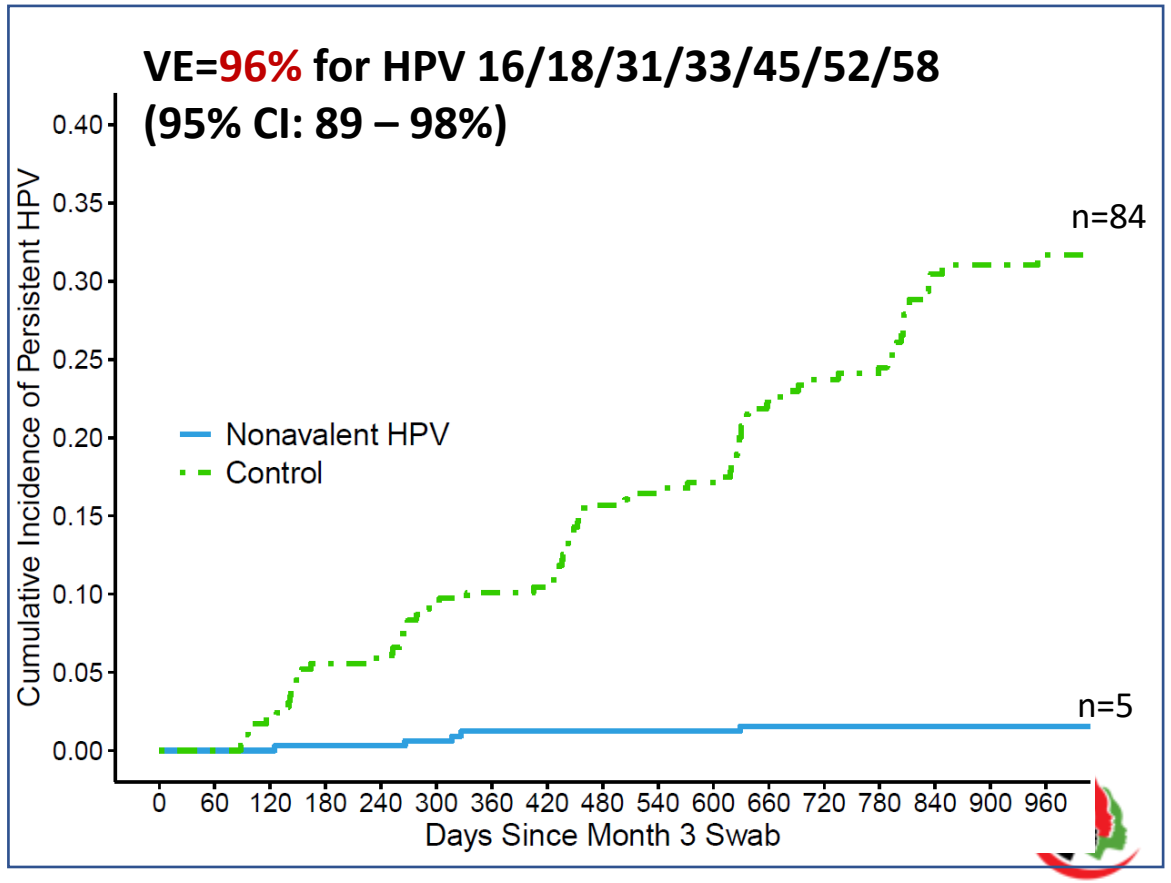
After three years, single-dose HPV vaccine efficacy remained high and durable (VE=98% for HPV 16/18 and VE=96% for HPV 16/18/31/33/45/52/58).

Month 36 VE results





Barnabas, R., Brown, E., and colleagues. KEN SHE Study 36 months VE results. Nature Medicine, Dec. 2023

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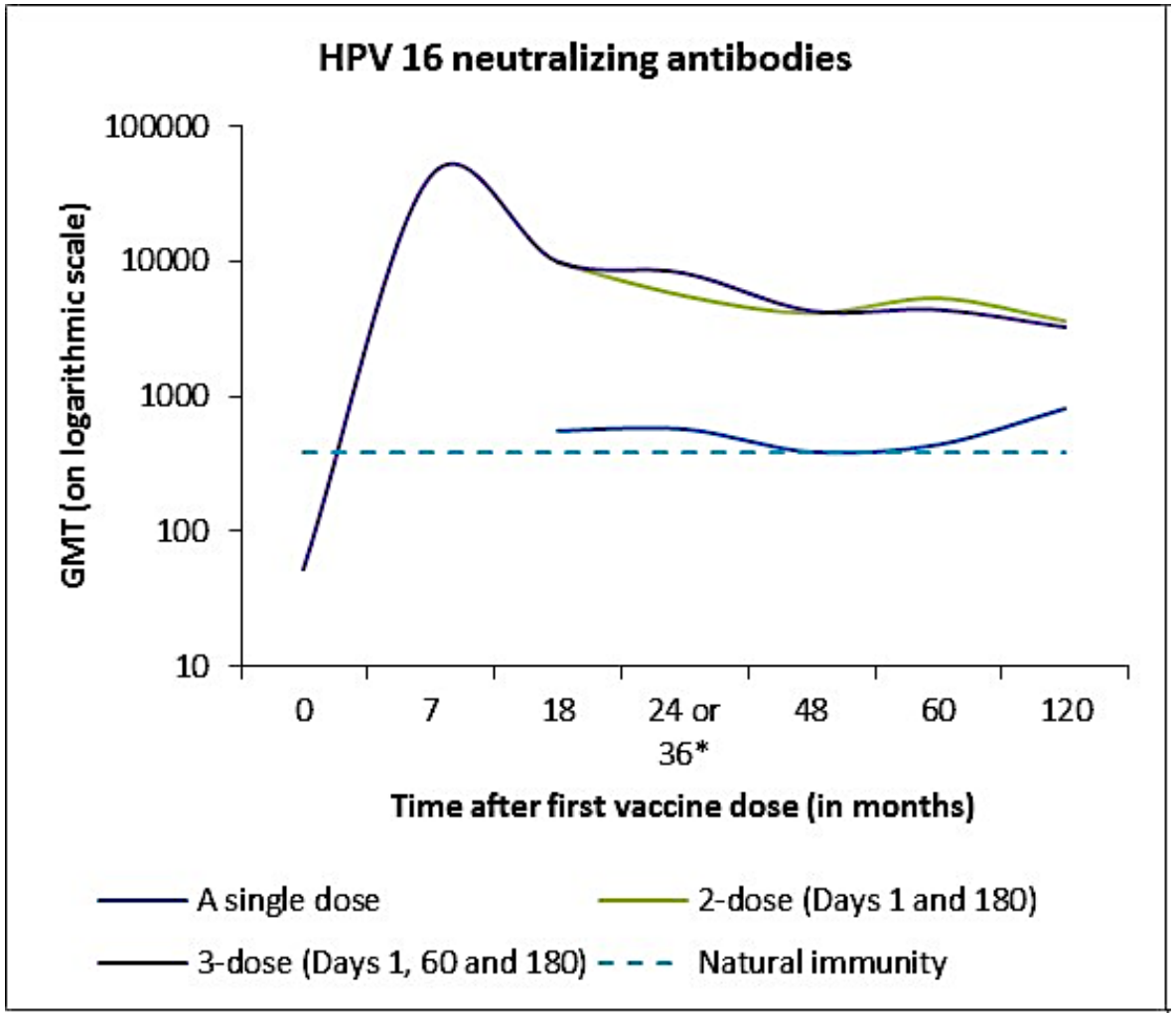
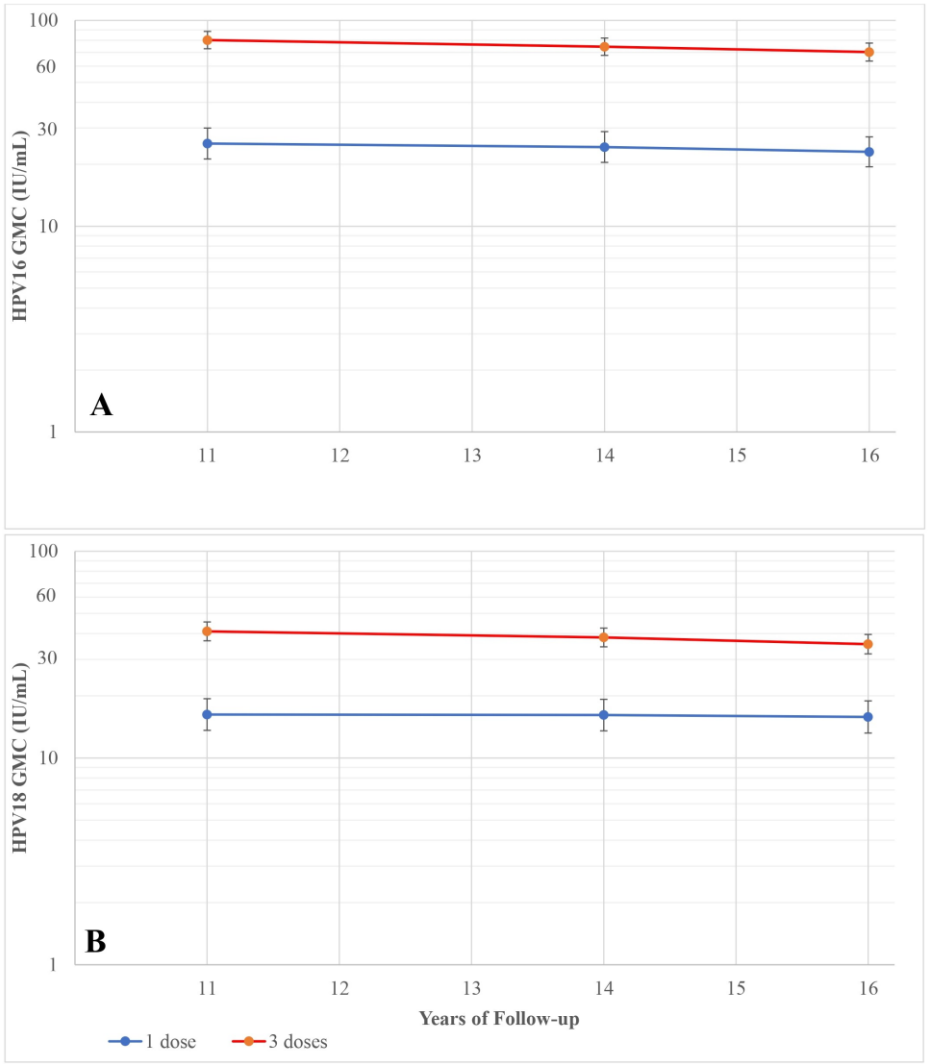
We hypothesized that single-dose vaccination would be effective and durable over 54-months based on sustained antibody levels over 16 years.



Joshi, S…Basu, P. Vaccine. 2023 Jan 4;41(1):236-245.



Porras, C … Kreimer, A. CVT, IPVC, 2023

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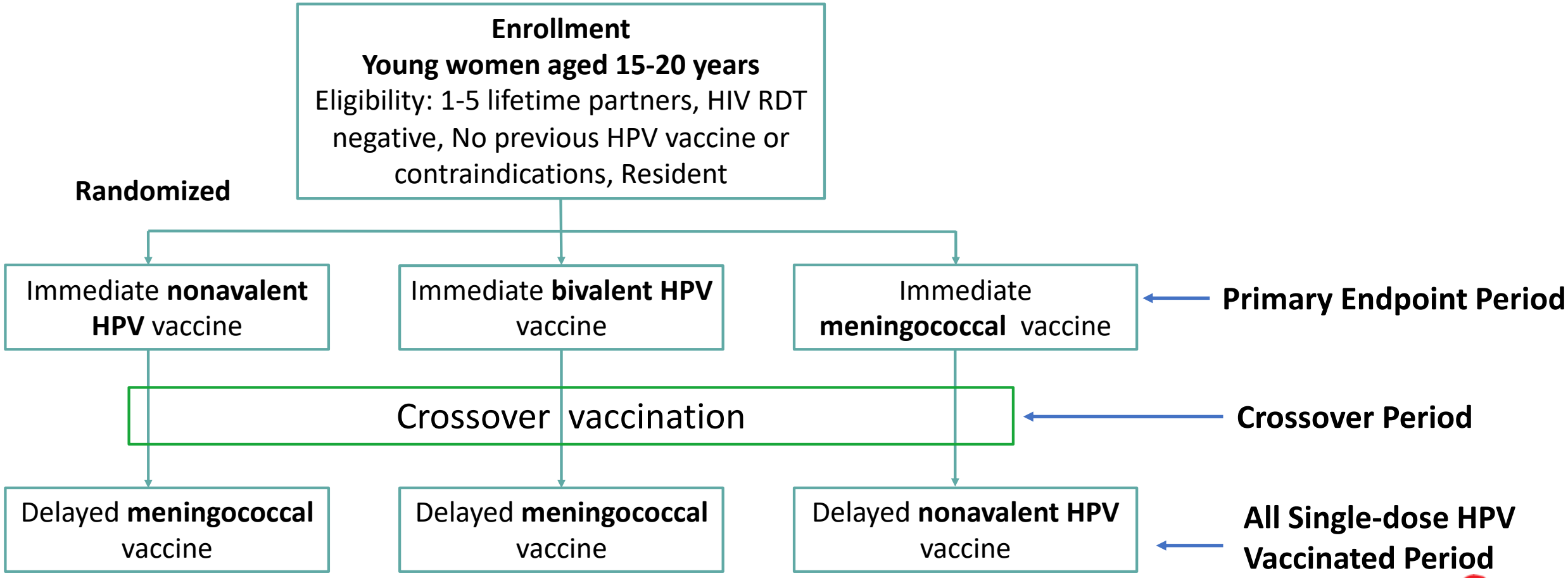
Participants in the KEN SHE Study were crossed over at month 30/36 while maintaining the study blind.



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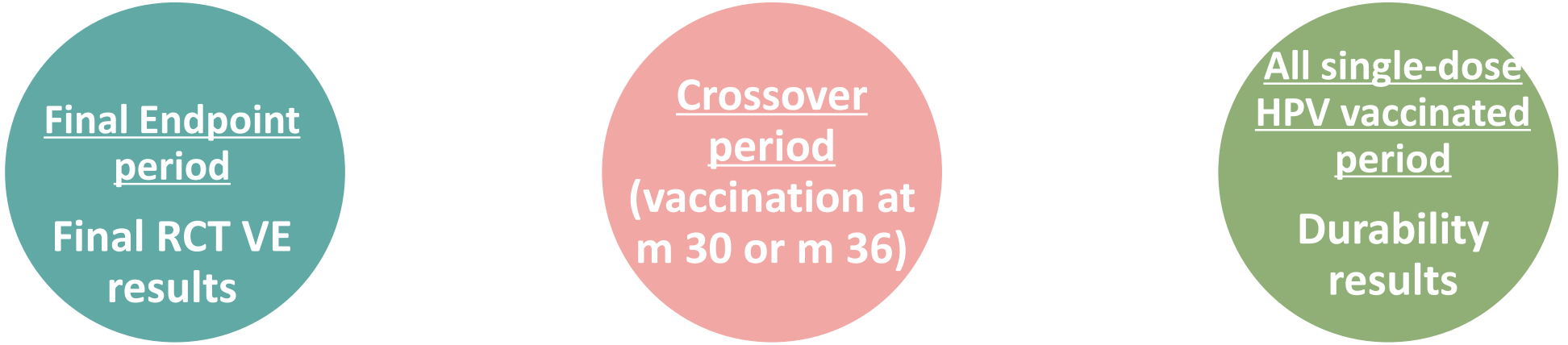

AIMS

1. To evaluate effectiveness of single-dose HPV vaccination for age 18-23, we compared the cumulative incidence of persistent HPV using Kaplan-Meier (cumulative incidence) curves and incident rate estimates for the immediate and delayed vaccine groups (graphic illustration)
2. To assess durability, vaccine efficacy was evaluated as a function of time since vaccination using a Cox regression model (accounting for time and time variable covariates)

- **Endpoint**: Incident persistent vaccine type-specific HPV infection measured at two time points 6 months apart
- Both analyses used the mITT cohorts

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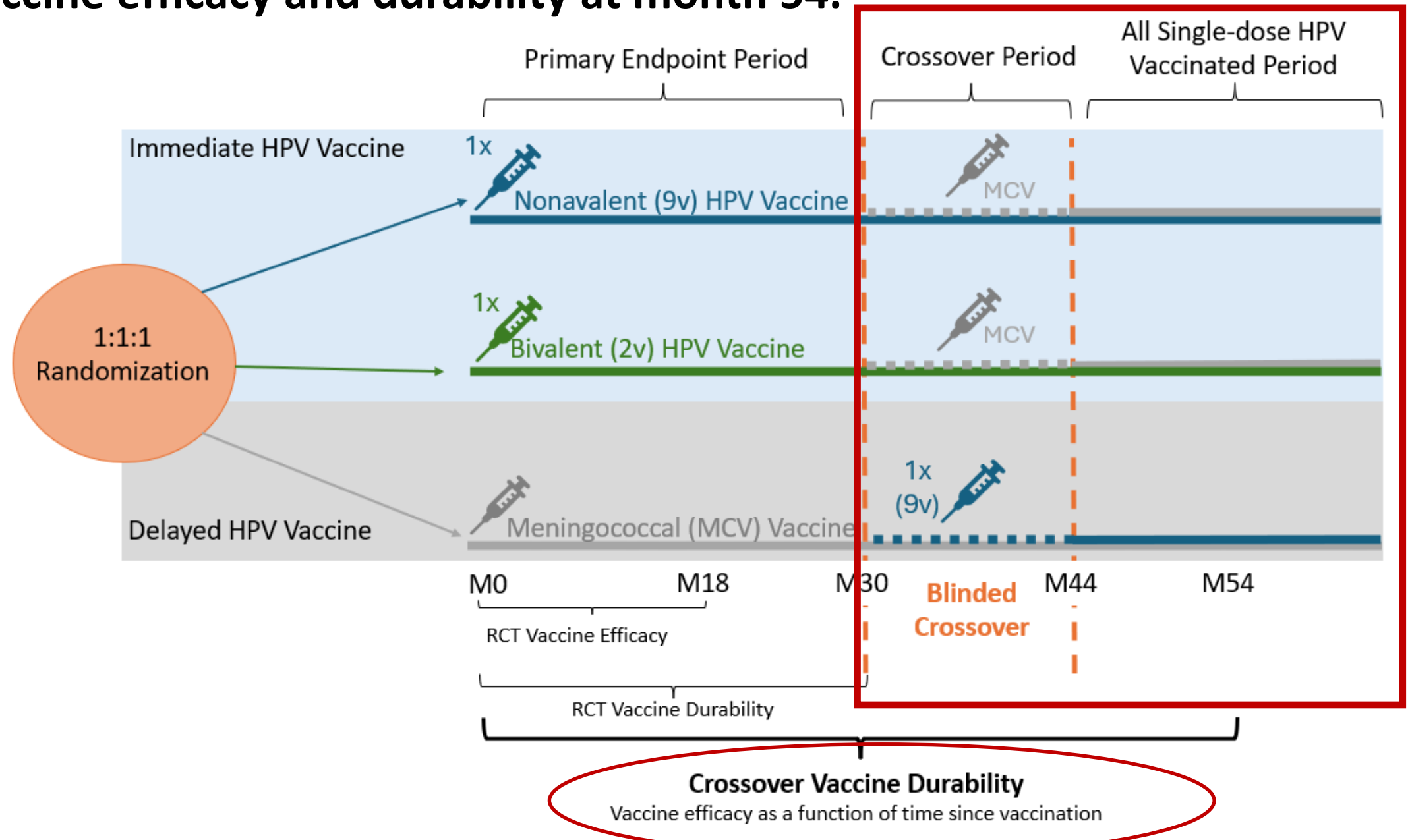
We extended the KEN SHE Study in a blinded cross-over trial design to assess vaccine efficacy and durability at month 54.



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There were no differences in baseline characteristics between study groups. Participants were age 18-23 years at cross-over vaccination.

Characteristics	Nonavalent HPV (n=758)	Bivalent HPV (n=760)	Control (n=757)
Age group 15-17 years (%)	60%	56%	56%
Median age (years)	17	17	17
Secondary school (%)	73%	73%	73%
Current steady partner (%)	72%	71%	72%
Chlamydia trachomatis positive (%)	12%	13%	14%

Prevalence of baseline characteristics for the ITT cohort

Retention was 90% for three or more swabs and the median time between endpoint swab collection was 6.00 months.

2,275 Participants enrolled

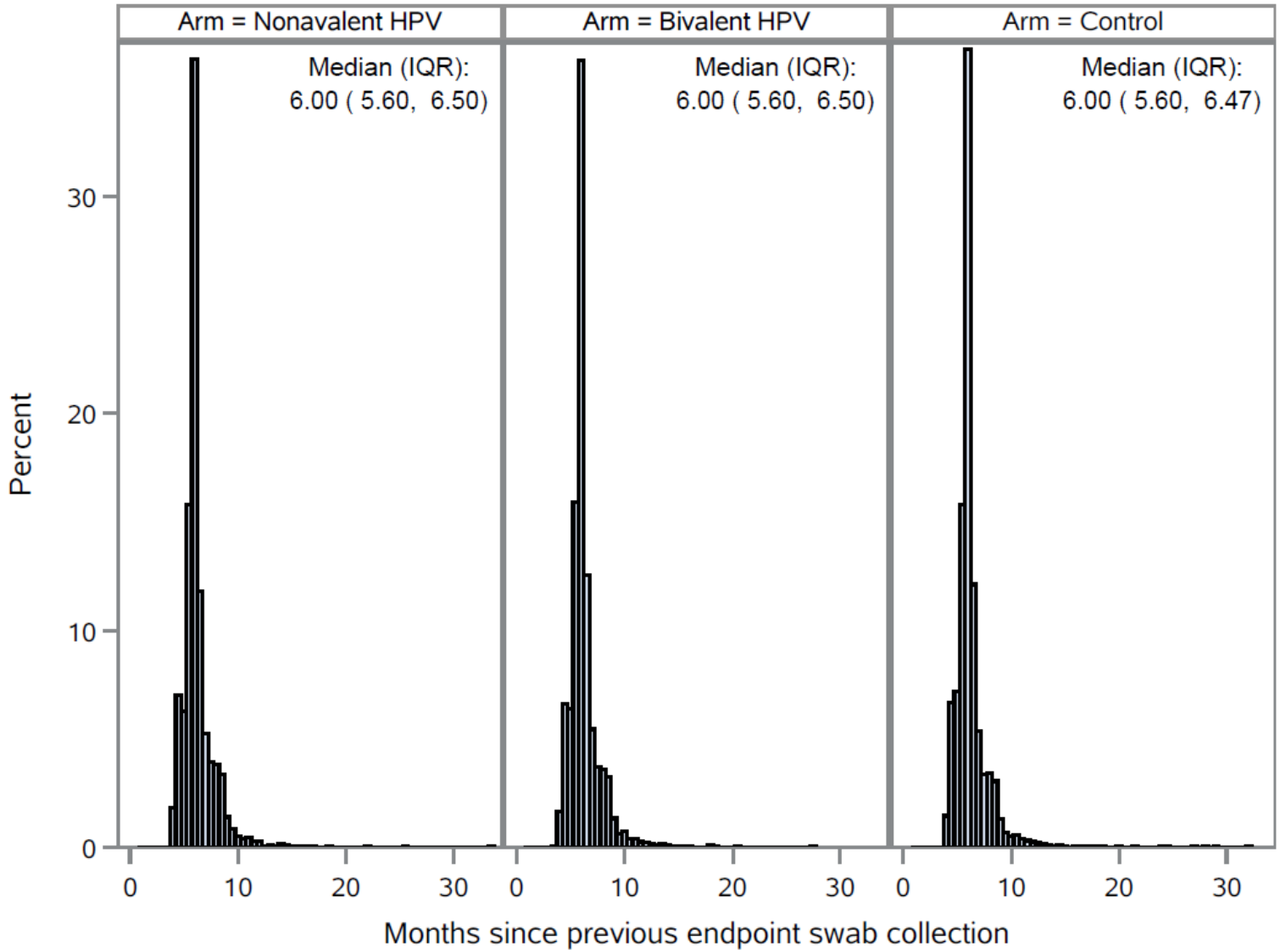
Retention 91% for 5 or more pre-crossover swabs

151 (6.6%) exited

2,124 (**95%**) Received crossover vaccine
No diff by study grp

Retention 90% for 3 post-crossover swabs

Median follow-up **53 months**



The incidence of persistent non-vaccine HPV types was stable across the time periods and between the study groups, indicating continued HPV exposure.

(26/35/39/40/42/43/44/51/53/54/56/59/61/66/68/69/70/73/82 in HPV 16/18 mITT cohort)

Incidence of persistent non-vaccine type HPV per 100 woman-years (95% CI)	Study Group		
	Delayed HPV vaccination	Immediate HPV vaccination	Overall
Primary Endpoint Period	19.5 (15.4-24.3)	20.7 (17.6-24.2)	20.3 (17.8-23.0)
All Single-dose HPV Vaccinated Period	22.0 (12.0-36.9)	22.5 (14.7-33.0)	22.3 (15.9-30.3)

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 26/35/39/40/42/43/44/51/53/54/56/59/61/66/68/69/70/73/82)

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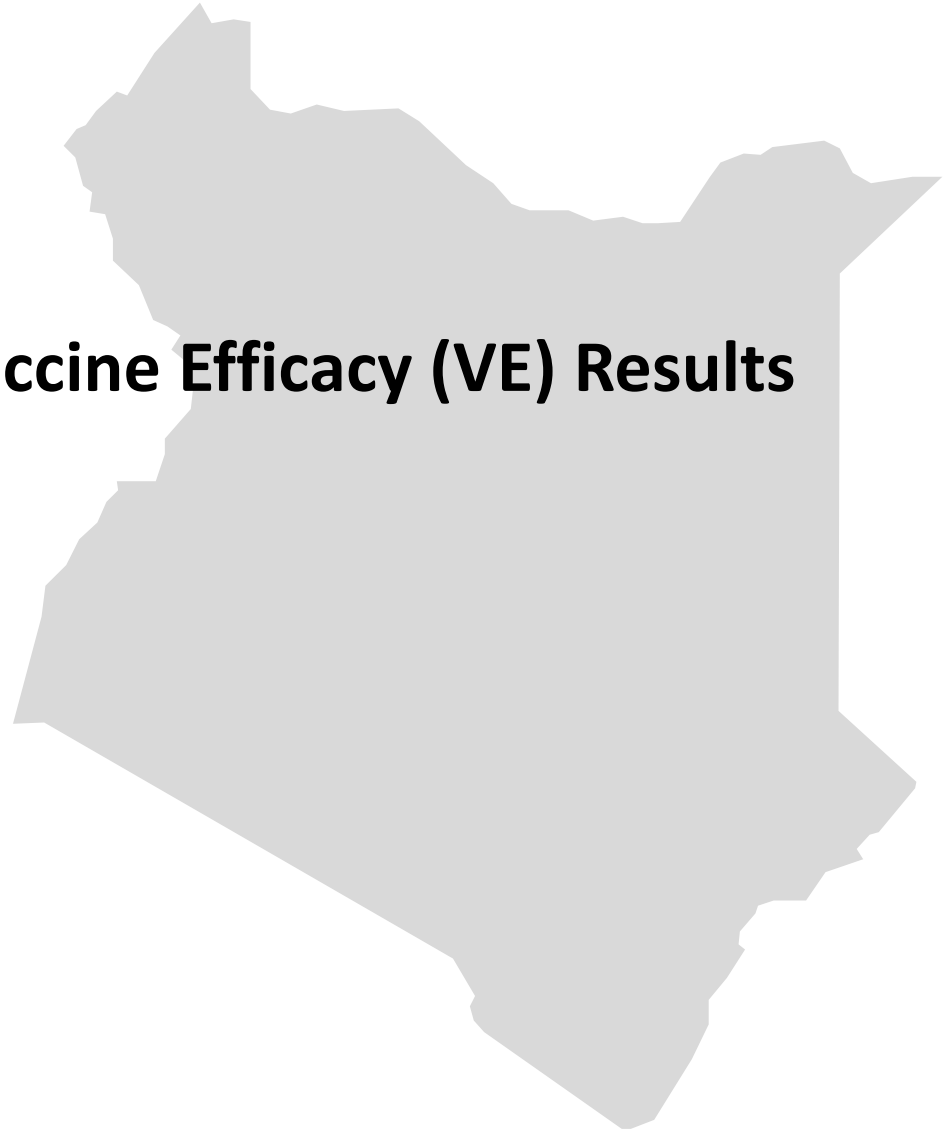
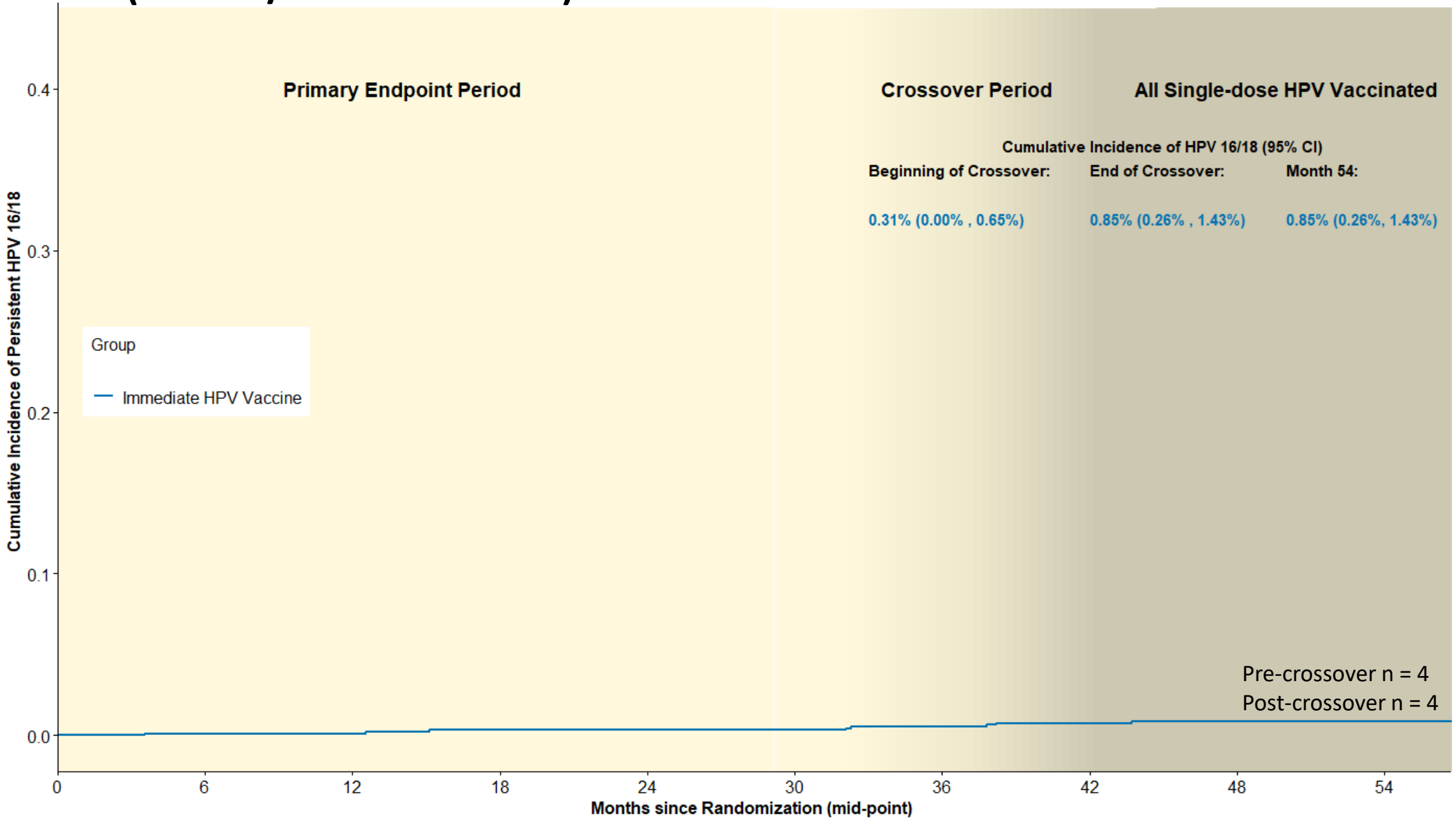
Durability and Vaccine Efficacy (VE) Results



Cumulative Incidence of Persistent HPV 16/18 by Original Vaccine Group and Study Period (HPV 16/18 mITT Cohort)



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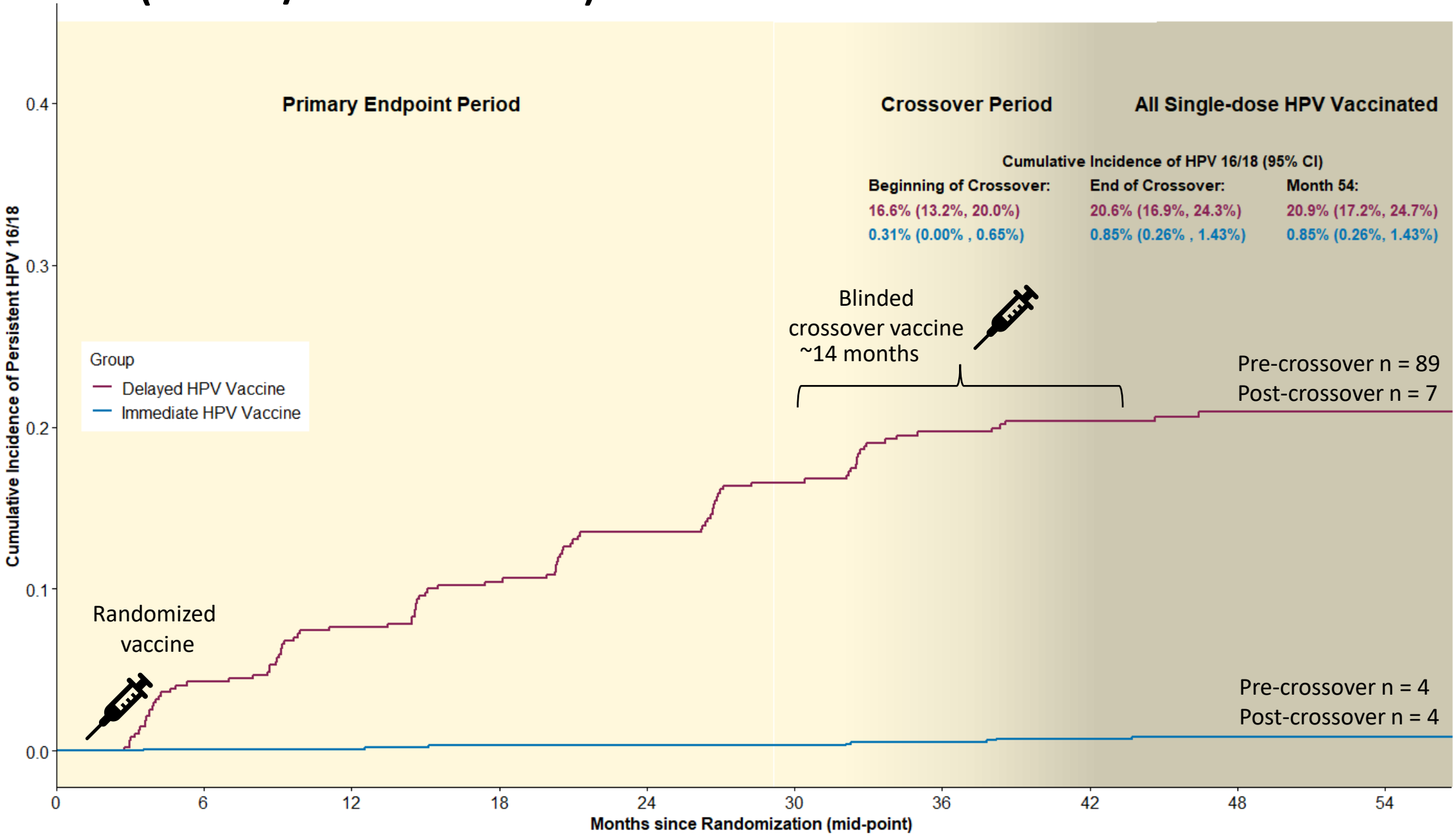

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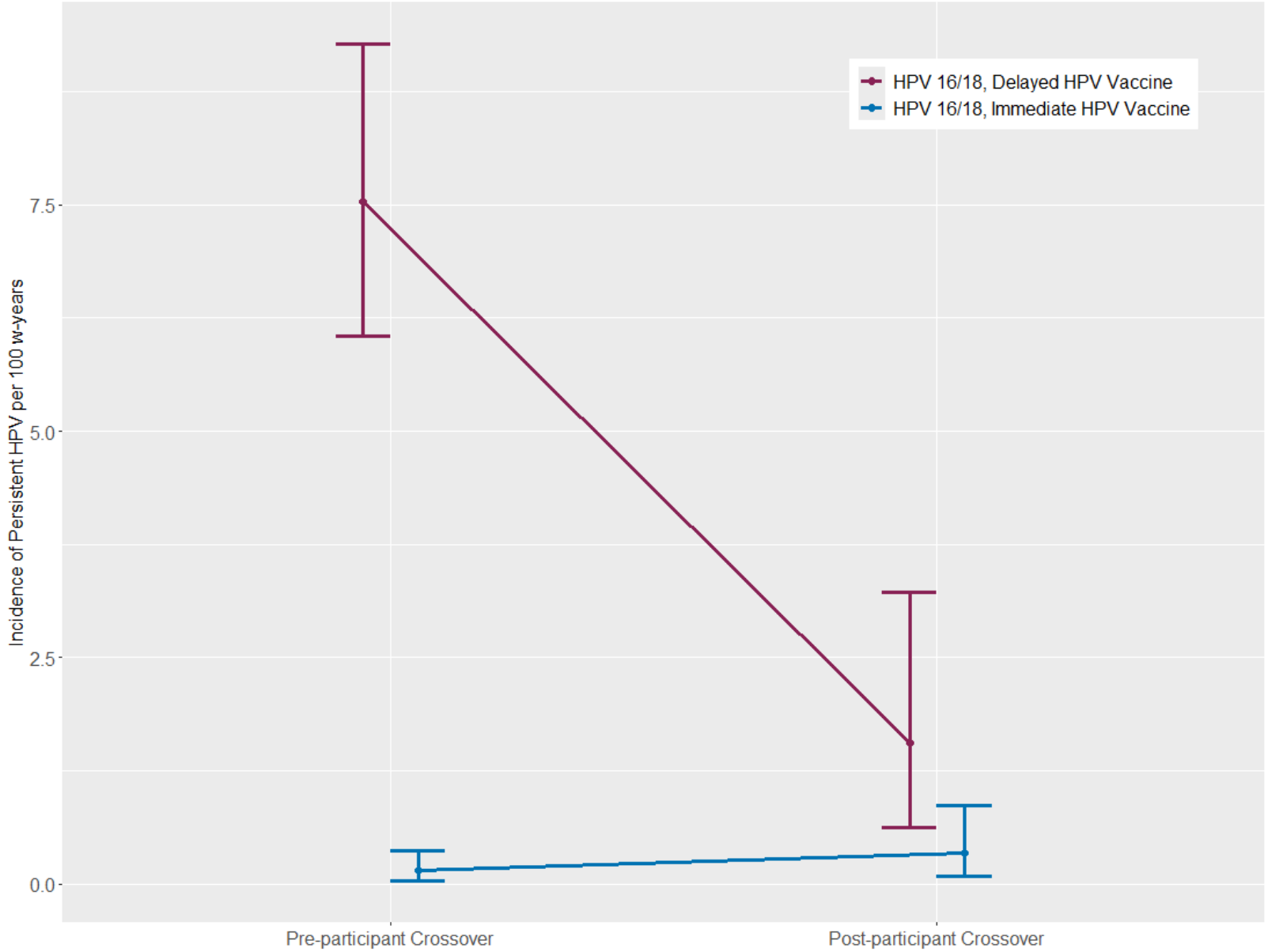
Participants vaccinated at age 18-23 years, had similar low rates of incident persistent HPV 16/18 infection compared to vaccination at age 15-20 years.



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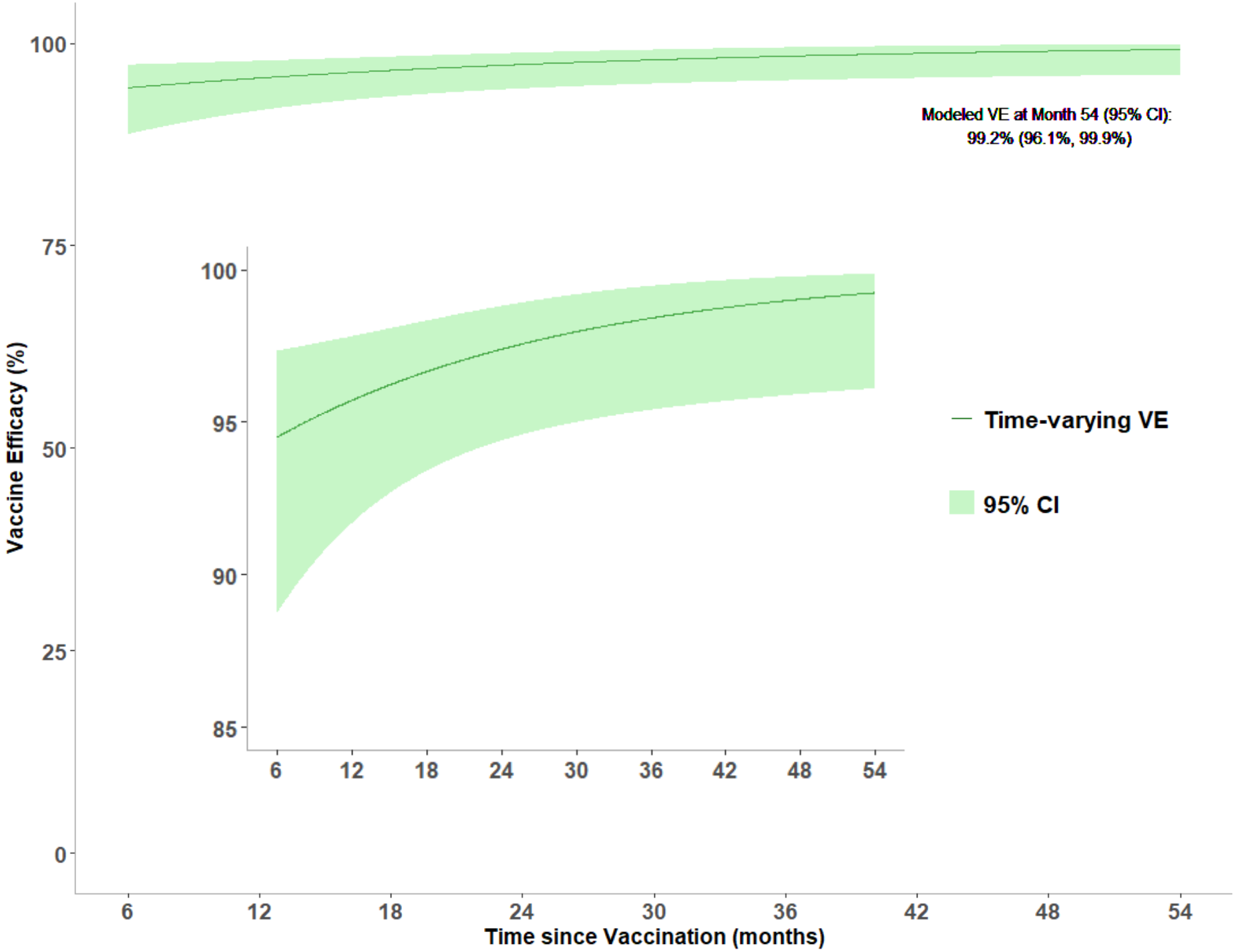

HPV 16/18 vaccine efficacy, VE=99.2% (95% CI 96.1-99.9%) is sustained over time without evidence for waning immunity.

VE to prevent HPV 16/18 as a function of time since HPV Vaccination (HPV 16/18 mITT Cohort)

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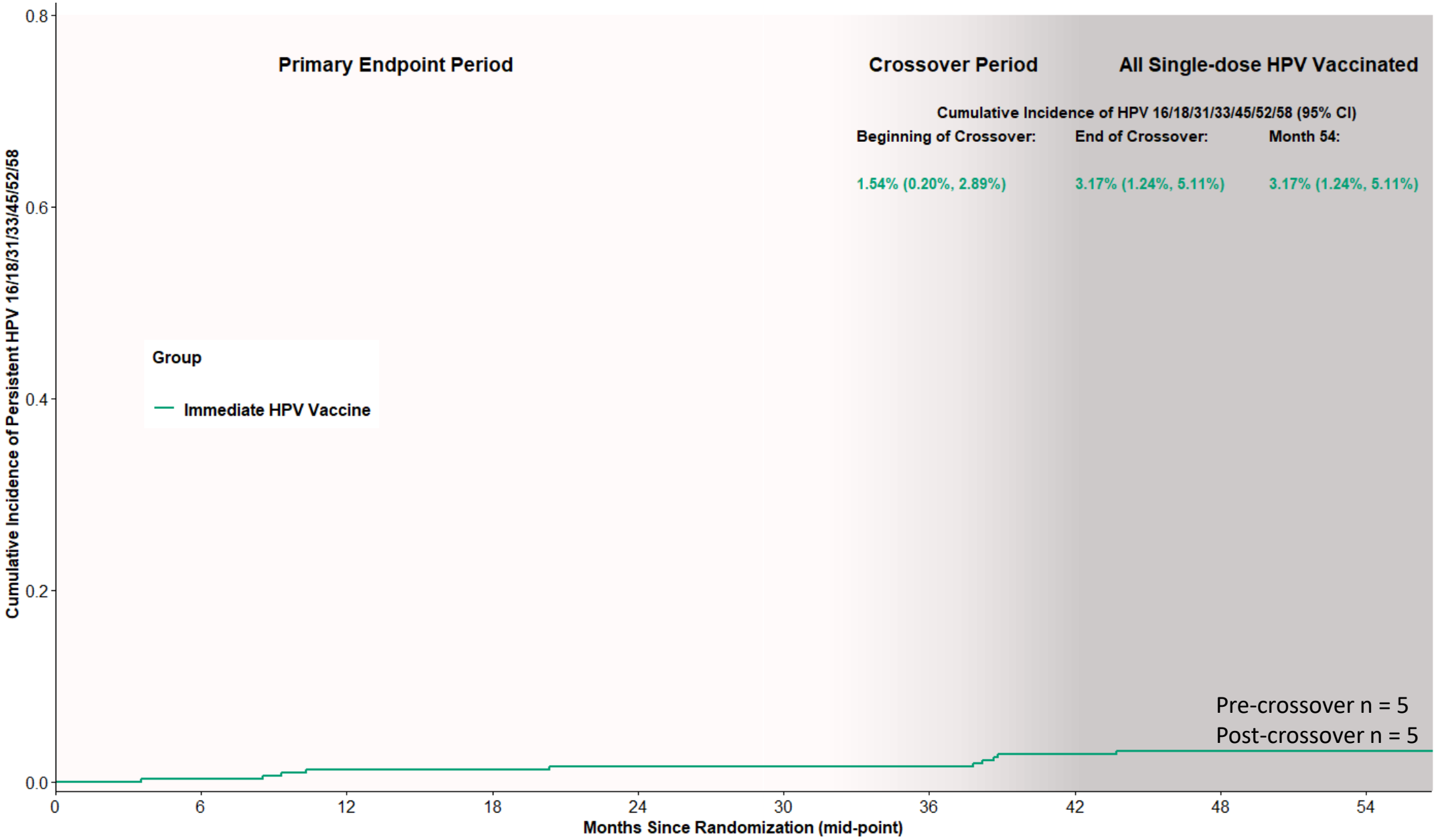
Cumulative Incidence of Persistent HPV 16/18/31/33/45/52/58 by Original Vaccine Group and Study Period (HPV 16/18/31/33/45/52/58 mITT Cohort)



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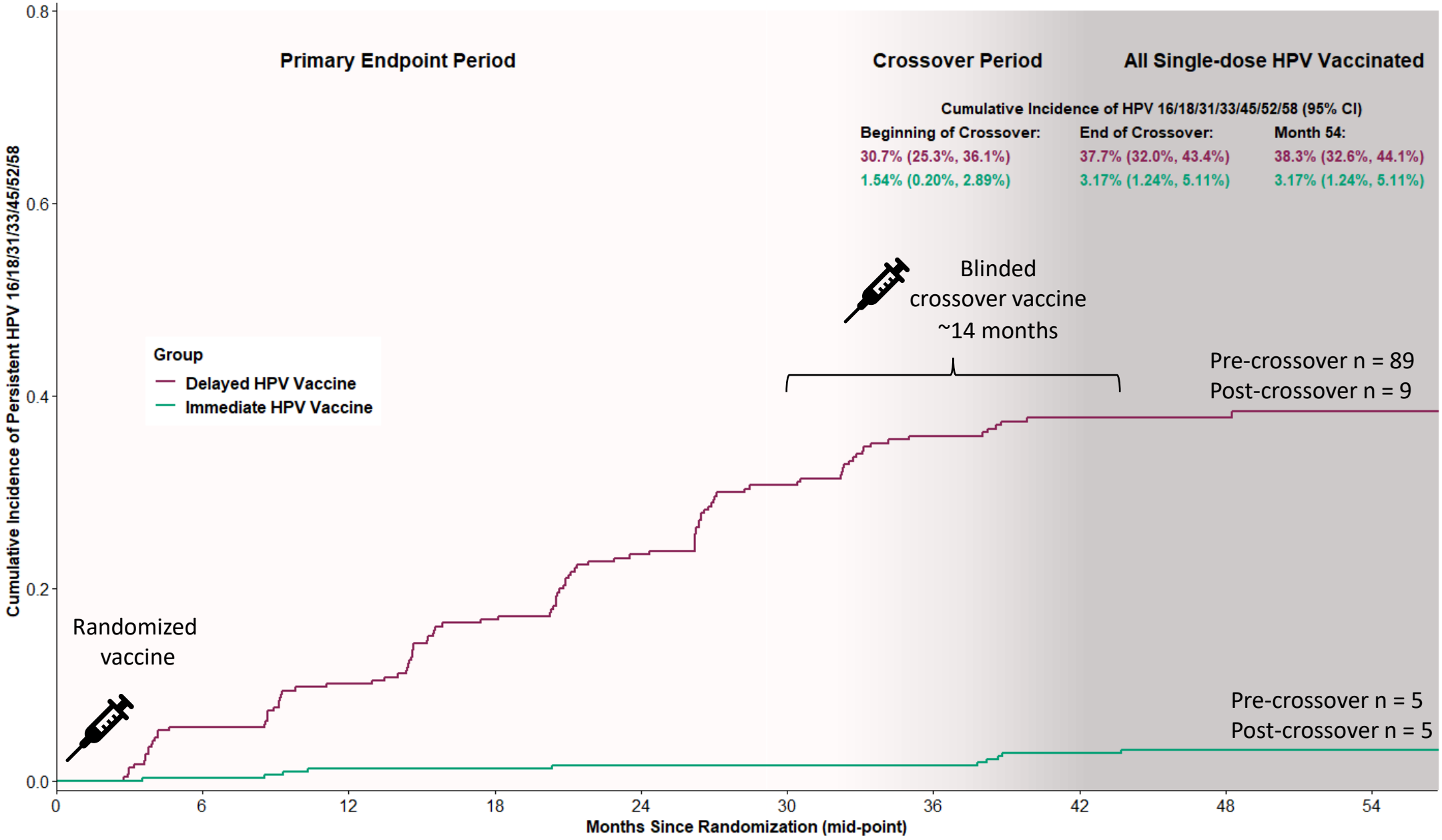
Cumulative Incidence of Persistent HPV 16/18/31/33/45/52/58 by Original Vaccine Group and Study Period (HPV 16/18/31/33/45/52/58 mITT Cohort)



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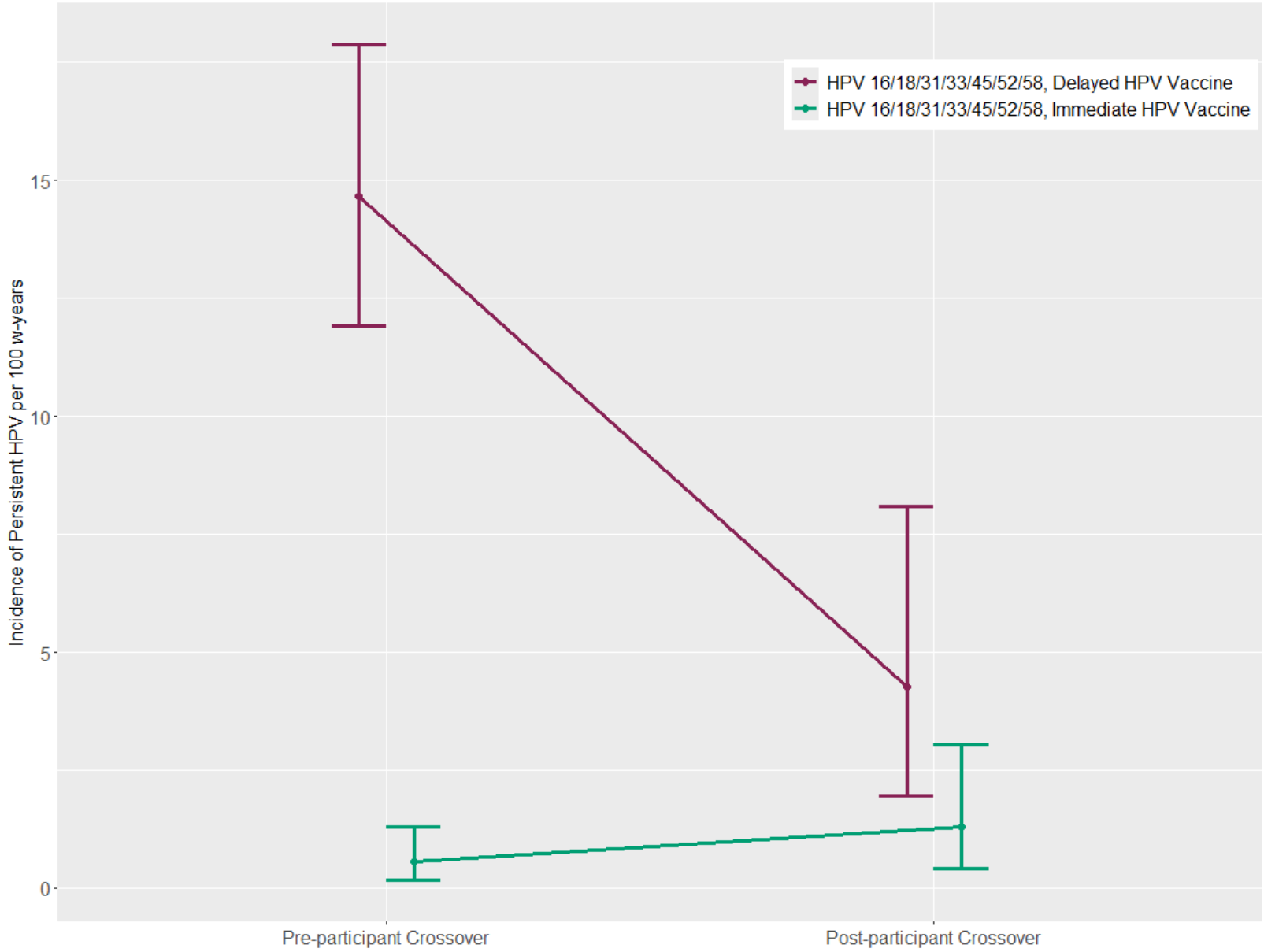
Participants vaccinated at age 18-23 years, had similar rates of incident persistent HPV 16/18/31/33/45/52/58 infection compared to vaccination at age 15-20 years.



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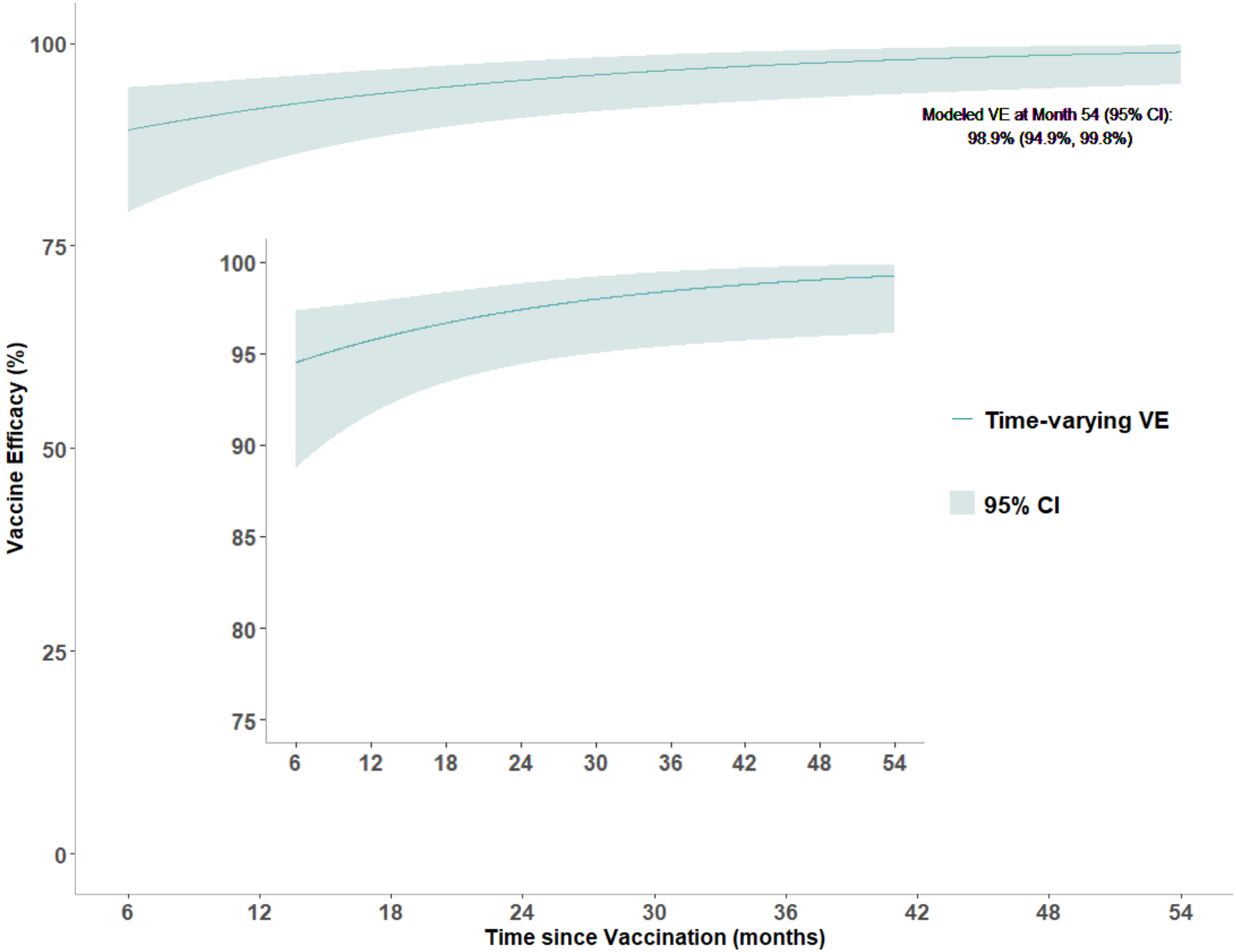

HPV 16/18/31/33/45/52/58 vaccine efficacy, VE=98.9% (95% CI 94.9-99.8%) is sustained over time without evidence for waning immunity.

Vaccine Efficacy to prevent HPV 16/18/31/33/45/52/58 as a function of time since HPV vaccination (HPV 16/18/31/33/45/52/58 mITT cohort)

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Discussion

- Adolescent girls and young women were effectively protected from HPV infection over the first 54 months post-vaccination
- Rigorous design, high fidelity to the protocol, high retention, clear ascertainment of outcomes → strong evidence for single-dose HPV vaccine efficacy for age up to 23 years
- Single-dose VE 16/18 and 16/18/31/33/45/52/58 – lower bound of the CI is >94% - in keeping with licensure trials for three doses without evidence of waning
- Adds to the growing body of evidence supporting the efficacy of single-dose HPV vaccine efficacy
- Next step: Extension to evaluate clinical endpoints

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Patient perspectives

Shared Clinical Decision Making

Increase Access to Prevention

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KEN SHE Study collaborators

Fred Hutchinson Cancer Center
University of Washington

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Grace Umutesi

Dr. Denise Galloway

Dr. Rachel Winer

Kenya Medical Research Institute (KEMRI)

Dr. Nelly Mugo

Dr. Betty Njoroge

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Massachusetts General Hospital

Kate Heller

Meighan Krows

Christine Hathaway

Odun Talabi

Jesse Heitner

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Thank you

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Thank you

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