

LONG-TERM EFFECTIVENESS OF VOLUNTARY MEDICAL MALE CIRCUMCISION FOR HIV PREVENTION

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BACKGROUND

- The efficacy of voluntary male medical circumcision (VMMC) for HIV prevention in men was demonstrated in three randomized trials. This led to the adoption of VMMC as an integral component of the United States President's Emergency Plan for AIDS Relief (PEPFAR) combination HIV prevention program in sub-Saharan Africa. However, evidence on the individual-level effectiveness of VMMC programs in real world, programmatic settings is limited.
- Our **primary objective** was to assess the impact of a PEPFAR-supported VMMC program on the risk of male HIV acquisition over time.
- We hypothesized that VMMC delivered through PEPFAR-supported programs would provide long-term protective effects against male HIV acquisition

METHODS

- Our study included initially HIV-negative, uncircumcised, non-Muslim men in the Rakai Community Cohort Study (RCCS), a longitudinal population-based study of HIV incidence in south-central Uganda.
- This study included 30 agrarian and semi-urban trading communities continuously surveyed during five survey rounds between 2008 and 2016 (denoted as RCCS study visits 13-17).during which period PEPFAR VMMC programs were implemented and scaled-up.
- The analysis was restricted to non-Muslim men who were uncircumcised at entry into this study period (Figure 1).
- VMMC using the dorsal slit procedure was performed under local anesthesia by trained clinical officers in mobile camps and in five health facilities.
- VMMC status** among male RCCS participants was assessed using self-report. Incident VMMCs were defined as those occurring among men who reported being uncircumcised at the prior study visit.
- Information on the exact date of surgery for newly circumcised RCCS participants was unavailable from the RCCS interview. In our primary analysis examining effectiveness of VMMC for HIV prevention, VMMC was assumed to have occurred at the start of the person-interval.
- Our **primary study outcome** was an incident HIV infection defined as cases in which a man was determined to be HIV-seropositive for the first time after an HIV-seronegative result at the prior visit, allowing for up to one missed study visit between consecutive tests
- Multivariable Poisson regression with generalized estimating equations was used to estimate the incidence rate ratio (IRR) of HIV acquisition in newly circumcised versus uncircumcised men, adjusting for sociodemographic characteristics and sexual behaviors.

- Risk of HIV acquisition was 53% lower among men who were circumcised through a PEPFAR-supported VMMC program in southern Uganda compared to men who remained uncircumcised.**
- The effectiveness of VMMC for HIV prevention was sustained with increasing time from surgery and was similar across age groups and calendar time.**

RESULTS

- There were 3,916 who were followed for 17,088 person-years (pys) over 9,469 person-intervals.
- Of these participants, **34% (n=1338) were circumcised** during follow-up, with an **overall incidence of VMMC of 9.8/100 pys (95% CI: 9.3-10.4)**.
- Over the course of the analysis period, there were **138 incident HIV infections detected**.

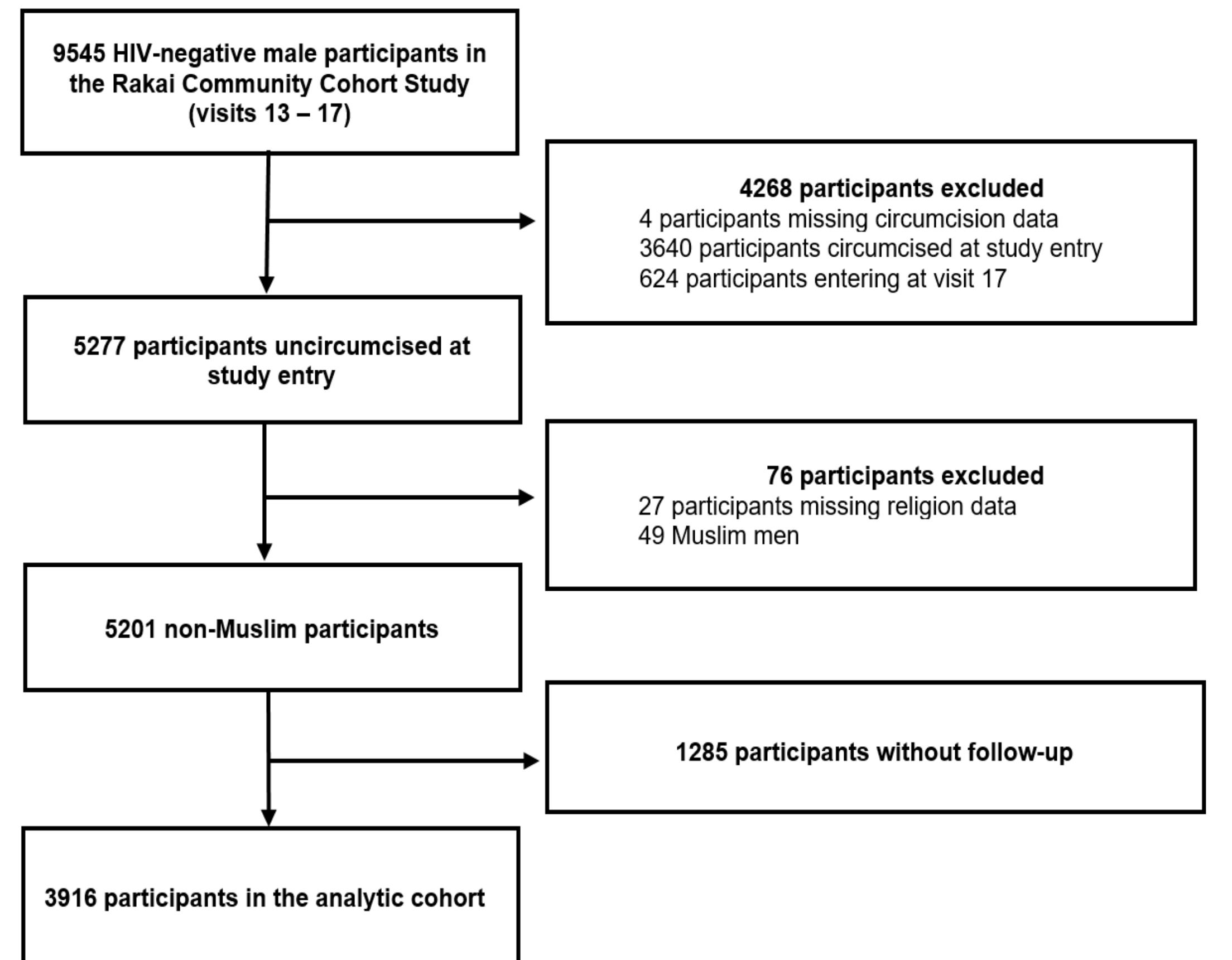


Figure 1. The analytic cohort

Table 1. Circumcision and HIV incidence

			Number of incident infections/pys	Incidence Rate per 100 person-years (95% CI)	Crude IRR (95% CI)	Adjusted IRR (95%CI)
			Uncircumcised	118/12095	0.98 (0.81-1.17)	REF
Age	15-24	Circumcised	20/4993	0.40 (0.26-0.62)	0.41 (0.25-0.66)	0.47 (0.28-0.78)
		Uncircumcised	25/3934	0.64 (0.43-0.94)	REF	REF
	25-34	Circumcised	5/1922	0.26 (0.11-0.63)	0.41 (0.16-1.07)	0.34 (0.09-1.33)
		Uncircumcised	60/3813	1.58 (1.22-2.03)	REF	REF
Study Visits	35+	Circumcised	11/1619	0.67 (0.37-1.23)	0.43 (0.23-0.82)	0.55 (0.29-1.06)
		Uncircumcised	33/4348	0.76 (0.54-1.07)	REF	REF
	13-14 (2008- 2011)	Circumcised	4/1452	0.27 (0.10-0.73)	0.36 (0.13-1.03)	0.47 (0.16-1.35)
		Uncircumcised	64/4821	1.33 (1.04-1.70)	REF	REF
	15-17 (2011- 2016)	Circumcised	8/936	0.86 (0.43-1.72)	0.64 (0.31-1.35)	0.53 (0.23-1.26)
		Uncircumcised	54/7274	0.74 (0.57-0.97)	REF	REF
		Circumcised	12/4057	0.30 (0.17-0.52)	0.40 (0.21-0.75)	0.44 (0.23-0.83)

IRR: Incidence rate ratio. CI: Confidence interval. REF: Reference group. Adjusted for study visit, age in years, marital status and educational attainment, sex with partners residing outside of the community in the prior year, sex with multiple partners in the past year, history of genital ulcer disease in the past year, and consistent condom use with casual partners.

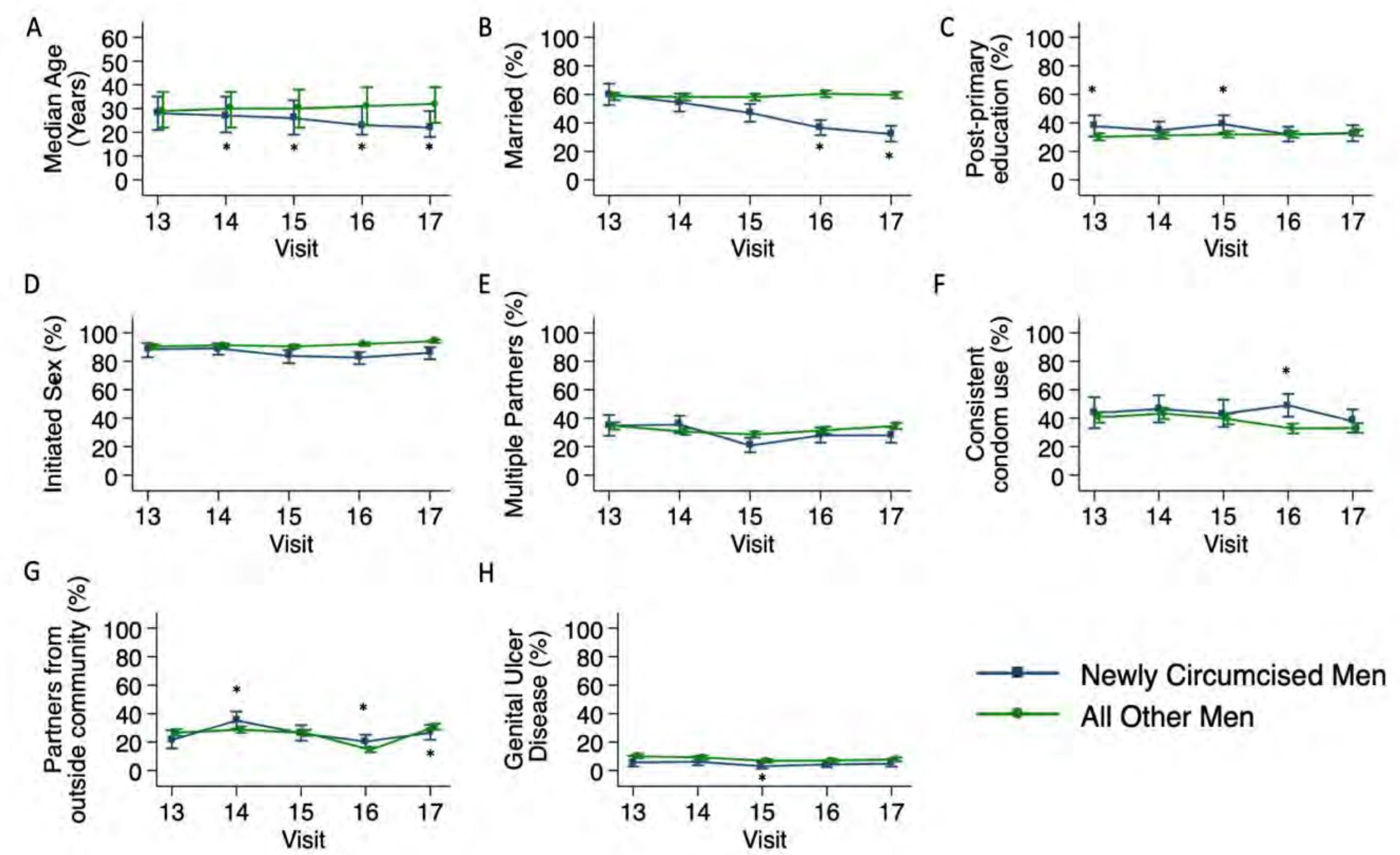


Figure 2. Demographic characteristics and sexual behaviors of newly circumcised men (since the prior study visit) compared to all other male participants. A) Error bars denote interquartile range of participants' age. B-H) Error bars denote 95% confidence interval for attribute prevalence. * Significant age-adjusted difference in prevalence between groups at the given study visit ($p<0.05$).

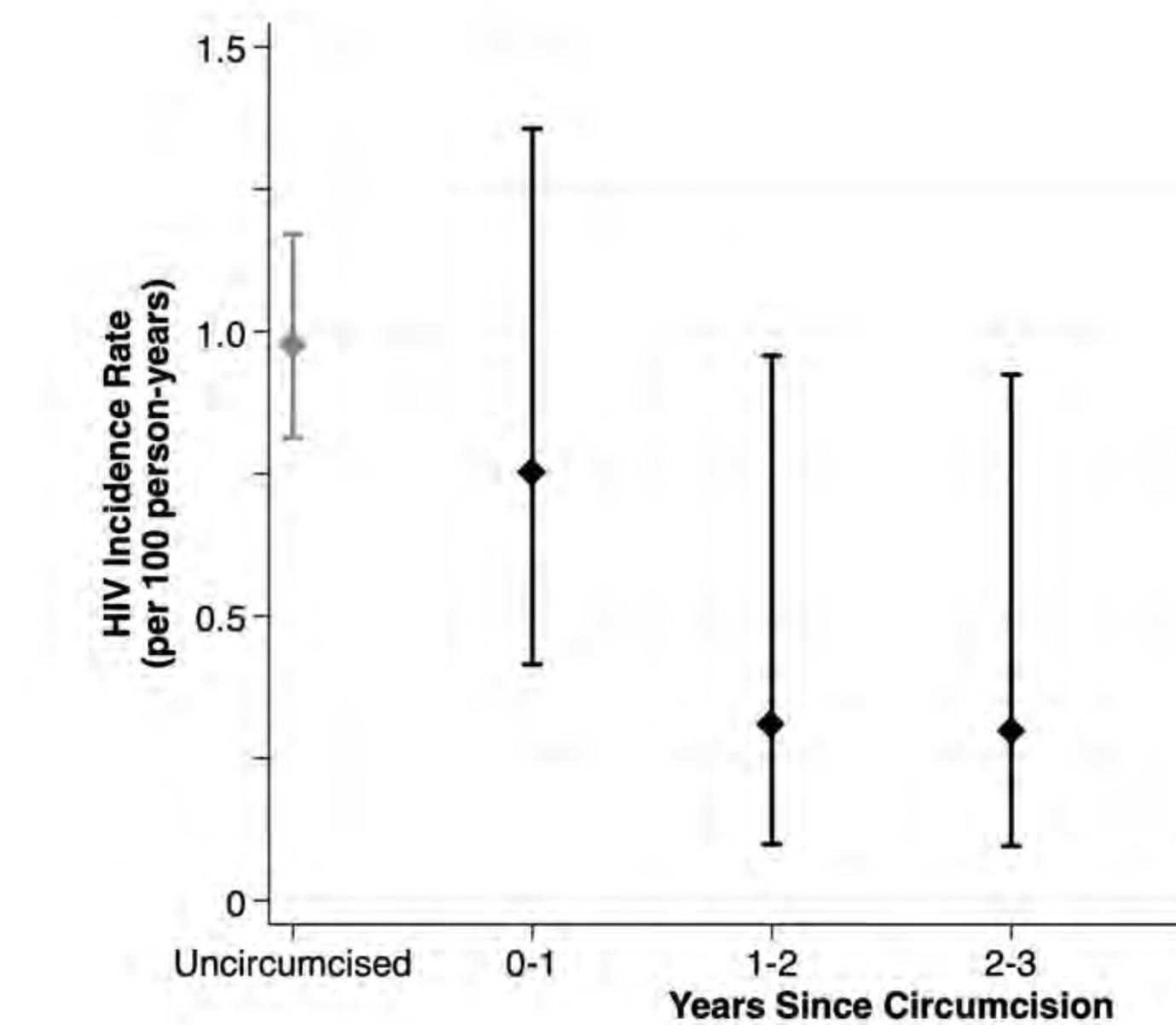


Figure 3. Long-term effectiveness of VMMC for HIV prevention; HIV incidence per 100 pys among non-Muslim uncircumcised and circumcised men by estimated time since surgery in years. Time since surgery was defined as the interval between the start of the person-period in which circumcision was reported to the midpoint of a given person-period.

- The age of men first reporting VMMC decreased consistently over time ($p\text{-trend} < 0.001$).
- HIV incidence was $0.40/100$ py ($20/4992.8$ py) among newly circumcised men and $0.98/100$ py ($118/12095.1$ py) among uncircumcised men with an adjusted HIV IRR of 0.47 (95% CI: $0.28-0.78$).
- HIV incidence declined substantially to $0.31/100$ py (95% CI: $0.09-0.95$) 1-2 years following VMMC and remained low with increasing years from surgery.

CONCLUSIONS

VMMC programs are highly effective in preventing male HIV-acquisition. The observed effectiveness is consistent with efficacy in clinical trials and supports current recommendations that VMMC is a key component of programs to reduce HIV incidence.

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