Examining PopART intervention impact on HIV in the general populations of Zambia and South Africa

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BACKGROUND

- HIV Prevention Trials Network (HPTN) 071 (PopART) cluster-randomized trial was conducted in 21 urban communities in Zambia and South Africa, 2013-2018, with 3 arms
  - A. combination prevention with universal HIV testing and antiretroviral therapy (ART) for all individuals with HIV
  - B. combination prevention with universal HIV testing and ART according to local guidelines
  - C. standard of care
- Interventions implemented in entire randomized communities; impact on HIV incidence measured on sampled "population cohort" members (i.e., HPTN071 sample)
- *Unexpectedly, no evidence of effect of arm A relative to C*
- But HPTN071 sample underrepresented men, older adults, alcohol users, and employed individuals compared to the general population (Table 1)

Table 1. Comparison of HPTN071 sample with population of interest represented by ZAMPHIA and SABSSMV

	HPTN071 Sample (n=29,130)	Population of Interest (n=5,076)
Sex and male circumcision (%)		
Female	68%	54%
Male, Uncircumcised	17%	24%
Male, Circumcised	15%	22%
Age category		
18-24	46%	36%
25-29	21%	20%
30-34	15%	19%
35-39	10%	14%
40-44	8%	11%
Educational attainment - Primary school or less	17%	15%
Alcohol use, past month		
Never	73%	59%
Monthly or less	16%	16%
More than once per month	11%	25%
Married	39%	38%
Currently employed	25%	38%
Number of sexual partners, past year		
0	30%	25%
1	64%	67%
2+	6%	8%
Ever had an HIV test	83%	80%

Weighting the HPTN071 sample to match demographics and HIV risk factors from the general population strengthened estimated intervention effects

METHODS

- Estimated effect of PopART interventions in adults 18-44 without HIV residing in urban areas of the five provinces where HPTN071 was conducted (*population of interest*)
- Population of interest is broader than trial communities
- Leveraged data from two probability-based surveys representing 4.5 million adults in population of interest
  - 2016 Zambia Population-based HIV Impact Assessment survey (ZAMPHIA)
  - 2017 South African National HIV Prevalence, Incidence, Behaviour and Communication Survey V (SABSSMV)
- Weighted the HPTN071 sample to match population of interest by demographics and HIV risk factors in Table 1

Table 2. Cumulative risk of HIV infection and risk differences, unweighted and weighted

	Cumulative Risk of HIV Infection (%)			Risk Difference (%)	
	Arm A	Arm B	Arm C (SOC)	Arm A vs SOC	Arm B vs SOC
Unweighted					
Yr 1	1.77	1.45	2.01	-0.24 (-1.21, 0.70)	-0.56 (-1.42, 0.31)
Yr 3	4.85	3.77	4.98	-0.14 (-2.22, 1.83)	-1.21 (-3.14, 0.64)
Yr 1 to Yr 3*	3.08	2.32	2.98	0.10 (-1.15, 1.25)	-0.66 (-1.88, 0.46)
Weighted					
Yr 1	1.33	1.14	1.82	-0.49 (-1.35, 0.33)	-0.68 (-1.53, 0.17)
Yr 3	3.83	2.80	4.66	-0.83 (-2.94, 0.99)	-1.86 (-3.80, -0.09)
Yr 1 to Yr 3*	2.50	1.66	2.84	-0.34 (-2.04, 0.96)	-1.18 (-2.85, 0.15)

*Change in cumulative risk from year 1 to year 3, i.e., Yr 3 – Yr 1

Note: SOC=standard of care. 95% confidence intervals for the risk difference are displayed in parentheses.

RESULTS

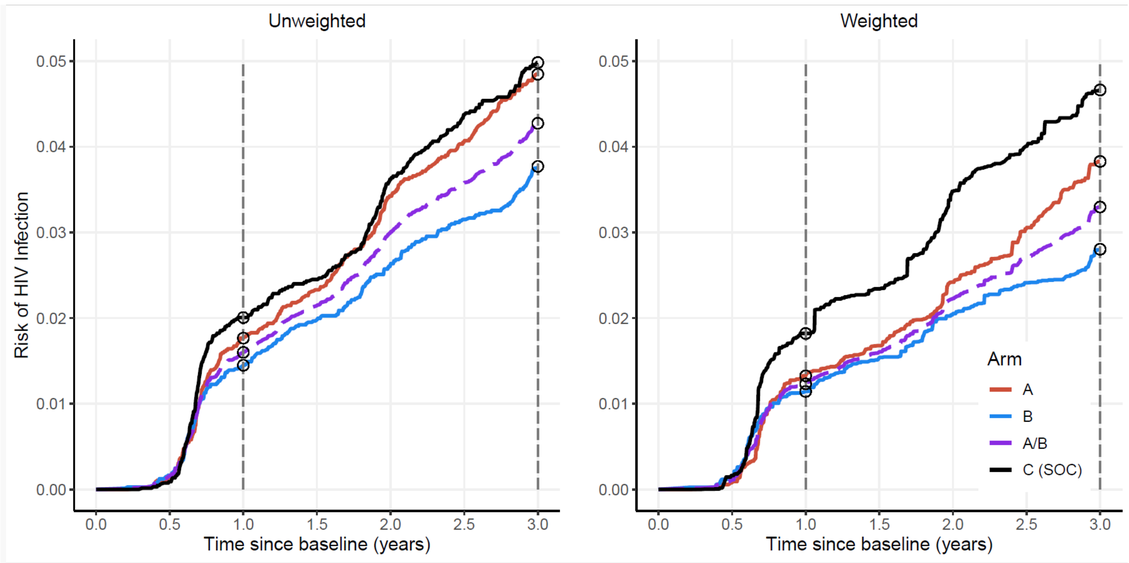


Figure. Cumulative risk of HIV over the study period, unweighted and weighted. These plots demonstrate that risk of HIV over the study period was estimated to be lower in all three arms in the population of interest (weighted) compared to the trial population (unweighted). Risk was similar in Arms A and C in the unweighted HPTN071 sample. Weighting reduced risk substantially in Arms A and B relative to C, resulting in strengthened effect estimates (Table 2).

CONCLUSIONS

- PopART interventions *more protective* in the population of interest than in the trial
- Difference likely due to HPTN071 *underrepresenting* individuals for whom intervention was most effective
- Randomized trials without missing data ensure internal validity by design (i.e., valid comparisons of interventions among trial participants)
- *External validity* a concern when trial sample differs from target population
- Highlights importance of accounting for selection bias, i.e., differences between trial participants and the population of interest
- Provides a partial explanation for the null A vs C comparison in HPTN071

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