

HPTN 071 (PopART)



Key Findings After the Third Year of the Intervention

HPTN 071 (PopART) is a community-based, randomized study evaluating the impact of a combination HIV prevention package on HIV incidence. This study is the largest community-randomized trial testing the universal HIV test and treat strategy and is being conducted across 21 high HIV burden, resource-limited urban settings in the Western Cape of South Africa and Zambia, with a total estimated population of 1 million.

Study communities were randomly assigned to one of three study arms (A, B and C). In the original study design, Arm A received a household intervention package with an offer of HIV treatment irrespective of CD4 count, Arm B received the household intervention package, but with HIV treatment offered per national guidelines, and in Arm C there was no household intervention and treatment followed national guidelines. The household intervention comprises annual rounds of home-based HIV counseling and testing delivered by Community HIV Care Providers (CHiPs) who also support linkage to care, antiretroviral therapy (ART) retention and other HIV-related services.



In late 2015, in response to mounting evidence of clinical benefit, the World Health Organization (WHO) revised its guidelines to recommend ART for all people living with HIV. The PopART study team responded by successfully incorporating this recommendation into the study design, making ART available for all people living with HIV (PLWH) in all study arms. As a result, Arms A and B now offer study participants the same intervention: the household intervention package plus HIV treatment irrespective of CD4 count.

HIV incidence, the study's primary outcome, will be assessed through a research cohort (the Population Cohort) of randomly-selected adults from all study communities, approximately 48,000 individuals, to be followed for three years. Findings from this study will also help inform the scale-up of future HIV programs and identify cost-effective interventions. The delivery of the intervention has now been completed. The follow-up of participants in the Population Cohort is on-going with a view to completion by the middle of 2018.

Finding Hard to Reach Populations – The PopART for youth study (P-ART-Y)

Nested within the HPTN 071 study, the PopART for youth study (P-ART-Y) aims to evaluate the acceptability and uptake of the PopART intervention among adolescents and young people.

To determine the uptake of home-based HIV testing and counseling (HTC) in four PopART intervention communities of the HPTN 071 (PopART) trial in Zambia, data on 15-19 year olds were analyzed from October 2015 to September 2016. Among 15 456 enumerated adolescents, 11 175 (72.3%) accepted the intervention. HTC uptake was 80.6% and was similar by sex. Adolescents that knew their HIV-positive status increased almost three-fold, from 75 to 210. Following visits from community HIV care providers, knowledge of HIV status increased from 27.6% to 88.5%. HTC uptake was associated with community, age, duration since previous HIV test, other household members accepting HTC, having an HIV-positive household member, circumcision, and being symptomatic for STIs.

HIV prevalence is known to be low among the 10-14y age group. As part of the P-ART-Y study, a screening tool was used to identify those in the 10-14y age range at high risk of being HIV-infected. The screening tool used was developed and validated elsewhere. Four questions probed for: 1) history of hospital admission, 2) recurring skin problems, 3) poor health in last three months, and 4) death of one or both natural parents. A “yes” response to ≥ 1 question identified an adolescent as “at-risk” for HIV, and these adolescents were prioritized for HB-HTC. The findings from Zambia for the period October 2015-August 2016 indicate that a total of 18,040 adolescents aged 10-14 years participated and had their health data recorded. The screening tool identified 12.1% of these adolescents as “at-risk”. HIV prevalence among those tested in the at-risk group was 2.4% compared to 0.6% in those not identified

by the screening tool, representing a 4.3-fold higher estimated odds of infection. The screening tool identified adolescents in the general population who are at relatively high risk of being HIV-infected; this can be exploited to allow targeted offer of HCT to 10-14 year-olds in resource-limited settings.

Overall, the proportion of adolescents who knew their HIV status increased substantially as a result of the PopART intervention (Figure 1). Delivering a community-level door-to-door combination prevention package is acceptable to many adolescents and can be effective if done in combination with targeted testing.

(1. Shanaube, K. et al. AIDS. 2017 Jul 1; 31(Suppl 3): S221–S232 // 2. MJ. Chaila Poster #TUPED1341, 25 July, 2017)

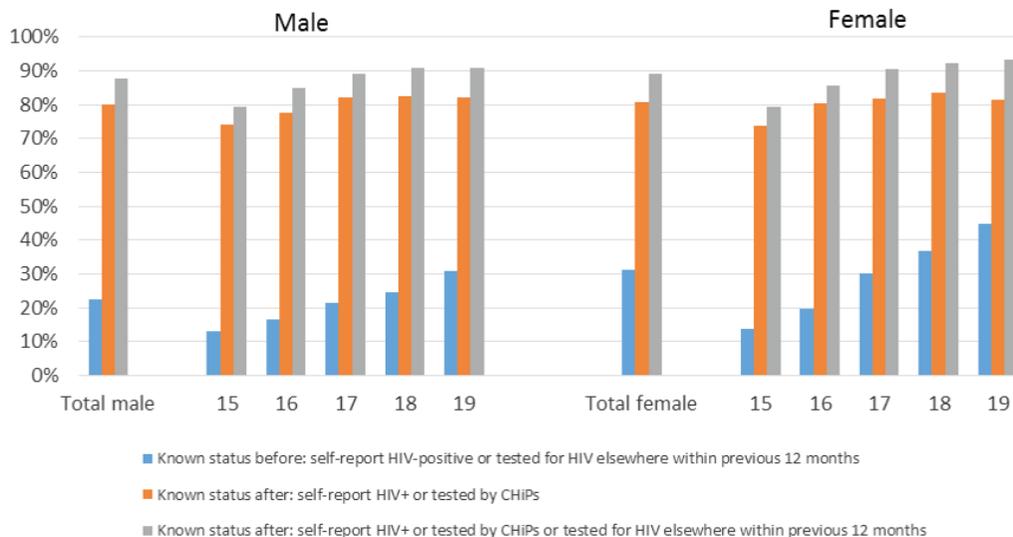


FIGURE 1: Knowledge of HIV-status before and after the intervention by age and sex

Increasing knowledge of HIV status among men: a cluster-randomized trial of community-based distribution of oral HIV self-test kits nested in four HPTN 071 communities in Zambia

Knowledge of status among HIV+ men, young adults and mobile individuals in HPTN 071 lags behind other groups. We nested a cluster-randomized trial within the main HPTN 071 study to evaluate the effect of Community HIV-care Providers (CHiPs) offering clients both oral HIV self-testing (HIVST) and rapid finger-prick HIV testing, compared to offering finger-prick testing only (non-HIVST).

TABLE 1: Knowledge of HIV status

	Standard of Care % (n/N)	HIV-ST % (n/N)	Adjusted OR (95% CI)	P-value
Overall	65.3 (8,952/13,706)	68.0 (9,027/13,267)	1.30 (1.03, 1.65)	0.03
Males	55.1 (3,571/6,486)	60.4 (3,843/6,368)	1.31 (1.07, 1.60)	0.009
Females	74.5 (5,381/7,220)	75.1 (5,184/6,899)	1.05 (0.86, 1.30)	0.62
Young adults (16-29)	70.2 (4,917/7,002)	73.5 (4,972/6,769)	1.31 (1.05, 1.63)	0.02
Older adults (30+)	60.2 (4,035/6,704)	62.4 (4,055/6,498)	1.22 (0.98, 1.52)	0.07
Resident in R1 and R2, and not previously tested in R1 or R2*	20.6 (117/567)	29.7 (173/583)	1.76 (1.25, 2.48)	0.001

*R1 & R2: First & second annual rounds of door-to-door home-based HIV testing provided by CHiPs (Community HIV Care Providers)

1.03-1.65; p=0.03) (Table 1). This effect was largely due to the effect among men, as a high proportion of women (approximately 75% in both HIVST and non-HIVST arms) were aware of their HIV status. Among men, however, knowledge of HIV status differed significantly between arms, with 60.4% knowing their status in the HIVST arm compared to 55.1% in the non-HIVST arm (adjusted OR 1.31, 95% CI 1.07-1.60, p=0.009). Almost 30% percent of residents who had previously not been tested during previous rounds of home-based testing accepted HIV-ST compared to under 21% who accepted fingerprick testing in the standard of care arm (adjusted OR 1.76, 95% CI 1.25-2.48, p=0.001). In qualitative studies, individuals indicated preference for HIVST over finger-prick testing due to privacy, sense of ownership and not having to interact with the health facility or health providers, among other reasons.

Introducing HIVST for three months in communities already exposed to door-to-door HIV testing services for three years increased the proportion of the population who knew their HIV status. This effect was most marked in men. (H. Ayles, Oral presentation, TUAC0406LB, 25 July, 2017)

In four Zambian communities participating in HPTN 071, 33 randomly-selected CHiPs teams provided the option of HIVST or fingerprick testing (HIVST arm) when offering HCT to clients in their work zone. They also offered to leave HIVST kits for partners absent from the household at the time of the visit. An equal number of CHiPs teams offered finger-prick testing only in their work zones (non-HIVST arm).

Over three months in early 2017, 68.0% (9,027/13,267) of adults enumerated in the HIVST arm knew their HIV status compared to 65.3% (8,952/13,706) in the non-HIVST arm (adjusted OR 1.30, 95% CI

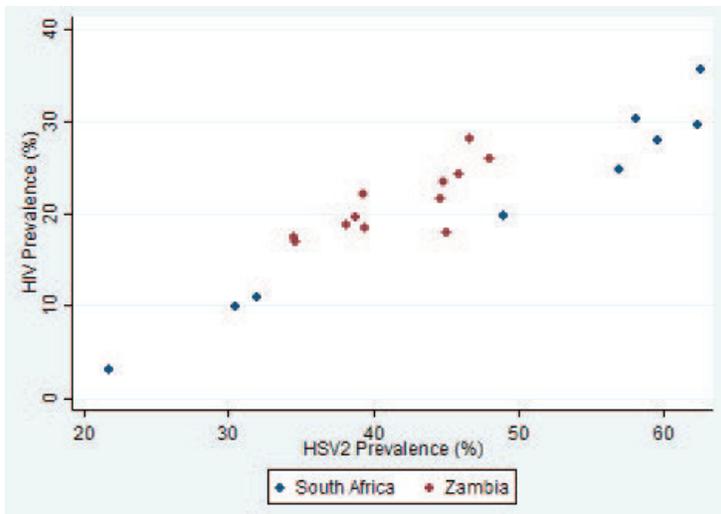
Sexually transmitted bedfellows: Exquisite association between HIV and HSV2 in 21 communities in Southern Africa

Serological tests were performed for HIV and HSV2 infection at baseline among all participants in the “Population Cohort”, comprising approximately 2,000 adults aged 18-44 selected randomly from each community to measure HIV incidence, the primary outcome of the HPTN 071 (PopART) study. Logistic regression was used to examine the association between HIV and HSV2 prevalence after adjustment for confounders. At community-level, HIV prevalence was plotted against HSV2 prevalence.

A total of 38,691 adults were enrolled in the cohort at baseline. Overall HSV2 prevalence in men and women was 22% and 50% in Zambia, and 27% and 60% in South Africa, respectively. A six-fold higher odds of HIV infection was seen in HSV2-infected individuals in both sexes, even after adjustment for other risk factors including lifetime number of sex partners (Table 2).

	HIV+ve/Total		OR (95% CI) [adj for age, community]	OR (95% CI) [adj for age, cty, partners, other]
	HSV2-ve	HSV2+ve		
MALES	372/7,657 (4.9%)	834/2,401 (34.7%)	6.84 (5.93, 7.90)	6.61 (5.91, 7.40)
FEMALES	790/11,380 (6.9%)	5652/13,305(42.5%)	7.70 (7.08, 8.37)	6.66 (5.41, 8.18)

TABLE 2: Association between HIV and HSV2 in 21 communities



At community-level there was a strong linear relationship between HIV prevalence and HSV2 prevalence as shown in Figure 2. This relationship remained strong after adjusting for median number of lifetime sexual partners ($p < 0.001$).

These data show the very strong association between these two infections, seen at both individual and community levels, likely due at least partly to a powerful biological cofactor effect of HSV2 on HIV acquisition. Renewed attention is needed to the development and evaluation of effective HSV2 control measures as tools for HIV prevention and to reduce the significant burden of disease associated with herpes infection itself.

(R. Hayes Poster #TUPEC0756, 25 July, 2017)

FIGURE 2: Community level association between HSV2 prevalence and HIV prevalence

Feasibility, uptake and yield of household based tuberculosis active case finding within the combination prevention package in the HPTN 071 (PopART) intervention in high TB/HIV burden communities in South Africa

We evaluated the feasibility, uptake and yield of household-based TB active case finding within a combination HIV prevention intervention.

Adults (≥ 18 years) who consented to participate and who were not already on TB treatment were eligible for TB screening. Community health worker (CHiPs) teams administered a TB screen that included four questions regarding weight loss, cough ≥ 2 weeks, night sweats and exposure to persons with TB in the household or at work. Two sputum specimens were collected from presumptive TB cases (≥ 1 symptoms or in contact with TB) for laboratory testing with Xpert MTB/RIF®, smear microscopy, or culture according to the testing algorithm.

Ninety-eight percent of eligible adults (101,630/103,455) received TB screening (43% males, median age 31 years). Of these, 2,709/101,630 (3%) were identified as presumptive TB cases and 2,263/2,709 (84%) were followed up, i.e. had 2 sputum samples collected and the results given to the individual. Of those followed up, 167/2,263 (7%) were pulmonary TB (PTB) cases and 143/167 (86%) initiated TB treatment.



A CHiP provides physiotherapy assistance outside the client's home to help the client produce sputum.

Adults aged ≥ 55 were more likely to be presumptive TB cases compared to younger age groups. Females were less likely to be presumptive TB cases. Among presumptive cases, females were less likely to be diagnosed with PTB. Active case finding for TB in a community HIV prevention intervention is feasible and can allow a single cadre of community-based health workers to address two of the most serious infectious diseases affecting communities with high burden of both conditions. (B. Yang Poster # WEPEC1030, 26 July, 2017)

Health-Related Quality-of-Life of people living with HIV in Zambia and South Africa: A comparison with HIV negative people in the baseline survey of the HPTN 071 (PopART) Trial

Life expectancy of HIV-positive individuals receiving antiretroviral therapy (ART) is approaching that of HIV-negative persons. However, little is known about the health-related quality-of-life (HRQoL) of HIV-positive individuals in resource-constrained settings.

Cross-sectional analysis of HRQoL was performed on baseline survey data from 38,691 adults aged 18-44 years in the Population Cohort, a random sample of the general population in 21 communities in Zambia and South Africa recruited as part of the HPTN 071 (PopART) study. In Zambia 21% and in South Africa 22% of enrolled individuals were HIV-positive at baseline. Differences in HRQoL scores were analyzed comparing five categories of HIV-positive individuals (unaware of their status, aware but not in care, in care but not on ART, on ART <5 years and on ART > 5 years) to HIV-negative individuals.

Multivariable regression models showed in both countries that individuals on ART for at least 5 years have the same HRQoL as HIV-negative individuals. For some other categories of persons with HIV infection (those aware of infection but not on ART in SA; those on ART for less than 5 years in Zambia) statistically significant differences were seen in the HRQoL in comparison to those without HIV infection, but the magnitudes of difference were small.

ART is successful in restoring HRQoL of HIV-positive individuals to that of HIV-negative individuals in this general population sample, providing further support for scale-up of testing and expansion of treatment to all HIV-positive individuals. (Thomas, R. et al. *Lancet Glob Health*. 2017 Nov;5(11):e1133-e1141. doi: 10.1016/S2214-109X(17)30367-4.)

Acceptability of the PopART immediate treatment intervention during the first annual round

A case-control study examining the factors associated with timely linkage-to-care and ART initiation (TLA) in the Arm-A intervention communities during the first year of the intervention, was conducted to assess the acceptability of the PopART immediate treatment intervention.

Of 7,572 individuals identified as PLWH (not on ART) during the first year of the PopART intervention, individuals who achieved TLA (controls) and those who did not (cases), were randomly selected for the study, with equal proportions from each community and of each gender. Standardized questionnaires were administered to explore factors potentially associated with TLA, including demographic and behavioural characteristics, and participants' opinions on HIV and related services.

Data from 705 participants (333 cases/372 controls) were analyzed. There were negligible differences between cases and controls by demographic characteristics including age, marital or socio-economic position. Prior familiarity with the CHiPs encouraged TLA. Participants who found clinics overcrowded, or opening hours inconvenient were less likely to achieve TLA, as were those expressing stronger feelings of shame about having HIV. Expressing "not feeling ready" and preferring to wait until they felt sick were similarly indicative of being a case. Worrying about being seen in the clinic or about how staff treated patients were not associated with TLA. While the association was not strong, we found that the greater the number of self-reported lifetime sexual partners the more likely participants were to achieve TLA. There was some evidence that participants with HIV-positive partners on ART were less likely to be cases.

The lack of socio-demographic differences between cases and controls is encouraging for a "universal" intervention that seeks to ensure high coverage across whole communities. Making clinics more "patient-friendly" could enhance treatment uptake further. The finding that those with higher risk behavior are more actively engaging with UTT holds promise for treatment-as-prevention. (Sabapathy, K. *J Int AIDS Soc*. 2017; 20(4):e25037)



BILL & MELINDA
GATES foundation

U.S. NATIONAL INSTITUTES OF HEALTH:
National Institute of Allergy and Infectious Diseases
National Institute of Mental Health
National Institute on Drug Abuse