



LESSONS LEARNED FROM A MAJOR TRIAL OF UNIVERSAL TESTING AND TREATMENT FOR HIV PREVENTION

The HPTN 071 (PopART) study is evaluating the impact of a combination prevention strategy – anchored in universal household HIV testing and linkage to immediate antiretroviral treatment initiation – to reduce HIV incidence. Currently ongoing in 21 large communities reaching nearly one million individuals in Zambia and South Africa, this study will provide answers to questions regarding how best to combine HIV prevention interventions in different populations and settings for maximum impact while also assessing cost-effectiveness.

In addition to strengthening all current routine HIV prevention and treatment services in the communities randomly allocated to receive the intervention, a novel cadre of staff, Community HIV-care Providers (CHiPs), have been recruited from within the study communities and trained to carry out the household interventions. Approximately 640 CHiPs have been deployed in the intervention communities to perform household-based HIV counseling and testing, linkage to HIV care and prevention services, tuberculosis and STI screening, condom distribution and referral for voluntary medical male circumcision (VMMC). HIV incidence will be assessed through a research cohort, recruited from all study communities, of approximately 37,000 randomly-selected adults (the “Population Cohort”), assessed annually for three years.



The HPTN 071 (PopART) research team has identified and overcome a number of challenges with delivering a universal testing and treatment (UTT) intervention at this scale (more than 600,000 individuals in the intervention communities). These critical findings have strengthened the intervention delivery in this study and provide critical insights for future large-scale, community-based and UTT studies and programs.

LESSON #1: FINDING HARD-TO-REACH POPULATIONS

A primary care level algorithm increases yield of HIV positive adolescents in a community intervention: HPTN071 (PopART) Study, Zambia (MJ. Chaila Poster #TUPED1341, 25 July, 2017, 12:30-14:30)

Within HPTN 071, the “PopART for Youth” (P-ART-Y) study aims to evaluate the acceptability and uptake of the intervention among adolescents. HIV prevalence is low among 10-14 year-olds, however, and so to prioritise HIV Counseling and Testing (HCT) within this group, a screening tool is used to identify those in this age range at high risk of being HIV-infected.

The screening tool used in HPTN 071 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 HCT. The poster

presents findings from Zambia for the period October 2015-August 2016.

A total of 18,040 adolescents aged 10-14 years participated and had their health data recorded. The screening tool identified 12.1% (n=2,181) of these adolescents as “at-risk”. HIV prevalence among those tested in the at-risk group was 2.4% (35/2,085) compared to 0.6% (44/7,755) in those not identified by the screening tool, representing a 4.3-fold higher estimated odds of infection (95% CI, 2.8-6.8; p=0.0001).

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.

Increasing knowledge of HIV status among men: a cluster-randomised trial of community-based distribution of oral HIV self-test kits nested in four HPTN 071 communities in Zambia (H. Ayles, Oral presentation, TUAC0406LB, 25 July, 2017, 14:30-16:00)

Knowledge of status among HIV+ men, young adults and mobile individuals in HTPN 071 lags behind other groups. We nested a cluster-randomised 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).

In four Zambian communities participating in HPTN 071, 33 randomly-selected CHiPs teams provided the option of HIVST or finger-prick 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 1.03-1.65; p=0.03). 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). 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.

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LESSON LEARNED #2: ASSESSING COMORBIDITIES AND QUALITY OF LIFE IN HIGH-RISK POPULATIONS

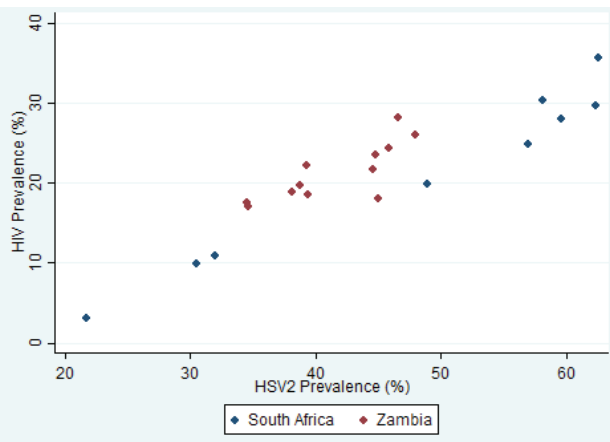
Sexually transmitted bedfellows: Exquisite association between HIV and HSV2 in 21 communities in Southern Africa (R. Hayes Poster #TUPEC0756, 25 July, 2017, 12:30-14:30)

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 1).

	HIV+vs/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 1: 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.

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 (B. Yang Poster # WEPEC1030, 26 July, 2017, 12:30-14:30)

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. 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.

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 (R. Thomas Poster # TUPEC0739, 25 July, 2017, 12:30-14:30)

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.



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

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LESSON LEARNED #3: IMPROVING ENROLLMENT AND RETENTION IN COMMUNITY-BASED HIV PREVENTION TRIALS

Impact of household visit schedule of field teams on the uptake of community-based HIV-prevention research; perspectives from the HPTN 071 (PopART) study (E. Nkuna Poster #TUPED1192, 25 July, 2017, 12:30-14:30)

We investigated the effect of different schedules for field teams on successful follow-up by those field teams of individuals enrolled in the Population Cohort (PC) in the HPTN 071 (PopART) study in South Africa.



Follow-up household visits were scheduled in three shifts: Midweek shifts (Monday-Friday, 8-hour duration) categorized as 'early' if ending before 4pm; as 'late' if ending after 4pm; and a Saturday shift (5 hours). A participant was considered successfully followed-up if the survey was completed during the household visit. The number of successful follow-up visits were calculated for each shift type and adjusted to account for variation in field work shift duration.

A total of 11,720 participants (8,251 females; 70%), were successfully followed-up during 223 days. The rate of successful visits per hour was 5.1 for early shifts, 6.8 for late shifts and 15.7 for Saturday shifts. Follow-up visits during Saturday shifts were more successful as compared to visits during early or late midweek shifts. For male participants, Saturday shifts resulted in 3.6-times more completed visits compared to early weekday shifts (incidence rate ratio (IRR), 95% CI 2.9-4.5) For female participants, Saturday shifts resulted in 2.9-times more completed visits compared to early weekday shifts (95% CI 2.3-3.7).

To efficiently follow-up participants (especially males) in a community-based study, more household visits should be scheduled during Saturday shifts instead of midweek shifts.

Recent Publications From HPTN 071

1. What works-reaching universal HIV testing: lessons from HPTN 071 (PopART) trial in Zambia.

Shanaube K, Schaap A, Floyd S, Phiri M, Griffith S, Chaila J, Bock P, Hayes R, Fidler S, Ayles H; HPTN 071 (PopART) Study Team. *AIDS*. 2017 May 3. doi: 10.1097/QAD.0000000000001514. [Epub ahead of print]

2. A universal testing and treatment intervention to improve HIV control: One-year results from intervention communities in Zambia in the HPTN 071 (PopART) cluster-randomised trial.

Hayes R, Floyd S, Schaap A, Shanaube K, Bock P, Sabapathy K, Griffith S, Donnell D, Piwowar-Manning E, El-Sadr W, Beyers N, Ayles H, Fidler S; HPTN 071 (PopART) Study Team. *PLoS Med*. 2017 May 2;14(5):e1002292. doi: 10.1371/journal.pmed.1002292. eCollection 2017 May.

3. HIV-related stigma and universal testing and treatment for HIV prevention and care: design of an implementation science evaluation nested in the HPTN 071 (PopART) cluster-randomized trial in Zambia and South Africa.

Hargreaves JR, Stangl A, Bond V, Hoddinott G, Krishnaratne S, Mathema H, Moyo M, Viljoen L, Brady L, Sievwright K, Horn L, Sabapathy K, Ayles H, Beyers N, Bock P, Fidler S, Griffith S, Seeley J, Hayes R; HPTN 071 (PopART) study team. *Health Policy Plan*. 2016 Dec;31(10):1342-1354. Epub 2016 Jul 3.

4. Good Health and Moral Responsibility: Key Concepts Underlying the Interpretation of Treatment as Prevention in South Africa and Zambia Before Rolling Out Universal HIV Testing and Treatment.

Bond V, Hoddinott G, Viljoen L, Simuyaba M, Musheke M, Seeley J. *AIDS Patient Care STDS*. 2016 Sep;30(9):425-34. doi: 10.1089/apc.2016.0114.

5. "The difference that makes a difference": highlighting the role of variable contexts within an HIV Prevention Community Randomised Trial (HPTN 071/PopART) in 21 study communities in Zambia and South Africa.

Bond V, Chiti B, Hoddinott G, Reynolds L, Schaap A, Simuyaba M, Ndubani R, Viljoen L, Simwanga M, Fidler S, Hayes R, Ayles H, Seeley J; HPTN 071 (PopART) study team. *AIDS Care*. 2016;28 Suppl 3:99-107. doi: 10.1080/09540121.2016.1178958.

6. A narrative analysis positioning HIV relative to personal (sexual) relationship challenges in an agony aunt column in the Western Cape, South Africa - Aunty Mona's "love advice".

Viljoen L, Thorne M, Thomas A, Bond V, Hoddinott G; HPTN 071 (PopART) team. *AIDS Care*. 2016;28 Suppl 3:83-9. doi: 10.1080/09540121.2016.1178957.

7. Implementing Community Engagement for Combination Prevention: Lessons Learnt From the First Year of the HPTN 071 (PopART) Community-Randomized Study.

Simwanga M, Bond V, Makola N, Hoddinott G, Belemu S, White R, Shanaube K, Seeley J, Moore A; HPTN 071 (PopART) study team. *Curr HIV/AIDS Rep*. 2016 Aug;13(4):194-201. doi: 10.1007/s11904-016-0322-z. Review.

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