

HPTN 071 (PopART) Population Effects of Antiretroviral Therapy to Reduce HIV Transmission is a research study that will determine the impact of a package of HIV prevention interventions on community-level HIV incidence. These prevention interventions include universal voluntary HIV counseling and testing and initiation of antiretroviral therapy (ART) regardless of CD4 count or clinical stage for all individuals living with HIV.

RATIONALE

HIV prevalence and incidence remain at very high levels in many parts of Southern Africa. Without bold, new, and effective HIV prevention strategies, the number of HIV infections will continue to rise, making lifelong provision of ART to all people living with HIV ever more challenging to achieve. Mathematical models have shown that universal voluntary HIV counseling and testing, with initiation of ART regardless of CD4 count or clinical stage for all people living with HIV, has the potential to achieve substantial reductions in HIV incidence at the population level.

HPTN 071 (PopART) will uniquely provide an accurate estimate of the effect on HIV incidence at the population level of a community-wide prevention package, including universal testing and treatment, in severely affected countries in Southern Africa.

In 2011, the HPTN 052 study showed that ART is an effective tool for prevention of HIV transmission at the individual level among stable serodiscordant couples. Participants who began ART early (with CD4+ counts between 350–550 cells/ml) were 96% less likely to transmit HIV to their partner than those who delayed ART until their CD4+ count was between 200–250 cells/ml. However, it has not yet been shown whether provision of early ART to all HIV-infected individuals in a community is feasible, acceptable and can reduce the overall rate of HIV transmission at the population level. HPTN 071 (PopART) will help researchers determine the effectiveness of this approach—referred to as “universal testing and treatment.”

This study will investigate the impact on HIV incidence of the ‘PopART intervention’, a combination of several interventions, based upon universal voluntary HIV counseling and testing (with referral to care) provided to the

HPTN 071 (PopART) Study Countries



Field work in Zambia



Field work in South Africa

whole community through a house-to-house campaign. The PopART intervention also includes ART initiation regardless of CD4 count or clinical stage for all individuals living with HIV, promotion of male circumcision for HIV uninfected men and other proven preventive interventions. HPTN 071 (PopART) will determine if such a program is feasible and acceptable when delivered on a large scale to entire communities. This study is a key global health priority and will inform policy for international agencies, funders and departments of health.

STUDY DESIGN

HPTN 071 (PopART) is being conducted in 21 communities—nine communities in the Western Cape Province of South Africa and twelve communities in Zambia. ‘Community’ is defined as the catchment area of a health care facility providing ART. The HIV combination prevention package (PopART intervention) that is being tested will be delivered by Community HIV-care Providers (CHiPs).

Full PopART Intervention

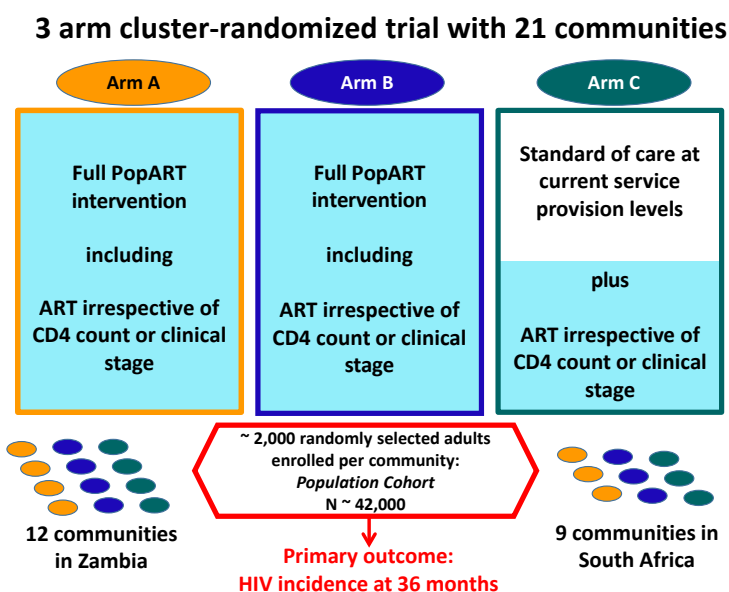
- Offering voluntary HIV counseling and testing annually through a house-to-house campaign
- Linking those with HIV to care at the local health center
- Offering ART to all those who are HIV-infected, irrespective of CD4+ count or clinical stage
- Promoting voluntary medical male circumcision for men who test HIV-negative
- Promoting services for the prevention of mother-to-child transmission (PMTCT) to HIV-infected pregnant women
- Referral for treatment of sexually transmitted infections
- Providing condoms in the community
- Screening and referral for tuberculosis (TB)

Preliminary mathematical modeling has shown that the full PopART intervention may reduce HIV incidence in adults by 50-60% over three years.

The 21 communities were formed into 7 matched triplets, with four triplets in Zambia and three in South Africa. Within each country, communities were matched based on the best available estimates of their HIV prevalence, with the aim of minimizing the variability in baseline HIV incidence between communities in each matched triplet.

In each matched triplet, one community was randomly assigned to each of three study arms. The PopART intervention is offered to every member of the study communities in Arms A and B, estimated to be approximately 800,000 individuals. The communities in Arm C will receive standard of care services with the addition of ART for all individuals living with HIV. To measure the impact of the PopART intervention, a Population Cohort, consisting of a random sample of approximately 2,000 adults aged 18–44 years, was recruited from the general population of each of the 21 communities (an overall total of around 42,000 across all communities) and will be followed up once a year for three years to measure HIV incidence and other outcomes.

In the original design of the HPTN 071 (PopART) study, Arm A communities received the full PopART intervention whereas Arm B communities received the PopART intervention except with ART initiation according to local guidelines (based on CD4 count or clinical stage). This design was to allow the study team to determine the additional benefit conferred by offering ART irrespective of CD4 count or clinical stage. In late 2015, in response to mounting evidence of clinical benefit, the World Health Organization (WHO) guidelines on HIV/AIDS were revised to recommend ART for all people living with HIV. The HPTN 071 (PopART) study team responded by incorporating this recommendation into the



study design, making ART available for all people living with HIV in all study arms.

The rationale for the HPTN 071 (PopART) study remains strong and its findings remain highly relevant to the scale-up of future HIV programming. Whereas the START study demonstrated individual benefit with early use of ART by HIV-infected patients, HPTN 052 showed efficacy of ART in prevention of HIV transmission among heterosexual discordant couples, and several observational studies indicate a decrease in the number of new infections with scale-up of treatment, HPTN 071 (PopART) will uniquely be able to provide an accurate estimate of the effect of a community-wide combination prevention package—one based on universal testing and treatment - on HIV incidence at the population level in severely affected countries in Southern Africa, as well as determining the feasibility and acceptability of delivering this intervention on a large scale.



Field work in Zambia

The majority of the communities participating in HPTN 071 (PopART) previously participated in the Zambia-South Africa TB and AIDS Reduction (ZAMSTAR) study, conducted by the investigators now leading the HPTN 071 (PopART) study. During the seven years of the ZAMSTAR study, these communities and investigators worked together to build strong community relationships and active community advisory boards and developed a robust infrastructure that is now supporting HPTN 071 (PopART).

The HPTN 071 (PopART) study began in late 2013 and is expected to continue until late 2018.

PRIMARY AND SECONDARY STUDY OBJECTIVES AND OUTCOMES

The **primary study outcome** will be HIV incidence over 3 years in members of the Population Cohort who are HIV-negative at baseline, and will be compared between the three study arms (A, B and C) to measure the population-level effectiveness of the PopART intervention.

Secondary outcomes will be measured using Population Cohort data as well as data from CHiPs, health centers and social science research to assess the effect of the intervention on a number of additional factors, including:

- HIV incidence during each year of follow-up
- HSV-2 incidence
- HIV disease progression and death
- ART toxicity
- Sexual risk behavior
- Case notification rate of tuberculosis
- HIV-related stigma
- Retention in care
- Community viral load (pending funding)
- ART adherence and viral suppression (pending funding)
- ART drug resistance (pending funding)
- Acceptance of HIV testing and re-testing
- Uptake of medical male circumcision among men testing HIV-uninfected
- ART screening and uptake
- Uptake of PMTCT services

Case-Control studies will be carried out to examine factors related to:

- Uptake of HIV testing during the first round of home-based testing in Arms A and B
- Uptake of immediate treatment in Arm A
- Uptake of HIV testing during the second round of home-based testing in Arms A and B

In order to inform the intervention before it was implemented in the communities, **social science** research was undertaken to better understand the communities, their prior and current HIV landscape, as well as attitudes toward different prevention approaches. During the study, further research is being carried out to examine the acceptability of the PopART intervention and to document the effects of the interventions on a number of factors, including risk behaviors, social networks, HIV identity and community-level HIV associated stigma.

Economic Evaluations will measure the incremental cost of the intervention packages and will assess the burden on local health centers of implementing them. **Mathematical models** fitted to the study data will be used to estimate the effectiveness and cost effectiveness of the intervention packages in the chosen study populations as well as other populations.

STUDY TEAM

The study is being conducted by the NIH funded HIV Prevention Trials Network (HPTN). The study is led by investigators at the London School of Hygiene and Tropical Medicine (LSHTM) in collaboration with Imperial College London, the Zambia AIDS Related Tuberculosis (ZAMART) Project and the Desmond Tutu TB Centre (DTTC) at Stellenbosch University, South Africa.



Imperial College
London



Zambart Project



STUDY FUNDERS

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To learn more about the HIV Prevention Trials Network, visit www.hptn.org or follow us on Facebook at www.facebook.com/HIVpntn or on Twitter at www.twitter.com/HIVpntn

The HIV Prevention Trials Network is a partnership between scientists and communities around the world to develop, evaluate and implement cutting-edge biomedical, behavioral and structural interventions to reduce the transmission of HIV. The HPTN has more than 80 research sites in 15 countries and more than 50 clinical trials ongoing or completed. The HPTN is funded by the National Institute of Allergy and Infectious Diseases (NIAID), and co-funded by the National Institute of Mental Health (NIMH), the National Institute on Drug Abuse (NIDA), and the Office of AIDS Research at the U.S. National Institutes of Health (NIH).