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 household voluntary HIV counseling and testing, linkage of HIV infected individuals to care and early initiation of antiretroviral therapy (ART) for all those testing HIV-positive.

RATIONALE

HIV prevalence and incidence remain at very high levels in many parts of Southern Africa and there is an urgent need for more effective prevention measures. Mathematical models have shown that universal voluntary HIV counseling and testing, with early initiation of ART for those who are HIV-infected, has the potential to achieve substantial reductions in HIV incidence at the population level. Evaluating the effectiveness of such a strategy is a key global health priority.

In 2011, the HPTN 052 study showed that ART is an effective intervention for prevention of HIV transmission in stable serodiscordant couples. HIV uninfected partners of participants with HIV who began ART early (with CD4+ counts between 350-550 cells/ml) were 96% less likely to acquire HIV than those whose partners delayed ART initiation 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 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 “treatment as prevention.”

HPTN 071 (PopART) will investigate the impact on HIV incidence of the full study intervention (described in detail on page 2), and whether it is feasible and acceptable when delivered on a large scale to entire communities.

Unless new and more effective strategies for preventing new HIV infections are identified and embraced worldwide, the number of new HIV infections will continue to rise, and providing lifelong ART to those who need it will become increasingly more challenging.
STUDY DESIGN

HPTN 071 (PopART) will be conducted in 21 communities—nine communities in the Western Cape of South Africa and twelve communities in Zambia. The HIV prevention interventions that will be tested (the full PopART intervention) include:

- Voluntary HIV counseling and testing annually through house-to-house testing
- Linking those with HIV to care at local health facility
- Offering immediate ART to those who are HIV-infected, irrespective of CD4+ count
- Referral for voluntary medical male circumcision for men who test HIV-negative
- Promotion of services for the prevention of mother-to-child transmission (PMTCT) to HIV-infected pregnant women
- Referral for treatment of sexually transmitted infections
- Provision of condoms in the community

The 21 communities were formed into 7 matched triplets, with 4 triplets in Zambia and 3 in South Africa. Within each country, communities were matched based on the best available estimates of 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 receiving the following interventions:

**Arm A**
- all of the HIV prevention strategies in the full combination intervention program, described above.

**Arm B**
- all of the HIV prevention strategies in the PopART combination prevention program, except HIV treatment will only be offered to those who are eligible according to national guidelines.

**Arm C**
- the current standard of care in their country.

The intervention will be offered to every member of the study communities in Arms A and B, estimated to be approximately 800,000 individuals.

MEASURING IMPACT OF THE INTERVENTION

A Population Cohort, consisting of a representative sample of 2,500 adults aged 18–44 years, will be randomly recruited from the general population of each study community (a total of 52,500 across all communities) and will be followed for the duration of the study for HIV incidence. A baseline survey of the Population Cohort will be carried out at the time the intervention is initiated to assess the comparability of the intervention and control arms. Follow-up questionnaires of the cohort will be carried out every 12 months during the study period to measure HIV incidence and other outcomes.

The majority of the communities that will participate 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 trial, these communities and investigators worked together to build strong community relationships and active community advisory boards and developed a robust infrastructure that can now be leveraged in support of HPTN 071 (PopART).
STUDY OBJECTIVES AND OUTCOMES

Primary study outcome: HIV incidence over 36 months in the Population Cohort who are HIV-uninfected at baseline will be compared between the three study arms (A-C) to measure the population-level effectiveness of the PopART intervention.

Secondary outcomes will include the following:
- HIV incidence during each year of follow-up
- HSV-2 incidence
- HIV disease progression and death
- ART toxicity
- Sexual risk behavior
- Tuberculosis rate
- HIV-related stigma
- Retention in care
- Community viral load*
- ART adherence and viral suppression*
- ART drug resistance*

Process variables measured in the intervention communities include:
- Acceptance of HIV testing and re-testing
- Uptake of medical male circumcision
- Evaluation of ART and uptake
- Proportion of those testing HIV-infected started on ART within three months
- 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

*Pending funding
Social science research will be undertaken to understand how HIV is impacting communities as well as attitudes toward different prevention approaches. During the trial, further research will be 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 trial 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.

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**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 (ZAMBART) Project and the Desmond Tutu TB Centre (DTTC) at Stellenbosch University, South Africa.

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**STUDY FUNDERS**

The study is sponsored by the National Institute of Allergy and Infectious Diseases (NIAID), with funding from the U.S. President's Emergency Plan for AIDS Relief (PEPFAR). Additional funding is provided through NIAID, the National Institute of Mental Health (NIMH), the National Institute on Drug Abuse (NIDA), and the International Initiative for Impact Evaluation (3ie) with support from the Bill & Melinda Gates Foundation.

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**ACKNOWLEDGMENTS**

To learn more about the HIV Prevention Trials Network, visit [www.hptn.org](http://www.hptn.org).

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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).