

PopART Phylogenetics (HPTN 071-2) study

The PopART trial, also known as HPTN 071, delivered community-wide HIV prevention interventions in combination with universal test and treat to 21 communities in Zambia and South Africa. This strategy was shown to reduce the number of new HIV infections by approximately 20%, when compared with standard care, preventing approximately 2,500 new cases over 3 years. PopART Phylogenetics, also called HPTN 071-2, is a complementary study to this trial. It aims to better understand the patterns of HIV transmission at a population level in selected PopART communities in Zambia. The study took place between 2016 and 2018 and the project is now entering the publishing phase.

In Zambia, the number of new HIV infections in 2018 was estimated at 48,000 by UNAIDS. The Zambian government is aiming to reduce this number to less than 5000 per year by the end of 2020. In order to achieve this goal, it is important to be able to characterise the transmission of HIV as accurately as possible.

Research has shown that the HIV epidemic in Sub-Saharan Africa is very variable, with different groups of people having different levels of risk of HIV, depending on factors such as age, sex and geographical location. PopART Phylogenetics has been designed to investigate the aspects that are thought to affect the success of the PopART intervention in reducing HIV incidence. It specifically studies the role of the following factors in shaping HIV transmission in PopART communities:

- Transmissions from individuals with acute and early HIV infection
- Contributions by specific sex and age groups
- Transmission occurring outside the trial communities
- Levels of antiretroviral drug resistance

Mathematical modelling and phylogenetic methods have been used in this investigation. Phylogenetics is a set of bioinformatics tools which leverage genetic information of HIV to obtain the evolutionary history of the virus and, from that, infer patterns of HIV transmission.

This is the largest phylogenetic study of HIV ever conducted. The results can help inform future interventions and ongoing research so that programmes can be more effective at stopping HIV transmission. Output from the phylogenetic study will specifically be used to inform projections of the long-term impact of the PopART intervention.

Key Findings

30-40% of HIV transmission occurred from people who had been HIV-positive for less than a year

Researchers found that approximately 30-40% of HIV transmissions arose from people who had been HIV-positive for less than a year. This means that people at risk of HIV infection will need frequent testing to ensure those with new infections know their status and can start treatment as soon as possible. Continuation of the community wide HIV prevention UTT programs have the capacity to continue conferring significant reductions in new HIV infections.

Men between the ages of 25-35 account for a disproportionate amount of HIV transmission

Men between the ages of 25 and 35 years account for a disproportionate amount of transmission of HIV. This group is less likely to be aware of their HIV status and have low treatment coverage. These findings suggests that encouraging young men to test for HIV with supported linkage to care will lead to a significant reduction in new HIV infections in the population as a whole, even though reaching them might require more effort per person. Furthermore, modelling investigations suggest that focusing HIV test and treat programmes on men and women under the age of 35 could be almost as effective as reaching everyone in the population, because older people are generally better linked into care already.

80% of HIV transmissions occurred within the same community

In this trial, 80% of HIV transmissions were found to occur within a given community, with the remaining 20% happening between partners from different communities. This means that one in every five transmissions happened between communities, likely due to high levels of mobility within Zambia. This emphasises the importance of having continued easy access to care for people living with HIV as they move between communities. The movement of people across communities may have also diluted the impact observed during the PopART trial. It is likely that a greater impact would be seen if the intervention were rolled out in a wider geographical area.

Levels of drug resistance to antiretroviral therapy increased across all communities

HIV viruses can adapt to become resistant to drugs used in treatment. The phylogenetic data show that levels of drug resistance to antiretroviral therapy have increased in the past few years across all communities. These findings suggest that

an increasing proportion of those HIV positive individuals who are not virally suppressed may be a result of undiagnosed first-line drug resistance. The phylogenetics study also showed increasing levels of transmitted HIV with drug resistant viruses to first line therapy. These findings strongly support current practice to switch to dolutegravir regimens and emphasize the importance of regular HIV viral load monitoring with national programmes for monitoring for antiretroviral drug resistance to develop robust strategies for programmatic HIV therapies.

Continuing PopART intervention would lead to steep reduction of rates of new infection between 2020 and 2030

Modelling suggests that continuation of the PopART intervention would result in a steep reduction in rates of new infection between 2020 and 2030. This stresses the importance of continued community-wide initiatives to encourage HIV testing, repeat testing for those at risk and enhanced linkage to care and retention on treatment, even across communities.

The data collected for PopART Phylogenetics will be contributed to the PANGEA-HIV Consortium (Phylogenetics and Networks for Generalised Epidemics in Africa) in September 2020. The involvement of this consortium provides access to crucial shared expertise in phylogenetic analysis. The data will be shared within the consortium via an accreditation system and externally with selected researchers that submit a successful concept sheet proposal. The PANGEA data sharing and storage policy will protect participant privacy. Zambart is one of the partners leading this international consortium.

The research team for this study was led by Prof Christophe Fraser, from the Big Data Institute at University of Oxford, Prof Richard Hayes, from London School of Hygiene and Tropical Medicine, Prof Helen Ayles, from Zambart and Prof Sarah Fidler, from Imperial College London. Samples were collected by the Zambart team. Sequencing was carried out at the University of Oxford. Key analyses were carried out by Dr Tanya Golubchik, Dr Matthew Hall, Dr David Bonsall, and Dr Will Probert at the University of Oxford.

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