



PopART Phylogenetics

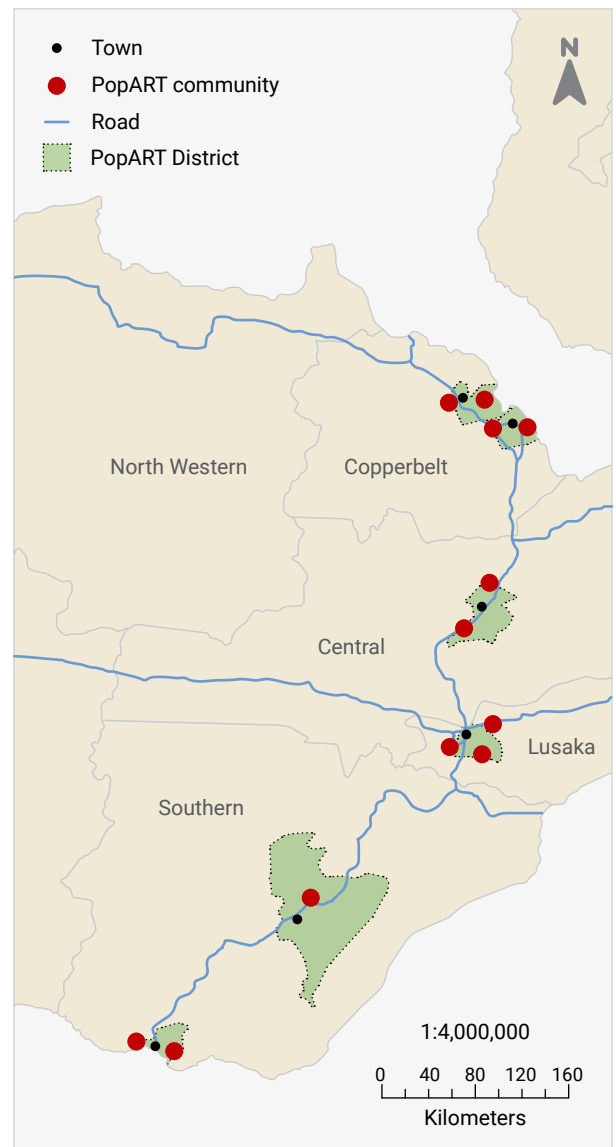
Characteristics of sources of HIV transmission in Zambia



About the PopART Phylogenetics study

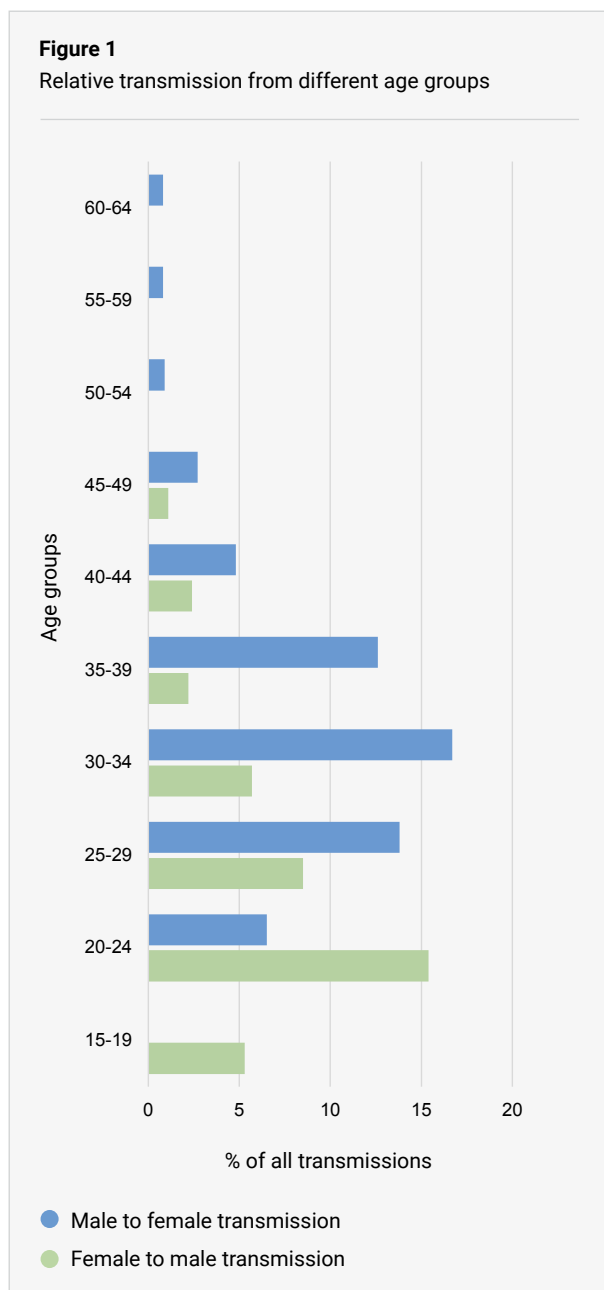
The HPTN 071 (PopART) trial took place in Zambia and South Africa between 2013 and 2018. The trial aimed to test the effectiveness of antiretroviral therapy (ART) in reducing new infections when given directly after diagnosis (universal testing and treatment) and the impact of an intervention package which aimed to provide universal household HIV testing at home, and then link infected individuals to care. The trial showed that the intervention package led to a 20% reduction in new infections. PopART Phylogenetics was conducted as an associated study in the twelve Zambian PopART communities. The study collected close to 7000 blood samples and determined the precise genetic sequence of the HIV virus in each of those samples.

The aim of the phylogenetics study was to learn more about the characteristics of people who are transmitting HIV. Phylogenetic methods can be used to compare the genetic sequences of different viruses and study how they are related to each other. Thereby, they can reveal who is close to whom in the local HIV transmission network and identify likely transmission pairs. By looking at the demographic characteristics of the sources in these pairs, it is possible to learn more about how HIV is transmitted between different groups in the population. For example, are transmissions originating from old or young people, men or women, within the trial communities or across different regions? The study also looked at the proportion of transmission which involved drug-resistant virus strains.



Transmission from men peaks at 30-34 years, transmission from women at 20-24 years of age

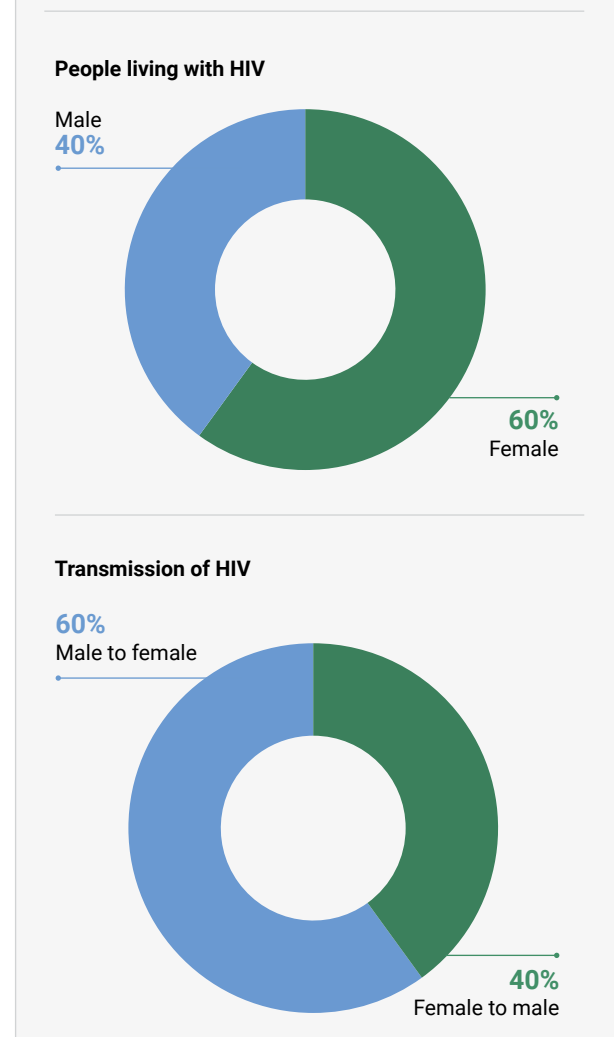
Different age groups contributed differently to overall transmission. The highest proportion of transmissions came from men between 30 and 34 years of age, with considerable additional transmission from the 25-29 and 35-39 year-old age groups. Men between 25 and 39 accounted for 43% of overall transmissions. Women were most likely to transmit at an earlier age, with a peak in the 20–24-year age group (Figure 1). Male partners were on average 5-6 years older than the female partner in male-to-female transmissions and 2-5 years older in female-to-male transmissions.



On average, a man living with HIV infects more than twice as many people as a woman living with HIV

The study shows that although the number of women living with HIV is higher than the number of men living with HIV, three out of five transmissions were from men to women. This means that, on average, a man living with HIV infected more than twice as many women as a woman infected men (Figure 2).

Figure 2
Relative transmission from men and women



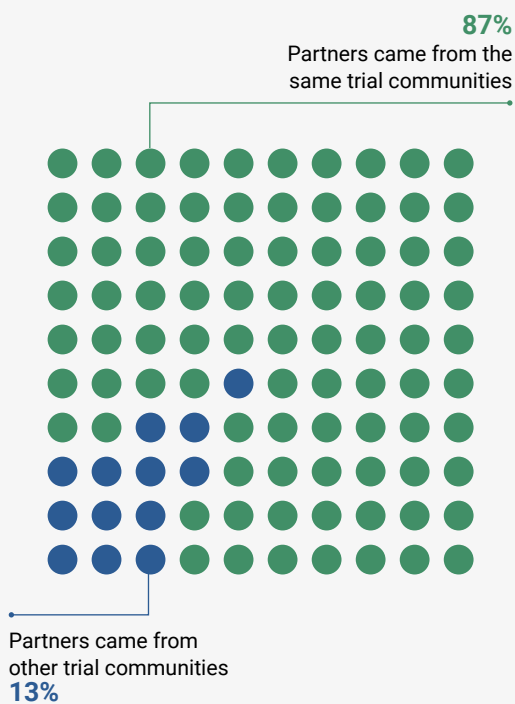
Previous studies have shown that men aged 25-40 are less likely to be aware of their HIV status and are less likely to be on treatment. These findings suggest that encouraging men in this age group to test for HIV with supported linkage to care will lead to a significant reduction in new HIV infections in the population, even though reaching them might require more effort per person.

At least 13% of HIV transmissions occurred between communities

13% of HIV transmissions detected in the study came from a partner living in a different trial community (Figure 3). However, most of the people in the surrounding areas did not participate in the study, so it is likely that the percentage of transmissions coming from outside the community is much higher. This means that the trial was most likely more successful than could be measured, and that making it easier for people to access treatment countrywide can help to substantially reduce the number of new infections.

Figure 3

Transmission from outside the trial communities



Phylogenetics and Networks for Generalised HIV Epidemics in Africa

PANGEA is a network of African, European and American researchers identifying individual and population-level factors that drive HIV transmission in sub-Saharan Africa. For more information visit our website www.pangea-hiv.org

11% of transmissions between 2014 and 2018 involved an HIV strain highly resistant to first-line therapy

During the trial period, first-line therapy did not yet include dolutegravir-containing regimens. In the transmission pairs, 79% of sources had drug-sensitive virus, 7% had HIV strains with low levels of resistance and 11% HIV strains with high levels of resistance (Figure 4). Overall levels of drug resistance to first-line antiretroviral therapy in newly diagnosed individuals, low and high, increased across all communities, from around 14% to around 23% during the trial period (Figure 5).

Figure 4

Drug resistance in sources of HIV transmission

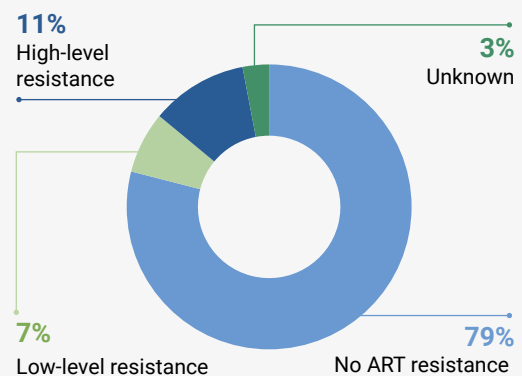
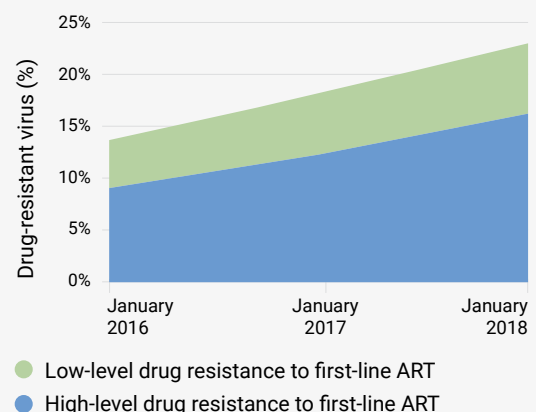


Figure 5

Drug resistance increased during the trial period



These findings strongly support the switch to dolutegravir-containing regimens which have dramatically decreased drug resistance since the trial ended. They also emphasize the importance of regular HIV viral load testing to catch the next rise of developing resistance early on.

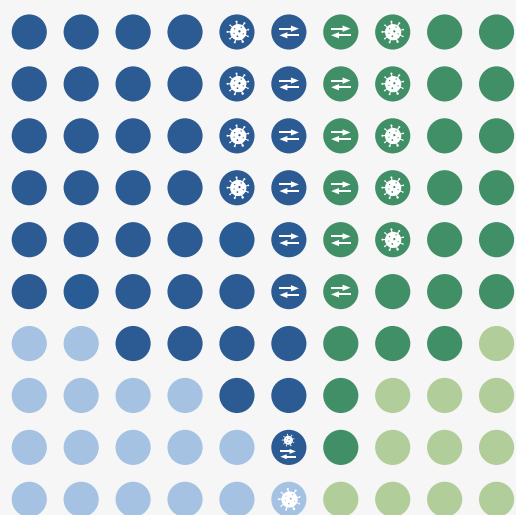
Conclusions

The PopART Phylogenetics study aimed to identify how and in which groups of the population the virus is spread, as this gives insights into the effectiveness of current approaches to reduce new infections. It also provides information about how to design strategies for HIV prevention in the future.

We found that men between the ages of 25 and 39 years account for a disproportionate fraction of HIV transmission, 43% in total. At least 13% of transmissions took place across trial communities, indicating that the impact of the trial would likely have been much greater if it had taken place country-wide. Drug resistance to first-line ART increased rapidly in the communities during the trial period, and 11% of transmissions analysed involved virus highly-resistant to first-line ART.

Figure 6

Characteristics of sources of HIV transmission



- 60 ● Men
- 43 ● Men between ages 25 and 39
- 40 ● Women
- 29 ● Women between ages 20 and 34
- 11 ⚙ Are infected with viruses with high resistance to first-line antiretroviral drugs
- 13 ⇄ Reside in a different community from the person they infected

Learning more about where transmission is happening in the population can inform prevention programmes and help to design more focussed and successful interventions in the future.

What must be done

1. Men aged 25-39 should be a focus of prevention strategies to control HIV transmission in Zambia. This group is less likely to access care and be on ART, which suggests that more efforts are required to support young and middle-aged men with HIV.
2. On average, each man living with HIV infects more than twice as many women than vice versa; programmes should therefore focus more strongly on also getting men into care even if more effort is required per person.
3. Young women at high risk of acquiring HIV should be one of the main focus groups for pre-exposure prophylaxis (PrEP) rollout.
4. Transmission across communities occurs frequently. This can reduce the impact of local prevention interventions and should be taken into account when evaluating these measures.
5. Drug resistance was rising rapidly before dolutegravir rollout and 11% of transmissions involved virus highly resistant to first-line ART. These findings strongly support current practice of switching to dolutegravir regimens.

The full manuscript, Hall et al., [Demographic characteristics of sources of HIV-1 transmission in the era of test and treat](#), is available on medRxiv. It is an unpublished preprint and has not yet undergone peer review. An additional manuscript on drug resistance is in preparation.

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Partners

PopART Phylogenetics was conducted by scientists from Zambart, the London School of Hygiene and Tropical Medicine and Oxford University. The study was funded by the National Institute of Health (NIH) and the Bill & Melinda Gates Foundation.

