Quantifying the Contribution of Different Aged Men and Women to Onwards Transmission of HIV-1 in Generalised Epidemics In Sub-Saharan Africa: A Modelling and Phylogenetics Approach from the HPTN 071 (PopART) trial

BACKGROUND
The HIV epidemic in Sub-Saharan Africa is known to be heterogeneous [2-4], and interaction with the HIV care cascade is known to vary by age and sex [1,5]. Young people may be less likely to be aware of their HIV status and less likely to be on antiretroviral therapy (ART) [figure 1] [5]. Heterogeneity in the epidemic highlights the importance of investigating targeted interventions informed by those most at risk of transmitting HIV, not just those at risk of acquiring the virus. Despite targeted programming based upon age and sex throughout SSA, there is limited information on the attributable fraction of transmissions arising from particular age groups of men and women. Mathematical modelling and phylogenetics provide a means for quantifying the contribution of different age groups of men and women to transmission of HIV.

HPTN 071 (PopART) was a 3-arm cluster-randomised trial in 21 communities in Zambia and South Africa that has been testing the impact of a combination prevention package including universal testing-and-treatment [7]. The PopART individual-based model (IBM) is a computer simulation model of the HIV epidemic in the communities of the trial developed to help interpret trial findings and investigate the PopART intervention in other settings. HPTN 071 is an ancillary study to HPTN 071 looking at phylogenetics in PopART.

RESULTS

AGE DIFFERENCE BETWEEN PARTNERS
Phylogenetics identified 224 probable transmission pairs and the direction of transmission between them. 60% of these transmissions were from men to women, 62% was predicted by the model.

Phylogenetics predicted men to be 5.4 years older than women in male-to-female transmission (model predicted 5.5 years). Phylogenetics predicted men to be 4.1 years older in female-to-male transmissions (model predicted 2.9 years) (figure 2).

OBJECTIVES 1 & 2: QUANTIFYING ONWARDS TRANSMISSION

According to phylogenetics, onwards transmissions peaked in 30-34 year old (y.o.) men. The model predicted onwards transmissions to peak in 25-29 y.o. men (figure 3).

OBJECTIVE 3: TARGETED INTERVENTIONS

The impact of suppressing transmissions from each age group of men and women was carried out using the computer simulation model. Modeling the prevention of all transmissions from 25-29 y.o. men and 20-24 y.o. women, those age groups identified as having the peak in onwards transmission, reduced cumulative incidence over the trial period (mid-2014 to 2018) by 20% and 19% respectively.

METHODS

MODELLING OF THE HIV EPIDEMIC
A simulated population, approximately the same size as the PopART community, was modelled. Several components model demography, the introduction of HIV, heterosexual partnership formation and dissolution, HIV progression through HIV diagnosis and antiretroviral therapy use, HIV transmission and transmission reduction from ART. The intervention is modelled as a combination of ART. The model contains a network of suppressing all infections from a group of men or women in a 5-year age group and summarises the difference in the number of infections with and without this group across the duration of the trial.

PHYLGENETIC ANALYSIS
Model predictions were tested against probable transmission pairs obtained with phylogenetics [8] from trial shell-read next-generation sequencing (NGS) data from trial communities in Zambia. Phylogenetic estimates were adjusted for sampling bias. The age discrepancy between the male and female partner in each pair was calculated by taking the difference in their recorded dates of birth.

LIMITATIONS

• Our results validate predictions of a mathematical model using phylogenetic data, with no sharing of parameter estimates across the two methods.

• Our results support observations that there is a significant contribution of young people to HIV transmission in Sub-Saharan Africa, especially 25 to 34 y.o. men, and that these groups should be prioritised for targeted interventions.

• These results agree with studies that use survey data of the reported age of an individual’s most recent sexual contact [9].

• Age groups of men and women who report lower awareness of status and ART coverage overlap substantially with those groups from which a large proportion of transmission events are predicted.

• Our work highlights that if universal testing-and-treatment (Utt) does not reach young people, and 25 to 34 y.o. men, then the effect of Utt on reducing incidences may be limited.

REFERENCES


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