

## Beyond risk compensation: Clusters of antiretroviral treatment users in sexual networks can modify the impact of ART on HIV incidence

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Early initiation of antiretroviral therapy (ART) significantly improves the survival of people living with HIV (PLWH) and greatly reduces HIV transmission to uninfected partners. Some mathematical models suggest that treatment-as-prevention (TasP) programmes could lead to HIV elimination, even in some of the most severely affected settings (1). International organizations including PEPFAR and the International AIDS Society have thus placed ART scale-up at the centre of their approach to achieving an “AIDS-free generation” (2, 3).

How the clinical efficacy of ART in preventing HIV transmission translates to real-life settings depends in large part on the capacity of HIV management and care programmes to engage and retain PLWH on a “HIV treatment cascade”, i.e., a series of clinical steps PLWH must go through to achieve viral suppression. In particular, for TasP programmes to be effective, a high proportion of PLWH must: 1) be diagnosed; 2) be linked to care; 3) remain in care; and 4) adhere to ART. Numerous implementation science initiatives have sought to improve each step of the HIV treatment cascade, e.g. (4-6).

The effects of ART on HIV incidence may also depend on changes in sexual network dynamics during the course of ART scale-up. The Health Belief Model suggests that “risk compensation” is one mechanism through which negative feedback loops between ART scale-up and HIV incidence may emerge. Risk compensation occurs when people increase their individual risk behaviours in response to the increased availability of interventions to prevent and manage HIV infection. Concerns about risk compensation after the initiation of ART have largely been dispelled in empirical studies, but other changes in sexual networking patterns may still modify the effects of ART on HIV incidence.

*ART patients engaging in sexual relationships with other ART patients*

For example, during the course of ART scale-up, ART patients may increasingly seek to form new relationships with other ART patients. Similarly, relationships between two ART patients may be less likely to dissolve than other relationships in which only one of the two partners is an ART patient. “ART homophily” – the tendency of ART patients to preferentially engage in, and maintain, sexual relationships with other PLWH who are also on ART – may lead to the emergence of ART clusters. These are subsets of the sexual network in which the density of ART patients is much higher than in the rest of the network.

Qualitative studies have documented several psychosocial mechanisms that may lead to such dynamics. For an ART patient, ART homophily may indeed reduce fear for further HIV transmission (7) and ease anxiety about HIV status disclosure (8). ART homophily also gives patients direct access to emotional support and facilitates sharing of coping strategies during episodes of drug-induced side effects or HIV treatment fatigue (9). In addition, ART patients may share common life histories, e.g., being widowed or having lost a previous partner. Finally, in a number of ART programmes, ART patients frequently interact with each other during dedicated ART clinics, in support groups or in various income-generating activities. This increased social proximity may lead to emotional closeness, and may provide additional opportunities to form new sexual partnerships with others who are also ART patients.

When ART clusters emerge, the rest of the sexual network is affected by compensatory changes. Since ART patients are no longer available for relationships with untreated PLWH or with HIV-negative individuals, these two groups must increasingly form relationships with each other if

they want to keep the number of sexual relationships that they engage in constant. The sexual network pattern of ART patients thus affects the partnerships formed by all other members of the sexual network.

#### *ART homophily impact differs according to epidemic characteristics*

Using a simple mathematical model, we showed that ART homophily may modify the prevention impact of ART in a complex manner, depending simultaneously on the performance of HIV testing and treatment programmes (e.g. coverage of HIV testing and ART adherence) and the epidemiological context (HIV prevalence).

In concentrated epidemics and in generalized epidemics where HIV prevalence is no more than 10%, ART homophily enhances the impact of ART on HIV incidence. The impact of ART clusters may be more nuanced in hyperendemic settings where the HIV prevalence among certain gender-age strata may reach or even exceed 35%, e.g. (10). In such settings, ART homophily also enhances the impact of ART on HIV incidence when HIV status awareness among PLWH and ART coverage are high, and adherence to ART is low. This is so because ART patients who do not adhere to treatment remain infective. In that case, ART clusters provide indirect protection to HIV-negative individuals by limiting their contact with potential sources of HIV transmission.

In contrast, in hyperendemic settings where HIV status awareness and ART coverage are low but adherence to ART is high, ART homophily may reduce the impact of ART on population-level HIV incidence. In this scenario, highly-adherent ART patients (who are significantly less infective than other PLWH) would have helped interrupt chains of HIV transmission in sexual networks connected to HIV-negative individuals. Instead, because of ART clusters, HIV-negative individuals are more likely to come into contact with undiagnosed (and untreated) and thus more infective PLWH. Since the combination of high ART adherence and low ART coverage characterizes most current ART programmes in sub-Saharan countries (11), ART may at the moment have a lower impact on HIV incidence than estimated by standard mathematical models without ART homophily.

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