**HIV treatment as prevention in Danish men who have sex with men, but would it work in sub-Saharan African settings?**

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Antiretroviral treatment (ART) decreases the risk of HIV acquisition in stable serodiscordant couples1 and the general population in high HIV prevalence settings.2 However, HIV elimination can likely not be achieved by a single prevention approach to fit all, but will require a combination of effective interventions contextualised to the specific epidemic3 to achieve virtual elimination, defined as one new HIV infection per 1,000 individuals.4

Okano and colleagues (ref) tested whether Treatment as Prevention (TasP) with ART can eliminate HIV in men who have sex with men (MSM) in the nationwide Danish HIV cohort study. They used CD4-staged Bayesian back-calculation to estimate the annual incidence in MSM in Denmark and the number of undiagnosed MSM likely to continue to transmit HIV infection. The unique civic registration number assigned to all Danish residents allowed linking the relevant registries. Estimated HIV incidence was 1.4 per 1000 MSM in 2013, and an estimated 21% of all HIV-infected MSM in Denmark remained undiagnosed. The incidence reduction was attributed to increasing ART coverage, with a significant effect when ART coverage reached 35%.

However, the context of this study needs to be appreciated: MSM drive the Danish HIV epidemic, are nearly universally engaged in HIV care, with extensive ART coverage immediately upon HIV diagnosis, and strict adherence and viral suppression; in these circumstances TasP works to curb the HIV epidemic. These essential optimal conditions have not been replicated elsewhere in Western Europe5 and this, coupled with behavioural risk compensation reported in MSM by Okano and elsewhere in Europe6 following ART-associated reduced morbidity and mortality, means TasP alone is unlikely to be the silver bullet that decision-makers hoped for.

The big question remains whether in heterosexually-driven HIV epidemics such as in sub-Saharan Africa (SSA), TasP will eventually reduce HIV incidence to such low levels that the end of the epidemic will be in sight. In a rural area in South Africa with high HIV prevalence and incidence and ART provided only to those with advanced HIV progression, ART coverage > 20% was associated with a reduction in an individual’s risk of HIV acquisition,2 albeit not to the low levels seen in Danish MSM. Whether this was due to later ART initiation in South Africa than in Denmark, whether a heterosexual epidemic differs from that in MSM and TasP alone is insufficient, or whether adherence, and thus viral suppression, was sub-optimal is unclear.

UNAIDS coined the 90:90:90 target to provide a structure for TasP to achieve its goal of epidemic containment: 90% of people to know their HIV status, 90% of HIV-infected people to be on ART and 90% of those on ART to be virally suppressed.7 In SSA, concentrated epidemics exist within the generalised HIV epidemic, and it has been suggested that focussing context-specific combination interventions to areas of high transmission and people at most risk of HIV infection achieves more impact than a uniformly-distributed intervention.8

Experience from ongoing studies and HIV treatment programmes in SSA, the region of highest need, shows that HIV care and treatment does not reach all those in need, that vulnerable groups including youth and men are failing to engage with health care, that asymptomatic people may be less likely to engage with, and be retained in, care and that life-long adherence to ART may be complex in settings where other health challenges prevail. With ART-eligibility expansion9, also in SSA, and consequent rapid increase in ART coverage coupled with adherence and viral suppression rates that are not as good as those observed in MSM in Denmark, the critical question now is whether earlier treatment will lead to drug resistance of the form and prevalence likely to compromise future elimination of HIV.10 Findings from four ongoing cluster-randomised trials,11 one of which is due to report later this year will provide further insight about the effectiveness of ART on HIV incidence at the population level and will also allow estimates of both acquired and transmitted resistance.

In the absence of an effective HIV vaccine, and the stringent treatment outcomes required for a TasP-only intervention to be successful, contextualised and targeted combination intervention that includes pre-exposure prophylaxis, circumcision and behavioural change will be needed to bend the epidemic curve. This requires political commitment.

**References**

1. Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med* 2011; **365**(6): 493-505.

2. Tanser F, Barnighausen T, Grapsa E, Zaidi J, Newell ML. High coverage of ART associated with decline in risk of HIV acquisition in rural KwaZulu-Natal, South Africa. *Science* 2013; **339**(6122): 966-71.

3. Jones A, Cremin I, Abdullah F, et al. Transformation of HIV from pandemic to low-endemic levels: a public health approach to combination prevention. *Lancet* 2014; **384**(9939): 272-9.

4. Granich RM, Gilks CF, Dye C, De Cock KM, Williams BG. Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model. *Lancet* 2009; **373**(9657): 48-57.

5. European Centre for Disease Prevention and Control. Thematic Report: HIV continuum of care. Stockholm: ECDC, 2015.

6. Phillips AN, Cambiano V, Nakagawa F, et al. Increased HIV incidence in men who have sex with men despite high levels of ART-induced viral suppression: analysis of an extensively documented epidemic. *PLoS One* 2013; **8**(2): e55312.

7. UNAIDS. 90-90-90 An ambitious treatment target to help end the AIDS epidemic. 2014. <http://www.unaids.org/sites/default/files/media_asset/90-90-90_en_0.pdf> (accessed 22 Jan 2015).

8. Anderson SJ, Cherutich P, Kilonzo N, et al. Maximising the effect of combination HIV prevention through prioritisation of the people and places in greatest need: a modelling study. *Lancet* 2014; **384**(9939): 249-56.

9. WHO. Guideline on when to start antiretroviral therapy and on pre-exposure prophylaxis to ART. 2015. <http://apps.who.int/iris/bitstream/10665/186275/1/9789241509565_eng.pdf?ua=1> (accessed 15/10/2015 2015).

10. Cambiano V, Bertagnolio S, Jordan MR, et al. Predicted levels of HIV drug resistance: potential impact of expanding diagnosis, retention, and eligibility criteria for antiretroviral therapy initiation. *AIDS* 2014; **28 Suppl 1**: S15-23.

11. AVAC, UNAIDS,,. Antiretroviral Treatment for Prevention of HIV and Tuberculosis. 2013 update on current and planned research efforts. 2014. <http://www.avac.org/sites/default/files/resource-files/ART%20for%20prevention%20study%20update%20report%20March%202014.pdf> (accessed 05 Feb 2015).