The Cascade of Care of HIV Seroconverters in the Context of Universal Test and Treat

Joseph Larmarange, Mamadou Hassimiou Diallo, Collins Iwuji, Joanna Orne-Gliemann, Nuala McGrath, Mélanie Plazy,
Frank Tanser, Rodolphe Thiebaut, Deenan Pillay, François Dabis for the ANRS 12249 TasP Study Group

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Background

The ANRS 12249 Treatment as Prevention (TasP) cluster-randomized trial aimed at evaluating the impact of a Universal Test and Treat (UTT) approach on population-based HIV incidence in rural KwaZulu-Natal, South Africa. Trial results (Dabis et al, AIDS conference Durban 2016, FRACO105LB) showed low rates of early linkage to HIV care and treatment and no significant reduction in incidence.

To optimize the impact of UTT, time to antiretroviral treatment (ART) initiation and viral suppression must be significantly shortened, in particular among newly infected individuals. We describe here the longitudinal cascade of care for those seroconverting during the course of the TasP trial.

Methods

TasP trial procedures
In this rural area with about 30% HIV prevalence, every six months between March 2012 and June 2016, resident members aged ≥16 years old were offered rapid HIV testing at home (for diagnosis) and asked independently to provide dried blood spot (DBS) samples (for incidence estimate). Those testing positive or who self-reported their positive status were referred to local trial clinics for ART initiation, regardless of their CD4 count (intervention arm) or according to national guidelines (control arm). They had also the opportunity to seek care in local government clinics where treatment was offered according to national guidelines.

Computation of residency, HIV and care statuses
Residency status of each participant was computed for each calendar day taking into account population exits (death, out-migration) and new eligible individuals (in-migration, 16th anniversary).

Cases of HIV seroconversion were identified using multiple sources: repeat DBSs, repeat rapid tests, HIV+ self-reports and clinic visits. Date of seroconversion was estimated using a random imputation approach between last negative and first positive known HIV status.

For those who were resident in the trial area at the estimated date of seroconversion, the HIV care status was computed, for each day following seroconversion (M0), using additional data (clinic visits, ART prescription, CD4 counts, viral loads) collected both in trial clinics and in local government clinics, linked at individual level with the authorization of the ethics committee.

Longitudinal cascade of HIV care since HIV seroconversion
Among those who seroconverted for HIV while residing in the trial area, we estimated the probability of being at a particular step within the cascade according to time since seroconversion by using a non-parametric multistate model, their follow-up being right-censored by date of death or date of trial closure (30 June 2016).

Care trajectories over the first year after HIV seroconversion
The analysis was restricted to those observed at least one year after HIV seroconversion. We plotted their detailed trajectories, i.e. the succession of their daily statuses over the first year following seroconversion, indicating whether the participants entered care in a local trial clinic or in a local government clinic and indicating successful contacts by trial team in subsequent survey rounds.

We stratified the results according to trial arm and according to the main care events occurring during the first 12 months following HIV seroconversion: (i) those not diagnosed during that period; (ii) those diagnosed but who did not enter care in a local trial or government clinic; (iii) those who did enter care but did not started ART; and (iv) those who initiated ART.

Fig. 1. Estimated longitudinal cascade of HIV care since HIV seroconversion
Both arms combined, TasP ANRS 12249 trial, multistate survival model

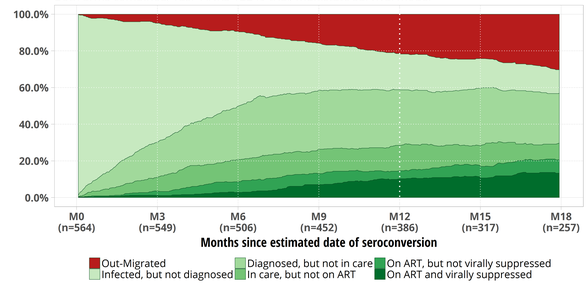
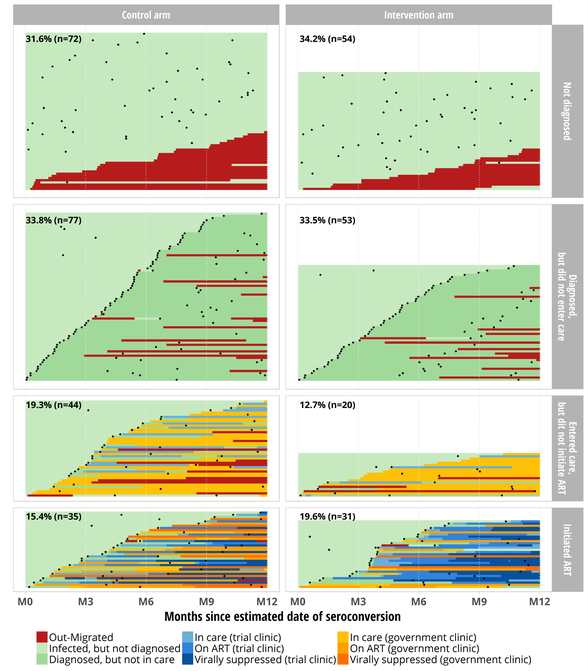


Fig. 2. Detailed individual HIV care trajectories (first year after seroconversion, n=386)
Stratified by arm and presentend in four sub-groups, TasP ANRS 12249.
Each row represents one individual. Black dots indicate contacts by a trial field worker (survey rounds).



Results

We observed 636 individuals acquiring HIV in the course of the trial. However, 72 of these cases occurred at an estimated seroconversion date where the participants were not residing in the trial area. Therefore, only 564 seroconversions (244 in intervention arm; 321 in control arm) were retained for the computation of the longitudinal cascade.

Longitudinal cascade of HIV care since HIV seroconversion
At M12, one year after seroconversion, 22% were non resident in the trial area; 20% were resident but not diagnosed; 30% were diagnosed but not actively in care in the trial area; 14% actively in care a local trial or government clinic; 4% on ART but not virally suppressed; and 10% on ART and virally suppressed (Fig. 1).

Care trajectories over the first year after HIV seroconversion
386 (228 in control arm; 158 in intervention arm) seroconverters were observed at least 12 months after seroconversion (Fig. 2).

HIV diagnosis
One-third (33%, 126/386) of these seroconverters was not diagnosed during the first year following HIV seroconversion, including 63% (80/126) who were contacted at least once by a trial field worker but refused to be re-tested.
Among the 67% (260/386) seroconverters who were diagnosed during that 12-month period, 75% (196/260) were diagnosed by a trial field worker; 21% (55/260) in a local government clinic (place of diagnosis being unknown for the remaining 9 participants).

Entry into care (first clinic visit)
For those diagnosed by a trial fieldworker, 23% (45/196) entered care in a trial clinic and 11% (21/196) in a government clinic. Those diagnosed in a local government clinic were, by definition, considered as having enter care the same day.
Overall, only a third of all seroconverters (34%, 130/386), i.e. half of those diagnosed (50%, 130/260), entered HIV care within 12 months after seroconversion: 78 in government clinics and 52 in trial clinics (first clinic visit).

CD4 count at first clinic visit and ART initiation
In trial clinics, baseline CD4 was documented for 48 of 52 and median count was 518 [IQR: 372-637]. 67% (35/52) initiated ART (84%, 21/25 in intervention arm, 52%, 14/27 in control arm, p = 0.0187). CD4 count at first clinic visit was documented for 67 of the 78 who entered care in a government clinic and the median count was 585 [IQR: 340-730]. Only 40% (31/78) initiated ART.
Overall, half of those who entered care (51%, 66/130) initiated ART within 12 months after HIV seroconversion, i.e. 17% (66/386) of all seroconverters.

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Discussion / Conclusion

Data collected through the ANRS 12249 TasP trial constitute a unique opportunity to make a fine description of individual trajectories over time through HIV services.

During the first year following HIV seroconversion, one third of individuals remained undiagnosed, one third discovered his/her HIV-positive status but did not enter care and one third linked to an HIV clinic. Among those linked to a trial clinic implementing treatment regardless of CD4 count, the proportion of seroconverters initiating ART was high.

Overall, the observed cascade of care was clearly suboptimal in seroconverters despite the introduction of UTT services and a trial environment. With only 17% initiating ART within 12 months after seroconversion, we are far from the 81% (90% × 90%) expected by the model of Granich *et al.* (*Lancet* 2009) to eliminate HIV transmission.

This poor outcome was aggravated in this rural setting by out-migration considered here as loss to the cascade. The dynamic between migration, the HIV epidemic and care trajectories through health system requires additional investigations. First, mobility is maybe associated with an higher risk of HIV acquisition, although we don't know with exactitude where seroconversions occurred or the location of seroconverters' sexual partners. Second, mobility could be an obstacle for rapid engagement with care (the proportion of migrants being higher among those not diagnosed).

Newly HIV-infected individuals need time to (re)test and enter HIV clinics, ART initiation and viral suppression being reached once linked to a clinic implementing universal treatment. This is one of the plausible explanations of the lack of effect of the UTT strategy on HIV incidence in our setting.

For a UTT approach to be effective, innovative strategies to identify seroconverters as soon as possible after seroconversion and support them to engage in ART care promptly are required.

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TasP ANRS 12249 Study Group (by alphabetical order):
Kathy Baisley, Eric Balestre, Till Bärnighausen, Brigitte Bazin, Sylvie Boyer, Alexandra Calmy, Vincent Calvez, Marie-Laure Chaix, François Dabis (co-PI), Anne Derache, Hassimiou Diallo, Hermann Donfouet, Rosemary Dray-Spira, Jaco Dreyer, Kamal El Farouki, Ken Freedberg, Andréa Gosset, Kobus Herbst, John Imrie, Maxime Inghels, Collins Iwuji (Coordinator South), Sophie Karcher, Joseph Larmarange, France Lert, Richard Lessells, Thembisa Makowa, Anne-Geneviève Marcelin, Laura March, Kevi Naidu, Colin Newell, Marie-Louise Newell (co-PI), Nuala McGrath, Nonhlanhla Okesola, Tulio de Oliveira, Joanna Orne-Gliemann (Coordinator North), Delphine Perriat, Deenan Pillay (co-PI), Mélanie Plazy, Mélanie Prague, Camélia Protopescu, Claire Rekacewicz, Tamsen Rochat, Bruno Spire, Frank Tanser, Rodolphe Thiébaut, Thierry Tiendrebeogo, Johannes Viljoen, Thembelile Zuma.