Care trajectories among people living with HIV and followed within a universal test and treat programme in rural South Africa (ANRS 12249 TasP trial)

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Background

- Retention in care is essential to optimize antiretroviral treatment (ART) impact on viral suppression and ensure the success of the universal test and treat (UTT) strategy
- In September 2016, South Africa adopted the latest World Health Organization (WHO) guidelines on Antiretroviral therapy (ART) suggesting to start ART immediately after HIV diagnosis, regardless of CD4 count
- Barriers to maintaining patients in care in a UTT setting need to be documented so that appropriate actions may be undertaken to address the difficulties
- The TasP cluster-randomized trial conducted in rural South Africa between 2012 and 2016 provided the opportunity to investigate retention in care among ART-eligible patients within a large UTT programme

Objectives

- To identify care trajectories among patients who linked to care after HIV diagnosis and who were ART-eligible at their first clinic visit
- To investigate factors associated with care trajectories

Methods

Setting:

- The ANRS 12249 TasP is a cluster-randomized trial implemented in the Hlabisa sub-district, located in northern KwaZulu-Natal in South-Africa, which is a largely rural area with scattered homesteads and an estimated HIV prevalence of 29%.
- Trial primary objective was to estimate the impact of immediate ART just after positive diagnosis on HIV incidence among the population of the Hlabisa sub-district.
- All trial participants identified as HIV-infected during home-based HIV testing were referred to trial clinic located at less than 5 km from their homes and offered immediate ART (intervention arm) or according to national guidelines (control arm).
- Clinical follow-up in trial clinics was offered monthly for patients initiating ART and quarterly for patients in pre-ART.

Study population = all HIV-infected patients

- Linked to a trial clinic
- ART-eligible at their first visit
- Having at least 18 months of follow-up at the end of data collection (30th June 2016)
- Still alive after the first three months of follow-up

Outcome variable = Retention in care defined each month as :

- 1 = lost from trial clinic
- 0 = retained in trial clinic

- A patient was considered to be exiting care if:
  - he/she was more than 3 months late for his last appointment
  - he/she was dead or transferred out

Statistical analysis:

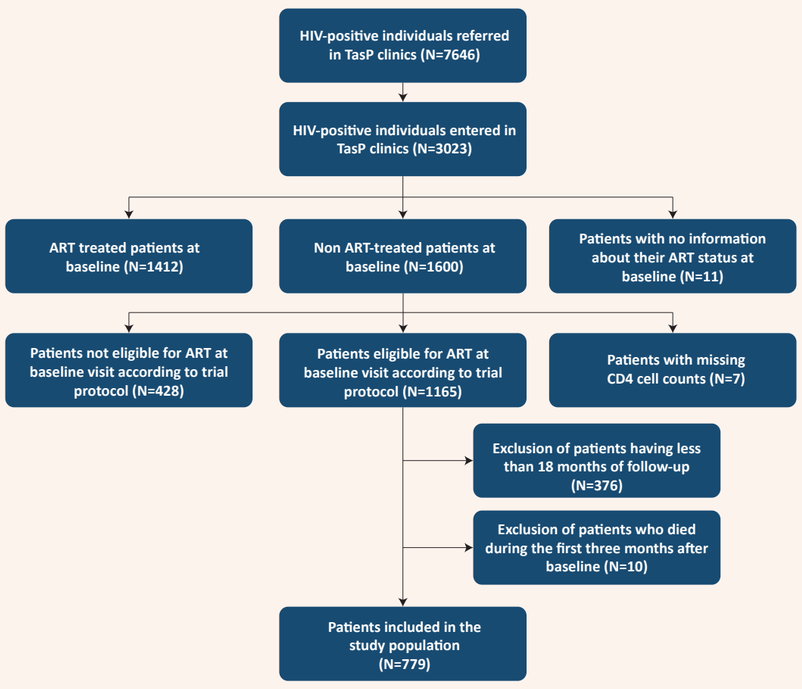
- Care trajectories assessed over 18 months of follow-up were estimated using Group-Based Trajectory Modelling (GBTM)
- GBTM is a semi-parametric mixture modelling procedure for longitudinal data that identify trajectories groups over time and analyse the factors associated with these groups
- The probability of group membership was estimated with a multinomial logistic model
- The optimal number of groups was determined using the Bayesian Information Criterion (BIC)

Covariates (defined at the first clinic visit except ART status defined at month 1):

- Socio-demographic characteristics : gender, age (16-29; 30-39; ≥40), partner
- Economic factors: household wealth assets, employment
- Psychosocial factors: disclosure, social support
- Stigma and treatment perception factors
- Clinical variables: newly diagnosed, CD4
- Geographical accessibility: distance to TasP clinic, and clusters
- Trial arm (intervention versus control)
- ART status at M1

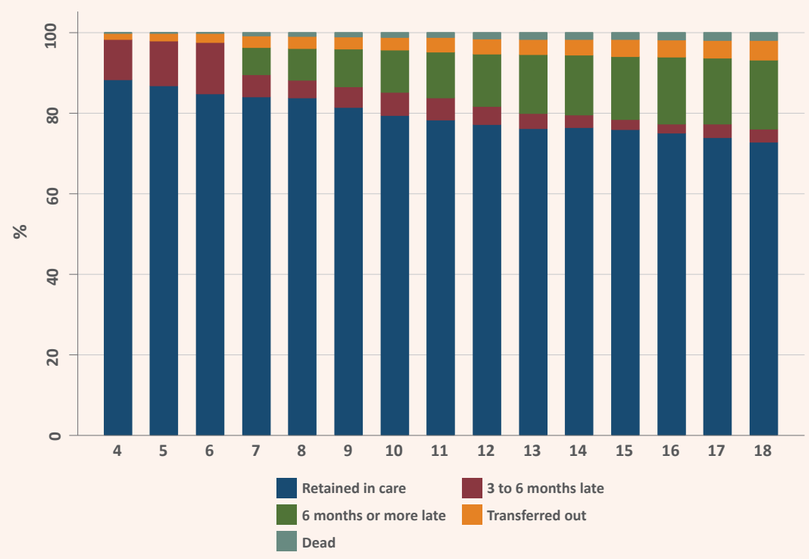
Results

Figure 1: Flow chart of the study population



- **The study population included 779 HIV-individuals**
- **Main characteristics of the study population:**
  - 66.5% entered in TasP clinic within 1 month after referral
  - 70.5% of women
  - Median [IQR] age : 35 [27.5; 46.6] years at the first clinic visit
  - Median [IQR] follow-up period: 7 [4; 11] months
  - 11.8% of patients were newly diagnosed at the time of referral
  - 19.6% had CD4 between 350 and 500 cells/mm3 and 26.3% had CD4 > 500 cells/mm3
  - 53.9% had initiated ART one month after the first clinic visit

Figure 2: Clinical follow-up status of ART-eligible patients at baseline visit from the 4th month to the 18th month of follow-up



- **Four trajectory groups were identified:**
  - **Group 1 = patients always in care:**
    - N=554 (71.1%)
    - 552/554 (99.6%) patients initiated ART during the period of follow up and 62.1% initiated ART within 1 month
    - Median [IQR] number of days between first clinic visit and ART initiation = 23 [15-42]
  - **Group 2 = patients leaving care then returned**
    - N=39 (5.0%)
    - Median [IQR] time to return in care = 4 [3-8] months
    - 33/39 (84.6%) patients initiated ART during the period of follow up and 5.1% initiated ART within 1 month
    - Median [IQR] number of days between first clinic visit and ART initiation = 351 [217-449]
  - **Group 3 = patients leaving care later**
    - N=87 (11.2%)
    - Median [IQR] time of leaving care = 11 [9-13] months
    - 76/87 (87.4%) patients initiated ART during the period of follow up and 56.3% initiated ART within 1 month
    - Median [IQR] number of days between first clinic visit and ART initiation = 24 [16 ; 41]
  - **Group 4 = patients leaving care rapidly:**
    - N=99 (12.7%)
    - Median [IQR] time of leaving care = 4 [4-6] months
    - 44/99 (44.4%) patients initiated ART during the period of follow up and 25.3% initiated ART within 1 month
    - Median [IQR] number of days between first clinic visit and ART initiation = 27.5 [15.5-49.5]

Figure 3: Follow-up trajectories in TasP clinics from the 4th to the 18th month of follow-up among ART-eligible patients at baseline visit

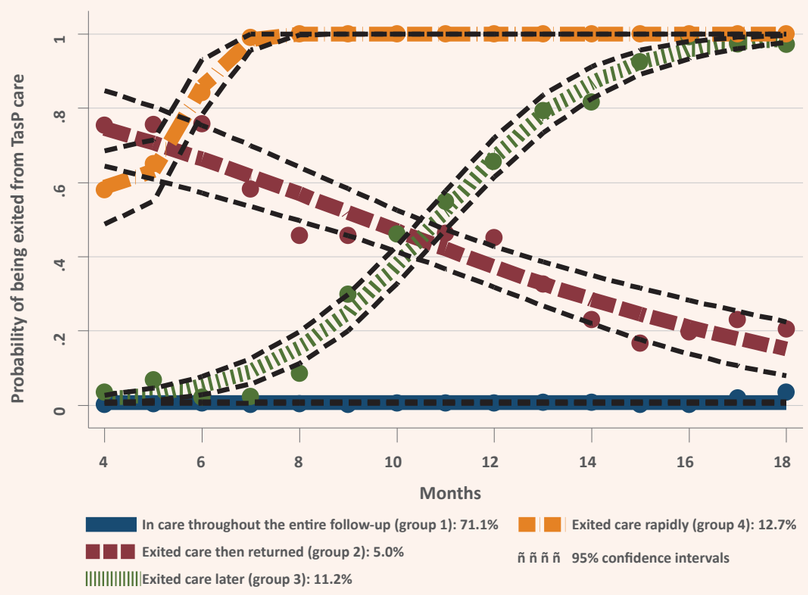


Figure 4: Clinical follow-up status of ART-eligible patients at baseline visit from the 4th month to the 18th month of follow-up, by trajectory group

Table 1: Factors associated with trajectory groups (N=738)

	Group 1 (Always in care) (ref.)	Group 2 (Leaving care then returned)	Group 3 (Leaving care later)	Group 4 (Leaving care rapidly)
Risk factors – OR [95% CI]				
Female & social support		1.00	1.00	1.00
Female & no social support		2.12 [0.7,6.2]	0.56 [0.2,1.4]	2.22* [1.2,4.3]
Male & social support		3.45** [1.4,8.3]	1.66 [0.9,3.1]	1.47 [0.8,2.8]
Male & no social support		3.01 [0.8,11.3]	1.55 [0.6,3.8]	1.59 [0.6,4.0]
+40 years old		1.00	1.00	1.00
30-39 years old		0.96 [0.3,2.8]	2.81** [1.3,5.9]	1.24 [0.6,2.5]
16-29 years old		3.43** [1.4,8.4]	4.80*** [2.4,9.8]	3.92*** [2.1,7.2]
Having a regular partner		1.00	1.00	1.00
No regular partner		2.82* [1.1,6.9]	1.28 [0.6,2.5]	1.62 [0.9,3.0]
Not newly diagnosed at referral		1.00	1.00	1.00
Newly diagnosed		0.90 [0.2,3.5]	5.62*** [3.0,10.7]	4.40*** [2.3,8.4]
CD4≤350		1.00	1.00	1.00
CD4 between]350-500]		7.81*** [2.6,23.4]	0.73 [0.4,1.5]	0.73 [0.4,1.4]
CD4>500		5.11** [1.7,15.5]	0.79 [0.4,1.5]	0.77 [0.4,1.4]
Not on ART at M1		1.00	1.00	1.00
On ART at M1		0.03*** [0.0,0.2]	0.80 [0.5,1.3]	0.17*** [0.1,0.3]

**** p<0.001 **p<0.01 *p<0.05*

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Conclusion

- About three quarters of patients were retained in care
- But a significant proportion of patients exited care at different follow-up times :
  - 12.7% exited care rapidly (in majority within 4-6 months after the first clinic visit)
  - 11.2% exited care later (in majority within 9-13 months after the first clinic visit)
  - 5% exited care and then returned
- No arm effect (intervention vs. control arm) but initiating ART rapidly (within the first month after the first clinic visit) was a major protective factor of exiting care
- Newly HIV diagnosed and young patients had a higher risk of exiting care
- Lack of social support was a risk factor of exiting care rapidly for women
- Men were at higher risk of exiting care and returning

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