HIV care trajectories in the era of Universal Test-and-Treat in rural South Africa

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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 showed low rates of early linkage to HIV care and antiretroviral treatment (ART) and no significant reduction in cumulative incidence by arm (immediate vs deferred ART) [1].
UTT strategies require that HIV-infected individuals enter care and start ART as soon as possible after diagnosis. Little is known yet about the care continuum in UTT contexts. We aimed to describe the timing and sequencing of individual HIV care statuses from clinic referral to viral suppression by identifying groups of individuals with similar care trajectories and identifying factors associated with each group.

Methods

TasP trial procedures

In this rural area where HIV prevalence reaches 30%, resident members aged ≥16 years old were offered rapid HIV testing at home, every six months between March 2012 and June 2016. Those testing HIV-positive or that 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 governmental clinics where treatment was offered according to national guidelines.

Study population

The analysis was restricted to individuals ever referred to HIV care in a trial clinic, not already in HIV care in a local governmental clinic at time of their first referral to a trial clinic and that were observed at least 18 months after the date of referral (death and out-migration being considered as right census events).

HIV care trajectories

An individual HIV care trajectory was defined as the succession of the daily HIV care statuses experienced following referral to a trial clinic.

Computation of daily HIV care statuses

Clinic visits, ART prescriptions, CD4 counts, viral loads (collected both in trial clinics and in local governmental clinics, linked at individual level with the authorization of the University of KwaZulu Natal ethics committee) were used to estimate the daily position of each individual through the HIV care continuum, from clinic referral (M0) to M18. The care statuses were: not in care, in care but not on ART, on ART but not virally suppressed (undocumented viral load or viral load over 400 copies/µL), on ART and virally suppressed.

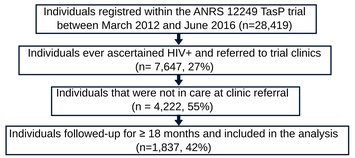
Statistical analysis

1. Identification of care trajectories groups: we used state sequence data analysis to identify homogeneous care trajectories groups: (i) a distance matrix between sequences was computed by optimal matching; (ii) sequences were classified hierarchically using Wald algorithm; (iii) the obtained dendrogram was partitioned based on the highest relative loss of inertia criterion.
2. Description of care trajectories groups: we described the different groups by depicting the timing and sequencing of major care events: entry into care, ART initiation, viral suppression and exit of care.
3. Analysis of factors associated with care trajectories groups: a multinomial logistic regression was used to identify the profile of each group in terms of individual and cluster characteristics.

Results

1,837 HIV+ participants were included (Fig. 1). Median age was 34 years (interquartile range: 27-45), 74% were female.

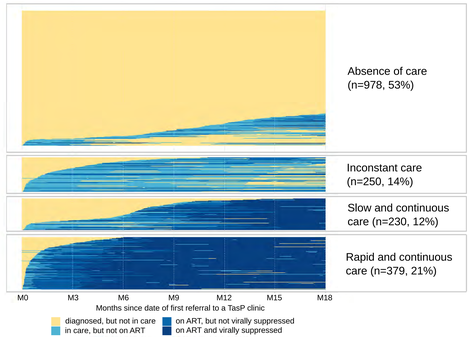
Fig. 1. Flow chart of inclusion of the study population (ANRS 12249 TasP trial, rural South Africa)



Description of care trajectories groups

The quantitative comparison of similarities between care trajectories allowed us to identify four homogeneous care trajectories groups (Fig. 2): (i) participants that mostly did not enter care (53%), (ii) participants with inconstant care, visiting a clinic occasionally but leaving care thereafter (14%), (iii) participants that took extensive time at each step of the care continuum (12%) and (iv) participants that rapidly progressed towards continuous care (21%).

Fig.2. Individual care trajectories by care trajectories group, participants to the ANRS 12249 TasP trial that were not already in care when referred to a trial clinic (n=1,837).



ART: antiretroviral treatment. Each horizontal line (Y-axis) represents a unique individual and the height of the group represents its proportion of the studied popul ation. The X-axis represents time since referral to HIV care. The colours represent the daily care statuses.

Analysis of factors associated with care trajectories groups

Participants from the care trajectories group "absence of care" were more likely to be newly diagnosed than those of the "rapid and continuous care" group (never in care and already diagnosed: adjusted odd ratio [aOR] = 0.25, 95% confidence interval [CI] = 0.14-0.43; previously in care but lost to follow up: aOR=0.14, CI = 0.08-0.25) (Tab. 1). They were also more likely to have been allocated to the control arm of the trial (aOR = 0.61, CI = 0.47-0.82). Similar results were found for participants to the "inconstant care" group (never in care and already diagnosed: aOR = 0.31, CI = 0.16-0.60; previously in care but lost to follow up: aOR = 0.36, CI = 0.18-0.71). On the contrary, participants from the care trajectories group "slow and continuous care" didn't present significant differences in terms of HIV care history when compared to those of the "rapid and continuous care" group. They were not significantly more likely to have been allocated to the control arm of the trial. Moreover, they were more likely to live in an area where the HIV prevalence was less than the median (35.3%) (HIV prevalence ≥35.3%: aOR: 0.63, CI = 0.43-0.88).

Tab.1. Adjusted multinomial logistic regression model with "rapid and continuous care" as the reference category, ANRS 12249 TasP trial, rural South Africa, 2012-2016 (n=1,835)

	"Absence of care" (n= 977) vs "rapid and continuous care" (n=379)		"Inconstant care" (n= 250) vs "rapid and continuous care" (n=379)		"Slow and continuous care" (n=229) vs "rapid and continuous care" (n=379)	
	aOR [CI95%]	p-value	aOR [CI95%]	p-value	aOR [CI95%]	p-value
HIV care history						
HIV care status at clinic referral						
Never in care, newly diagnosed in TasP	1		1		1	
Never in care, already diagnosed	**0.25 [0.14-0.43]**	**<0.01**	**0.31 [0.16-0.60]**	**<0.01**	1.19 [0.49-2.88]	0.70
Previously in care but lost to follow up	**0.14 [0.08-0.25]**	**<0.01**	**0.36 [0.18-0.71]**	**<0.01**	1.40 [0.57-3.43]	0.47
Socio-demographic and economic characteristics						
Age (years)						
16-19	1		1		1	
20-29	1.37 [0.69-2.69]	0.37	1.10 [0.48-2.52]	0.82	1.04 [0.42-2.56]	0.86
30-39	0.85 [0.43-1.66]	0.63	0.70 [0.31-1.61]	0.40	0.99 [0.41-2.40]	0.97
40-49	0.67 [0.34-1.32]	0.77	0.45 [0.19-1.07]	0.07	0.57 [0.22-1.42]	0.22
Over 50	**0.40 [0.20-0.78]**	**<0.01**	**0.27 [0.11-0.64]**	**<0.01**	**0.35 [0.14-0.88]**	**0.02**
Household wealth assets						
Low	1		1		1	
Middle	1.03 [0.77-1.37]	0.84	0.71 [0.48-1.04]	0.08	1.14 [0.78-1.66]	0.49
High	**1.42 [1.00-2.01]**	**0.05**	1.08 [0.69-1.69]	0.74	0.94 [0.58-1.53]	0.81
Health system						
Local HIV prevalence (%)						
< 35.3	1		1		1	
≥ 35.3	1.03 [0.77-1.34]	0.85	1.12 [0.77-1.64]	0.55	**0.63 [0.43-0.93]**	**0.02**
Distance from home to the nearest TasP clinic (km)						
< 1	1		1		1	
[1-2[	**1.32 [1.00-1.74]**	**0.05**	1.06 [0.74-1.51]	0.76	1.10 [0.77-1.60]	0.59
≥2	1.35 [0.90-2.01]	0.14	0.61 [0.34-1.10]	0.10	0.61 [0.34-1.07]	0.09
Distance from home to the nearest governmental clinic (km)						
<3	1		1		1	
[3,5[	**0.63 [0.42-0.95]**	**0.03**	1.04 [0.60-1.80]	0.89	1.36 [0.78-2.38]	0.28
[5,7[	**0.47 [0.32-0.69]**	**<0.01**	0.65 [0.38-1.12]	0.12	1.06 [0.62-1.81]	0.82
≥7	**0.53 [0.34-0.82]**	**<0.01**	0.75 [0.41-1.38]	0.4	0.88 [0.47-1.64]	0.69
Trial-specific						
Trial arm						
Control arm	1		1		1	
Intervention arm	**0.61 [0.47-0.80]**	**<0.01**	**0.75 [0.41-1.38]**	**<0.01**	0.72 [0.51-1.01]	0.06

aOR: adjusted odd ratio, 95CI%: confidence interval, ART: antiretroviral treatment

Discussion and conclusion

Complex entry into care in the era of UTT

Our results show a high heterogeneity of the care trajectories of participants to the TasP trial that were not in care at referral to a trial clinic. A vast majority of trial participants experienced difficulties with regard to linkage to care: no linkage to care (group "absence of care"), unsuccessful linkage to care (group "inconstant care") or late linkage to care (≥6 months) (group "slow and continuous care"), confirming that linkage to care is a major point of attrition of the care cascade in this rural area of South Africa [2, 3].
Our study also brings evidence of people's difficulty to be successfully retained on ART: even though TasP participants have blood drawn for a CD4 count once in a clinic, many of them never return to the clinic to initiate ART (and therefore contribute to HIV transmission) [4, 5]. Such result participates in questioning the potential of eliminating CD4 thresholds to increase retention and achieve the full preventive benefits of ART.

Potential of repeat referral to HIV care to improve care trajectories

This work shows that there is an heterogeneity in care trajectories in terms of speed and care utilization patterns, including individuals that never enter care. New diagnosis of HIV infection was strongly associated with suboptimal care trajectories (groups "absence of care" and "inconstant care"). Repeated contacts with health care workers, including repeated referral to HIV clinic-based care, have the potential to re-engage in care people who had previously slipped through the cracks of the continuum of care [6, 7].

Potential of immediate ART to improve care trajectories

Our study shows that the most important factor associated with successful care trajectories is the suppression of the pre-ART period and the delivery of ART regardless of immunological or clinical staging (intervention arm), suggesting that structural characteristics of the health system such as the availability of health services, are more likely to drive people towards successful care trajectories than individual profiles. Interventions to increase demand for immediate ART as well as improved retention on ART are needed [8].

The longitudinal approach of our work highlighted the heterogeneity of individual care utilization behaviours, as well as identified typical patterns in the trajectories. By embracing a person-centred approach, it complements the traditional population-based approaches and brings a new perspective on the features of the leaky HIV care cascade. The present study highlights that, to maximise the impact of UTT strategies, differentiated care and support should be scaled-up.

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