Measuring the Impact of Test and Treat on the HIV Cascade: the Challenge of Mobility

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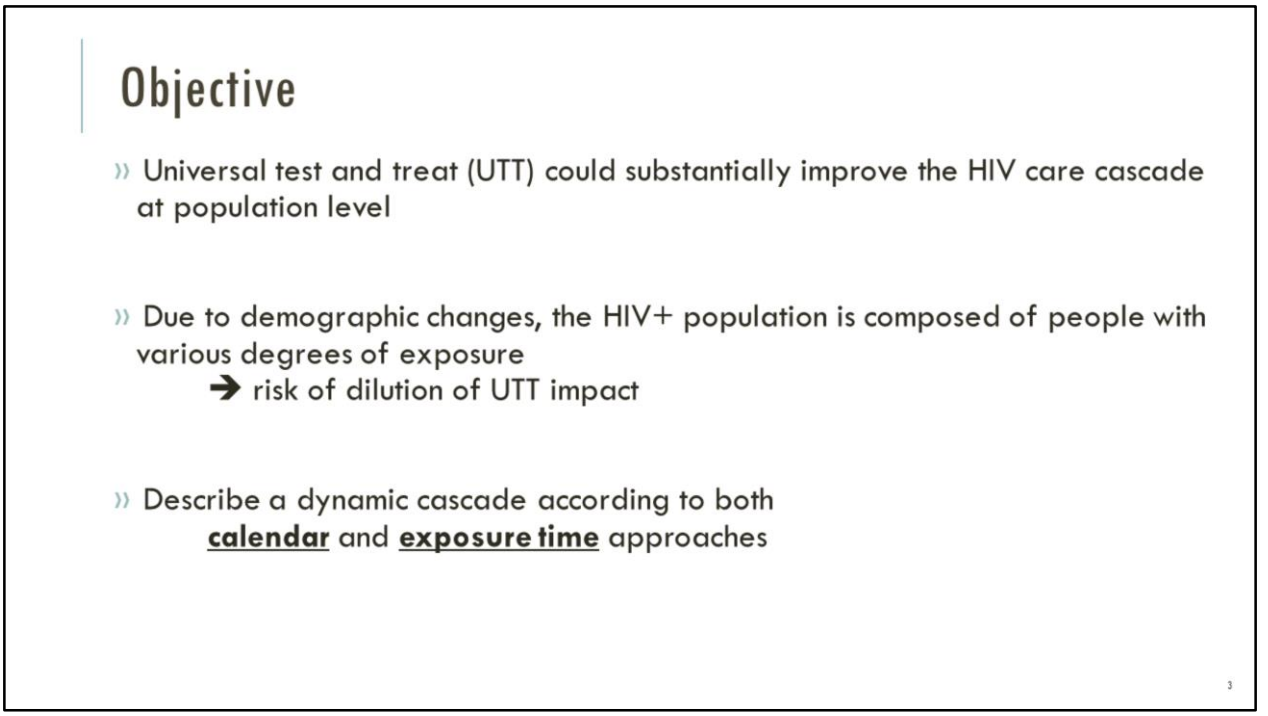
Good morning and thank you for providing me this opportunity to present some preliminary results of the ANRS 12249 Treatment as Prevention TasP trial.

Disclosure

Joseph Larmarange has no financial relationships with commercial entities to disclose.



Universal test and treat (UTT) could substantially improve the HIV care cascade at population level (i.e. the proportion of all HIV-infected people being diagnosed, on ART and virally suppressed at a given date) and thus reduce HIV incidence.

Due to demographic changes, the study population of HIV-infected individuals is composed of people with various degrees of exposure to any UTT interventions. This structural effect could potentially dilute the impact observed at population level of a UTT strategy.

Here, we describe a dynamic cascade according to both calendar and exposure time approaches. I will define these two approaches later in my talk

Context: the ANRS 12249 TasP trial

- Cluster-randomized trial
- Proof of concept study of a Universal Test & Treat (UTT) approach strategy
- Implemented in rural KwaZulu Natal
- Among ~28,000 individuals 16+ years
- HIV prevalence ~24%
- 22 clusters: phased implementation
  - 4 clusters opened in 2012
  - 6 clusters opened in 2013
  - 12 clusters opened in 2014
- The trial will end in June 2016

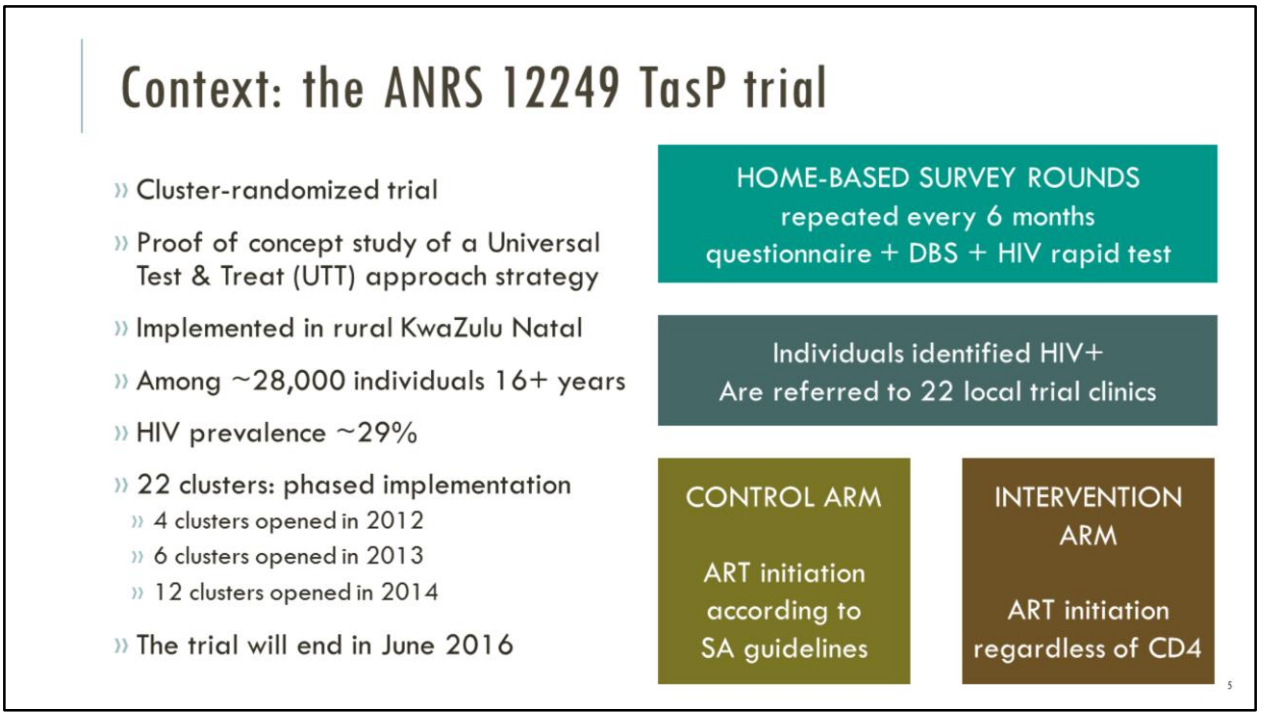
The TasP trial is a cluster-randomized trial implemented to test the hypothesis whether HIV testing of all adult members of a community, followed by immediate ART initiation of all HIV-infected participants, will prevent onward transmission and reduce HIV incidence in this population.

It is implemented in the Hlabisa sub-district, in rural northern KwaZulu-Natal in South Africa.

The size of the eligible trial population is approximatively 28,000 individuals aged 16 or more. The HIV prevalence in the sub-district is one of the highest in the world, with around 24% of adults infected with HIV.

The trial has been implemented over time in 22 clusters: 4 clusters opened in 2012, 6 in 2013 and 12 in 2014.

The trial is still ongoing and we hope to report results this summer.

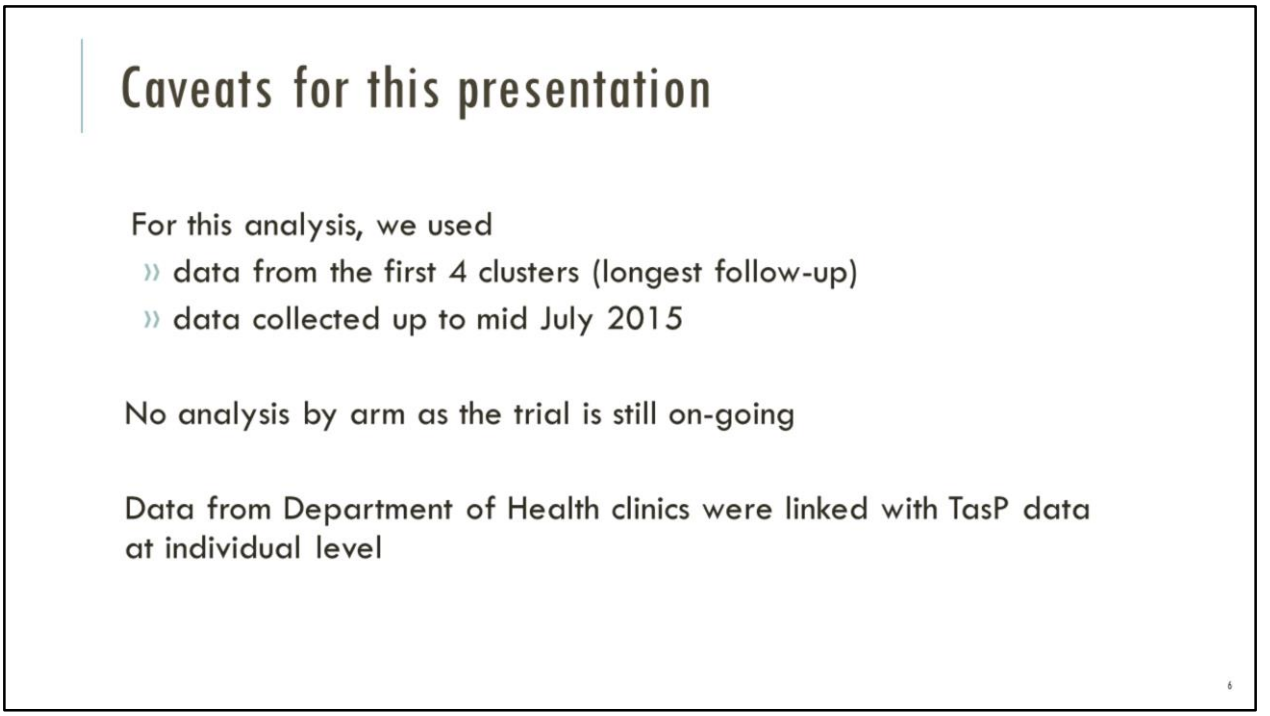


In both trial arms, rounds of home-based HIV testing are repeated every six months. All contacted individuals are invited to complete an individual questionnaire, to provide a blood sample by DBS and to perform a rapid HIV test.

All trial participants identified as HIV-infected are referred to a local TasP trial clinic situated in the trial cluster in which they live.

In the control clusters, HIV infected adults are offered ART according to current South African guidelines. In summary, it was a CD4 count less than 350 at trial start in 2012, and less than 500 CD4 since January 2015.

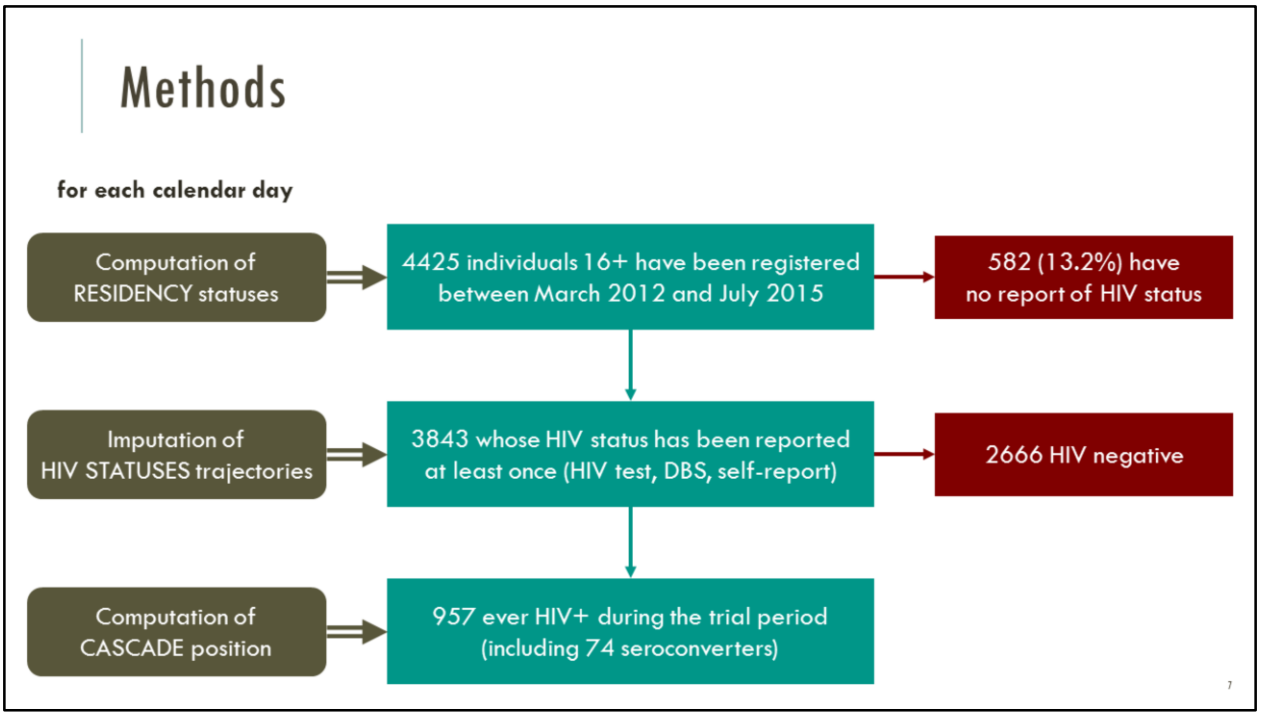
In the intervention clusters, all HIV infected adults are offered the opportunity to begin ART immediately regardless of CD4 count or clinical staging. HIV infected individuals have also the opportunity to receive HIV care in three clinics operated by the Department of Health where ART is offered according to national guidelines only.



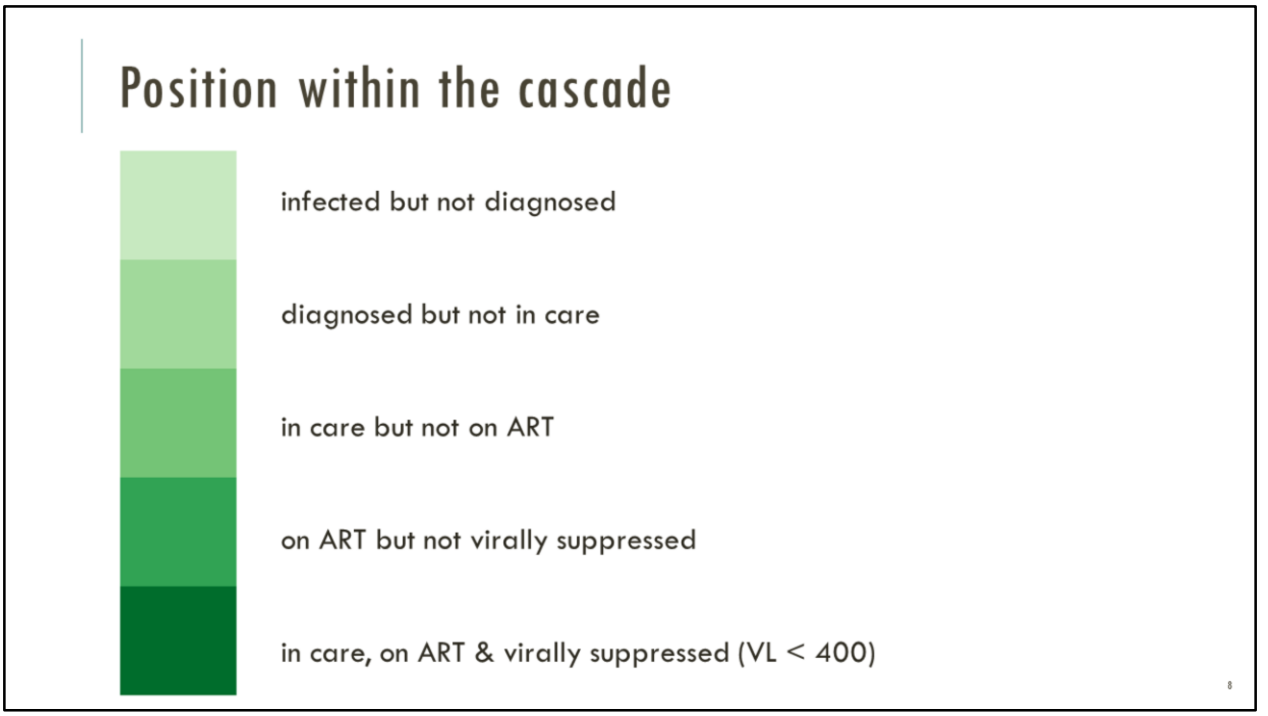
For this presentation, we used preliminary data from the TasP trial, collected in the four initial trial clusters between March 2012 and July 2015.

As the trial is still on-going, we didn't perform any analysis by trial arm.

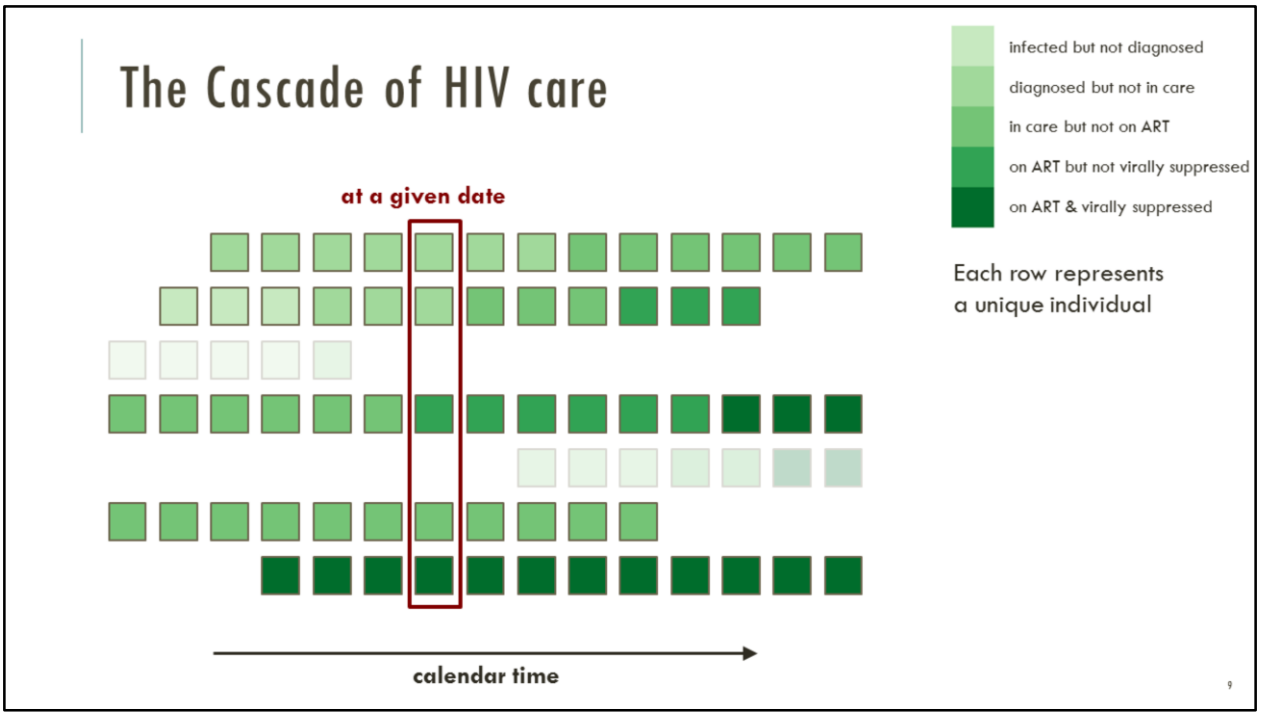
With the authorization of the ethical committee, we were also able to link individual level data from the HIV care and treatment program of the Department of Health with our trial data.



- 4425 individuals 16+ have been registered between March 2012 and July 2015 in the initial 4 clusters.
- Residency status, defined as spending 4 nights per week in the study area, has been computed for each individual and each day, taking into account trial registration, migration and deaths.
- 582 individuals have no report of HIV status, meaning no DBS, no rapid test and no self-report as being HIV infected. They were excluded of this analysis.
- For the 3843 whose HIV status has been reported at least once, HIV statuses trajectories have been imputed, assuming a random seroconversion date between the last negative and the first positive observed statuses. Probability of seroconversion by sex and cluster was also used to estimate possible seroconversion prior a positive status or after a negative one.
- We identified 957 individuals ever HIV positive during the trial, including 74 seroconverters.
- Position within the cascade was estimated for each day using data collected within TasP and data from Department of Health clinics linked at individual level.



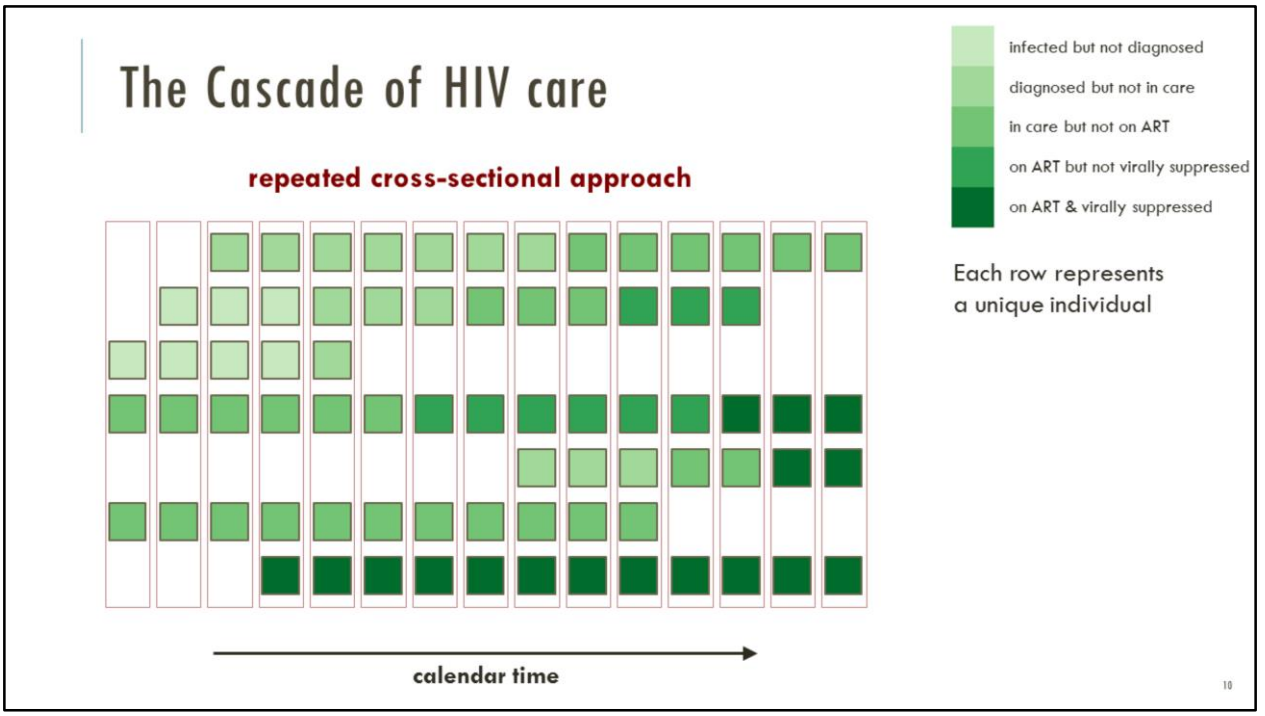
Position within the cascade has been defined in 5 common categories: individuals who are HIV infected but not diagnosed, individuals diagnosed but not currently in HIV care, individuals in HIV care but not on ART, individuals on ART but not virally suppressed, and finally individuals in care, on ART and virally suppressed, the last "90" to echo the 90-90-90 target of UNAIDS. In the results, we will focus more specifically on this last category.



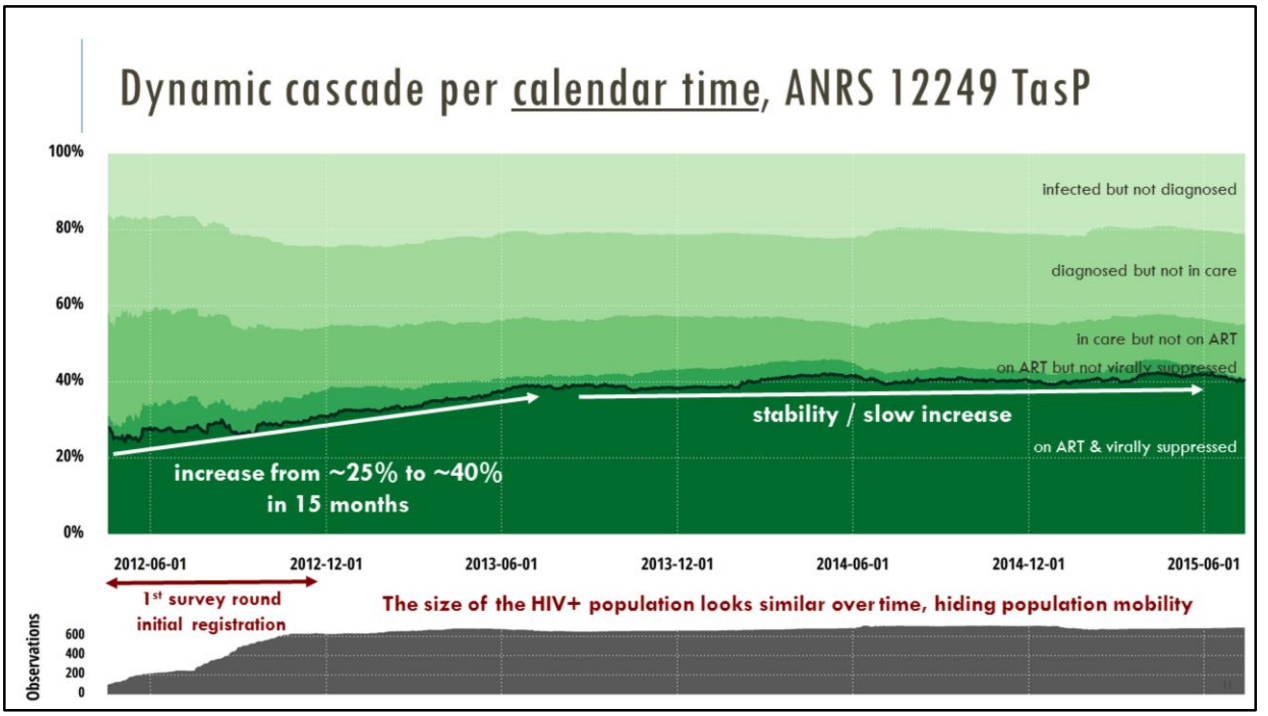
Here, each row represents the successive positions within the cascade of a unique individual, according to calendar time

What is commonly called the “cascade of HIV care” is computed at a given date among the overall population of individuals infected by HIV and residing in the area of interest.

It means that individuals who are not part of that population at that time, because they were not residing in the area or because they were not HIV infected at that time, would be excluded from the computation of the cascade at that date.



The TasP trial collects longitudinal data at different time points. Therefore, we computed a dynamic cascade, for each calendar day between March 2012 and July 2015, adopting a repeated cross-sectional approach.

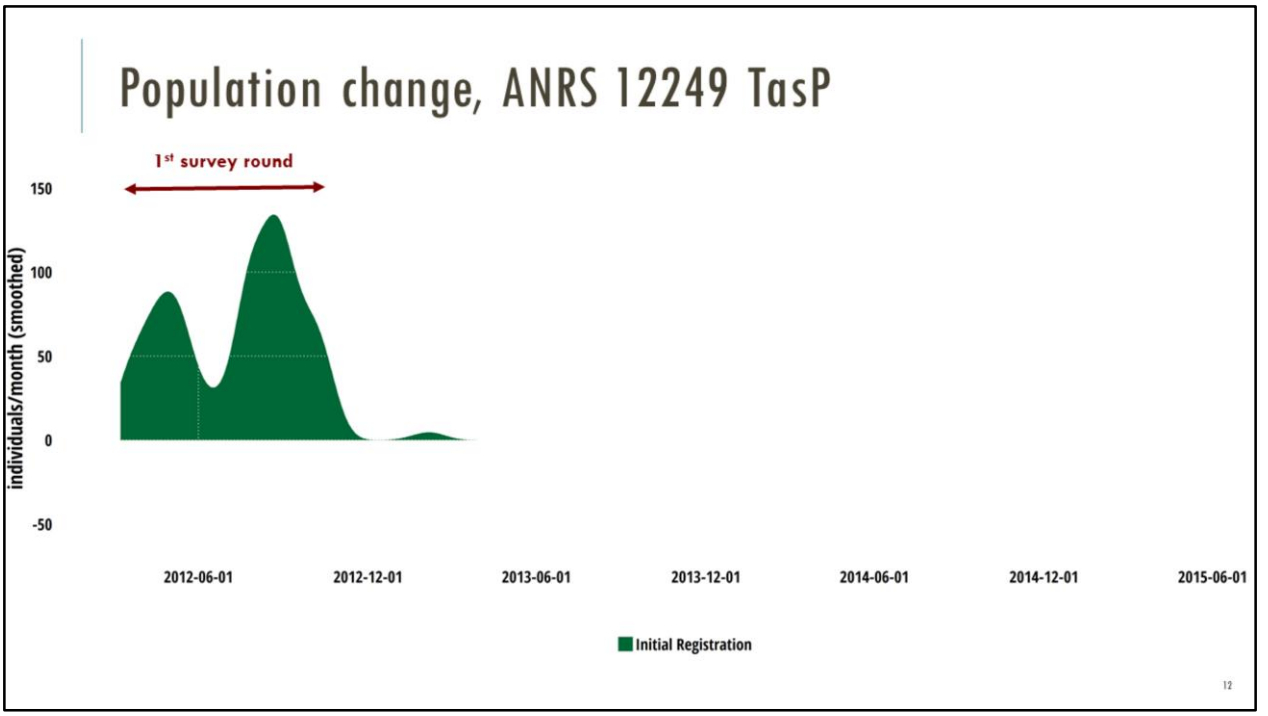


The top graph presents the dynamic cascade per calendar time as observed within the four first clusters of the TasP trial.

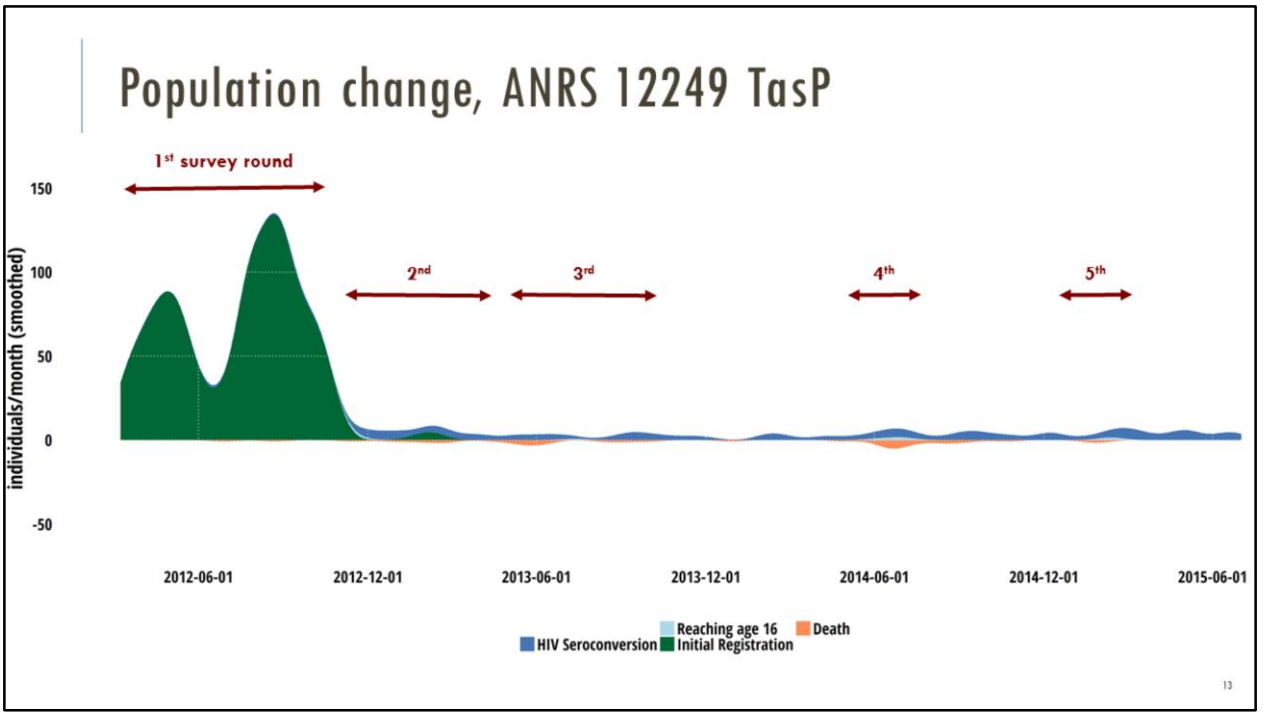
If we focus on the proportion of individuals virally suppressed, we first observed an increase from approximatively 25% to 40% during the first 15 months of the trial.

However, we observed afterwards a slower increase as if we reached a sort of “plateau”.

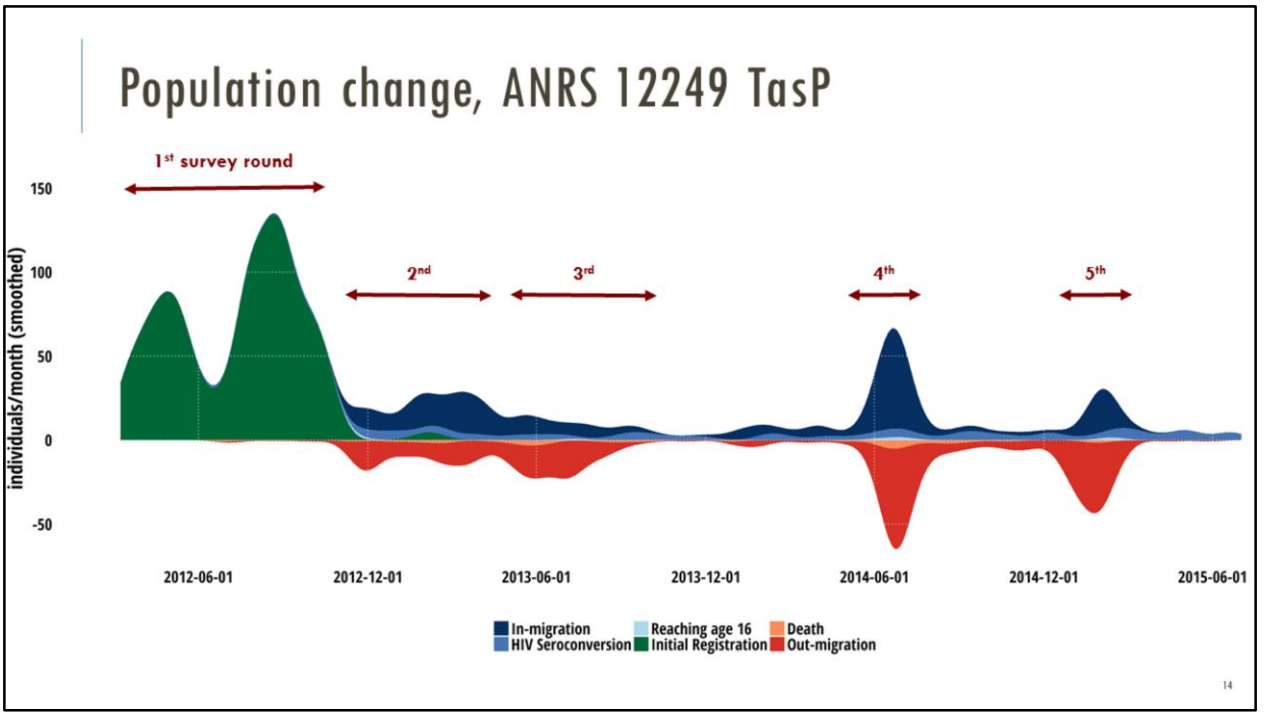
The bottom graph presents the population size. After the first survey round with the initial registration of the resident population, population size looks similar over time. This apparent stability is hiding population mobility.



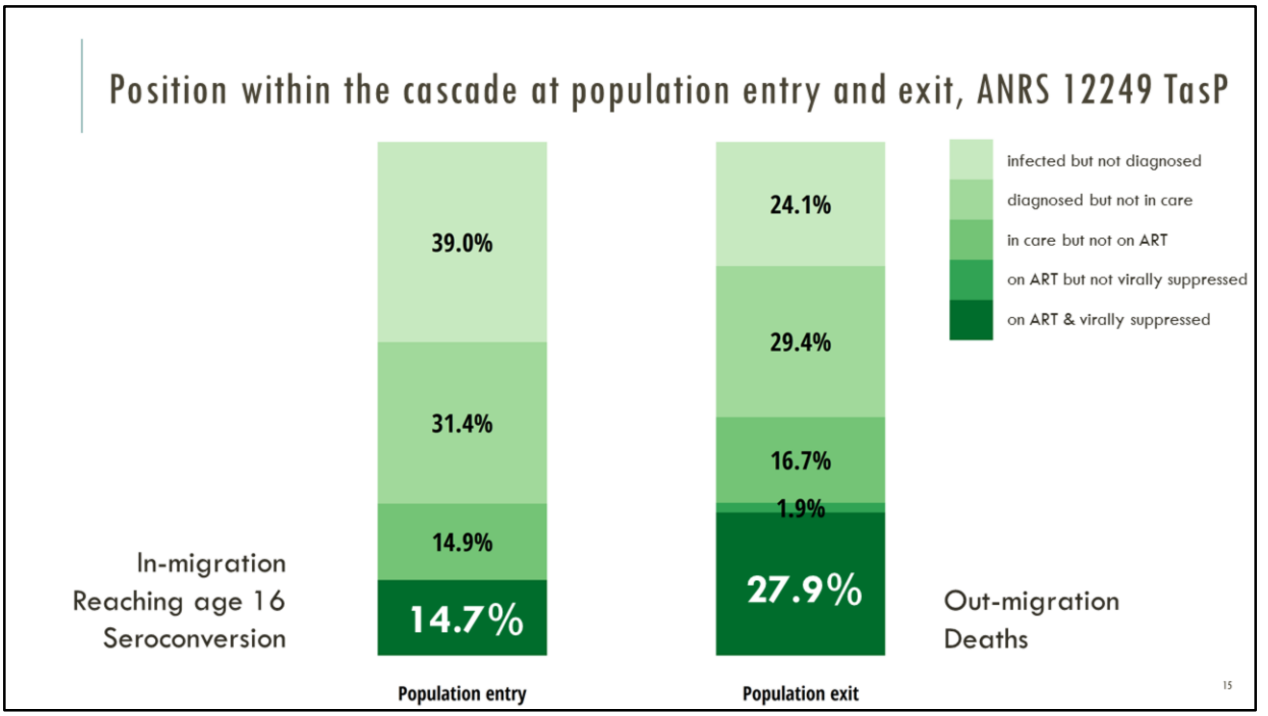
During the first survey round of the trial, fieldworkers registered the resident population aged 16 or more.



In the following survey rounds, the HIV+ population has been changing due to death in orange, few individuals reaching the age of 16 (in light blue) and HIV negative participants acquiring HIV and seroconverting (in blue).

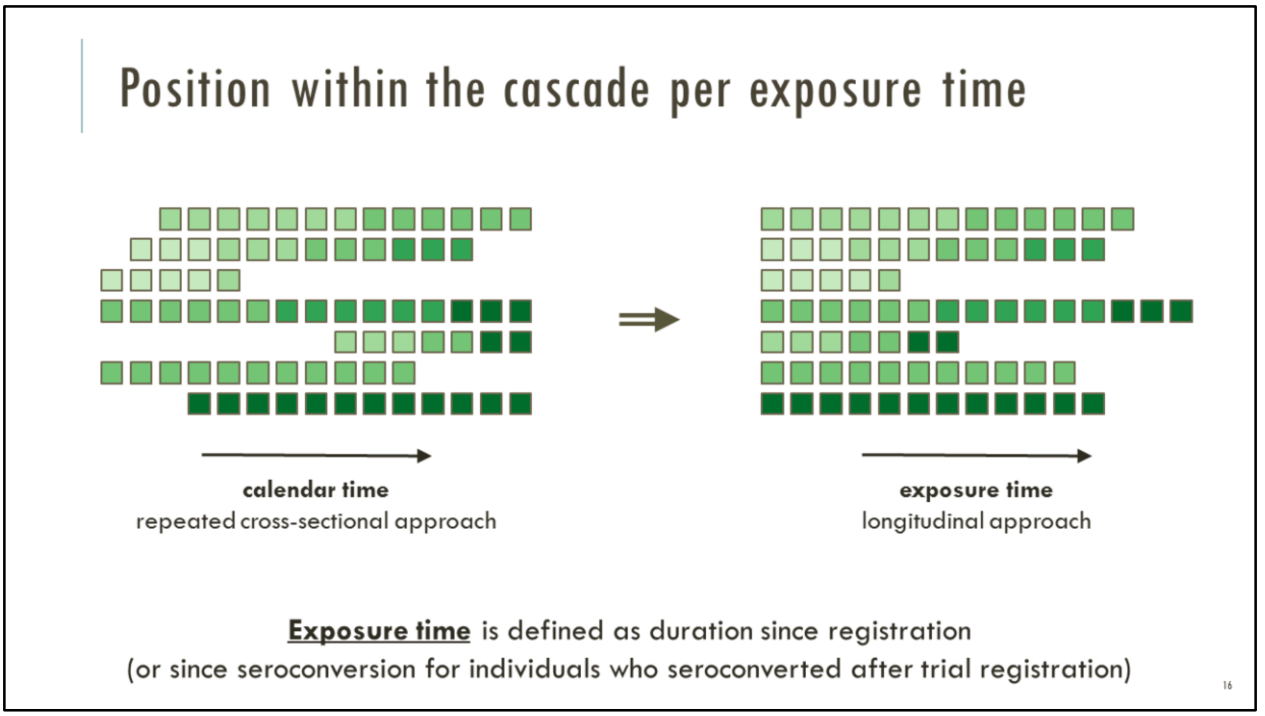


But the major change within the HIV infected population is due to high levels of in- and out-migration from the study area. In-migration is represented in dark blue and out-migration in dark red.

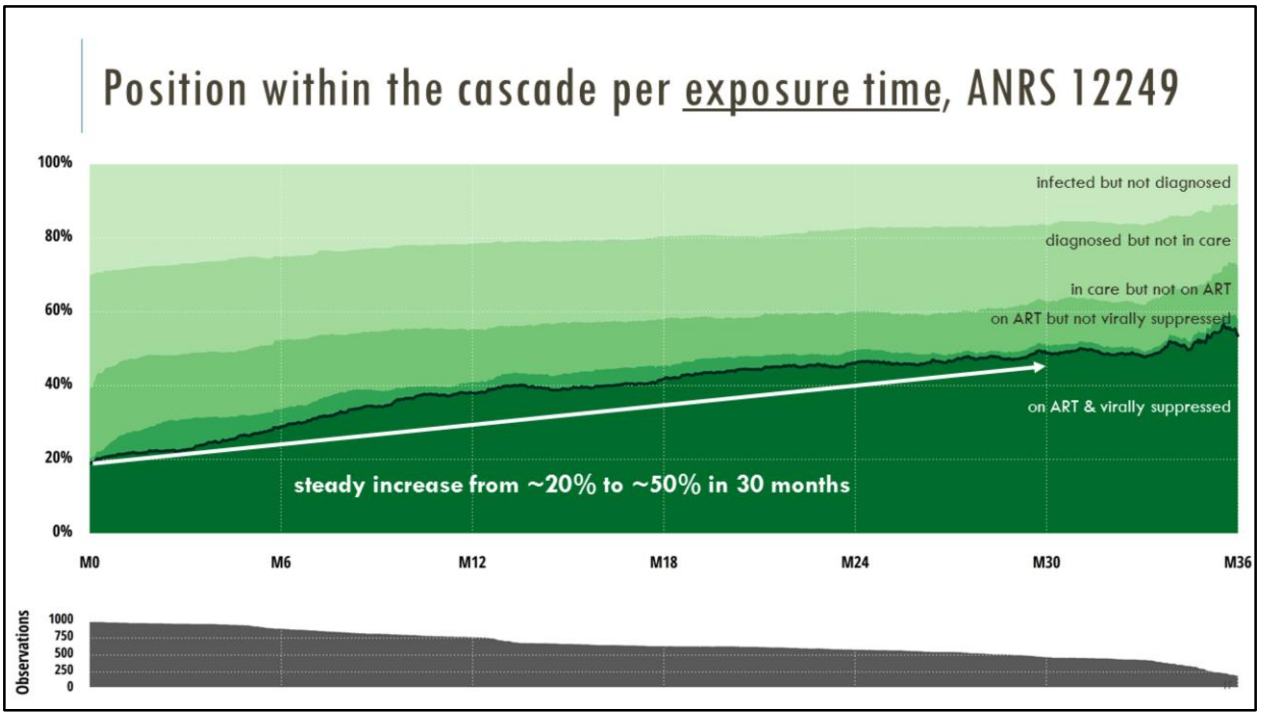


This graph presents the position within the cascade of individuals when they entered or when the exited the resident HIV infected population.

It appears that only 15% of individuals entering are already on ART and virally suppressed vs. 28% for individuals exiting.

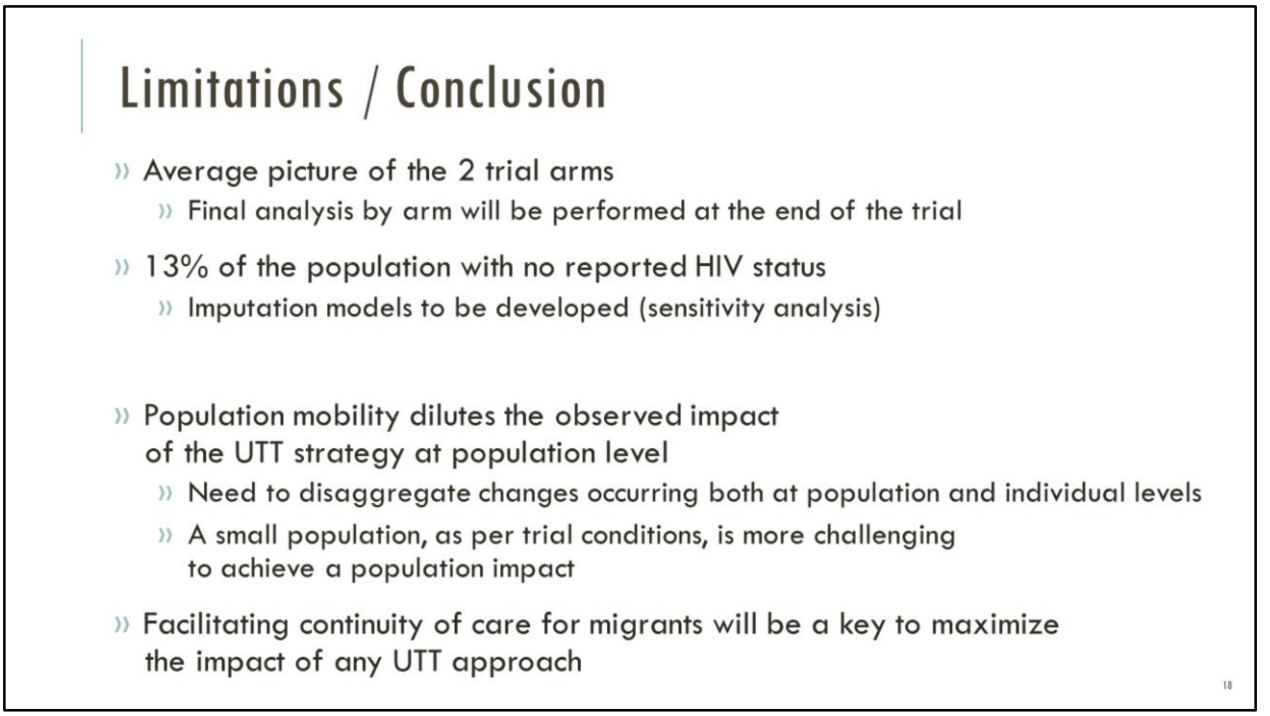


To better understand the trajectories of individuals within the HIV care cascade, we adopted an individual perspective by recalculating the position within the cascade of each individual according to their exposure to the trial interventions. Exposure time is defined as duration since registration or, for individuals who seroconverted after trial registration, duration since seroconversion.



The impact of the trial on individual trajectories within the cascade is higher compared to the population perspective.

In 30 months, the proportion of individuals being virally suppressed increased from 20% to 50%.



Our results provide an average picture of the two trial arms. Final analysis, including comparison by arm, will be performed at the end of the trial, planned in June this year.
We didn't have any HIV status for 13% of the resident population who were excluded from this analysis. These individuals are likely to have different trajectories within the cascade of care. Imputation models and sensitivity analysis are required to investigate how it could impact the cascade picture.

Population mobility dilutes the observed impact of UTT interventions on the cascade at population level. In this high mobile population, we need to disaggregate the impact both at population and individual levels. Working on a small population, as per trial conditions, is more challenging to achieve any population impact.
Our findings also suggest that the impact of a UTT approach could be maximized as long as there is a coordination to facilitate continued access to care when people move. Continuity of care for migrants will be a key for maximizing the impact of any UTT approach.

Thank you for your attention. I would also like to acknowledge all trial participants, Africa center staff, traditional authorities, South African department of health and our funders and sponsors. Thank you.