Temporal trends of population viral suppression in the context of Universal Test and Treat: results from the ANRS 12249 TasP trial in rural South Africa

Joseph Larmarange, Mamadou Hassimiou Diallo, Nuala McGrath, Collins Iwuji, Mélanie Plazy, Rodolphe Thiébaut, Frank Tanser, Till Bärninghausen, Joanna Orne-Gliemann, Deenan Pillay, François Dabis for the ANRS 12249 TasP Study Group
Universal Test and Treat (UTT) aims to maximize PLWHIV on ART and virally suppressed in a community.

According to mathematical modelling, UTT would lead to reduction in HIV incidence.
THE **ANRS 12249 TASP TRIAL**

› One of 5 international trials aiming at evaluating UTT approaches

› **Design:** cluster-randomised trial

› **Timeline:** March 2012-June 2016

› **Study setting:** Hlabisa sub-district
  
  › ~28 000 individuals aged 16+
  
  › isiZulu speaking
  
  › HIV prevalence ~30%
  
  › frequent migration
  
  › low marital rates & late marriage
  
  › only 10% are employed
**TASP TRIAL PROCEDURES**

**Homestead Identification**

**Homestead visit**
1. Registration of resident adults
2. Update of resident members list
3. Exit forms

repeated every ~six months

**Homestead procedures**
1. Individual questionnaires
2. DBS sample (lab tests)
3. Rapid HIV testing

**Trial clinics**
- **Intervention arm**: immediate ART
- **Control arm**: ART according to national guidelines

**Local governmental clinics**
- Matching between trial and governmental database at individual level
- CD4 and viral load results / clinic visits
- ART according to national guidelines

if ascertained HIV+ (rapid test or self-report) referred to trial clinic
TIMING OF FIELbWORK

› 4 clusters (opened in 2012)
› 6 clusters (opened in 2013)
› 12 clusters (opened in 2014)

Light areas indicate the time required to complete the initial census of the population
PREVIOUS RESULTS

› Main results were presented in Durban in 2016 (Iwuji et al. Lancet HIV 2017)

› No significant difference in HIV incidence between trial arms

RESEARCH QUESTION

› Did population viral suppression improve during the course of the trial?

› Differentially by arm?

› According to trial interventions or contextual changes?
**APPROACH: COMPUTATION OF DAILY STATUSES**

28,419 adult residents were registered

- Initial census of the population, 16th birthday, in-migration events, out-migration events and deaths
  - among those residents

- Repeat DBS, repeat rapid tests, HIV-positive self-reports and HIV clinic visits; seroconversion date imputed (random point approach)
  - among those HIV-positive

- Clinic visits, ART prescription, CD4 counts and viral loads; trial clinics and local governmental HIV clinics

For each calendar day:

- **RESIDENCY status** (resident / not resident)
- **HIV status** (HIV positive / negative)
- **HIV CARE position**
  - Viral Suppression (<400)
CLUSTER-LEVEL
POPULATION
VIRAL SUPPRESSION

% being in care, on ART and virally suppressed

Computed at different time points (pre-intervention + daily)
OVERALL RESULTS

At baseline, population viral suppression slightly lower in intervention arm

Significant increase in both arms

A slightly higher increase in intervention arm

No significant difference between arms at the end of the trial
MODELLING POPULATION VIRAL SUPPRESSION

› Mixed linear model
› One record per cluster and per day
› Outcome: cluster-level population viral suppression
› Factors:
  › calendar time
  › time since cluster opening
  › trial arm
  › interaction between trial and time since cluster opening
  › socio-demographic characteristics (cluster-level)
MODEL RESULTS: POPULATION VIRAL SUPPRESSION, TASP ANRS 12249

**Contextual changes**
- Calendar time (2012-2013)
- Calendar time (2014)
- Calendar time (2015-2016)

**Effect of Universal Testing**
- Time since cluster opening (first year)
- Time since cluster opening (second year)
- Time since cluster opening (third year)

**Baseline difference between trial arms**
- Intervention arm (vs. control)

**Effect of Universal ART**
- Interaction of intervention arm on time since cluster opening (first year)
- Interaction of intervention arm on time since cluster opening (second year)
- Interaction of intervention arm on time since cluster opening (third year)

The coefficients correspond to PVS annual change.
LIMITATIONS

- Care received in governmental clinics probably **underestimated** due to participants not matched between governmental and trial datasets.

- Care received in **private sector** or **outside the trial area** not captured.

- 9.5% of trial population with no observed HIV status and excluded from the analysis.

- Sensitivity analysis: results unchanged.
Although suboptimal, the TasP strategy **significantly improved** population viral suppression over time.

Mainly due to **universal testing** rather than **universal treatment**

Increase similar between arms ➔ explain the null effect of HIV incidence

*Changes in treatment guidelines not enough to increase population viral suppression*
ACKNOWLEDGMENTS

ANRS 12249 Study Group (by alphabetical order):
Kathy Baisley, Eric Balestre, Till Bärnighausen, Sylvie Boyer, Alexandra Calmy, Vincent Calvez, François Dabis (co-PI), Anne Derache, Adama Diallo, Hermann Donfouet, Rosemary Dray-Spira, Jaco Dreyer, Ken Freedberg, Andréa Gosset, Kobus Herbst, John Imrie, Collins Iwuji (Coordinator South), Sophie Karcher, Joseph Larmarange, France Lert, Richard Lessells, Thembisa Makowa, Anne-Geniève 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, Camélia Protopescu, Bruno Spire, Frank Tanser, Rodolphe Thiébaut, Thierry Tiendrebeogo, Joanna Viljoen, Thembelile Zuma.

• Trial participants
• Africa Centre staff
• Traditional Authorities
• Department of Health, South Africa
• Merck/Gilead