The impact of Universal Test and Treat on HIV incidence in a rural South African population

François DABIS
for the ANRS 12249 TasP study team
Disclosures

- Research grants from Gilead, MSD
- Study drugs were provided by Merck / Gilead
ART as prevention

- Plasma HIV viral load: primary determinant of the risk of HIV transmission (*Quinn, NEJM 2000*)

- Good evidence that ART reduces sexual transmission of HIV in serodiscordant stable couples (*Cohen, NEJM 2011*)

What is the effectiveness of using ART as prevention (TasP) or Universal Test and Treat (UTT) at the population level in an HIV hyper-endemic community in rural KwaZulu-Natal?

- Population well characterized in terms of ART use and effect on transmission (*Tanser, Science 2013 & Oldenburg, CID 2016*)
ANRS 12249 TasP trial

- **Objective:** To evaluate the effect of early ART, initiated irrespective of CD4 count criteria, on HIV incidence in the general population in the same setting.

- **Design:** Cluster-randomized trial (*Iwuji et al. Trials 2013*; *Orne-Gliemann et al. BMC Public Health 2015*).

### 6-monthly rounds of home-based HIV-testing

**Intervention**
- Treat all HIV+ individuals regardless of CD4 count and clinical stage.

**Control**
- Treat all HIV+ individuals according to South African guidelines
  - (≤350 CD4, WHO stage 3 or 4 until Dec 2014, ≤500 since Jan 2015)

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**Phase 1:** 2012 - 2014

**Phase 2:** 2014 - 2016
**Trial area**

**Country:** South Africa  
**Region:** KwaZulu-Natal  
**Sub-district:** Hlabisa  
- 1,430 Km²  
- 228,000 Zulu speaking people

4 clusters  
+ 6 clusters  
+ 12 clusters  
**Total of 22 clusters**
Trial procedures

Homestead identification (GPS)
Trial procedures

Homestead identification (GPS)

Homestead visit every 6 months
1. Head of household verbal consent
2. Registration of individuals

Inclusion criteria
- Resident member of a household
- 16 years or older
- Able to give informed consent

Exclusion criteria
- Untreated psychiatric disorder
- Neurological impairment
Trial procedures

**Homestead identification (GPS)**

**Homestead visit every 6 months**
1. Head of household verbal consent
2. Registration of individuals

**Homestead procedures**
1. Household assets questionnaire
2. Individual questionnaire
3. DBS sample, rapid HIV testing
4. TasP card
Trial procedures

Homestead identification (GPS)

Homestead visit every 6 months
1. Head of household verbal consent
2. Registration of individuals

Homestead procedures
1. Household assets questionnaire
2. Individual questionnaire
3. DBS sample, rapid HIV testing
4. TasP card

TasP clinic
- One per cluster (45 min walk max)
- HIV care and treatment according to arm
- Study questionnaires

HIV +
HIV -

Referral to TasP clinics
Repeat HIV test 6 mths later
ANRS 12249 TasP trial

primary outcome

- Cumulative incidence of new HIV infections
  - Powered to detect a 34% reduction in incidence in intervention arm vs control arm
- Measured on longitudinal/repeat Dried Blood Spot (DBS) using HIV-ELISA
- Computed among those individuals with a first HIV-negative test
- Compared by Poisson regression taking into account cluster effect
Results: UTT is feasible and acceptable
### Description of trial population, HIV burden and ART coverage at the beginning of the trial

<table>
<thead>
<tr>
<th>Socio-demographics at registration</th>
<th>Intervention (n=13,236)</th>
<th>Control (n=14,917)</th>
<th>Total (n=28,153)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>37%</td>
<td>38%</td>
<td><strong>37%</strong></td>
</tr>
<tr>
<td>Median age in years (IQR)</td>
<td>30 (22-50)</td>
<td>30 (22-49)</td>
<td><strong>30 (22-50)</strong></td>
</tr>
</tbody>
</table>

**Baseline cluster characteristics**

<table>
<thead>
<tr>
<th>Average HIV prevalence (95% CI) (DBS)</th>
<th>Intervention</th>
<th>Control</th>
<th>Total</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>30% (29-31)</td>
<td>31% (30-32)</td>
<td><strong>31% (30-31)</strong></td>
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**ART coverage**

<table>
<thead>
<tr>
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<th>Control</th>
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<tr>
<td>ART coverage*</td>
<td>31%</td>
<td>36%</td>
<td><strong>34%</strong></td>
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*Estimated from Department of Health data*
# Trial process indicators

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<tr>
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<th>Control</th>
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<tbody>
<tr>
<td><strong>Contact</strong> rate per survey round (range)</td>
<td>61% – 84%</td>
<td>66% – 90%</td>
</tr>
<tr>
<td><strong>HIV ascertainment</strong> rate per survey round (range)</td>
<td>70% – 83%</td>
<td>77% – 88%</td>
</tr>
<tr>
<td><strong>Entry into care</strong> among individuals not in care</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Within 3 months</td>
<td>28%</td>
<td>29%</td>
</tr>
<tr>
<td>Within 6 months</td>
<td>36%</td>
<td>37%</td>
</tr>
<tr>
<td>Within 12 months</td>
<td>47%</td>
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</table>
## Trial process indicators (ctd)

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<tr>
<td><strong>ART initiation within 3 months in TasP clinics</strong> among patients not on ART at first TasP clinic visit</td>
<td>91%</td>
<td>52%</td>
</tr>
<tr>
<td><strong>Viral load</strong> &lt;400 copies/ml among patients not on ART at first TasP clinic visit**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>At month 6</td>
<td>93%</td>
<td>92%</td>
</tr>
<tr>
<td>At month 12</td>
<td>95%</td>
<td>95%</td>
</tr>
<tr>
<td><strong>Estimated ART coverage</strong>* (as of 1\textsuperscript{st} January 2016)</td>
<td>45%</td>
<td>43%</td>
</tr>
<tr>
<td><strong>ART coverage improvement since baseline</strong></td>
<td>+14</td>
<td>+7</td>
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</table>

*Estimated from TasP + Department of Health data*
Incidence analysis - flowchart

Intervention arm

Registered
N = 13,296

Ever contacted
N = 12,449 (94%)

First DBS test negative
N = 8,349

Control arm

Registered
N = 14,954

Ever contacted
N = 13,912 (95%)

First DBS test negative
N = 9,233

No result = 500
First confirmed DBS test positive = 4,179

No result = 535
First confirmed DBS test positive = 3,565
**HIV incidence**

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<th>Person-years</th>
<th>Incidence for 100 person-years</th>
<th>95% CI</th>
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<tr>
<td>Control</td>
<td>268</td>
<td>11,787</td>
<td><strong>2.27</strong></td>
<td>2.00-2.55</td>
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<tr>
<td>Intervention</td>
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<td><strong>TOTAL</strong></td>
<td><strong>495</strong></td>
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## ANRS 12249 TasP: HIV incidence comparison

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### Adjusted risk ratio*

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<th>95% CI</th>
<th>P-value</th>
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<tr>
<td>Intervention vs control</td>
<td>0.95</td>
<td>0.79-1.14</td>
<td>0.5821</td>
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*Estimated with Poisson regression, adjusted on sex, age, change in national ART guidelines, baseline cluster HIV prevalence and ART coverage*
Estimated cascade of care

UNAIDS target

- 90.0% diagnosed
- 90.0% on treatment
- 90.0% virally suppressed

= 72.9%
ANRS 12249 TasP - Estimated cascade of care

UNAIDS target
- Diagnosed: 90.0%
- On treatment: 90.0%
- Virally suppressed: 90.0%
= 72.9%

TasP trial (1st January 2016)

Control
- Diagnosed: 93.4%
- On treatment: 46.0%
- Virally suppressed: 93.6%
= 40.2%

Intervention
- Diagnosed: 92.3%
- On treatment: 49.2%
- Virally suppressed: 93.4%
= 42.4%
Summary

- No significant difference in HIV incidence between trial arms
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- Nearly all individuals living with HIV in the trial communities are aware of their HIV status
- More than 90% individuals on ART achieved viral suppression
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- No significant difference in HIV incidence between trial arms
- Nearly all individuals living with HIV in the trial communities are aware of their HIV diagnosis
- More than 90% individuals on ART achieved viral suppression
- Sub-optimal and delayed linkage to care
- Small ART coverage difference between arms
Further analyses

- Specific secondary outcomes: clinical, behavioural, socio-economic, health services
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- Profile of people reached and not reached by TasP intervention
- Reasons for non linkage
  - Models of care
  - Community attitudes and stigma....
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- Profile of people reached and not reached by TasP intervention
- Reasons for non linkage
  - Models of care
  - Community attitudes and stigma....
- In and out migrations
- Location of sexual partners
- Community viral load and phylogeny
Acknowledgements

- Trial participants
- Africa Centre staff
- Traditional Authority
- Department of Health, South Africa
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