Uptake of home-based HIV testing, linkage to care, and community attitudes about ART in rural KwaZulu-Natal, South Africa: descriptive results from the first phase of the ANRS 12249 TasP Cluster-Randomised Trial

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**Abstract**

**Background:** The 2015 WHO recommendation of antiretroviral treatment (ART) for all immediately following HIV diagnosis is partially based on anticipated impact on HIV incidence in the surrounding population. We investigated this approach in a cluster-randomised trial in a high HIV prevalence setting in rural KwaZulu-Natal. We present findings from the first phase of the trial and report on uptake of home-based HIV testing, linkage to care, uptake of ART and community attitudes about ART.

**Methods and findings:** Between 03/2012 and 05/2014, five clusters in the intervention arm (immediate ART offered to all HIV-positive adults) and five clusters in control arm (ART offered according to national guidelines, i.e. CD4 ≤350 cells/µL) contributed to the first phase of the trial. Households were visited six monthly. Following informed consent and administration of study questionnaire, each resident adult (≥ 16 years) was asked for a finger prick sample, which was used to estimate HIV prevalence, and offered a rapid HIV test using a serial HIV testing algorithm. All HIV-positive adults were referred to the trial clinic in their cluster. Those not linked to care three months after identification were contacted by a linkage-to-care team. Study procedures were not blinded.

12,894 adults were registered eligible for participation (5,790 in intervention; 7,104 in control), of whom 9,927 (77.0%) were contacted at least once during household visits. HIV status was ever ascertained for a total of 8,233/9,927 (82.9%), including 2,569 ascertained HIV-positive (942 tested HIV-positive and 1,627 reported a known HIV-positive status). Of the 1177 HIV-positive individuals not previously in care and followed for at least six months in the trial, 559 (47.5%) visited their cluster trial clinic within six months. In the intervention arm, 89% (194/218) initiated ART within three months of their first clinic visit. In the control arm, 42.3% (83/196) had a CD4 count of ≤ 350 at first visit, of whom 92.8% initiated ART within three months.

93% (8,802/9,460) of participants agreed with the statement they would want to start ART as soon as possible if HIV-positive. Estimated baseline HIV prevalence was 30.5% (2,028/6,656) (95% CI: 25.0%, 37.0%).

HIV prevalence, uptake of home-based HIV testing, linkage to care within six months or initiation of ART within three months in those with CD4 ≤ 350 did not differ significantly between intervention and control clusters. Selection bias related to non-contact could not be entirely excluded.

**Conclusion:** Home-based HIV testing was well-received in this rural population, although men were less easily contactable at home; immediate ART was acceptable, with good viral suppression and retention. However, only about half of HIV-positive people accessed care within six months of being identified and nearly two-thirds by 12 months. The observed delay in linkage to care would limit individual and public health ART benefits.

The trial is registered at ClinicalTrials.gov, numberNCT01509508

**Author Summary**

**Why Was This Study Done?**

* A study in stable sexual partners in which one partner was HIV-positive and the other partner HIV negative and both partners had disclosed to each other showed that if the HIV positive partner was on antiretroviral therapy, there was a 96% reduction in HIV transmission from the HIV-positive partner to the HIV-negative partner.
* However, we do not know if antiretroviral therapy prescribed to HIV-positive individuals in the general population, and where individuals may not have disclosed their HIV status would have a similar impact on HIV transmission.
* To achieve a high impact, we decided we would prescribe antiretroviral therapy to all HIV-positive individuals regardless of whether their HIV has progressed to the point in which the local HIV treatment guidelines recommend HIV-positive individuals should start treatment.

**What did the Researchers Do and Find?**

* We designed an experiment to investigate whether antiretroviral therapy can reduce new HIV infections in the general population, and piloted the trial in five communities in each comparison group to check whether the idea is feasible and acceptable.
* We visited people in their homes, offered HIV rapid tests every six months to all those 16 years and above and referred identified HIV-positive individuals to trial clinics where they were offered antiretroviral therapy either regardless of their CD4 count (intervention group) or when treatment eligible as per local guidelines (control group).
* During the two-year period, we contacted 9,927 (77%) of 12, 894 eligible individuals and ascertained the HIV status of 80% of contacted women and 75% of men.
* HIV positive status was obtained for 1,339 adults who were not previously in care; 1,177 were followed in the trial at least six months after referral, of whom 559 (47.5%) engaged with care within this period

**What do These Findings Mean?**

* Our findings show good acceptance of home-based HIV testing in rural South Africa but highlight challenges in reaching adequate number of people to offer HIV tests especially men.
* We also show that linkage to care was slower than expected, but amongst those who reached the clinics, uptake of antiretroviral therapy was high with majority of individuals achieving good control of the virus.
* Our study informs health care professionals, planners and policy makers about the challenges that need to be addressed to achieve the UNAIDS target of 90% of people living with HIV aware of their HIV diagnosis; 90% on antiretroviral therapy and 90.% achieving good control of the virus, with testing and treatment offered to all

**INTRODUCTION**

Although significant gains have been made in the control of the HIV epidemic in many sub-Saharan countries, the annual number of new HIV infections remains unacceptably high [[1](#_ENREF_1)]. Approximately 6.3 million people were estimated to be living with HIV in South Africa alone in 2013, of whom 3.1 million were on antiretroviral therapy (ART) [[2](#_ENREF_2)]. Adult HIV prevalence in KwaZulu-Natal province was estimated as high as 30% [[3](#_ENREF_3)], making it an ideal setting to evaluate the impact of universal test and treat on HIV incidence.

HIV viral load (VL) of the HIV-positive individual is the dominant determinant of transmission [[4](#_ENREF_4)]. Effective ART lowers VL and thus substantially decreases the risk of HIV transmission. In heterosexual couples in stable relationships, ART provided to the HIV-positive partner with T-cell lymphocytes CD4+ (CD4) between 250 and 550 cells/µL reduced transmission to the HIV-negative partner by 96% [[5](#_ENREF_5)]. Repeat annual population-based HIV surveys in rural KwaZulu-Natal, South Africa have shown that individual level HIV-acquisition risk decreased by 38% when ART coverage in the surrounding community was 30-40% compared to ART coverage <10%, under national treatment guidelines (first CD4 <200 cells/µL, then 350 cells/µL)[[3](#_ENREF_3)]. The impact on HIV transmission at population level of ART initiation of all HIV-positive individuals soon after HIV diagnosis has not yet been evaluated in a trial setting.

Mathematical models have suggested significant reductions in HIV transmission could be achieved with optimisation of every step of the HIV care cascade starting with high uptake of regular HIV testing of all adults with immediate treatment initiation of those found to be HIV-positive [[6](#_ENREF_6)]. The Joint United Nations Programme on HIV/AIDS (UNAIDS)’ targets that by 2020, “90% of all people living with HIV will know their status; 90% of all people with diagnosed HIV infection will receive sustained antiretroviral therapy and 90% of all people receiving antiretroviral therapy will achieve viral suppression” [[7](#_ENREF_7)]. However, the impact of the HIV care cascade on HIV incidence would additionally depend on sexual networks (such as heterogeneity, concurrency and mixing) in which HIV transmission would occur [[8-10](#_ENREF_8)].

Experience from public health HIV treatment programmes highlights the challenges of reaching high uptake of HIV testing, linkage to care, ART initiation and long-term treatment adherence [[11](#_ENREF_11)]. A recent meta-analysis of 28 studies that evaluated several approaches to HIV testing including door-to-door HIV testing amongst 555,267 participants reported an 80% (95% CI: 76.9, 83.1%) HIV test acceptance, higher in community-based than in facility-based programmes, although the former identified less HIV-positive people and with substantially less advanced disease [[12](#_ENREF_12)]. There are limited data on repeat HIV testing, but one population-based study in rural Malawi reported a repeat HIV testing uptake of 96% amongst participants who tested HIV-negative in a previous survey and were re-contacted [[13](#_ENREF_13)]. Linkage to care and ART initiation present further challenges in the HIV care cascade, with results from a further meta-analysis of sub-Saharan African data showing that for every 100 patients with a positive HIV test, 72 had a CD4 count performed, 40 were deemed ART-eligible by national treatment criteria and only 25 started ART [[14](#_ENREF_14)]. However, somewhat more positively, a recent evaluation of self-testing for HIV and linkage to care in Blantyre, Malawi reported 56% of individuals who tested HIV-positive linked to care within the first 12 months [[15](#_ENREF_15)]. There is little, if any, data on the acceptability and uptake of immediate ART for HIV prevention in African populations [[16](#_ENREF_16), [17](#_ENREF_17)].

In early 2012, we initiated a cluster-randomized trial in rural KwaZulu-Natal to evaluate whether immediate ART in HIV-positive individuals could significantly reduce HIV incidence at population level. At the time of implementation, similar trials were still in their planning phase [[18](#_ENREF_18), [19](#_ENREF_19)]; with the complexity of implementing such a large trial and a lack of available data to inform the design and sample size, we opted to start the interventions in a limited number of clusters randomised for the main trial. We were able to evaluate process indicators such as uptake of initial and repeat home-based HIV testing, linkage to care, uptake of ART and community attitudes and beliefs about HIV which are important for the success of the main trial as well as for HIV treatment programmes more generally.

# Methods

**Ethics statement**

The trial was approved by the Biomedical Research Ethics Committee (BFC 104/11) at the University of KwaZulu-Natal and the Medicines Control Council of South Africa. (Clinicaltrials.gov: NCT01509508; South African Trial Register: DOH-27-0512-3974). All participants provided written/witnessed thumbprint informed consent.

## Study design

ANRS 12249 TasPis a cluster-randomised trial including 22 clusters (2×11) at full implementation. The full trial protocol has been published previously [[20](#_ENREF_20)]. The protocol underwent some modification in response to changes in South African national ART guidelines and to optimise the trial implementation procedures involving the introduction of an active linkage-to-care team in both arms in May 2013 to facilitate linkage to trial clinics for those not linked to care within three months of being referred. These amendments were also approved by the Biomedical Research Ethics Committee of the University of KwaZulu-Natal and the trial data and safety monitoring board.

We here present results on process indicators from the first phase of the trial in ten (2 ×5) clusters; four (2×2) of the ten clusters began enrolment in March 2012 and the remaining six (2×3) in January 2013. A total of three HIV survey rounds were conducted in the initial four clusters between March 2012 and August 2013 and two in the remaining six clusters between January 2013 and March 2014. Follow up for all those identified HIV-positive receiving care in trial clinics started in March 2012, depending on cluster implementation date, to May 2014.

## Trial setting

This cluster-randomised trial was implemented in the Hlabisa sub-district, uMkhanyakude district, northern KwaZulu-Natal, South Africa. The area is largely rural, with scattered homesteads and a national road on the boundary, adjacent to the Africa Centre for Population Health and its demographic surveillance area. It is served by the Hlabisa Department of Health HIV treatment and care programme [[21](#_ENREF_21)].

## Study procedures

The study procedures and instruments have been fully described previously [[20](#_ENREF_20), [22](#_ENREF_22)]. Procedures relevant to the first phase of the trial are summarised below.

### Home-based procedures

In each six-monthly home-based HIV testing and survey round, homestead (a bounded physical structure usually comprising one household but occasionally two or more households with different household heads) visits took place between 8am and 4.30 pm weekly from Tuesday to Saturday. Where required, a separate homestead visit took place between 10am and 6.30pm Thursday to Sunday to accommodate adults not contacted during those times, mainly students and employed individuals.

Individuals were eligible for trial participation if aged ≥16 years and resident (defined as spending ≥four nights per week) members of a household in the designated cluster. Individuals were ineligible if they did not fulfil the criteria for residency or lacked the mental capacity to give informed consent.

Verbal consent from the homestead owner was obtained before entering any homestead. After explaining the study, each household head was asked to enumerate all eligible household members and complete a household asset form. Eligible individuals present on the day were taken to a private area and consented in writing to respond to a social and sexual behaviour questionnaire and give a finger-prick sample, collected on filter paper as dried blood spots (DBS). An individual was considered a trial participant if they agreed to complete a study questionnaire, although opting-out of providing a DBS was accepted. DBS samples collected longitudinally during survey rounds were tested using HIV ELISA in the Africa Centre laboratory in Durban for identification of new cases of HIV infection which is the primary outcome of the main trial. Researchers and study participants were blinded to these longitudinal DBS results.

HIV pre-test counselling and a finger-prick rapid HIV test were offered following a separate written consenting process to individuals who completed the study questionnaire, using a serial HIV testing algorithm[[23](#_ENREF_23)]. Gold HIV-1/2 screening test (G-Ocean, Hong Kong, China) was used as first test for screening and Alere Determine HIV-1/2 (Alere Pty Ltd., Kempton Park, South Africa) was used as second test for confirmation of HIV-positive result in line with the provincial Department of Health protocol. This was later amended in September 2012 to Alere Determine HIV-1/2 for screening and First Response HIV-1/HIV-2 WB (Premier Medical Corporation Ltd., Kachigam, India) for confirmation, following changes in the Department of Health directive.

The result of the rapid HIV test was given to each participant, with counselling as appropriate and further psychological support offered for any serious distress observed. Those who newly tested HIV-positive or who self-reported to be HIV-positive were referred to the TasP trial clinics in their cluster. Those who self-reported as HIV negative were documented as having refused to be tested.

Procedures offered to eligible individuals were the same in each repeat survey round, irrespective of their HIV status recorded in the previous round.

### TasP trial clinic procedures

HIV-positive participants attending TasP trial clinics were asked to provide written consent to: (i) complete clinical history and examination questionnaires and provide blood specimens for VL testing and (ii) receive care as per national guidelines and ART as per cluster allocation. HIV-positive participants comprised those newly diagnosed as HIV-positive and those who self-reported as HIV-positive during home-based survey visits; they could be either ART-naïve or ART-experienced from their previous HIV care provider.

All consenting HIV-positive participants underwent clinical evaluation and a point-of-care CD4 measurement (Alere PIMA device tool, Alere Inc., Waltham, MA, USA). All participants eligible for ART attended adherence and ART-literacy sessions and initiated ART within two weeks of the baseline visit or sooner if severely immunocompromised. A fixed dose combination of Tenofovir/Emtricitabine/Efavirenz (Atripla) was used for first-line ART, except if a participant’s clinical condition indicated otherwise. Second-line ART was informed by the results of genotypic resistance tests in participants failing first-line ART.

Participants receiving ART underwent monthly clinical evaluation including scheduled safety monitoring bloods and HIV viral load measurements (Abbott m2000 RealTime System, Abbott Molecular Inc., Des Plaines, IL, USA) at the first visit, three and six months after ART initiation and six monthly thereafter. They were also interviewed for clinical adverse events. Non-scheduled clinic visits were also allowed for participants with clinical complaints. In the control clusters, patients not yet eligible for ART were invited to return to the study clinic in four to six months for pre-ART care, positive prevention services, repeat clinical assessment and CD4 count measurement. Participants missing a trial clinic appointment were phoned, and where possible, a new appointment was scheduled. Participants who failed to link to care three months after being referred by the field team were contacted by a trial linkage-to-care team either by phone or through a home-visit.

**Intervention**

In the intervention clusters, HIV-positive individuals were informed during home-based HIV testing that they would be provided ART irrespective of CD4 count and clinical stage. In the control clusters, HIV-positive individuals were informed that ART would be offered according to the national South African guidelines: CD4 ≤350 cells/µL, World Health Organization (WHO) clinical stage 3 or 4, multi-drug resistant or extensively drug-resistant tuberculosis.

**Definition of variables and outcomes**

S1 Table presents the outcomes measured in phase 1 and presented here, and those that will be measured after trial completion.

HIV prevalence was estimated on the basis of antibody test result from the DBS collected during the first survey round only. We estimated the ART coverage at the start of the trial (proportion of all HIV-positive on ART) among those with positive DBS results (first survey round) using linked information from the Department of Health (DoH) clinics and pharmacy records (ARTemis and iDART databases). Matching between the three databases was based on first names, last name, date of birth, South African ID number and cell phone numbers.

Mean, median (interquartile) age at registration was computed among individuals who completed at least one individual questionnaire at home; similarly for other demographic variables.

Proportion of individuals contacted and whose HIV status was ascertained was computed per home-based survey round, i.e. an individual eligible in three survey rounds (taking into account round of registration and population exits), fully contacted in two rounds, but accepting a HIV rapid test only in one round, will contribute three episodes in the denominator and two episodes in the numerator for estimation of contact; two episodes in the denominator and one in the numerator for HIV ascertainment. The HIV status of an individual was ascertained if that person accepted an HIV rapid test and obtained a valid result (i.e. invalid/indeterminate results excluded) or if he/she self-reported being HIV-positive.

Rapid HIV test uptake was computed amongst individuals contacted, not self-reporting to be HIV positive, who accepted a rapid HIV test.

Linkage to care within six months was computed among individuals ascertained HIV-positive at home, not previously in care (in DoH clinics in the study area) and observed at least six months (taking into account population exits and the end date of data collection). Linkage to care was defined as having a first clinic visit either in DoH clinic in the study area or TasP clinic and obtained by individual linkage in the databases as described above

ART uptake was computed in TasP clinics only, within three months from the first clinic visit, among participants not on ART at the first clinic visit, regardless of ART eligibility criteria. ART uptake was further stratified by CD4 count at first visit in TasP clinics.

Viral suppression was defined as having a viral load <400 copies/mL on ART.

We estimated the status within the HIV care cascade (diagnosed, ever on ART, ever virally suppressed during the trial follow-up) of trial participants who were contacted and identified to be HIV-positive (through DBS and/or HIV rapid test) who linked to TasP or DoH clinics, using linked information from DoH clinics. In order to present a population cascade, we also estimated the number of HIV infected individuals who had not been reached by the trial field activities by applying the observed HIV prevalence (from DBS) to the total population of registered individuals. This assumes there was no selection bias.

Attitude indicators were computed (i) among individuals having completed at least one individual questionnaire at home (the first questionnaire being used for individuals who completed several questionnaires over the trial) or (ii) among HIV-positive participants who linked to TasP clinics, at their first visit, and if they were not already on ART at this first clinic visit.

**Sample size**

The main trial at full implementation was 80% powered to detect an overall 34% reduction in cumulative HIV incidence over 4 years (N= 22,000; 22 clusters), with an incidence of 2.25% per year in the control clusters. The calculation made allowance for 20% of loss to follow up and assumed a coefficient of variation of 0.25 to account for variation between clusters [[20](#_ENREF_20)]. Assumptions for attaining this incidence reduction were that the level of population contact would need to be 90%, HIV status ascertainment 80%, linkage to care 70%, and baseline HIV prevalence 24%.

**Randomisation**

Randomisation was performed by the trial statisticians before the start of the trial. 211 local areas were aggregated into 48 clusters. Initial sample size calculation showed 34 clusters (2×17) would be required and these were randomly allocated to two arms; control and intervention. Randomisation was carried out within each stratum to derive an equal number of control and intervention communities per stratum. Random number generation and the randomisation procedure were performed in MapInfo version 11.0. The sample size was subsequently amended to 2×11 with an increase in the duration of follow-up through a revision of the protocol for the main trial. For this initial phase only ten (2×5) of the 22 clusters were used. To minimise the degree of between-cluster variation, clusters were stratified on the basis of predicted HIV prevalence, extrapolating from HIV surveillance data from the Africa Centre’s demographic surveillance area and data from antenatal clinics (six strata).

## Statistical analyses

Process indicators were summarised by arm and described according to key baseline characteristics (sex, age, education level, marital status and professional status). They were then compared by arm using Pearson’s Chi² test with Rao-Scott second-order correction which is appropriate in the context of cluster sampling [[24](#_ENREF_24)]. The p-values are computed with a Satterthwaite approximation to the distribution and with denominator degrees of freedom as recommended by Thomas and Rao [[25](#_ENREF_25)] or a design-based t-test (taking into account clustering for variance computation).

# Results

**Registration and enrolment of participants**

Three consecutive rounds of home-based HIV testing were conducted in four initial clusters (2×2) from March 2012, and two rounds in six additional clusters (2×3) from January 2013. A total of 12,894 individuals were registered as eligible between March 2012 and May 2014 (Fig 1). During this period, 9,927 (77.0%) were contacted by the fieldworkers at least once, with no difference between arms (77.7% and 76.4%, respectively). Of the 9,927 individuals ever contacted, 9,490 (95.6%) agreed to complete a social and sexual behaviour questionnaire at least once and HIV status was ascertained at least once for 82.3% (3 698/4 496) and 83.5% (4,535/5,431) in the intervention and control arms, (Fig 1), this translates to ascertained HIV status for 63.9% (3,698/5,790) and 63.8% (4,535/7,104) of all registered individuals respectively.

Overall, the HIV prevalence was 30.5% (95% CI: 25.0%, 37.0%).

**Fig 1.** Flow diagram of enrolment by trial arm and sex in the ANRS 12249 TasP trial  
DBS: Dried Blood Spots; DoH: Department of Health

**Baseline characteristics**

The median age (inter-quartile range [IQR]) of participants was 32.3 years (22.1, 52.4) and the majority were female (67.9%). A third of participants had primary level education or less. The majority were never married; very few were formally employed. No difference was observed between arms (Table 1).

**Table 1.** Baseline characteristics of participants in intervention and control arms, first phase of the TasP ANRS 12249 trial, 2012-2014

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable** | **Intervention arm** | **Control arm** | **p-value** |
| **Number of registered individuals** | 5790 | 7104 |  |
| **Estimated baseline HIV prevalence (n/N)** | 29.0% (880/3036) | 31.7% (1148/3620) | 0.672 |
| **Estimated baseline ART coverage (n/N)** | 36.0% (317/880) | 39.8% (457/1148) | 0.271 |
| **Number of participants who completed at least one questionnaire** | 4244 | 5246 |  |
| **Sex (Female)** | 68.4% | 67.4% | 0.486 |
| **Mean age (years) at registration** | 39.0 | 38.1 | 0.944 |
| **Median age (inter-quartile range)** | 33.3 (22.4-53.3) | 31.6 (21.9-51.8) |  |
| **Never been married** | 67.0% | 69.1% | 0.678 |
| **Primary education or less** | 42.6% | 39.7% | 0.133 |
| **Employed** | 9.4% | 9.9% | 0.842 |
| **Condom use at last sexual act (IQ1)** | 29.3% | 32.2% | 0.342 |

*p-values correspond to Pearson’s Chi² test with Rao-Scott second-order correction or a design-based t-test (taking into account clustering) between intervention and control arms. IQ1: first-administered questionnaire at home.*

**Contact and uptake of HIV testing per round**

The proportion of registered individuals contacted per survey round was 66.8%, similar in both arms, p=0.530 but lower in males than females (53.3% vs. 75.2%). Uptake of rapid HIV test at first contact was 73.1% overall, similar in both arms (Table 2). Amongst those contacted, HIV status ascertainment (rapid HIV test uptake + self-reported HIV positive) per survey round was 77.6%; also similar between arms, p=0.676 (Table 2).

**Table 2.** Process indicators by trial arms and by sex, first phase of the TasP ANRS 12249 trial, 2012-2014

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Process indicators** | **Women** | **Men** | **Overall** | **Women vs. Men** | |
| **Difference in proportions   % [95% CI]** | **p-value** |
| **Intervention arm** |  |  |  |  |  |
| Contact per home-based survey round | 74.4% (5554/7465) | 50.3% (2305/4587) | 65.2% (7859/12052) | 24.1 [21.4; 26.9] | <0.001 |
| HIV ascertainment per home-based survey round | 76.8% (4264/5554) | 76.6% (1765/2305) | 76.7% (6029/7858) | 0.2 [-4.1; 4.5] | 0.932 |
| Linkage to care within 3 months (individuals not in care at referral) | 36.7% (159/433) | 38.1% (67/176) | 37.1% (226/609) | -1.3 [-9.7; 7.0] | 0.770 |
| Linkage to care within 6 months (individuals not in care at referral) | 47.4% (188/397) | 48.2% (79/164) | 47.6% (267/561) | -0.8 [-5.0; 3.3] | 0.724 |
| Linkage to care within 12 months (individuals not in care at referral) | 62.6% (134/214) | 62.6% (57/91) | 62.6% (191/305) | 0.0 [-3.4; 3.4] | 0.991 |
| ART initiation within 3 months of first clinic visit (CD4 ≤ 350 at baseline) | 95.0% (57/60) | 85.0% (34/40) | 91.0% (91/100) | 10.0 [-2.9; 22.9] | 0.073 |
| ART initiation within 3 months of first clinic visit (CD4 > 350 at baseline) | 89.8% (79/88) | 80.0% (24/30) | 87.3% (103/118) | 9.8 [-3.5; 23.1] | 0.168 |
| **Control arm** |  |  |  |  |  |
| Contact per home-based survey round | 75.8% (6426/8475) | 56.0% (2904/5189) | 68.3% (9330/13664) | 19.8 [16.6; 23.1] | <0.001 |
| HIV ascertainment per home-based survey round | 80.4% (5165/6426) | 73.9% (2146/2904) | 78.4% (7311/9326) | 6.5 [3.9; 9.0] | 0.009 |
| Linkage to care within 3 months (individuals not in care at referral) | 35.6% (190/534) | 39.3% (72/183) | 36.5% (262/717) | -3.4 [-7.8; 0.3]] | 0.137 |
| Linkage to care within 6 months (individuals not in care at referral) | 47.3% (218/461) | 47.7% (74/155) | 47.4% (292/616) | -0.4 [-4.5; 3.6] | 0.838 |
| Linkage to care within 12 months (individuals not in care at referral) | 62.9% (146/232) | 66.1% (39/59) | 63.6% (185/291) | -3.2 [-17.9; 11.5] | 0.700 |
| ART initiation within 3 months of first clinic visit (CD4 ≤ 350 at baseline) | 93.3% (56/60) | 91.3% (21/23) | 92.8% (77/83) | 2.0 [-6.3; 10.3] | 0.587 |
| ART initiation within 3 months of first clinic visit (CD4 > 350 at baseline) | 9.8% (9/92) | 14.3% (3/21) | 10.6% (12/113) | -4.5 [-21.4; 12.4] | 0.565 |
| **Intervention vs. Control**  **Difference in proportions between arms % [95% CI]**  **p-value** |  |  |  |  |  |
| Contact per home-based survey round  HIV ascertainment per home-based survey round | -1.4 [-9.1; 6.3]  0.730  -3.6 [-11.7; 4.5] | -5.7 [-17.1, 5.6]  0.353  2.7 [-5.0; 10.4] | -3.1 [-12.1; 6.0]  0.530  -1.6 [-9.3; 6.0] |  |  |
| Linkage to care within 3 months (individuals not in care at referral) | 0.386  1.1 [-11.8; 14.1] | 0.525  -1.3 [-9.4; 6.9] | 0.676  0.6 [-10.4; 11.6] |  |  |
| Linkage to care within 6 months (individuals not in care at referral) | 0.866  0.1 [-10.4; 10.5] | 0.525  0.4 [-8.7; 9.6] | 0.921  0.2 [-9.5; 9.9] |  |  |
| Linkage to care within 12 months (individuals not in care at referral) | 0.990  0.3 [-16.6; 16.0] | 0.929  -3.5 [-25.5; 18.6] | 0.970  -1.0 [-17.4; 15.5] |  |  |
| ART initiation within 3 months of first clinic visit (CD4 ≤ 350 at baseline) | 0.971  1.7 [-3.9; 7.2] | 0.766  -6.3 [-24.5; 11.9] | 0.912  -1.8 [-11.2; 7.7] |  |  |
| ART initiation within 3 months of first clinic visit (CD4 > 350 at baseline) | 0.571  80.0 [73.2, 86.8] | 0.518  65.7 [43.2; 88.2] | 0.719  76.7 [68.4; 85.0] |  |  |
|  | <0.001 | 0.003 | <0.001 |  |  |

*p-values correspond to Pearson’s Chi² test with Rao-Scott second-order correction (taking into account clustering) between intervention and control arms.  
Proportion of individuals contacted and whose HIV status was ascertained was computed per home-based survey round, i.e. an individual eligible in three survey rounds, fully contacted in two rounds, but accepting a HIV rapid test only in one round, will contribute three episodes in the denominator and two episodes in the numerator for estimation of contact; two episodes in the denominator and one in the numerator for HIV ascertainment.*

Repeat HIV test uptake was 85.3% at second contact in those initially testing HIV-negative. Cumulatively in all survey rounds, 2,569 adults were ascertained HIV-positive (942 tested HIV-positive and 1,627 reported a known HIV-positive status) and referred to TasP clinics in their cluster (Fig 1).

Amongst the 1,694 individuals who were contacted at least once but whose HIV status was never ascertained, 573 (33.8%) did not provide any reason for refusal. Amongst the remaining 1,121 individuals; 545 (48.6%) ever reported they thought they were HIV negative, 353 (31.5%) were afraid to test, 96 (8.6%) would test only with their partner and 323 (28.8%) provided other reasons (Overall proportion differs from 100% due to multiple reasons per individual).

**Linkage to care**

Of the 2,569 adults ascertained HIV-positive and referred to TasP clinics, 1,230 were actively engaged with care in DoH clinics at the time of referral (Fig 1). Amongst the remaining 1,339 adults; 1,177 were followed in the trial at least six months after referral (Table 2). Of these, 559 (47.5%) linked to care within six months of referral with no significant difference between arms (p=0.970). The corresponding estimate at 12 months was 63.1% (376/596) overall, again not significantly different between arms (p=0.912).

**Uptake of ART and retention**

In the intervention arm, among participants not already on ART, followed at least 3 months in TasP clinics, 103/118 (87.3%) participants with CD4 >350 cells/µL initiated ART within three months of the first clinic visit (Table 2). There was no difference between arms in the proportion of treated individuals who achieved viral suppression (448/526; 85.2% in the intervention arm and 440/518; 84.9% in the control arm). The median (IQR) duration on ART was 265 days (162-383).

Retention in care in trial clinics at 12 months was 84.4%, slightly higher in the intervention than in the control arm (86.2% vs 82.5%).

**HIV care cascade**

Among an estimated total of 3,933 (30.5% HIV prevalence × 12,894) HIV infected individuals ≥16 years living within the trial area, 2,706 (68.8%) were diagnosed (2,569 ever ascertained within TasP plus 137 not ascertained within TasP but ever in care in DoH), of whom 1,898 (70.1%) were ever in care in TasP and/or DoH clinics, of whom 1,343 (70.8%) achieved viral suppression (Fig 2). Overall, 34.1% (1,343/3,933) of all HIV-positive individuals were ever virally suppressed.

**Fig 2.** Estimated HIV care cascade among all HIV-infected individuals at population level  
\* the number of non-observed HIV+ individuals was estimated under the assumption there was no selection bias, i.e. the observed HIV prevalence of 30.5% was applied to individuals whose HIV status was not observed within TasP. 2983 amongst HIV-infected in column 1 refers to total number of individuals ascertained HIV-positive within TasP in both arms of the trial, 2569 (Fig 1) plus those who declined HIV rapid tests but whose DBS HIV ELISA was positive and matched that of 137 individuals on ART within the department of Health clinics.

**Attitude indicators and other observations**

Almost all participants in both arms are of the opinion that people should test regularly and agreed that they would start ART as soon as possible if diagnosed HIV-positive, with no difference by arm (Table 3).

**Table 3.** Attitudes towards repeat home-based HIV testing and early treatment by trial arms, first phase of the TasP ANRS 12249 trial, 2012-2014

|  |  |  |  |
| --- | --- | --- | --- |
| **Attitude indicators** | **Intervention arm** | **Control arm** | **p-value** |
| Consider that people should test regularly (IQ1) | 93.3% (3961/4244) | 92.9% (4876/5246) | 0.846 |
| Consider that best place to get HIV tested is 'at home' (IQ1) | 60.4% (2564/4244) | 56.5% (2965/5246) | 0.505 |
| Agree that would want to start ART as soon as possible if HIV positive (IQ1) | 93.1% (3951/4244) | 92.5% (4851/5246) | 0.688 |
| Believe that antiretroviral drugs make people with HIV less infectious (IQ1) | 78.7% (3340/4244) | 75.3% (3948/5246) | 0.472 |
| Less worried about HIV now that treatments have improved (IQ1) | 81.9% (3476/4244) | 84.2% (4419/5246) | 0.258 |
| Agree that ART will reduce transmission to sexual partners (HIV+ patients, first visit in TasP clinic, not already on ART) | 77.1% (219/284) | 82.9% (252/304) | 0.601 |

*IQ1: first-administered questionnaire at home.   
p-values correspond to Pearson’s Chi² test with Rao-Scott second-order correction (taking into account clustering) between intervention and control arms*

One female participant newly identified HIV-positive among the 6,155 individuals who underwent 10,445 HIV rapid tests in the home suffered an acute adjustment reaction with suicidal intent; she was referred to a clinical psychologist for support and care. There were no reports of study-related gender-based violence, partnership dissolution or breach of confidentiality.

# Discussion

This two-year initial phase of a trial evaluating a Treatment as Prevention strategy in a rural South African setting confirmed programmatic challenges in reaching optimum numbers of individuals for HIV testing at home during working hours, especially men, hindering HIV-status ascertainment. However, among those contacted, ascertainment of initial and repeat HIV status was high. Further, linkage to care in newly HIV diagnosed adults was slower than expected, but of those who reached the trial clinic uptake of ART was high regardless of CD4 count with good viral suppression and retention. These observations are particularly relevant with the most recent WHO guidelines recommending ART to be initiated in anyone diagnosed with HIV, irrespective of CD4 cell count [[26](#_ENREF_26)]. We show a drop-off at each of the first two steps of the HIV care cascade, which would undermine the effectiveness of such a universal testing and treatment policy in reducing HIV transmission.

We were unable to contact one-quarter of the potential target population, especially men; however home-based HIV testing was effective in ascertaining the HIV status of those contacted. Our results are in line with those from a meta-analysis including 28 studies which showed a pooled 80% uptake of home-based HIV testing [[12](#_ENREF_12)]. Individuals unaware of their HIV positive status cannot benefit from ART for their own health and as they would remain potential transmitters, the population as a whole would not benefit either. Mobile HIV testing has recently been shown to be more efficient than home-based approaches in increasing contact and testing uptake in men [[27-29](#_ENREF_27)] and in younger individuals and should be considered as a complementary approach in settings such as ours. Concerns about stigma and breach of confidentiality are often cited as reasons for HIV test refusal, but actual harm is rarely reported in published studies [[12](#_ENREF_12)]. We identified only one serious adverse event following nearly 11,000 home-based tests, which highlights the quality of the pre- and post-test counselling.

First-time clinic engagement was limited, with only 47.5% of participants not already in care attending the trial or DoH clinic within six months of referral; with up to 12 months required to reach 63% linkage. Our findings are in line with what was observed in a study in Malawi of HIV self-testing and linkage to care [[15](#_ENREF_15)] as well as those from a systematic review and meta-analysis of 11 sub-Saharan African studies, which reported only 57% of those diagnosed HIV positive had been linked to care [[30](#_ENREF_30)]. The delay in accessing the trial clinics in our study may be associated with the earlier HIV identification, while asymptomatic, in home-based testing. Furthermore, we did not show much difference between those in the intervention (who were told that ART would be provided to all) and those in the control (who were told that ART would be provided for those who were treatment-eligible) arm. However, there were some anecdotal reports that fear of stigma may have discouraged rapid linkage to care as trial clinics only provided service to HIV positive individuals; on-going social science work embedded within the trial may shed more light on this issue [[22](#_ENREF_22)]. Further, about one-fifth of HIV-positive individuals who entered into care reported to be unaware of the link between viral load and HIV transmission; this highlights the need to incorporate this information into ART literacy and adherence counselling sessions.

The observed uptake of ART once linked to care was high both in treatment-eligible and not yet-eligible individuals, with 85% of those initiating ART achieving viral suppression in both arms. Retention was equally high in the first year following treatment initiation. In contrast, in a study in urban Soweto one in five HIV-positive individuals eligible for ART refused to initiate ART [[31](#_ENREF_31)]. In that study “feeling healthy” was the commonest reason for ART refusal despite a median CD4 count of 110 cells/µL and high rates of tuberculosis. In a qualitative study in Kenya to explore HIV serodiscordant couples’ attitudes toward early initiation of ART, most participants reported interest in initiating ART early, citing individual health benefits and preventing HIV transmission as motivators [[16](#_ENREF_16)]; with side effects, life-long adherence and stigma emerging as potential barriers.

Overall, we estimated that only one-third of all individuals living with HIV in this population were on ART and virally suppressed. However, we were able to link data from DoH clinics only for the trial participants who were contacted and observed HIV-positive (through DBS and/or ascertainment). We do not have this information for nearly one-quarter of individuals not reached by the trial or who refused to participate, who may be in HIV care at DoH clinics. Hence the overall proportion of HIV-positive individuals in the population with viral suppression should be considered an underestimate, while the value of 45.0% (1,343/2,983) computed only among observed HIV-positive individuals constitutes an upper estimate. There remains an important gap in reaching the 73% (90% of 90% of 90%) of all people living with HIV to be virally suppressed, which is the UNAIDS target.

The 2013 WHO guidelines for ART recommended initiation at CD4 counts ≤500 cells/µL and immediate ART initiation among specific groups including serodiscordant couples. Following the results of two large randomised clinical trials [[32](#_ENREF_32), [33](#_ENREF_33)] reporting health benefits in individuals initiating ART at higher CD4 counts, the WHO recently concluded that universal testing and treatment should become the standard of care [[26](#_ENREF_26)]. Many African countries, including South Africa from January 2015, had already adopted the 2013 guidelines. Trials, including ours, currently underway in South Africa, Zambia, Botswana, Uganda and Kenya which were originally designed to show a decrease in HIV incidence with ART initiated at a CD4 count of ≤350 cells/µL in the control arm have had to adapt to these expanding treatment eligibility criteria [[18](#_ENREF_18), [19](#_ENREF_19)]. It is likely that when the 2015 WHO HIV treatment guidelines are adopted and implemented in country the research focus in these trials may shift to evaluations of programmes which aim to achieve the WHO/UNAIDS 90-90-90 targets (90% of people living with HIV aware of their HIV status, 90% of people diagnosed HIV-positive on ART, 90% of people on ART virally suppressed) by 2020 [[7](#_ENREF_7)] which our study shows could potentially be challenging. As these changes have not yet been implemented in South Africa, they do not affect the analysis in this paper.

Study limitations include use of a subset of the original randomisation for the initial phase of the trial comprising fewer clusters but this did not seem to have affected the distribution of baseline characteristics between the two arms. Although household contact rates were high, we were unable to contact all individuals identified as eligible for the trial, in particular men. Non-contact could potentially be a source of bias if different between arms. These limitations highlight the challenges of a universal test and treat policy.

In summary, we show that home-based HIV testing was well-received in this population, although men were less easily contactable during the day of home visits, and that immediate ART was acceptable, with good viral suppression and retention. However, only about half of the HIV-positive people identified accessed care within six months and nearly two-thirds by 12 months; the improvement with time would suggest that people need time in accessing care, rather than refuse to link to care altogether.

These findings inform the now topical debate of how to identify HIV positive people in the community and the rate of linkage to care and provides important input in further statistical projections about the burden of HIV and treatment need for populations with high HIV prevalence, such as in sub-Saharan Africa.

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**Supporting Information**

S1 Table. TasP trial outcomes measured in Phase 1 and 2

S1 Text. Trial protocol

S2 Text. CONSORT checklist