CASCADE

Evidence-Based Structural Intervention
Evidence-Based for Engagement in HIV Care
Evidence-Based for Viral Suppression

INTERVENTION DESCRIPTION

Goal of Intervention
- Improve engagement in HIV care
- Improve viral suppression

Target Population
- Adults who tested positive for HIV and who are antiretroviral treatment (ART)-naïve

Brief Description

The *CASCADE* intervention offers same-day ART initiation to individuals who tested HIV positive and are ART-naïve during a home-based testing campaign (HBT). During the home visit after HIV testing, participants receive point-of-care laboratory blood work, results of their lab work, and pre-ART counseling with a leaflet summarizing the importance of ART adherence. After counseling, study nurses offer ART to participants. Participants who decide to initiate ART receive a 30-day supply of ART, and instructions to visit their health facility within 2 to 4 weeks for their first clinic visit and ART refill. For follow-up visits including ART refills, participants receive usual care for ART patients (per national and WHO guidelines), with exception of longer intervals between visits at 1.5, 3, 6, 9, and 12 months after ART initiation.

Theoretical Basis
- None reported

Intervention Duration
- One home-based session with follow-up visits to the nearest health facility at 2-4 weeks and 1.5, 3, 6, 9, and 12 months after ART initiation

Intervention Setting
- Missionary hospital
- Public hospital
- Public nurse-led health centers
- Residential homes

Deliverer
- Lay counselors
- Study nurse
- Team leader

Delivery Methods
- Residential home visits

Structural Components

- Access
  - Provided same-day ART initiation, a 30-day supply of ART, and ART refills
  - Provided follow-up HIV care appointment at nearest health facility
- Physical Structure – Service in a non-traditional setting
  - Provided same-day ART initiation, a 30-day supply of ART, and lab work results in the homes of participants
- Policy/Procedure – Institutional policy/procedure
  - Implemented same-day ART initiation for patients who tested HIV positive

INTERVENTION PACKAGE INFORMATION

An intervention package is not available at this time. Please contact **Niklaus D. Labhardt**, Division of Infectious Diseases and Hospital Epidemiology, University Hospital Basel, Basel, Switzerland.

E**mail:** n.labhardt@unibas.ch for details on intervention materials.

EVALUATION STUDY AND RESULTS

Study Location Information

The original evaluation study was conducted in rural Lesotho, South Africa between 2016 and 2017.

Key Intervention Effects

- Improved engagement in HIV care
- Improved viral suppression

Recruitment Settings

- Household participating in home-based testing (HBT) campaign in Lesotho

Eligibility Criteria

Participants were eligible if they were adults (≥ 18 years old) who tested HIV positive and were ART naïve.

Study Sample

The baseline study sample of 274 participants (137 Same-day ART and 137 Usual care) is characterized by the following:

- *66% female, 34% male*
- *65% married or living with partner*
- *Median age of 39 years*
- *77% without regular income*
- *44% had CD4 cell count of <350 cells/μL*
- *74% newly diagnosed with HIV*

Assignment Method

Participants (N = 274) were randomized to same-day ART (n = 137) or usual care (n = 137).

Comparison

Participants in the usual care comparison group received a referral letter for an appointment at the nearest health facility within 28 days after the HBT campaign. Once participants were linked to care, they had a minimum of two pre-ART health facility visits. The first visit consisted of laboratory blood work and a pre-ART counseling session. At the second visit, participants were provided with laboratory results and assessed for readiness to start ART. Participants were offered to initiate ART based on the judgment of the health facility staff. Participants who initiated ART were given monthly follow-up visits and drug refill dates.

Relevant Outcomes Measured

- Engagement in HIV care was defined as attending at least one health facility visit within 90 days after testing HIV positive during the home-based testing visit.
- Viral suppression at 12 months was defined as viral load <100 copies/mL between 11 and 14 months after enrollment.

Participant Retention

Because participant retention is not a criterion for the Structural Interventions (SI) chapter, the Prevention Research Synthesis (PRS) project does not evaluate that information.

Significant Findings on Relevant Outcomes

- A significantly greater percentage of intervention participants were engaged in HIV care within 90 days after enrollment than comparison participants (68.6% vs. 43.1%; absolute difference = 25.6%, 95% CI = 13.8 – 36.3, $p < 0.001$).
- A significantly greater percentage of intervention participants were virally suppressed (<100 copies/mL) between 11 and 14 months after enrollment than comparison participants (50.4% vs. 34.3%; absolute difference = 16.0%, 95% CI = 4.4 – 27.2, $p = 0.007$).

In post hoc analyses:

- A significantly greater percentage of intervention participants were engaged in HIV care between 11 and 14 months after enrollment than comparison participants (63.5% vs. 48.2%; absolute difference = 15.3%, 95% CI = 3.6 – 26.5, $p = 0.01$).
- A significantly greater percentage of intervention participants than comparison participants were engaged in HIV care at any time > 11 months after enrollment (64.2% vs. 49.6%; absolute difference = 14.6%, 95% CI = 2.9 – 25.8, $p = 0.02$).
- A significantly greater percentage of intervention participants-initiated ART vs. comparison participants (68.6% vs. 32.1%; absolute difference = 36.5% (95% CI, 24.9% - 46.7%, $p < 0.001$).

Strengths

- None identified

Considerations

Additional significant positive findings on non-relevant outcomes

In post-hoc analyses:

- Having a drug refill between 11 and 14 months after enrollment was significantly higher for intervention participants vs. comparison participants ($x^2 = 6.84$, $p = 0.009$).
- Among participants who engaged in HIV care within 3 months, having a drug refill between 11 and 14 months after enrollment was significantly higher for intervention participants vs. comparison participants ($x^2 = 6.22$, $p = 0.02$).

Non-significant findings on relevant outcomes

- There were no significant intervention effects for viral suppression 6 months after enrollment (absolute difference = 11%; 95% CI = -0.1% - 21.6%, p = 0.05), viral suppression between 11 and 14 months after enrollment among those with a documented viral load (absolute difference = 4.1%, 95% CI = -5.4% - 15.6%, p = 0.38) or lost to follow-up at 12 months after enrollment (absolute difference = 1.5%, 95% CI = -5.2% - 8.2%, p = 0.66).

Negative findings

- None reported

Other related findings

- The study also meets evidence-based criteria for the Linkage to, Retention in, and Re-engagement in HIV Care chapter of the *Compendium*.

Implementation-related findings

- None reported

Adverse events

- Of the 214 patients ever initiating ART, 205 (96%) started on tenofovir disproxil fumarate, lamivudine and efavirenz. Due to an estimated creatinine-clearance <50mL/min, 7 (3%) received zidovudine and 2 (1%) abacavir instead of tenofovir. Cotrimoxazole prophylaxis was given to 84 (39%) of participants at ART initiation. During follow-up, ART side-effects were reported in 8 participants: 6 in same-day ART intervention group: rash (n = 2), nausea (n = 1), dizziness (n = 1),gynecomastia (n = 1),elevated alanine aminotransferase levels [200 IU/L] (n = 1) and 2 in the usual care comparison group: rash (n = 2). Due to side-effects, the ART regimen was changed in 4 participants (3 in the same-day ART intervention group and 1 in the usual care comparison group), 3 were changed from efavirenz to nevirapine, and 1 changed from efavirenz to ritonavir-boosted lopinavir.
- Two deaths occurred after enrollment, and both were in the same-day ART intervention group. One woman, aged 39 years, was started on tenofovir disoproxil, lamivudine and efavirenz, and died from anemia and renal failure 16 days after enrollment. At enrollment, she had a CD4 cell count of 342 cells/µL, a serum creatinine of 46 µmol/L, hemoglobin of 6.7g/dL, and body weight of 35kg (77 lbs). The event was classified as late-presenting AIDS (e.g., wasting, anemia). Another woman, aged 71 years, was started on tenofovir disoproxil, lamivudine and efavirenz, and died from a possible cardiovascular event. At enrollment, she had a CD4 cell count of 323 cells/µL, a serum creatinine of 57µmol/L, hemoglobin of 13.7g/dL, and body weight of 53kg (117 lbs). The village health worker reported her death to the study team, and no further information about the circumstances of her death was available.

Funding

Grant R4D Open Call IZ07Z0_160876/1 from the Swiss National Science Foundation, Stiftung für Infektiologie beider Basel, and the Gottfried and Julia Bangerter-Rhyner Stiftung

REFERENCES AND CONTACT INFORMATION

Labhardt, N. D., Ringera, I., Lejone, T. I., Klimkait, T., Muhairwe, J., Amstutz, A., & Glass, T. R. (2018). Effect of offering same-day ART vs usual health facility referral during home-based HIV testing on linkage to care and viral suppression among adults with HIV in Lesotho: The CASCADE randomized clinical trial. *JAMA Journal of the American Medical Association, 319*(11), 1103-1112.

Labhardt, N. D., Ringera, I., Lejone, T. I., Masethothi, P., Thaanyane, T., Kamele, M., . . . Glass, T. R. (2016). Same day ART initiation versus clinic-based pre-ART assessment and counselling for individuals newly tested HIV-positive during community-based HIV testing in rural Lesotho - A randomized controlled trial (CASCADE trial). *BMC Public Health, 16*, 329.

Researcher: **Niklaus D. Labhardt, MD**
Division of Infectious Diseases and Hospital Epidemiology
University Hospital Basel
Basel, Switzerland

Email: **n.labhardt@unibas.ch**