Protocol For A Trial Of The Impact Of Intensive Case Management Approach In Adults HIV Positive

Jacques Lukenze Tamuzi, Jonathan Lukusa Tshimwanga

Community Health Division, Faculty of Medicine and Health Sciences,
Stellenbosch University, Matieland, South Africa
Division of Family medicine, Faculty of Medicine and Health Sciences,
Stellenbosch University, Matieland, South Africa
drjacques.tamuzi@gmail.com

Abstract: Background: Among the global gap in HIV epidemic to achieve the 90–90–90 target in 2015 was 13.0 million people living with HIV were not virally suppressed (UNAIDS 2016). In fact, the viral load is the mirror of HIV disease progression. Achieving the last 90 target is challenging because an estimated 38% [35–41%] of people living with HIV worldwide are virally suppressed. Disruptions of viral suppression of those on treatment, due to lack of adherence or viral resistance, limit the potential gains of treatment. Adherence is the best predictor of treatment success among clients. Near-perfect adherence is needed for clients to achieve good results, such as decreasing viral loads in the bloodstream, and preventing HIV-related complications. Maximum adherence to ART in patients with HIV improves health outcomes and prevents drug resistance. This trial will use intensive case management approach to improve adherence in adults HIV-infected whose viral load is >=1000 copies/ml. **Objectives:** -To improve the viral load in adults HIV-infected with viral load equal or above 1000 copies/ml. -To enhance the adherence in HIV-infected in adults with viral load >= 1000 copies/ml. **Methods:** This is a trial assessing viral load before and after the intervention. Participants will be selected in Otavi Health Centre. We will assess database in Otavi Health Centre and adults HIV-infected whose viral load is equal or above 1000 copies/ml will be selected. Data will be captured and entered into EpiInfo, then after converted to Stata14 for validation and analysis. The statistical analyses will be based on comparing the baseline viral load to post intervention viral load. Knowing that the viral load is continuous data, paired t-test will be used. We will use STATA 14 to analyze data. **Conclusion:** this trial will highlight the importance of intensive case management approach in improving ARV adherence.

I. Background

Enormous progresses against HIV/AIDS over the last 15 years have inspired a global commitment to end the epidemic by 2030 (UNAIDS 2016). The United Nations General Assembly agreed in June 2016 that ending AIDS by 2030 requires a Fast–Track response to reach three milestones by 2020: Reduce new HIV infections to fewer than 500 000 globally by 2020 (UNAIDS 2016). Reduce AIDS-related deaths to fewer than 500 000 globally by 2020 (UNAIDS 2016). Eliminate HIV-related stigma and discrimination by 2020 (UNAIDS 2016). Remarkable scale up of antiretroviral therapy has put the world on track to reach the target on AIDS-related deaths (UNAIDS 2016). Intensive efforts to eliminate mother-to-child transmission of HIV have achieved steep declines in the annual number of new HIV infections among children in 2015 (UNAIDS 2016). Therefore, ending AIDS by 2030 should involve international as well as national policies. Reviewing the literature, each country is facing its own challenges in fighting HIV/AIDS. Data from 146 countries show that some have achieved declines in new HIV infections among adults of 50% or more over the last 10 years, while many others have not made palpable progress, and yet others countries have experienced worrying increases in new HIV infections (UNAIDS 2016). In Namibia, HIV prevalence amongst people aged 15 – 49 is estimated to be 16% and the total population of PLHIV aged 15 and above is estimated at 260,000 (Ministry of Health and Social Services 2015). The revised 2015 estimated projects People living with HIV to increase to over 273,000 in 2017, and over 296,000 by 2020 (Ministry of Health and Social Services 2015). Meanwhile, the preventative effect of antiretroviral therapy has been limited because 40% [35–44%] of people living with HIV do not know their HIV status and 62% [59–65%] of people living with HIV are not virally suppressed well shy of the 90–90–90 target (UNAIDS 2016). Reaching the third 90 which translates to 73% of people living with HIV virally suppressed can only achieve up to 50% of the incidence reduction required to end the AIDS epidemic by 2030 (UNAIDS 2016). The global gap to achieving the 90–90–90 target in 2015 was around 10.9 million people living with HIV who did not know their status, 12.7 million people in need of antiretroviral therapy, and 13.0 million people living with HIV who were not virally suppressed (UNAIDS 2016). In fact, viral load is the mirror of disease progression. Achieving the last 90 target is challenging because an estimated 38% [35–41%] of people living with HIV worldwide are only virally suppressed (UNAIDS 2016). The preventative benefits of treatment are not being realized fully due to failure to reach people soon after infection, when viral load levels are high (UNAIDS 2016). Disruptions of viral suppression of those on treatment, due to lack of adherence or viral resistance, limit the potential gains of treatment (UNAIDS 2016). Adherence is the best predictor of treatment success among clients (Kassaye 2015). Near-perfect adherence is needed for clients to achieve good results, such as decreasing viral loads in the bloodstream, and preventing HIV-related complications (Kassaye 2015). Maximum adherence to ART in patients with HIV improves health outcomes and prevents drug resistance (Lester 2010). Authors (Giami 1996: Abelhauser 1998; Chesney 2000; Tamuzi 2017) have argued adherence is: "l'arbre qui cache la foret", meaning that patient adherence is multidisciplinary, multifocal and complex (Tamuzi 2017). Several factors among socio-economic, psychological, socio-environmental and socio-cultural could impact on patient adherence. Due to the multifactorial nature of the determinants of patient adherence and diversified research efforts to respond to each of these factors, mobile phones have emerged as a potentially useful tool to improve adherence rates (Mbuagbaw 2013). Policy makers should

propose the combination of more than two community-based interventions to strengthen patient adherence (Tamuzi 2017). Patient adherence should involve medical staffs, families and communities. In this trial, we will emphasize the role of medical staffs in enhancing patient adherence. Authors have shown that frequent contact with health care and other social services within a case management–based system may further facilitate good adherence in particular patient populations (Smith-Rohrberg 2006 ; Conway 2007). Thus, a multidisciplinary individualized approach that proactively addresses potential adherence issues with regular reinforcement may be the most practical way to support adherence in persons with HIV infection (Frick 2006 ; Conway 2007). Case management based system that includes Motivational interviewing (which, by its design, is meant to mitigate this concern) has shown modest favorable impacts on subsequent adherence (Golin 2006). In addition, maintaining an honest, open, nonpaternalistic care provider–patient relationship is critical to addressing adherence and its barriers (Conway 2007). Then, authors call all those intervention "intensive case management approach".

II. Research question and objectives

- To improve the viral load in adults HIV-infected with viral load equal or above 1000 copies/ml.
- To enhance the adherence in HIV-infected in adults with viral load >= 1000 copies/ml.

In adults HIV-infected with viral load >= 1000 copies/ml, is intensive case management approach effective in enhancing the viral load before and after interventions?

III. Methods

We hypothesize that intensive case management approach will enhance the viral load and the adherence in adults HIV-infected adults. The study is a mini-trial assessing the outcome before and after the intervention. Participants will be selected in Otavi medical centre. We will assess database in Otavi Medical Centre. Adults HIV-infected whose viral load is equal or above 1000 copies/ml will be selected.

➢ Study Population and Study Sample

Between October 2016 and July 2017, we will identify a convenience sample of 50 adults HIV infected in Otavi Medical Centre. Patients will be aged between 15-64 years. Otavi is a town located in the Otjozondjupa Region of northern Namibia with a population around 11000 residents (Hope for hopeless project 2009). It is the district capital of the Otavi electoral constituency. The community is variable and consists of people from a variety of tribes, even if its largest tribe consists of the Damara people (Hope for hopeless project 2009). Otavi is a traffic hub where the national roads B1 and B8, as well as the main street 1039 are in intersection (Support ulm e.v 2015). These hubs present so called "hot-spots" are known as being high-risk areas for the spreading of HIV-infections (Support ulm e.v 2015). According to recent estimates for this region, the accumulation of HIV-infections among the adult population is likely to be over 50% (Support ulm e.v 2015). A discussion hold among youth in Otavi in 2006 identified several problems that could allow the HIV pandemic to progress. During the discussion, the youth acknowledged the fact that they drink too much alcohol, having many partners and unprotected sex (WIMSA 2006).

- Inclusion criteria
  We will include adults HIV-infected aged from 15-64 years with VL>= 1000 copies that are follow up in Otavi clinic.
- Exclusion criteria
  HIV/TB co-infection patients, inpatients and HIV-infected pregnant women will be excluded from this trial.

➢ Interventions

We developed our interventions through a process of identifying main barriers and solutions to improve adherence in adults HIV-infected. The principal investigator will use Life-Steps protocol during his medical consultations. Life-Steps is a single session intervention utilizing cognitive-behavioral, problem-solving (D'Zurilla, 1986; Safran 2001), and motivational interviewing (Miller1991; Safran 2001) techniques to enhance motivation, rehearse adherence- related behaviors, and solve problems that interfere with adherence to HIV medications. We will call HIV-infected adults with VL>=1000 copies/ml in Otavi clinic. The medical doctor will assess the holistic needs of patients through medical consultation. With the help of the client, family members, nurses and community support, we will prioritize the needs of the client. In collaboration with case manager, adherence will be enhanced through regularly advice calls, SMS (one monthly call and weekly SMS) and medical discussions. The duration of the intervention is estimated six months. Those symbiotic interventions are called 'intensive case management approach'.

➢ Outcomes assessment

The primary outcome will be the proportion of adults with viral load less than 1000 copies/ml after three and six months of intervention. Primary outcomes will be assessed through medical laboratory results. The secondary outcome is adherence assessment; through self-reported HIV treatment adherence.

IV. Data collection and management

The principal investigator will choose the files in which the VL will be equal or above 1000 copies/ml. Once eligibility has been confirmed, the nurse will contact eligible participants if they are ready to decide whether or not to join the trial. If so, she will give the participant a consent form (See annex). After patient has checked that the consent form is understood, the nurse will invite the participant to sign the form, add her own name and countersign it. One copy of the consent form will be given to the participant, another will be filed in the clinic case notes, and the third will be posted to the Trial team. Data collection will be conducted by the principal investigator in medical consultation room. Medical records will be used to assess demographic details and primary outcome.

The completeness of the intervention will be assessed through the intervention description form. A self-administered questionnaire will be design to assess the secondary outcome. Baseline data (3 months before the intervention) will be collected for all outcomes. Then, the trial team will assess data trough database creates specifically for the trial. Data will be handled, computerized and stored in accordance with the Data Protection Act, 1998. Participants will be identified on the study database using a unique code and initials. The investigator will maintain accurate patient records/results detailing observations on each patient enrolled. All participant contact information data will be stored on spreadsheets within the recruiting internet site, which will have restricted access from password protected computers.

V. Discontinuation / Withdrawal of Participants from Trial

Each participant has the right to withdraw from the trial at any time. In addition, the Investigator may discontinue a participant from the trial at any time if the Investigator considers it necessary for any reason including:

- Significant protocol deviation
- Withdrawal of Consent
- Loss to follow up

VI. Ethics

In the start of trial, investigators will obtain ethical approval from the Otavi Clinic. Then after, clearance will be also obtained from Otjozondjura Region and the Namibian Ethic committee. Questionnaires and consent forms will be created in English, translated into, and back-translated; all translations and back-translations will be submitted for Ethics Committee review. Once all these approvals will be granted, verbal consent will be obtained from the participants in the study. Investigators collecting the data will be trained to deal with study. We will assure respondents of privacy and confidentiality as such names and HIV status will not be included in the study. Respondents will also be informed that participation in the study will be voluntary and that, their treatment will not depend on whether or not they accept to participate. The risk of stress and anxiety due to discussion about HIV, HIV testing, and disclosure of HIV status will be minimized by conducting all discussions in a private space. Investigators will assure that none of the information collected through the trial will likely affect a subject's relationship with other individuals (e.g., patient-physician, family relationships) or influence the subject's HIV treatment at the research site. All data will be protected in locked cabinets or in password-protected computers equipped with anti-virus.

VII. Analysis plan

Data will be captured and entered into EpiInfo and converted to Stata14 for validation and analysis. The Excel datasheets will be cleaned and scanned. Excel datasheets will be imported into STATA 14 format for analysis. Normality checks on all data will be conducted prior to further analysis. No imputation of missing values will be carried out for subjects.

- Ground rules for the statistical analyses

The statistical analyses will be based on comparing the baseline viral load to post intervention viral load. Known that the viral load is continuous data, paired t-test will be used. We will use STATA 14 to analyze data.

- Subgroup analysis

Subgroup analyses will be performed after stratification of primary outcome in different barriers affecting adherence among which food security, limited access to care, co-morbid conditions, forgetfulness and gender.

VIII. Post recruitment retention strategies

Support from the study team will be offered to participants to resolve any such problems. An information sheet will be given to all participants during the intervention period reminding stage of the study procedures. The fees of N$30 will be a reminder of the strategies suggested during training, but will also be informed by feedback from the routine telephone contacts made with the trial research in the four weeks after patients recruitment starts. Participants, who completed one-week questionnaire has not been received by the research team three weeks post-recruitment, will receive a reminder from the study researcher. Reminders will be issued by telephone as indicated in the participant contact details given during the recruitment. Attempts to contact non-responders will continue until contact is made or for a maximum of one week. A similar process will be followed for the 8 weeks.

IX. Registering the trial

This study will be registered to clinical trials (www.clinicaltrials.gov). The clinical trial will be registered based on with the criteria of World Health Organization (WHO) or International Committee of Medical Journal Editors (ICMJE). After registering the study, a unique trial number will be assigned which will be mentioned in the published protocol and the final report. And then, the trial registration date is recorded.

X. Good clinical practice (GCP)

The investigator will ensure that this trial is conducted in accordance with relevant regulations and with Good Clinical Practice. Then, trial staff will be trained as clear as possible in GCP. Regular monitoring will be performed according to GCP. Data will be evaluated for compliance with the protocol and accuracy in relation to source documents. Following written standard operating procedures, the monitors will verify that the clinical trial is conducted and data are generated, documented and reported in compliance with the protocol, GCP and the applicable regulatory requirements. The Investigator will ensure that this trial will be conducted in accordance with the principles of the Declaration of Helsinki. The protocol, informed consent form, participant information sheet and any proposed advertising material will be submitted to an appropriate Research Ethics Committee, regulatory authorities, and host institution(s) for written approval. The principal investigator will submit during the clinical trial, a monthly ongoing Report to the research ethics committee, host organisation and Sponsor. In

addition, an end of Trial notification and final report will be submitted to the host organisation and Sponsor.

XI. Reporting, dissemination and notification of results

The CONSORT guidelines (Schulz 2010) will be used for reporting the results. The following ways of dissemination will ensure the widest possible distribution:

a) Publication of major findings in a mainstream journal.
b) Publication of major findings in national journals.
c) Reporting of trial findings in WHO publications.
d) The practical implications of the trial results can be incorporated within a short time into other WHO activities such as The WHO guidelines for HIV.

Trial results will be disseminated even if the outcome is negative. We will assume participant's confidentiality will be maintained when reporting the results.

XII. Conclusion

This trial will highlight the importance of intensive case management approach in improving ARV adherence. The particularity of this intervention is considering a holistic approach in enhancing adherence.

XIII. References

[1]. Conway B. The role of adherence to antiretroviral therapy in the management of HIV infection. Journal of acquired immune deficiency syndromes (1999) 2007;45 Suppl 1:S14-8.

[2]. D'Zurilla, T. J. Problem solving therapy: a social competence approach to clinical interventions. In: Springer. New York, 1986.

[3]. Frick P, Tapia K, Grant P, Novotny M, Kerzee J. The effect of a multidisciplinary program on HAART adherence. AIDS patient care and STDs 2006;20(7):511-24.

[4]. Golin CE, Earp J, Tien HC, Stewart P, Porter C, Howie L. A 2-arm, randomized, controlled trial of a motivational interviewing-based intervention to improve adherence to antiretroviral therapy (ART) among patients failing or initiating ART. Journal of acquired immune deficiency syndromes (1999) 2006;42(1):42-51.

[5]. Hope For The Hopeless Project. https://hopeforthehopelessproject.wordpress.com/about-otavi-namibia/) 2009.

[6]. Manuel Kassaye, Ismael Ahmed, Getachew Feleke. ART Structured Adherence Counseling Session Guide. Addis Ababa: I-TECH Ethiopia team, 2015.

[7]. Lester RT, Ritvo P, Mills EJ, Kariri A, Karanja S, Chung MH, et al. Effects of a mobile phone short message service on antiretroviral treatment adherence in Kenya (WelTel Kenya1): a randomised trial. Lancet (London, England) 2010;376(9755):1838-45.

[8]. Mannheimer SB, Morse E, Matts JP, Andrews L, Child C, Schmetter B, et al. Sustained benefit from a long-term antiretroviral adherence intervention. Results of a large randomized clinical trial. Journal of acquired immune deficiency syndromes (1999) 2006;43 Suppl 1:S41-7.

[9]. Mbuagbaw L, Thabane L, Ongolo-Zogo P. Opening communication channels with people living with HIV using mobile phone text messaging: insights from the CAMPS trial. BMC research notes 2013;6:131.

[10]. Miller, W. R., & Rollnick, S. Motivational interviewing: preparing people to change addictive behavior. In: Guilford Press. New York, 1991.

[11]. Ministry of Health and Social Services. THE NAMIBIA AIDS RESPONSE PROGRESS REPORT 2015. unaids, 2015.

[12]. Safren SA, Otto MW, Worth JL, Salomon E, Johnson W, Mayer K, et al. Two strategies to increase adherence to HIV antiretroviral medication: life-steps and medication monitoring. Behaviour research and therapy 2001;39(10):1151-62.

[13]. Smith-Rohrberg D, Mezger J, Walton M, Bruce RD, Altice FL. Impact of enhanced services on virologic outcomes in a directly administered antiretroviral therapy trial for HIV-infected drug users. Journal of acquired immune deficiency syndromes (1999) 2006;43 Suppl 1:S48-53.

[14]. Support e.v. https://www.support-ulm.de/en/namibia/relief-operations-in-namibia/ 2015.

[15]. Jacques L. Tamuzi; Charles I. Okwundu. Mobile Phone Communication for Improving Uptake of Antiretroviral Therapyin HIV-infected Pregnant Women: Review. International Annals of Medicine 2017;1:1.

[16]. UNAIDS. Prevention gaps report. 2016;(www.unaids.org/en/resources/documents/2016/prevention-gap).

[17]. WIMSA 2006. Discussions on HIV:A Hai||om Community Assessment Oshivelo, Otjiwarongo, Otavi & Outjo. Summary Report. wwwisis.unam.na/hivdocs/.../HIV%20.../WIMSA_2006%20Oct_Hai%20om%20com 2006.