MÉDECINS SANS FRONTIÈRES

VIRAL LOAD TOOLKIT

AN IMPLEMENTER'S GUIDE TO INTRODUCING HIV VIRAL LOAD MONITORING

MEDECINS SANS FRONTIERES

SAMU
SOUTHERN AFRICA MEDICAL UNIT

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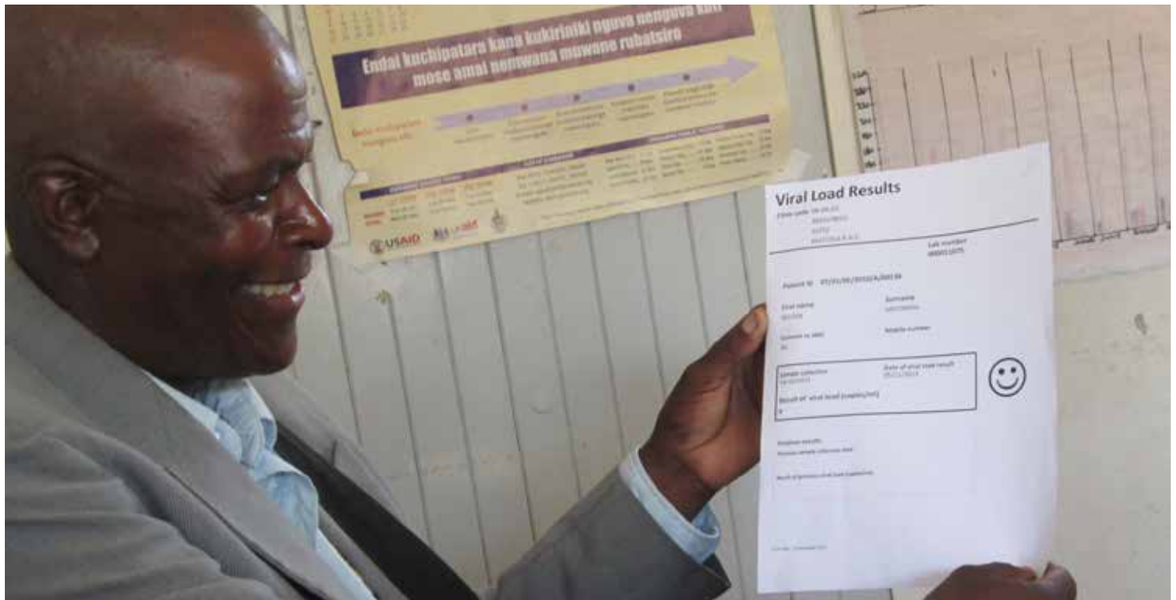


1. INTRODUCTION:

HIV viral load (VL) testing has been the gold standard for monitoring the response to antiretroviral therapy (ART) in high-income settings for many years and is increasingly recognized as an important tool for the management of ART in resource-limited settings. Benefits of VL monitoring include the ability to diagnose poor adherence and treatment failure early, prevent unnecessary switches to second line ART and to allow optimization of treatment response in order to avoid development of resistance and prevent transmission.[1,2,3] Guidelines for ART management issued by the World Health Organization (WHO) have recognized the importance of VL monitoring since 2003 and routine VL monitoring is now strongly recommended as the monitoring strategy of choice.

This toolkit is designed to provide implementers with a set of tools to aid in implementation of VL monitoring including aspects related to sample preparation, activities for clinical and counselling staff, and education and empowerment of the patients themselves. The tools and algorithms form a basis for implementation, but will need to be adapted to the local context.

A training pack for clinicians and counsellors is also attached in Annexes 4 and 5 that incorporate these key components.

1. Sigaloff KCE, Hamers RL, Wallis CL, Kityo C, Siwale M, Ive P, Botes ME, Mandaliya K, Wellington M, Osibogun A, Stevens WS, van Vugt M, Rinke de Wit TF: **Unnecessary Antiretroviral Treatment Switches and Accumulation of HIV Resistance Mutations; Two Arguments for Viral Load Monitoring in Africa.** *J Acquir Immune Defic Syndr* 2011, **58**:23-31.

2. Lynen L, Van Griensven J, Elliott J: **Monitoring for treatment failure in patients on first-line antiretroviral treatment in resource-constrained settings.** *Curr Opin HIV AIDS* 2010, **5**:1-5

3. Keiser O, Chi B, Gsponer T, Boulle A, Orrell C, Phiri S, Maxwell N, Maskew M, Prozesky H, Fox MP, others: **Outcomes of antiretroviral treatment in programmes with and without routine viral load monitoring in Southern Africa.** AIDS 2011

2. SAMPLE PREPARATION:

For centralised viral load processing, samples may either be sent to the VL laboratory as **whole blood, plasma or dried blood spots (DBS).** When blood is drawn at a peripheral clinic in either EDTA or plasma preparation tubes (PPT), samples should be transported at room temperature but must reach the district laboratory or site where centrifugation may occur preferably within 6 hours.[4] If centrifugation is feasible at peripheral clinic level, plasma samples can be stored up to 5 days at room temperature with PPT and up to 14 days at 2° - 8° from EDTA-derived tubes (longer if frozen at -20° to -80°). In the same way, transport of plasma samples to the viral load laboratory requires cold chain, which increases the costs related to sample storage and transport. The practical implications of these requirements for the patients are that they are either asked to visit their clinic again on a specific specimen collection day or are forced to travel to the district level hospital to have blood drawn.

A strategy to simplify sample transport is to prepare whole blood samples on dried blood spots (DBS). At present DBS samples can only be processed reliably using a NASBA platform (e.g Biomerieux) if a threshold of 1000 copies/ml is required for clinical action. DBS samples offer multiple operational advantages: they can be stored and transported at room temperature for longer periods of time without affecting RNA stability; they can be prepared by non-laboratory staff with minimal training either from capillary or venous blood; and the small volume of blood needed to impregnate the filter paper reduces the biohazard risk related to sample collection.

The decision on sample type will be determined by availability and level of staff in the clinics; for example, collection of capillary blood by the finger-prick method can be performed by both lay counsellors and nurses, whilst venesection is restricted to trained medical staff. Although the procedure to prepare DBS is straightforward, training and ongoing mentorship is essential when task shifting the collection and preparation of samples to lower levels of health workers.

Standard operating procedures for preparation of DBS samples from EDTA whole blood and finger prick capillary blood are given below (Figures 1 and 2).

4. Some studies suggest that EDTA whole blood samples can be stored at room temperature for up to 7 days before testing, with negligible impact on RNA stability. However, these results only apply to samples with high HIV viral loads (>5,000 copies/ml), thus, further investigation is needed in samples with low viral loads (<5,000 copies/ml).

ANNEXE 1: SAMPLE PREPARATION
Also available at http://samumsf.org/blog/portfolio-item/viral-load-vl-toolkit/

- Standard Operating Procedure (SOP) Preparation of EDTA DBS
- SOP Preparation of Finger prick DBS
- Training powerpoint for preparation of EDTA DBS
- Training powerpoint for preparation of Finger Prick DBS

FIGURE 1: PREPARING A DBS FROM EDTA WHOLE BLOOD

How To Prepare An Acceptable Blood Spot Specimen From EDTA Whole Blood

A1 Preparation

A1.1 Wash hands vigorously.

A1.2 Wear powder-free gloves and change gloves between patients.

A1.3 Confirm identity of patient and ensure that all data elements on the form are complete, accurate and consistent.

A2 Phlebotomy

A2.1 Write name and number of the patient on a purple cap EDTA tube (4mL) with an indelible marker.

A2.2 Use a tourniquet or get the patient to clamp his/her fist to locate the veins.

A2.3 Clean the puncture site with alcohol or disinfectant. Do not touch again after cleaning.

A2.4 Insert the needle into a holder and then into the patient's vein, bevel upwards. The back of the needle is used to pierce the top of the vacutainer tube.

A2.5 The vacuum makes the tube fill to the required level.

A2.6 Remove the tube and mix gently by inverting several times to mix the blood with the anticoagulant.

A2.7 Blood collection can be difficult on a patient with low blood pressure. In this case, use a syringe. The use of a butterfly can also assist in the collection of blood.

A3 DBS Preparation

A3.1 Write patient name, number and date on the space provided on the card.

A3.2 Position the DBS card in a way that the circles do not touch the surface of the bench.

A3.3 Mix the blood gently once again by inverting several times.

A3.4 Open the EDTA tube.

A3.5 Squeeze the end of the Pasteur pipette before inserting it in the tube.

A3.6 Insert the pipette in the blood and release the end to suck up the blood.

A3.7 Gently apply enough blood to each circle to fill them completely. Apply blood to one side only.

A3.8 Make sure that the individual blood circles do not touch each other.

A3.9 Place completed DBS cards on the rack to dry. Make sure that the cards do not touch each other.

A3.10 Let the DBS cards dry for at least 3-4 hours. Keep out of direct sunlight.

A3.11 All used items should be disposed of in an appropriate biohazard container.

A3.12 When dry, each card should be packed individually in a plastic zip-lock bag with 2 desiccant sachets and a humidity indicator card.

A3.13 Store the packed DBS at room temperature and send to the laboratory within a week after preparation.

A4 Pitfalls

A4.1 Avoid touching the area within the circle before and after blood spotting.

A4.2 DBS cards should always be handled with gloves and only touched on the edges, never on the circles.

A4.3 DBS's should be prepared in a dry and clean room, free of wind and dust.

A4.4 Blood can be collected from several (5-10) patients before preparing the DBS's. Make sure that the collected blood is spotted within 1 hour.

A4.5 Do not pack the DBS cards in the plastic zip-lock bag until thoroughly dry. Insufficient drying adversely affects test results.

FIGURE 2: PREPARING A DBS FROM FINGER PRICK CAPILLARY BLOOD

How To Prepare An Acceptable Blood Spot Specimen From Capillary Blood

A1 Preparation

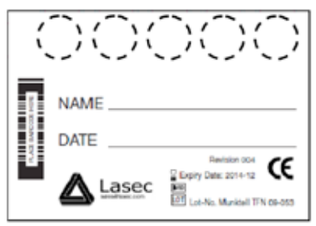
A1.1 Wash hands vigorously.

A1.2 Wear powder-free gloves and change gloves between patients.

A1.3 Confirm identity of patient and ensure that all data elements on the form are complete, accurate and consistent.

A2 Finger-Prick And DBS Preparation

A2.1 Write patient name, number and date on the space provided on the card.



A2.2 Position the DBS card in a way that the circles do not touch the surface of the bench.

A2.3 Clean the puncture site on the finger with alcohol or disinfectant.

A2.4 Let air-dry and do not touch again.

A2.5 Keep the puncture site below heart level.

A2.6 Prick the site with a lancet, off the center of the finger.

A2.7 Wipe away the first drop of blood with sterile gauze.

A2.8 With the finger extended, allow a large hanging drop of free flowing blood to accumulate at the puncture site.

A2.9 Hold the Microsafe pipette horizontally and allow it to fill by capillary action to the defined volume.

A2.10 Dispense the blood in the center of the first circle of the card.

A2.11 Allow another large drop of blood to form at the puncture site and collect it to fill the next circle.

A2.12 Repeat A2.7 until all circles are filled.

A2.13 Try to fill all 5 circles. If not enough blood can be collected, at least 3 circles should be filled.

A2.14 Do not layer successive drops of blood on top of each other and only apply blood on one side of the paper.

A2.15 Make sure that the individual blood circles do not touch each other.

A2.16 Place completed DBS cards on the rack to dry. Make sure that the cards do not touch each other.

A2.17 Let the DBS cards dry for at least 3-4 hours. Keep out of direct sunlight.

A2.18 All used items should be disposed of in an appropriate biohazard container.

A2.19 When dry, each card should be packed individually in a plastic zip-lock bag with 2 desiccant sachets and a humidity indicator card.

A2.20 Store the packed DBS at room temperature and send to the laboratory within a week after preparation.

A4 Pitfalls

A3.1 Do not squeeze or milk the finger.

A3.2 Avoid touching the area within the circle before and after blood spotting.

A3.3 DBS cards should always be handled with gloves and only touched on the edges, never on the circles.

A3.4 DBS's should be prepared in a dry and clean room, free of wind and dust.

A3.5 Do not pack the DBS cards in the plastic zip-lock bag until thoroughly dry. Insufficient drying adversely affects test results.

3. VIRAL LOAD REQUEST FORM

The number of variables included on the HIV viral load (VL) request form will depend on the analyses required by the programme managers. Essential variables will include a minimum of two key patient identifiers, sample collection date, VL result and VL result date. The example given below allows one portion of the VL form (on the left) to be kept at clinic level and allows the clinician to record the result upon its receipt, plus ensure that all VL results have been received. Bar codes are also included (one each for the VL form, sample and clinic held portion) in order to reduce sample identification errors.

FIGURE 3: EXAMPLE OF A VIRAL LOAD REQUEST FORM (ZIMBABWE)

Tear here

Viral Load Laboratory Request form

Province _____ **District** _____

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Clinic name _____
Clinician name _____

Sample Collection date ____ / ____ / ____ Time ____:____
First name_____ Surname_____

Patient OI Number ␣␣/␣␣/␣␣/ 20␣␣/ A␣␣␣␣␣

Sex (**tick one**): Male ☐ Female ☐ Date of ART initiation ____ / ____ / ____ Current ART regimen _____

Date of birth ____ / ____ / ____ If no DOB, Age_____ years If < 1 year Age _____ months

Currently pregnant (**tick one**): Yes ☐ No ☐ Currently breastfeeding (**tick one**): Yes ☐ No ☐

Patient consents to SMS: Yes ☐ No ☐ If Yes, mobile number _____

Date of last viral load tested ____ / ____ / ____ Result last viral load _____ copies/ml

Reason viral load requested (**tick one**): Routine ☐ Target clinical failure ☐ Targeted Immunological failure ☐

Repeat After Enhanced Adherence ☐ Other ☐ _____

If After Enhanced Adherence: Poor Adherence was identified Yes ☐ No ☐ Number of Enhanced Sessions: 1 ☐ 2 ☐ 3 ☐ >3 ☐

Date of sample collection:
____ / ____ / ____

Time of sample collection:
_____ : _____

Patient name and surname:
_____

Patient OI number:
␣␣/␣␣/␣␣/ 20␣␣/ A␣␣␣␣␣

Patient phone number:
_____

Viral Load result:
_____ Copies/ml

Date VL received:
____ / ____ / ____

FOR LABORATORY USE ONLY

VL Platform (**tick one**): BioMérieux ☐ Roche ☐ Abbott ☐ POC ☐

Specimen Type (**tick one**): EDTA DBS ☐ FP DBS ☐ DPS ☐ PLASMA ☐ WHOLE BLOOD ☐

Test method (**tick one**): Individual ☐ Minipool ☐ Other Pooling algorithm ☐

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Date of result ____ / ____ / ____ Viral Load result _____ copies/ml

If no result _____ Approved by_____

Laboratory officer comments | Date received stamp

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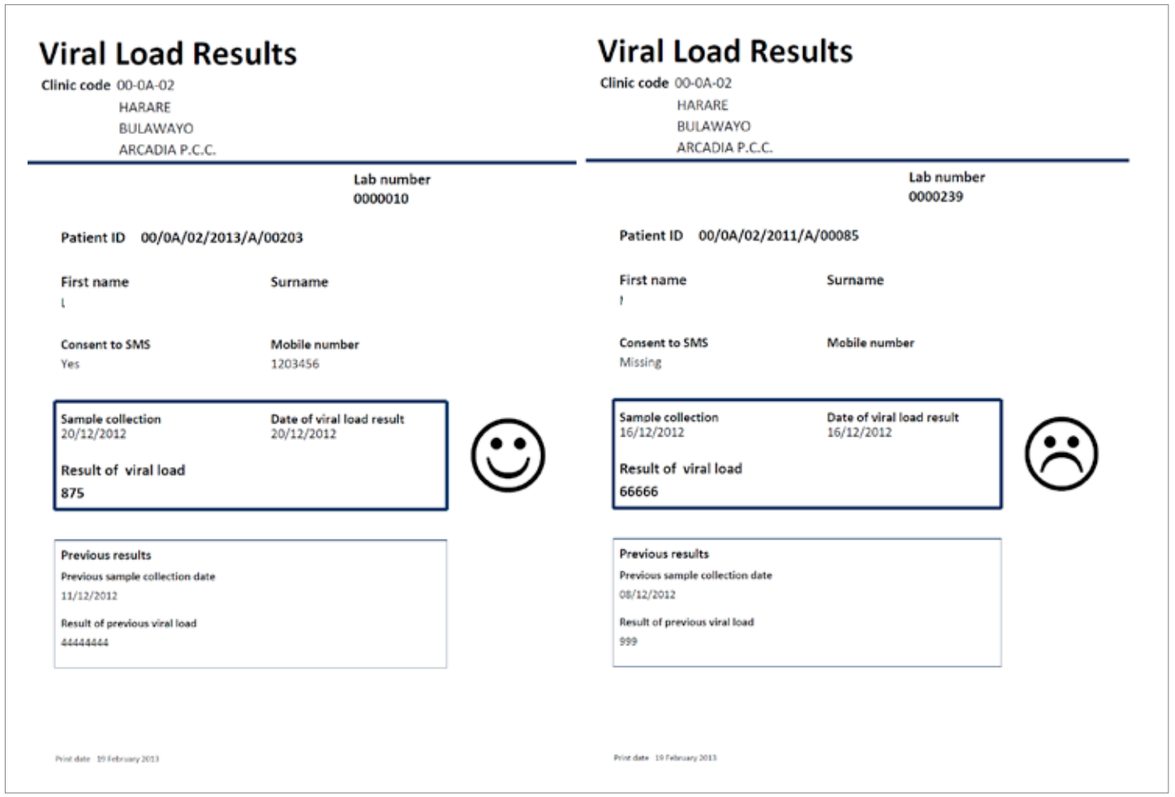
ANNEXE 2: VIRAL LOAD REQUEST FORM
Also available at http://samumsf.org/blog/portfolio-item/viral-load-vl-toolkit/

4. RESULT DELIVERY

To assist in interpretation of VL results, particularly where HIV care has been task shifted to lower levels of health care workers, a flagging system for abnormal results should be employed. Figure 4 shows schematics of results less than and greater than 1000 copies/ml.

M-health activities may also improve the number of patients receiving their results and ensure that appropriate action is taken. Results may be sent directly to the clinics and/or to patients themselves with specific messages that depend on the result.

FIGURE 4: SCHEMATICS FOR FLAGGING VIRAL LOAD RESULTS

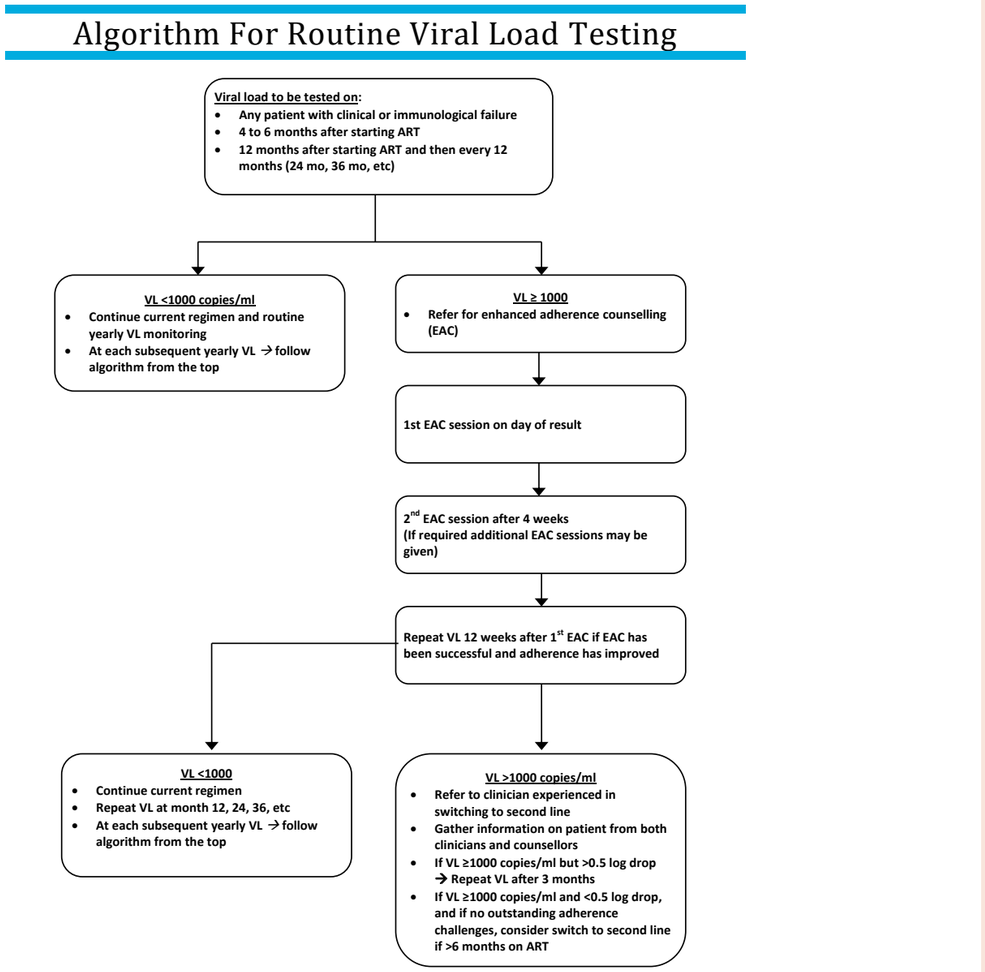


5. VIRAL LOAD CLINICAL ALGORITHM

According to the WHO viral load algorithm, the threshold for triggering an adherence intervention is an HIV viral load result > 1000 copies/ml. Following the adherence intervention (usually performed over a three-month period) a repeat VL test is carried out. If this second viral load result is > 1000 copies/ml, the patient should be considered for a switch to second line ART.

Ideally the first VL test should be performed between 4-6 months after ART initiation in order to detect early poor adherence. Following this early VL test, the next test is usually taken at twelve months on ART and ideally yearly thereafter. A simple way of reminding patients and nurses when to take the VL is to perform the test annually during the month of ART initiation. Figure 5 outlines the steps in a typical viral load clinical algorithm.

FIGURE 5: VIRAL LOAD ALGORITHM



When a patient becomes eligible for second line ART, a multidisciplinary team discussion between counsellor and clinician should be carried out. Figure 6 demonstrates a tool that may aid in documentation of the key areas that should be considered in this discussion. Where HIV care and treatment (i.e. ART) have been decentralised, an effort should be made to also decentralise the decision to switch to second line ART. Cases eligible to be switched can be booked for the day of the mobile mentoring/ supervising team visit or discussed by telephone, if feasible, using the summary forms. A system for establishing a structured approach to switching to second line ART needs to be developed locally.

In addition, adequate supervision, through monitoring and evaluation and site visits, is needed to ensure systematic implementation of the VL clinical algorithm. Lists of patients having VL results > 1000 copies/ml should be generated automatically and provided by the laboratory to clinic coordinators and programme supervisors in order to assist in follow up and to ensure that those patients who may be adhering poorly and/or be failing their ART regimen are being managed appropriately.

FIGURE 6: HIGH VIRAL LOAD PATIENT SUMMARY FORM

HIGH VIRAL LOAD FORM
(For Enhanced Adherence Counselling and Second Line Consideration)

Patient Information

Name:_____ **Health Centre:**_____
Age: _____ **Sex: M F** **Pt Number:**_____

ARV Information		***Viral Load Results***	
ARV Regimen:	Date of initiation:	**Viral Load before EAC:** _____ c/ml	Date: ____/____/____
_____	____/____/____	**Previous VL (if any) :** _____ c/ml	Date: ____/____/____
_____	____/____/____	_____ c/ml	Date: ____/____/____
_____	____/____/____	_____ c/ml	Date: ____/____/____
_____	____/____/____		

Enhanced Adherence Counselling (To be filled by the Counsellor)

For each session, assess major barriers for possible poor adherence (cognitive, behavioral, emotional, socio-economic).
Date of 1st session:___/___/___ **Summary:**_____
_____
_____
ARV-intake demonstration by patient/caretaker done? **Y N** Pill count done? **Y N** Pill intake: ___%

Date of 2nd session: ___/___/___**Summary:**_____
_____
_____Pill count done? **Y N** Pill intake: ___%

Date of extra session (if any): ___/___/___**Summary:**_____
_____
_____Pill count done? **Y N** Pill intake: ___%

Did the patient attend all the appointments? **Y N** If no, any reason? _____
Your impression about patient's adherence before EAC:
Likely to be good Likely to be **NOT** good (relevant barriers identified) clearly poor (defaulter)

Your impression about patient's adherence during and after EAC:
Likely to be good Likely to be **NOT** good (relevant barriers identified and not cleared) clearly poor (defaulter)*
(*) *If patient is defaulting, repeat Viral Load should be deferred and EAC extended. Share decision with the team.*

Major remaining barriers identified after EAC sessions: • Behavioral **Y N** If yes: _____
• Cognitive **Y N** If yes: _____ • Socio-economic **Y N** If yes:_____
• Emotional **Y N** If yes: _____ • others (Disclosure, Religion...) **Y N** If yes:_____

Date of collection of repeat Viral Load:____/____/_____
Counsellor: _____ Date of assessment: ____/____/_____

OUTCOME (To be filled by the Nurse)

Repeat Viral Load result:_____ c/ml Date: ____/____/____
Was it a significant drop in the Viral Load (fulfilling criteria of good response to EAC)? **Y N**

Is this patient currently a TB suspect? Y N Investigations done? **Y N** If yes, results:_____

Is this patient presenting any other OI or signs of immunosuppression? **Y N** If yes, describe:_____
Hx of chronic diarrhea or vomiting? **Y N** Use of traditional medications? **Y N**
Hx of side-effects with ARV? Y N If yes, describe symptom and possible drug:_____

Other investigations: **CD4 count:** _____ **Hepatitis B screen:** _____ **Creatinine Clearance**: _____ **Hb:** _____

Regarding the ARV regimen, what is the plan? continue current regimen refer to doctor for further management

Nurse:_____ Date of assessment: ____/____/_____

Outcome for patients with persistent high Viral Load (To be filled by the Doctor)

What is the plan for this patient? Patient is suitable for Second-line Regimen. New regimen:_____
extend adherence sessions before new Viral Load (in 2-3 months time).
Comment:_____

Doctor:_____ Date: ____/____/_____

6. PATIENT EDUCATION FOR VIRAL LOAD

Patient literacy on the need for VL testing to monitor their response to treatment, and interpretation of VL results, is essential to support the demand for viral load, and is likely to aid adherence. For many patients changes in CD4 count levels have been the traditional way to understand treatment efficacy, and changing this paradigm will require concerted patient literacy and counseling, both within the clinic and through awareness raising in the community. Visual tools that help to explain the concept of viral load testing may aid in management, as can having clear written instructions on patient-held records describing when viral load testing should be performed. The aim is to empower the patient to both request that a viral load test be performed and to understand the result. A simple approach for patients to know when to request their yearly viral load is for the test to be performed during the month they were initiated on ART.

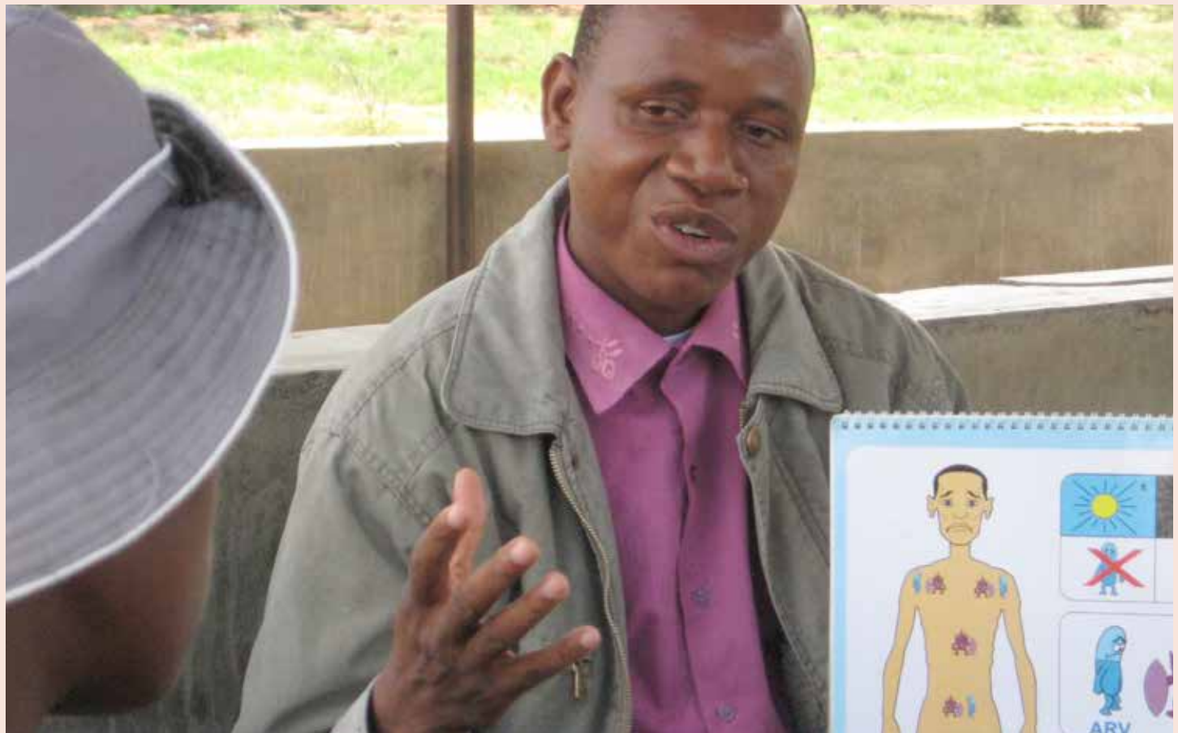
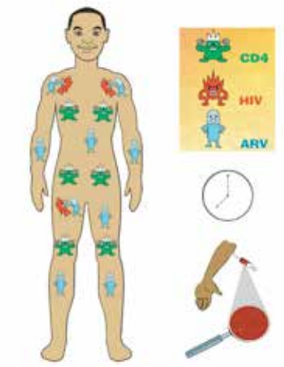
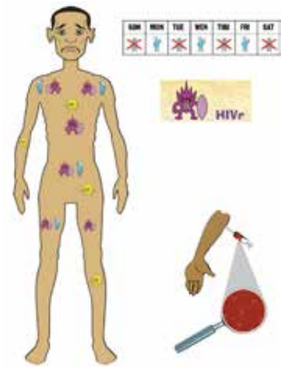


FIGURE 7: VISUAL AIDS AND KEY MESSAGES ON VIRAL LOAD



TOPIC	MESSAGES
What is the goal of ART therapy?	You are taking ARVs on a daily basis to fight HIV in your body. Due to the ARVs the number of HIV particles will decrease in your body, while your soldiers (CD4 cells) will increase and protect you from diseases.
What is the viral load test?	A viral load test measures the number of viruses in your blood. The test is done by taking a sample of blood for the lab by a finger prick of dy drawing blood.
When to have a viral load test?	All those on ART treatment will be offered a viral load test as part of your routine follow-up at X months or according to your health condition. You can always remind health your health worker for your need to get a viral load test or ask them the results of your test. It is important not to miss your appointment date for your viral load test and to come for the results on time.
What does an undedectable viral load result mean?	Undetectable viral load means that you have less HIV in your blood. Undetectable viral load in the blood does not mean that you no longer have HIV, but that it is too low to be measured. Undetectable viral load means your treatment is working well, because your ARVs are fighting HIV and thus reducing the amount of HIV in your blood.



TOPIC	MESSAGES
What does a detectable viral load result mean?	Detectable viral load means that there is a lot of HIV in your blood. When your viral load is detectable, the health worker will suspect treatment failure. Treatment failure means your HIV treatment is no longer working as it should: HIV is multiplying in your body while your soldiers (CD4 cells) reduce and opportunisitic infections might appear.
What could explain a detectable viral load?	You have problems taking your treatment on a regular basis: stopping to take your pills for a while, skipping many doses,... Resistance has developed to the treatment, which means that the HIV in your blood has changed in the absence of lower than normal levels of ARVs and your treatment is no longer able to fight the changed HIV. The resistant virus is now multiplying rapidly in your blood. You have good adherence but there is another unidentified medical problem.
What to do when you have a detectable viral load?	Together with the counsellor you will identify the reason for your detectable viral load and look at ways how to address any adherence problems. If your viral load persists being detectable and there is no longer and adherence problem, you might be changed to another drug regimen, which often consists of more pills to take and more potential side effects.
How to avoid resistance and treatment failure?	Adhere to your ARV treatment in order to maintain undetectable viral load, a strong immune system and a long life.

7. ENHANCED ADHERENCE COUNSELLING

Enhanced adherence counselling (EAC) refers to the counselling intervention for a patient with an elevated viral load result. A package for EAC consists of one to four sessions, which may be given individually or with specific sessions as a group. The objective of these sessions is to assess the barriers to adherence and to identify and evaluate strategies to overcome these barriers. The first of these sessions is given on the day the high viral load result is given to the patient, with subsequent sessions following monthly drug refill intervals. The repeat VL test is performed twelve weeks after the initial viral load result was given.

Suggested recording tools to aid in the management of patients with a high viral load result include the High Viral Load Patient Summary form shown in Figure 6 and a clinic-based register for all those patients undergoing EAC (Figure 8). This register gives an overview of all patients being offered enhanced adherence, whether they have attended their sessions or not, and the outcomes of their repeat viral load testing. In this way it also serves as a useful tool to give immediate feedback to the counsellors performing the intervention and may be used as a supervision tool by programme managers.

FIGURE 8: ENHANCED ADHERENCE REGISTER

OI Number	First Name and Surname	Age	Sex	Date first VL taken	First VL Result	First EAC on day result given (Date)	Second EAC (Date)	If further sessions write date	If further sessions write date	Expected Date Repeat VL due	Date Repeat VL taken	Result Repeat VL	Date 2nd Repeat VL taken	Result 2nd Repeat VL	Outcome: 1. Switched to second line 2. Remain on first line	Outcome date

ANNEXE 3: ENHANCED ADHERENCE SESSION CONTENTS
Also available at http://samumsf.org/blog/portfolio-item/viral-load-vl-toolkit/

6. TRAINING PACKAGES

A training package for clinicians and counsellors can be found in Annexes 4 and 5 respectively.
Also available at http://samumsf.org/blog/portfolio-item/viral-load-vl-toolkit/

These packages cover why we need routine viral load, the use of the viral load algorithm, details of the flow of samples and result delivery and the detailed content of the enhanced adherence sessions.

7. ADVOCACY MATERIALS

ANNEXE 6
Also available at http://samumsf.org/blog/portfolio-item/viral-load-vl-toolkit/

Undetectable: How Viral load monitoring can improve HIV treatment in developing countries.

Putting HIV Treatment to the test: A product Guide for Viral load and point of care CD4 Diagnostic Tools

Video: Reaching Undetectable: Why I need Viral Load.
This video shares the experience from a patient in Malawi who has had access to routine viral load and how she dealt with her result.

8. ACKNOWLEDGEMENT

The Southern Africa Medical Unit (SAMU) would like to acknowledge the work of the field teams in Zimbabwe, Malawi and South Africa who have contributed to the tools illustrated in this document and to the successful implementation of routine viral load.

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