



MÉDECINS SANS FRONTIÈRES

VIRAL LOAD TOOLKIT

**AN IMPLEMENTER'S GUIDE TO INTRODUCING
HIV VIRAL LOAD MONITORING**



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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.

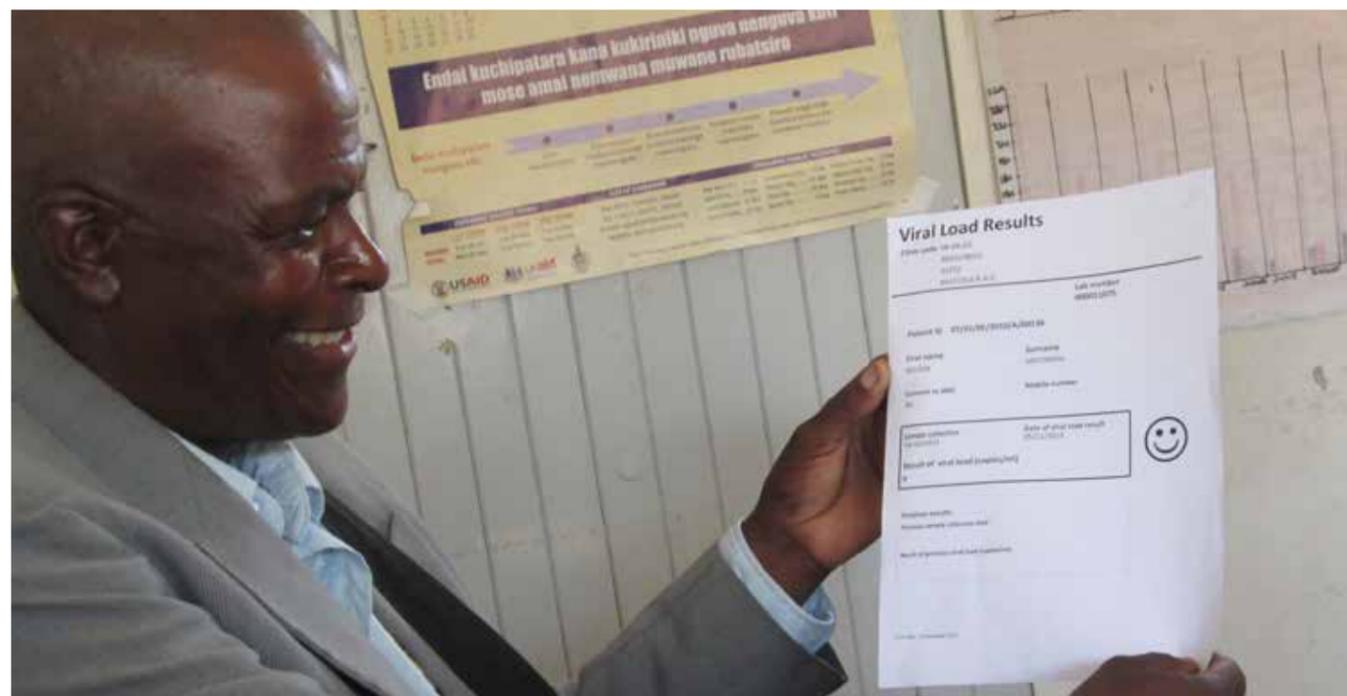
This toolkit is designed to provide implementers with a set of tools to aid in implementation of VL monitoring including aspects related to sample preparation, activities for clinical and counselling staff, and education and empowerment of the patients themselves. The tools and algorithms form a basis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

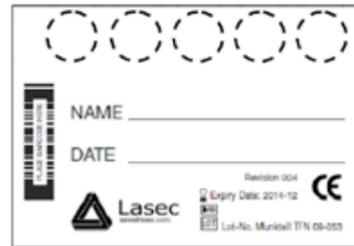
A1.2 Wear powder-free gloves and change gloves between patients.

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.

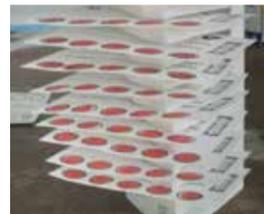
A2.12 Repeat A2.7 until all circles are filled.

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)


00000001



Viral Load Laboratory Request form

Province _____ District _____

Clinic name _____ Sample Collection date dd / mm / yyyy Time _____

Clinician name _____ First name _____ Surname _____

Patient OI Number dd/mm/yy/20yy/A_____

Sex (**tick one**): Male Female Date of ART initiation dd / mm / yyyy Current ART regimen _____

Date of birth dd / mm / yyyy 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 dd / mm / yyyy 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

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

Date of result dd / mm / yyyy Viral Load result _____ copies/ml

If no result _____

Approved by _____

Viral Load result: _____ Copies/ml

Date VL received: dd / mm / yyyy

Laboratory officer comments

Date received stamp


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00000001

ANNEXE 2: VIRAL LOAD REQUEST FORM

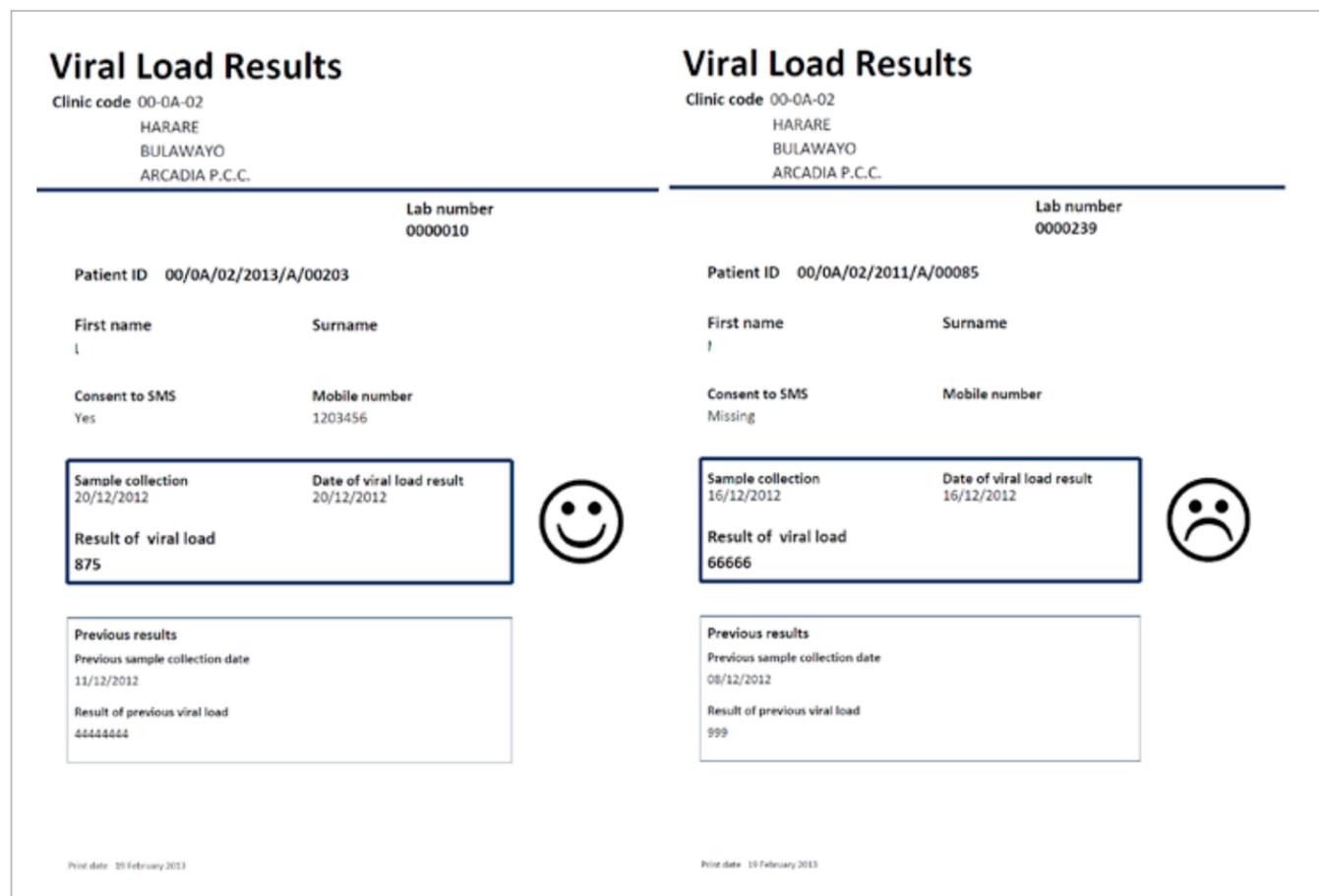
Also available at <http://samumsf.org/blog/portfolio-item/viral-load-vl-toolkit/>

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

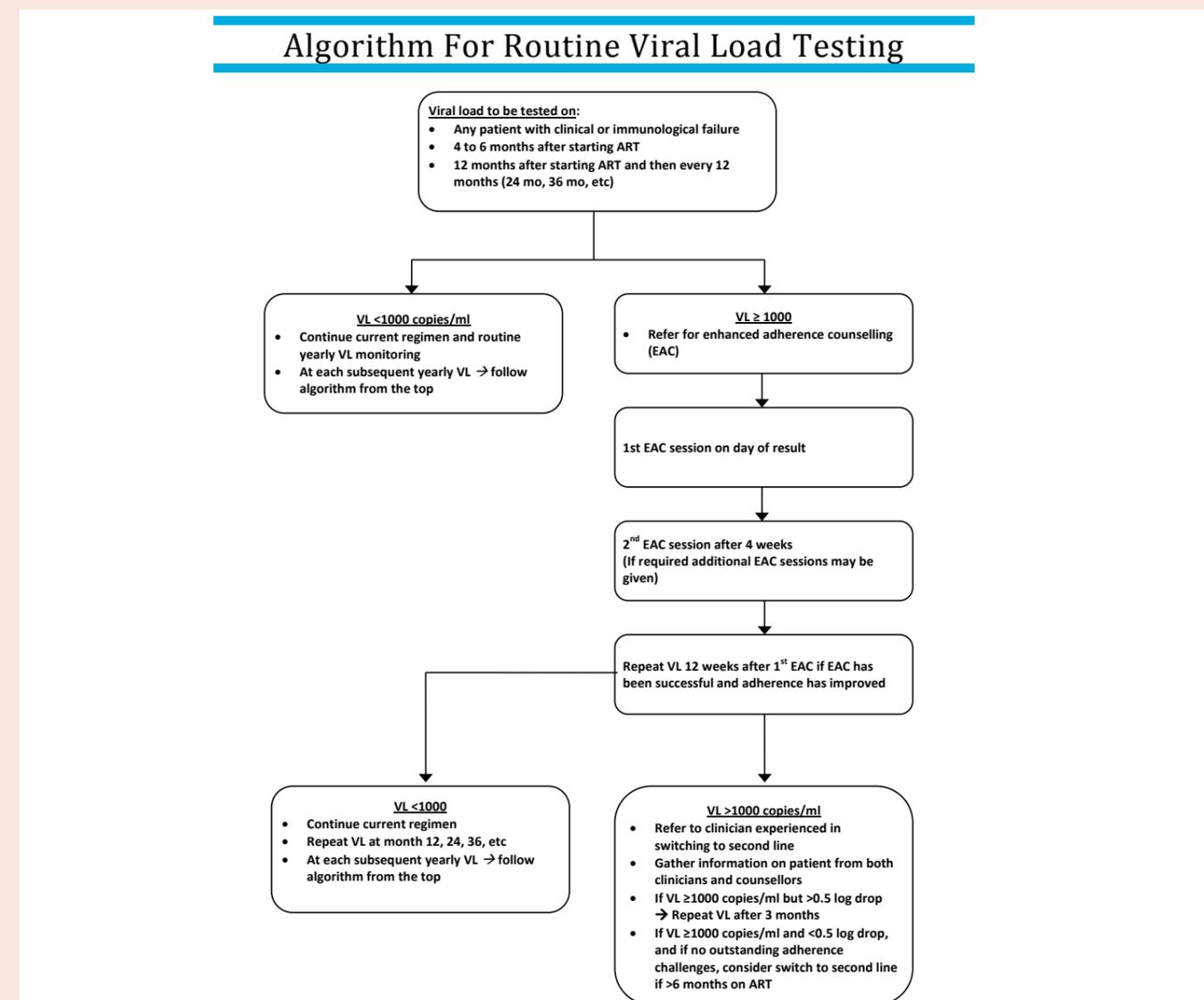


5. VIRAL LOAD CLINICAL ALGORITHM

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.

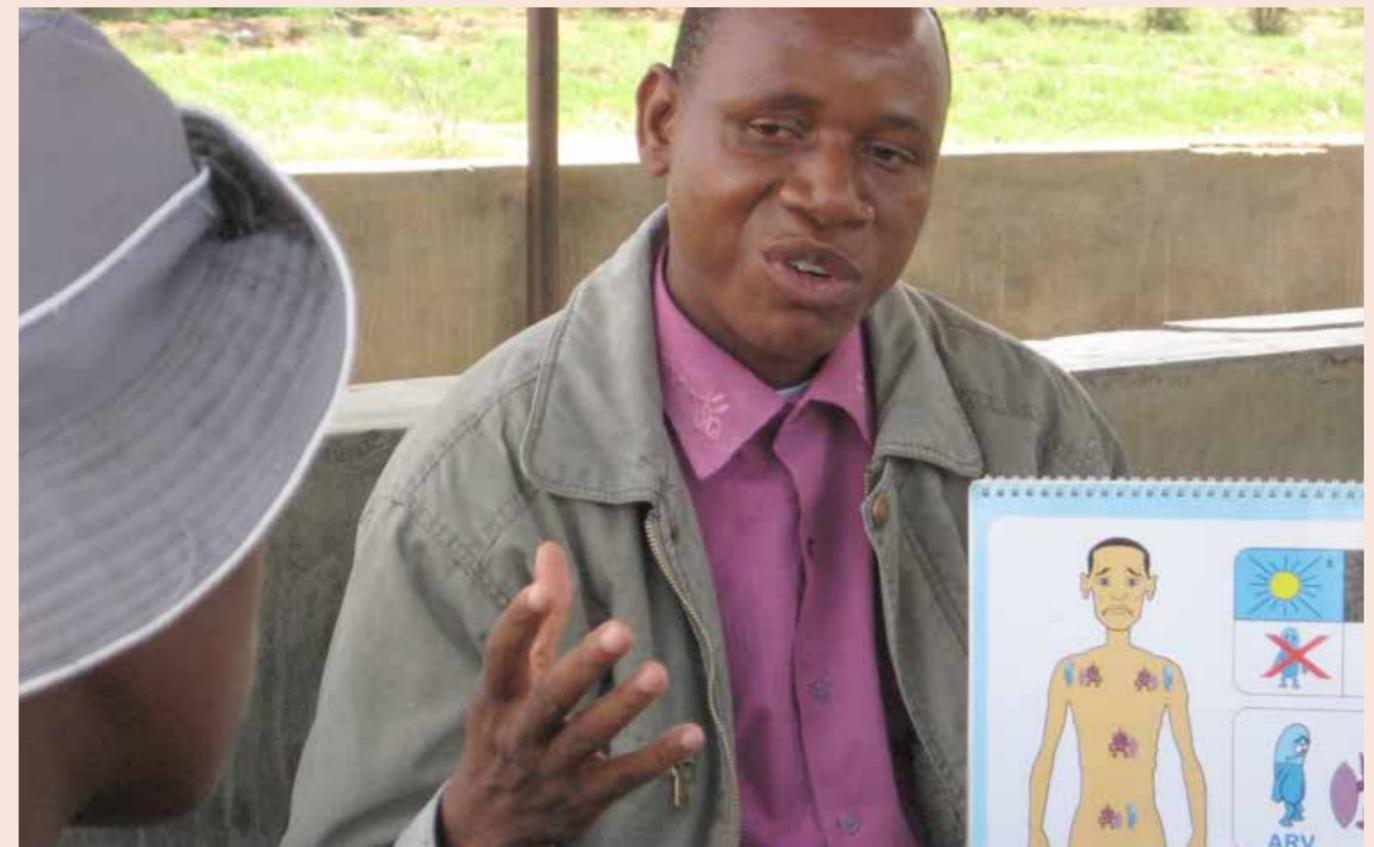
In addition, adequate supervision, through monitoring and evaluation and site visits, is needed to ensure systematic implementation of the VL clinical algorithm. Lists of patients having VL results > 1000 copies/ml should be generated automatically and provided by the laboratory to clinic coordinators 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: _____	Sex: M F	Health Centre: _____	
Age: _____		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)			
<i>For each session, assess major barriers for possible poor adherence (cognitive, behavioral, emotional, socio-economic).</i>			
Date of 1 st session: ____/____/____ Summary: _____			
ARV-intake demonstration by patient/caretaker done? Y N Pill count done? Y N Pill intake: ____%			
Date of 2 nd 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: _____			
• Emotional Y N If yes: _____			
• Socio-economic 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.



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.

