

MAKING VIRAL LOAD ROUTINE

Successes and challenges in the implementation of routine HIV viral load monitoring

PART 1: PROGRAMMATIC STRATEGIES



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CONTENTS

| | |
|--|----|
| Abbreviations | 3 |
| Foreword | 5 |
| Executive Summary | 6 |
| Introduction | 8 |
| Step 1: Achieving Coverage of Viral Load Testing | 14 |
| Human resources for viral load testing | 17 |
| Clinic organisation | 18 |
| Differentiated ART delivery | 19 |
| Creating demand for viral load testing | 19 |
| Introducing Routine VL – What Did We Find? | 22 |
| Step 2: Acting on the Result | 26 |
| Does a good result matter? | 28 |
| Identifying patients with high viral load | 28 |
| Approaches to enhanced adherence counselling (EAC) | 28 |
| Who is performing EAC? | 29 |
| What did we find? | 29 |
| Step 3: Switching to Second-line ART | 30 |
| Monitoring, Evaluation and Supervision of the Viral Load Cascade | 33 |
| What About CD4 Count? | 33 |
| The Way Forward | 35 |
| References | 35 |

ABBREVIATIONS

| | |
|---------------|---|
| aRR | adjusted risk ratio |
| ART | antiretroviral therapy |
| CI | confidence interval |
| CSO | civil society organisation |
| DBS | dried blood spot |
| EAC | enhanced adherence counselling |
| EMR | electronic medical record |
| HCW | health care worker |
| HR | human resources |
| ITPC | International Treatment Preparedness Coalition |
| MoH | Ministry of Health |
| NAPHAM | National Association of People living with HIV and AIDS of Malawi |
| PMTCT | prevention of mother-to-child HIV transmission |
| POC | point of care |
| RR | risk ratio |
| SOP | standard operating procedure |
| TB | tuberculosis |
| VL | viral load |
| WHO | World Health Organisation |



FOREWORD

When I met Juliana, an activist for women living with HIV in East Africa, earlier this year she told me that despite being born HIV positive she was not diagnosed and put on treatment until she was 11. Now, at 23, she is happy and proud to be still receiving first-line treatment in full knowledge that it is working. Juliana knows this because a test shows her viral load – the amount of HIV in her blood – to be undetectable.

Viral load testing is the most important tool that we have to determine whether HIV treatment is having the desired effect. Not everyone is as fortunate as Juliana because this kind of testing is not widely available.

So how can countries today bring routine viral load testing to people on antiretroviral treatment? This is the question that this report seeks to address, based on lessons learned over the past four years in the course of a UNITAID-funded project implemented by Médecins sans Frontières (MSF). The project aimed to establish the feasibility of viral load testing in resource-limited and challenging environments and the extent to which its use can be decentralised.

For much of the last decade, healthcare workers have relied on measuring the CD4 cell count to monitor how people living with HIV respond to treatment. The CD4 cell count measures the blood cells that play an important part in the body's defences against infection and illness.

A patient's CD4 cell count decreases as HIV progresses but recovers when an HIV positive person is put on antiretroviral treatment. Although useful, this test does not quickly pick up what the virus is doing in the body. And as a monitoring tool it is not as effective as viral load testing at indicating treatment failure.

A viral load test quickly detects exactly how much HIV is in the blood. If treatment is not working, the virus will replicate. By monitoring how well antiretroviral therapy is controlling the virus, a viral load test can help prevent a treatment failure and avert a switch to more expensive and toxic second-line treatment regimens.

A Harvard University epidemiologist, Phyllis Kanki, presented the first study to show viral load testing was the only sure way to determine promptly if antiretroviral treatment was not working. Unveiled at a meeting of HIV specialists in 2009, the study prompted a call to make the

tests available to all. Their adoption was initially held up by high costs and the challenge of deploying the tests in resource-limited locations.

In 2013, WHO guidelines recommended viral load testing over CD4 count in the monitoring of people on antiretroviral treatment (ART). UNAIDS' 90-90-90 targets call, among other things, for 90 percent of all people receiving antiretroviral therapy by 2020 to have viral suppression, meaning that they have no detectable HIV in the blood. UNAIDS estimated in June 2015 that more than 15.8 million people are accessing ART – but less than 30 per cent of them have ever had a viral load test.

In 2012, UNITAID funded its first grant with MSF to demonstrate the feasibility of monitoring HIV treatment using viral load testing. Almost four years on, this richly detailed report provides guidance on how we can make viral load testing routine for all those on antiretroviral therapy. The authors pull together lessons learned and make recommendations to support countries as they move to viral load testing. A key finding is that viral load diagnostic tools and approaches need to be adapted to the setting they will be used in. Also a key factor contributing to success is to work with clinicians, health workers and people living with HIV in order to create awareness and stimulate demand.

We have a long way to go if we want to reach global health targets. For this reason UNITAID has invested more than US\$180 million in the last three years in a range of projects that address the diagnostic needs of countries, assess innovative and adapted solutions, and generate essential evidence to inform countries and global stakeholders on how to invest more effectively in this key area of the HIV response.

The recommendations in this report will prove invaluable for countries seeking to scale up use of this vital monitoring tool.

Lelio Marmora
Executive Director
UNITAID

EXECUTIVE SUMMARY

From 2013-2016 the UNITAID-funded MSF HIV viral load initiative has supported the programmatic and/or laboratory scale-up of viral load testing in seven countries (DRC, Lesotho, Malawi, Mozambique, Swaziland, Uganda and Zimbabwe) performing almost 320,000 viral load tests. The three years of implementation have seen both laboratory and programmatic strategies developed to enhance the uptake of routine viral load. Success withstanding, significant challenges still remain.

Based on a survey performed across ten MSF supported ART sites and seven viral load testing laboratories in February 2016, "Making viral load routine" aims to share practical lessons from the field with Ministries of Health and implementing partners. The report reflects both on the programmatic strategies required within the clinic (for clinicians, counsellors and patients) and the realities of both setting up and keeping a viral load testing laboratory functional in such settings. National viral load scale up plans must link both programmatic and laboratory planning if viral load tests are to be taken, processed and results utilised.

Part 1 of this report, *Programmatic Strategies*, examines the outcome of the viral load cascade from coverage of routine viral load testing through to an appropriate switch to second line ART. Coverage of routine VL in the MSF supported sites ranged from 32-91% whilst the chance of having a second VL test following an initial high viral load was as low as 23% in Changara, Mozambique, and as high 71% in Chiradzulu, Malawi. In all sites more than half (50-78%) of patients who received a second VL had persistent viraemia > 1000 copies/ml. Although second line initiation rates have significantly increased with the introduction of viral load monitoring, the proportion of patients with persistent viraemia who were switched remained low. To address the leaks in the viral load cascade four essential programmatic investments were identified to make viral load routine: (1) Strengthening of health systems to identify those in need of viral load and enhanced adherence counselling (EAC) (2) ensuring a dedicated health care worker can provide psychosocial

support for those with high viral load (3) creating demand for viral load testing through patient education and engagement of civil society, and (4) the decentralisation and task shifting of second line ART provision.

Part 2 of this report, *The Viral Load Laboratory*, demonstrates that scale up of viral load testing was feasible in these settings. The choice of viral load platform must remain context specific and take into account the ability to prepare and transport specific sample types, the sample throughput and the clinical urgency of the test. Where polyvalent platforms exist, testing needs beyond HIV-VL should also be considered. Although plasma remains the gold standard, if it is to be used in decentralised settings significant investment in both sample transport or establishing the ability to centrifuge and store samples at peripheral clinics is needed. The use of dried blood spot samples (DBS) and near point-of-care technologies (POC) overcame the challenges of sample transport for plasma and significantly facilitated the scale up of viral load. In some settings either because of instability within the country or as an initial phase in the scale up of VL, testing was outsourced to established private laboratories. In some laboratories, prolonged turn-around time of results triggered outsourcing of viral load testing so as to maintain provision of the service for patients. When setting up a laboratory, the option to lease the viral load platform provided cost savings, flexibility and assured service and maintenance provision. Finally those responsible for scaling up viral load also have a responsibility to manage the waste that is produced, an area that still requires technical guidance, regulation and funding.

Our MSF field teams in collaboration with Ministries of Health have made great strides to begin the scale up of viral load testing, developing models of care that optimize the use and benefits of viral load. We hope that learning from the successes and failures documented in this report will result in more patients having access to viral load testing and have the test results acted upon. For the success of this scale up, sustainable funding must be assured, whilst Ministries of Health, donor agencies and implementing partners must develop a coordinated response. If they succeed we may truly make viral load monitoring routine.



Since I started working with MSF in 2006, I have been crying out for viral load testing to improve the clinical care of patients we are treating. It is fantastic to see this scale up happening with patients finally being reassured their ART treatment is working and counselling support being provided to those with high viral load.

However there is a danger if viral load machines are provided in isolation and not accompanied by training, mentorship and supervision of the clinicians and counsellors, money will be spent on tests that are simply not utilised. It is only if ART programme managers and laboratory services come together to address this challenge that we will truly make viral load routine for our patients. The test alone, is not enough.

Dr Helen Bygrave, Medical Doctor.

INTRODUCTION

From 2013 to 2016 MSF has supported the programmatic scale-up of viral load (VL) testing across 10 sites in six countries. Through field visits and the outcomes of a programmatic survey conducted in February 2016, our field teams have identified the successes and ongoing challenges of “making viral load routine”. Having access to VL testing is only the first step in achieving routine VL monitoring, and by sharing this experience we hope to assist Ministry of Health (MoH) ART programme managers and other implementing partners as they support the scale-up of VL monitoring.

The global goal to reach '90-90-90' includes 90% of people living with HIV knowing their status, 90% of HIV-positive people receiving sustained antiretroviral therapy and 90% of people on ART having viral suppression by 2020. In 2010 WHO recommended a “phased-in” approach to the use of VL testing, waiting until 2013 to clearly recommend VL as the monitoring strategy of choice. However to date, less than 30% of patients on ART globally have access to VL monitoring.

Current WHO guidelines recommend the first VL test to be taken when the patient has been on ART for 6 months, the second at 12 months and then annually thereafter. The threshold to trigger a counselling intervention is a VL more than 1000 copies/ml. If when repeated the VL remains above this threshold a subsequent switch to second line is considered (1).

The 2013 WHO recommendation has galvanised both donors and national ART programmes to recognise the benefits of VL monitoring. However, despite high rates of inclusion of VL testing into policy, coverage remains low. At the end of 2015 VL coverage rates were estimated at 17% in Malawi, 30% in Swaziland and just 5% Zimbabwe. In addition, due to resource limitations, variations in both the frequency of testing and the threshold for action have been adapted across countries (Table 1).

FROM POLICY TO PRACTICE: KNOWING YOUR VIRAL LOAD CASCADE

Mirroring the steps of the WHO VL algorithm, the figure on page 9 outlines the steps of the VL ‘cascade’, from VL coverage to an appropriate switch to second line. Each of these steps must be assessed by ART programme managers if VL monitoring is to have the desired impact on early identification of failure and reducing transmission. Analysis of the VL cascade not only assesses the quality of an ART programme but also provides essential data to plan resource requirements for counselling and second-line drugs.

In 2015 an analysis of the VL cascade was undertaken in MSF-supported sites. Table 1 summarises the outcomes.

Coverage of routine VL in the MSF supported districts ranged from 32% to 91%. Documentation of patients with a VL >1000 copies/ml receiving enhanced adherence counselling (EAC) ranged from 56% to 82%, whilst the chance of a second VL test following an initial high result was as low as 23% in Changara, Mozambique, and as high as 71% in Chiradzulu, Malawi. In all sites, more than half (50-78%) of patients who received a second VL had persistent viraemia >1000 copies/ml. Patients who were switched to second-line therapy after a persistent high VL, according to national guidelines, ranged from 10% to 68%. This very wide difference in switch rates is further explored on page 30.

Tremendous efforts have been made towards developing laboratory capacity and in training and mentorship of clinical and counselling staff. However, VL testing is clearly far from routine, with leaks occurring throughout the VL cascade. By analysing each step of the cascade MSF field teams have identified interventions that have both supported and hindered the successful implementation of routine VL. These findings are further explored in this report.

THE VIRAL LOAD CASCADE

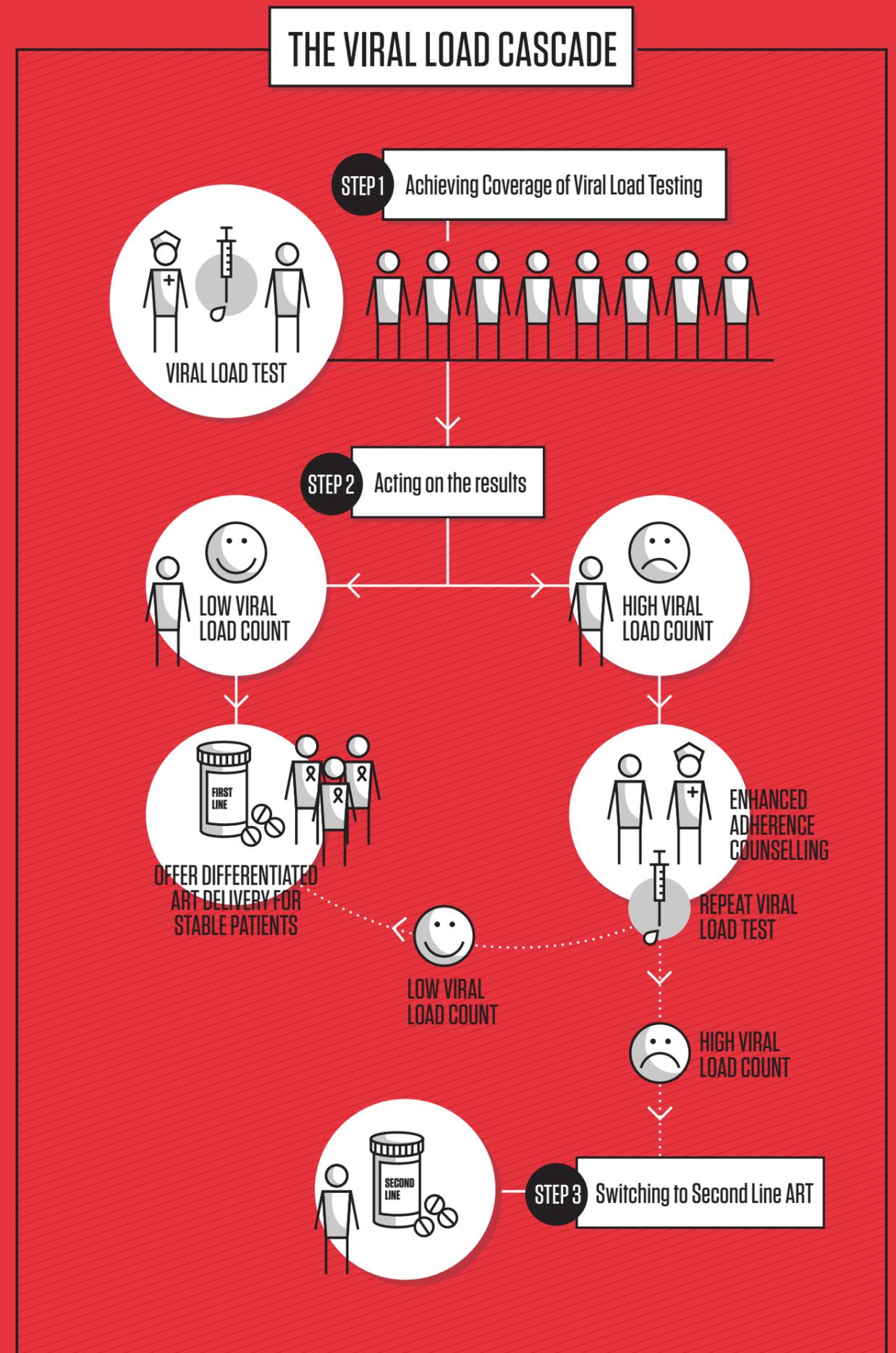


TABLE 1: MSF SUPPORTED ART COHORTS: BACKGROUND AND VIRAL LOAD CASCADE OUTCOMES

| Sites |  |  |  |  |  |  |  |  |  |  |
|--|--|--|--|--|---|--|---|--|--|--|
| HIV prevalence |  15.7% |  14.5% |  14.5% |  16.3% |  17.0% |  23.0% |  7.0% |  16.8% |  31.0% |  3.0% |
| Year routine VL testing started | 2012 | 2013 | 2012 | 2013 | 2013 | 2014 | 2013 | 2013 | 2012 | 2013 |
| Frequency of routine viral load testing after 12 months on ART | Annual | Annual | Every 2 years | Every 2 years | Every 2 years | Annual | Annual | Annual | Annual | Annual |
| ART cohort eligible for VL testing |  19 289 |  11 944 |  42 003 |  15 382 |  19 036 |  6 032 |  3 534 |  45 591 |  20 000 |  6 984 |
| Number of ART sites with access to VL testing |  28 |  19 |  28 |  14 |  5 |  10 |  10 |  7 |  25 |  3 |
| Sample type used |  DBS |  DBS |  DBS |  DBS |  PLASMA SAMBA 1 |  DBS |  DBS |  DBS |  PLASMA |  PLASMA SAMBA 1 |
| Coverage of routine VL testing |  91% |  74% |  56% |  32% |  60–80% (across 5 sites) |  70% |  62% |  69% |  85% |  85% |
| VL > 1000 copies/ml |  14% |  15% |  9% |  20% |  12% |  10% |  40% |  27% |  9% |  21% |
| Threshold for triggering adherence intervention (copies/ml) | 1000 | 1000 | 1000 | 1000 | 1000 | 1000 | 3000* | 3000* | 1000 | 1000 |
| EAC documented for patients with VL above the threshold | 57% | 76% | 62% | 56% | NA | 70% | 70% | NA | 82% | NA |
| Repeat VL test performed (VL2) | 68% | 67% | 55% | 40% | 71% | 42% | 23% | 36% | 57% | 64% |
| Suppressed to < 1000 copies/ml |  43% |  39% |  46% |  32% |  31% |  50% |  22% |  26% |  24% |  24% |
| Threshold for switch to second line ART (copies/ml) | 1000 | 1000 | 5000* | 5000* | 5000* | 5000** | 3000* | 3000* | 1000 | 1000 |
| Eligible patients switched to second-line ART |  37% |  35% |  15% |  38% |  68% |  37% |  10% | Not known: referred to tertiary centre |  17% |  41% |

High VL = > 1000 copies/ml Suppressed VL = < 1000 copies/ml

*Will change to 1000 in next guideline review **Changed to 1000 beginning 2015



KEY IMPLEMENTATION STRATEGIES TO MAKE VIRAL LOAD ROUTINE

A VL focal person dedicated to identifying those in need of VL and enhanced adherence counselling greatly facilitated uptake at all steps of the VL cascade.

Systems to flag patients in need of VL using paper based and electronic medical records improved coverage.

A patient triage system, clinic flow and tools (EAC register and high VL form) adapted to identify patients in need of VL and enhanced adherence counselling improved uptake.

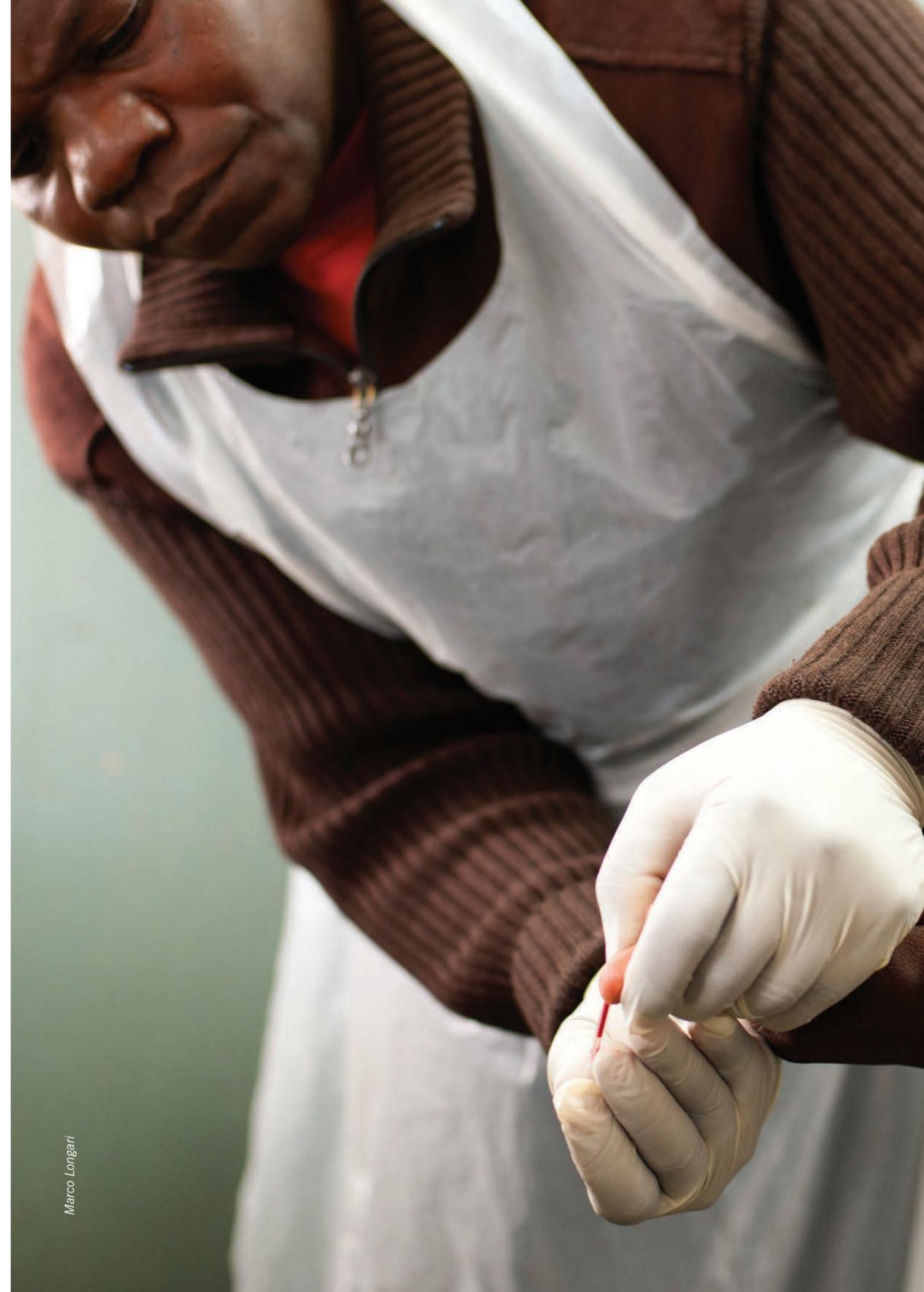
Investing in patient education and demand creation for viral load should be at the foundation of any VL scale up strategy.

Near point of care (SAMBA I) VL facilitated 80% of patients receiving results on the same day.

Sites with high rates of switch to second line decentralised initiation and follow up of second line ART to primary care. Chiradzulu, Malawi, had significantly higher rates of switch attributed to:

- Results being received on the same day
- Clinicians authorised to switch being on site at least once a week
- Second-line drugs being available on site for new patients

Elsewhere, switch decisions were centralised to a district or even national second-line committee.



Marco Longari

STEP 1

ACHIEVING COVERAGE OF

VIRAL LOAD TESTING



Coverage of routine VL testing in MSF supported sites:



LESSONS LEARNED

MOVING FROM TARGETED TO ROUTINE VIRAL LOAD MONITORING

- During the initial phase of routine VL monitoring, clinicians continue to prioritise patients with clinical and immunological failure. Rates of detectability (>1000 copies/ml) should therefore be interpreted with caution during this initial phase.
- There are pros and cons of implementing a 'catch-up' phase (testing anyone regardless of time on ART) when VL monitoring is introduced.
 - » *Pros: A catch-up phase provides an opportunity to quickly make staff and patients aware of VL and ensures access for the existing cohort*
 - » *Cons: A catch-up approach generates a peak in counselling workload and second-line needs and does not allow the development of clinic systems required to identify patients for ongoing routine monitoring*

HUMAN RESOURCES

- Healthcare workers require continuous training as to the benefits of VL monitoring and why it should be 'routine'.
- Setting monthly VL targets for each clinic is useful for supervision and provided motivation to enhance performance.

“ The supervision team gave each of our clinics a target number of VLs to take every month. We shared the results each month with the other clinics in the district on WhatsApp so we could see how each clinic was performing. ”

(Nurse, Zimbabwe)

IDENTIFYING PATIENTS FOR VIRAL LOAD TESTING

- Use existing documentation (ART cards/patient-held records) to identify those in need of VL according to time on ART.
- Where electronic medical records (EMRs) exist, they should be programmed to immediately flag a patient who is due VL testing or produce lists to support clinical management – e.g. a weekly list to identify attendees due a VL test.
- Where uptake of VL is poor, laboratory triggered testing (VL performed automatically if CD4 requested) may be considered.

THE ROLE OF DIFFERENTIATED ART DELIVERY

- Using VL to differentiate ART delivery (resulting in clinic decongestion) may act as a motivating factor for VL to be taken.
- Differentiated ART delivery models where patients attend in groups for annual clinical review and VL testing achieve higher coverage of VL.

CREATING DEMAND FOR VIRAL LOAD TESTING

- Programmes should invest in the training of counsellors and development of educational material to ensure quality patient education on VL.
- Funding for civil society organisations to support VL awareness campaigns should be integrated into national VL scale-up plans.

“ Having my viral load result motivated me to continue taking my treatment; it really told me that my drugs are controlling the virus. ”

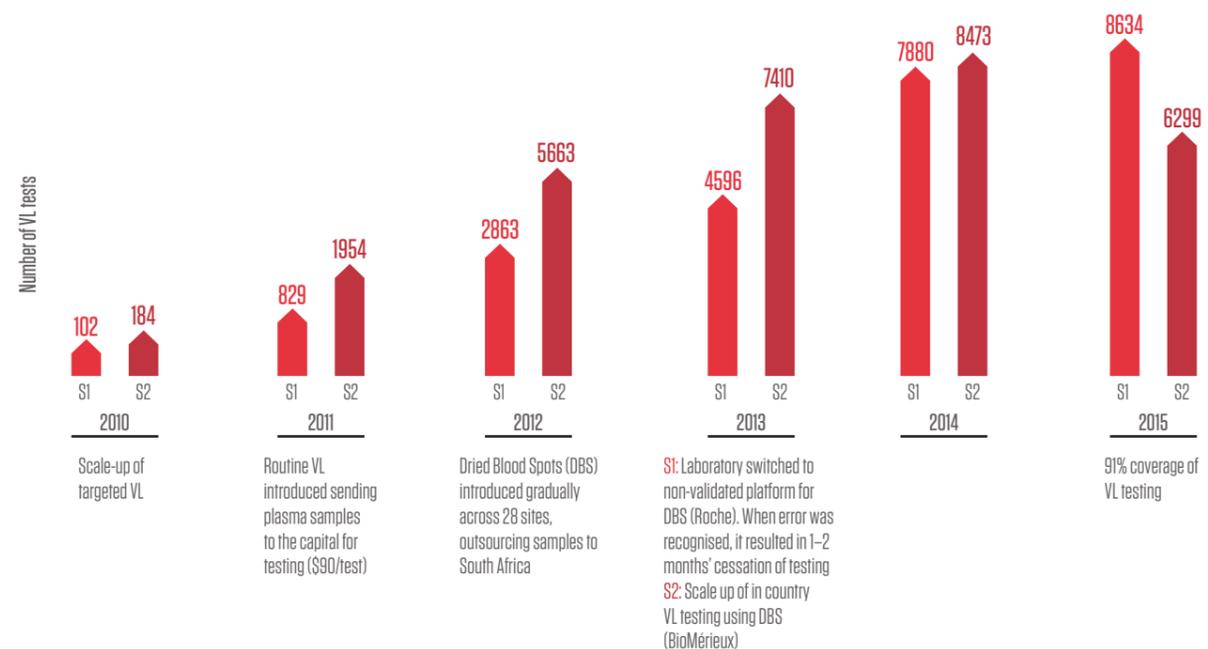
(Patient Shiselweni, Swaziland)

The first step in the VL cascade is to take the VL sample at the appropriate time, and at the appropriate frequency. Achieving this has required investment in training of healthcare workers and in creating the demand for VL from

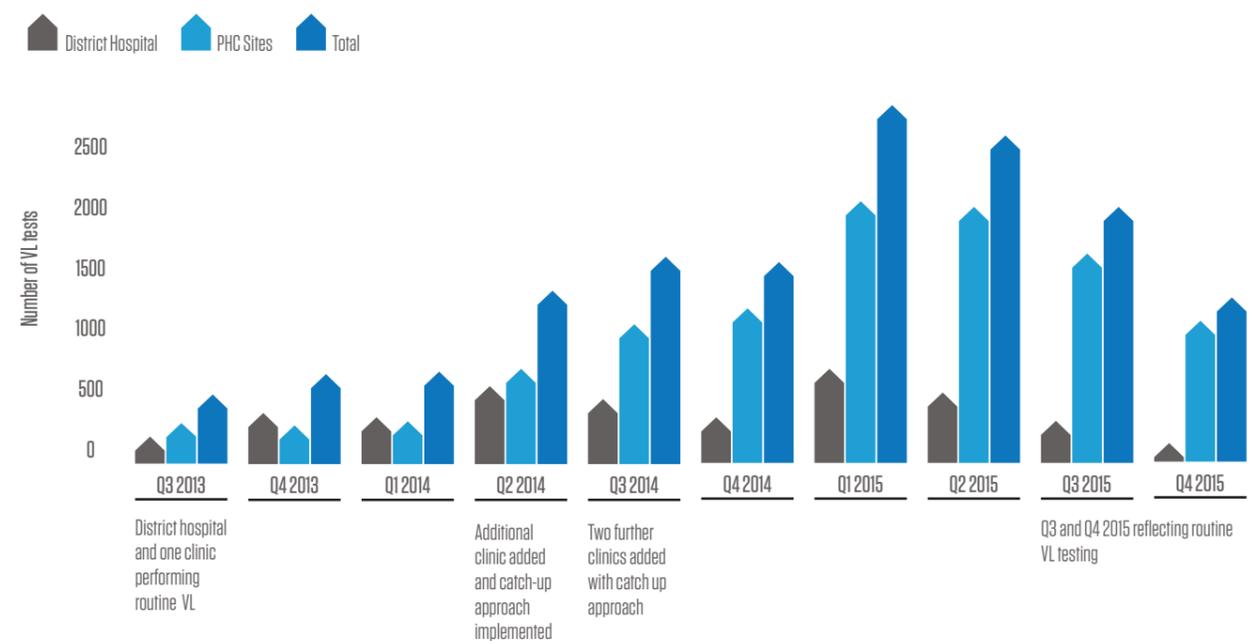
patients themselves. Fig 1 shows the rate of scale-up of VL testing in one site using a centralised VL testing approach with dried blood spots (Buhera, Zimbabwe) and one SAMBA I near point of care site (Chiradzulu, Malawi).

FIG 1: SCALE UP OF VIRAL LOAD (VL) TESTING

i. BUHERA, ZIMBABWE (28 SITES) 2010–2015



ii: CHIRADZULU, MALAWI (SAMBA 1): PHASED APPROACH ACROSS 5 SITES (2013–2015)



PROMOTING AN INTENSIVE 'CATCH-UP PHASE' OF VL TESTING

In some sites, where initial scale-up was slow, a catch-up phase of testing was planned. This was done by taking a VL test for any patient attending for routine ART follow-up regardless of their time on ART. In Maputo, Mozambique, laboratory triggered testing was also introduced to kick start testing. This was done by taking a viral load sample on DBS for all patients sent by their clinician for CD4 monitoring (CD4 for monitoring had not yet been stopped).

Catch-up testing allows healthcare workers to rapidly become familiar with sample preparation procedures and gives a clear message that VL is available to both healthcare workers and patients. However, this approach generates an artificially high workload for the laboratory and counselling staff, and increases second-line needs. Furthermore, it does not allow a triage and patient flow system to be developed that will identify patients who are due their routine annual test.

SETTING TARGETS

In Zimbabwe and Lesotho, a monthly target of VL tests to be performed was calculated for each clinic.

Regular feedback of performance was given during mentorship visits. The target was calculated based on the cohort size and the estimated number of repeat VL tests needed after enhanced adherence.

Example:

- Cohort of 1,200 patients on ART
- Estimated 10% with VL >1000 copies/ml
- This clinic would need to perform 100 routine VL tests per month and 10 repeats
- Target number of VL tests to be performed per month = 110

HUMAN RESOURCES FOR VIRAL LOAD TESTING

Field teams reported low health care worker knowledge on the benefits of VL testing. Healthcare workers and patients have needed to shift their understanding from the benefits of CD4 to why VL is the monitoring strategy of choice. In

particular, the shift to understand the need to switch the treatment regimen of a patient who is virologically failing but who may be clinically well has required significant investment in training, mentorship and supervision.

For both clinicians and patients, prolonged turnaround times for results caused considerable confusion, resulting in patients having repeat samples taken and staff demotivation. This was directly observed in Kibera, Kenya, in 2015, where supply chain and human resource issues prevented communication of 10-20% of test results.

WHO CAN REQUEST A VIRAL LOAD TEST?

In Maputo, Mozambique, VL testing is only requested by the clinician during their consultation, resulting in a high number of patients being missed. An 'automatic' approach in Zimbabwe and Lesotho improved uptake. There, lay workers and nurses performing triage identify patients needing VL at entry to the clinic and direct such patients immediately to give a blood sample. The VL form is then completed by the nurse or lay worker performing the sample preparation.

WHO CAN PREPARE THE VIRAL LOAD SAMPLE?

The World Health Organisation (WHO) does not make a specific recommendation regarding the preparation of VL samples but does make a good practice statement in the 2016 guidelines: "Trained and supervised non-laboratory staff including lay persons can undertake blood finger prick for sample collection" (1). Ensuring that national policies adapt to the human resource (HR) reality of who is available to both draw blood and perform sample preparation will be essential for the effective scale-up of VL monitoring.

Existing routine CD4 testing assisted the transition to VL load testing in some sites. A cadre to take blood and prepare the sample was selected at each site according to local human resource constraints. In sites with higher rates of VL testing coverage, a specific healthcare worker was delegated to identify patients and take samples on a daily basis. In Malawi, where CD4 monitoring was not routine, an additional cadre, the HIV diagnostic assistants, have recently been recruited.

TASK SHIFTING OF VL SAMPLE PREPARATION IN LESOTHO AND SWAZILAND

In Lesotho, the nurse draws blood from the patient when they arrive in the morning. The lay counsellor completes the request form and prepares the DBS sample. The sample is then left to dry until the afternoon when the lay counsellor packs the DBS according to the standard operating procedure (SOP). This task was successfully shifted to lay workers without any policy restrictions from national government.

The project in Swaziland relied on phlebotomists. These are lay people with high school (level 5) education undertaking 5 days theoretical and 4 weeks practical training, enabling them to perform all diagnostic tests offered in primary health clinics, including phlebotomy. For the VL scale-up, they were additionally trained to centrifuge whole blood samples, allowing samples to be kept refrigerated at decentralised primary health facility level. This means that blood can be drawn daily but sample transport can be reduced to twice weekly. This approach, supported by the MoH, will be adapted for the national VL scale-up.

The majority of sites are heavily dependent on lay workers both to complete administrative tasks and to perform sample preparation. In most sites, these same lay cadres also perform adherence counselling. Funding for this spectrum of work is not assured. In Malawi and Swaziland, all such functions are funded through either MSF or other partners; in Lesotho, although funded through the Global Fund, the salaries have not been paid consistently. National governments should recognise the role these cadres now play in the scale-up of VL testing and should develop standardised job descriptions, training and remuneration packages to reflect the work they do (2).

CLINIC ORGANISATION

FLEXIBILITY OF THE TIMING OF VIRAL LOAD

In Thyolo, Malawi, restrictive instructions to healthcare workers as to when they should perform VL (e.g. exactly at 24 or 48 months on ART) resulted in patients not

being tested, especially when multi-month refills of ART were given. The need for a degree of flexibility in testing schedules should be made clear during clinical training of healthcare workers. In Zimbabwe, during the initial phases of implementation, a simple instruction was given to both staff and patients that VL should be tested according to the patient's month of initiation. The month was clearly highlighted on the front of the ART card and the patient tested at their routine appointment two months before or after the highlighted month.

REMINDER SYSTEMS

Reminder systems using both paper and electronic methods to identify those in need of VL testing are essential but were poorly utilised.

The following methods were used:

- Highlighting the month VL testing was due on the ART card
- Indicating on the patient-held record the service due at the next visit: e.g. to come back for ART refill and VL on 31/1/16. This information is used by the healthcare or lay worker performing triage and the patient is immediately directed for VL testing
- Electronic medical records (EMRs)
 - » *Where EMRs are used during direct patient contact (at registration or consultation), an automatic flag appears for any patient due a routine or repeat VL test*
 - » *EMRs can produce an automatic weekly report of those attending for ART and those due for VL testing. This function of EMRs has been underused.*

PATIENT TRIAGE

Patient triage is an essential element of any clinic service to identify patients both according to their medical need (e.g. acutely unwell, coughing) and according to the services they require on the day of the visit. The concept of patient triage is essential throughout the VL cascade to identify not only those due for routine VL testing but also those due for counselling and repeat VL. Having an appointment system that indicates which services the patient requires and having a patient-held record indicating which service is needed, enables patients to be directed to the appropriate service in the most efficient sequence. In particular, where DBS samples need to be prepared and to ensure that POC results can be given on the same day identifying patients on arrival, facilitated sample preparation and processing.

DIFFERENTIATED ART DELIVERY

Differentiated ART delivery distinguishes the specific needs of patients at different times in their ART journey. Using VL results to identify patients whose refill and clinical appointments may be spaced is an important outcome that, in itself, may make VL testing cost effective (3). Although access to VL testing should not be a pre-requisite to differentiate ART delivery for stable patients, access to VL may simplify eligibility criteria. In all sites, a VL of <1000 copies/ml was used as a criterion to differentiate ART delivery (fast track, adherence clubs or community ART groups).

Receiving ART through a group rather than an individual approach may also enhance uptake of VL. In Khayelitsha, South Africa, members of adherence clubs were more likely than non-club members to have both heard of viral load (90% vs 76%) and had a test performed (67% vs 49%). In Changara, Mozambique, coverage of VL testing was higher among patients who were members of community ART groups (72% vs 47%). In Zimbabwe, community ART group members attend the clinic as a group once a year for their clinical review and VL tests. The group attendance easily permits the simultaneous scheduling of a routine yearly VL test.

Although a VL <1000 copies/ml has been used as a criterion to place individuals into differentiated ART models for stable patients, those whose VL becomes detectable are not forced to leave the group. They receive a period of more intensive clinical and counselling follow-up but remain a member of the group, which often provides valuable psychosocial support.

CREATING DEMAND FOR VIRAL LOAD TESTING

Supporting patients to become empowered to request a VL test and understand the result is the foundation of any VL scale up plan. In Khayelitsha, South Africa, where VL testing has been available for over a decade, 83% (429/519) of patients had heard of VL but only 62% (267/429) could describe what the test measured. In Nsanje, Malawi, where VL was introduced at the end of 2013, education sessions on VL were held in the ART waiting area of the health facility and key messages given before blood sampling. A 2015 survey found that 70% (267/384) of patients on ART had heard of VL testing, of those 77% (205/267) knew that VL tests measure the amount of HIV in the blood and 88% (235/267) understood that an undetectable VL means there is still HIV

in the blood and that they are not cured. However, 79% did not know what VL result requires action by their healthcare worker. In both sites, a relatively high proportion of patients (36% in Khayelitsha and 24% in Nsanje) believed that the most common reason for having a high VL was having unprotected sex.

In conjunction with civil society, a survey (performed by the International Treatment Preparedness Coalition (ITPC) with the support of MSF and UNITAID) of 1189 people living with HIV was carried out in nine countries (Mozambique, Kenya, Zimbabwe, Swaziland, Uganda, Malawi, DRC, Lesotho, South Africa), all of which, apart from South Africa, are in the early phases of rolling out VL testing. In all sites, except Malawi where routine CD4 monitoring is not provided, patients still valued CD4 testing over VL. Although most respondents had heard of VL, a small minority could correctly explain the purpose of the test or what threshold would require action.

Further qualitative work was carried out in Swaziland to assess patients' perceptions of their VL result. Findings suggested that knowing their VL improved adherence, while having an undetectable VL was seen as a positive affirmation of treatment: *"It encourages me to hold on and take my treatment as prescribed"* (4).

THE ROLE OF PATIENT EDUCATION

Over the past decade, patient education programmes have promoted the message that CD4 count is the measure of wellbeing and treatment response. This effort has resulted in many patients knowing their latest CD4 counts and proactively requesting to be tested. With the introduction of VL, the concept of what the test measures and why CD4 is no longer monitored needs to be explained.

Patient education strategies for VL have been developed across all MSF sites using generic tools adapted to the local context (5). All patients starting ART go through a number of structured *ART initiation education and counselling sessions*. In most projects, patient education is organised as a session before starting ART, a session at initiation (=month 0) and follow-up counselling sessions (months 1, 3 and 6 on ART) until the first VL. While the first sessions focus on HIV/ART education and build adherence skills, the session before VL testing explains how ART can be monitored, how to interpret a VL result, and the common reasons for and risks of an elevated VL. At the same time, the session communicates the message that a VL of <1000 copies/ml is a criterion to enter a differentiated model of ART delivery such as clinic-based pharmacy fast track or a community ART group. Depending on cohort size, sessions may be conducted individually or as a group.

While newly initiated patients will learn about VL monitoring as they start treatment, the large number of existing ART experienced patients still need to receive this information. Specific strategies need to be set up during the initial year of VL implementation to ensure that all patients receive the key messages related to VL. Strategies used to promote these messages include:

Health talks – commonly organised in the ART waiting areas or within group ART refill strategies such as adherence clubs. Interactive methods such as a quiz, theatre play and the use of visual aids have been promoted.

Promotional material has been used to draw patients' attention to VL, including leaflets and posters (see opposite) in waiting areas, consultation rooms and laboratories, with simple messages encouraging the patient to request a VL and drawing the link between good adherence and a suppressed VL. Additional materials such as T-shirts, caps and stickers promoting VL have also been used in some settings.

In some projects, patient education on VL has been organised in the community, targeting places where clients

on ART gather, such as support groups and community ART groups. These activities can be carried out with other partners and networks of PLHIV.

All the tools developed to support patient education on VL are available in the viral load toolkit (5).

THE ROLE OF CIVIL SOCIETY

People living with HIV and civil society organisations (CSOs) have long been recognised for their positive role in the HIV response through their activities in mobilisation, awareness raising and advocacy. The survey, performed by ITPC clearly identified not only gaps in knowledge but in some sites personal financial costs of accessing VL testing. The outcomes of this survey have been fed back to CSOs to spearhead in-country campaigns aimed at increasing the knowledge of VL among people living with HIV. An activist toolkit (Annex 1) is available to empower CSOs with resources to undertake advocacy initiatives that will challenge donors and governments to prioritise the strategic scale-up of routine VL monitoring.

NSANJE, MALAWI

In 2013 routine VL monitoring was introduced in Nsanje district, Malawi. To increase patients' awareness, short patient education sessions on VL were conducted by nurses or community health workers in the ART waiting areas of the health facility on ART consultation days, often targeting over 50 patients on ART. Patients commonly asked questions such as: "How can my viral load be high if I always use condoms?", "How often should I get a viral load test?", "I got a viral load test, but I never received the result. Why?"

To address these gaps in patients' awareness the following additional strategies were introduced:

- ART education counselling has been reviewed. All patients receive a session at month 6, before their first VL test, to explain its role and how to interpret the results.
- Support group leaders of the National Association of People living with HIV and

AIDS of Malawi (NAPHAM) in Nsanje district gather monthly. Support group leaders will be trained to give the key messages for VL to group members and are provided with visual aids. This will be followed by an event in a community venue for all patients on ART, with music and theatre performances to promote VL.

- Theatre plays on VL will be performed by support group members at the health facility.
- Promotional material in the form of Chitenge have been produced. This is a local fabric that women traditionally wear, with the message "On ART for more than 6 months? Ask for your viral load test today" in local language. This fabric will be given to support group members and healthcare workers involved in VL education.

MY VIRAL LOAD IS UNDETECTABLE.

I AM CONTROLLING THE VIRUS!



INTRODUCING ROUTINE VL

WHAT DID WE FIND?



LESSONS LEARNED

- 9–21% of all VL tests performed were >1000 copies/ml except in Mozambique, where rates of failure were significantly higher.
- Regular analysis and feedback of the proportion of VL tests > 1000 copies/ml is essential during initial scale up in order to estimate laboratory needs for re-testing, workload for counselling and second-line drug requirements.
- Rates of failure in children and adolescents were significantly higher than in adults.
- In Zimbabwe and Swaziland, rates of virological suppression in women in the B+ (prevention of mother-to-child HIV transmission) PMTCT programme were high and similar to the non-pregnant female cohort.
- In a “start all” pilot in Swaziland, after 3-9 months on ART, virological suppression was ≥95% in patients with baseline CD4 350–500 and >500 cells per μL.

“ When we looked at our data over the first 6 months it helped us a lot to plan. At first we thought introducing VL testing was going to mean a massive increase in workload. What we know now is that for every 100 VLs we send, around 10-15 patients will need tracing and counselling. This has helped us to plan. ”

(Nurse Thyolo, Malawi)

MOVING FROM TARGETED TO ROUTINE VIRAL LOAD

In Buhera, Zimbabwe, during the first year of routine VL implementation (2011-2012), clinicians continued to prioritise VL testing for patients in need of confirmation of immunological or clinical failure. Of all patients tested, 30% (95%CI 28-33) had a VL >1000 copies/ml. 33% (95% CI 19-47) of patients with clinical failure and 34% (95% CI 30-39) of patients with immunological failure had a VL >1000 copies/ml. By 2015, when coverage of routine VL had reached 91%, the proportion testing >1000 copies/ml had dropped to 16%.

PROPORTION OF PATIENTS WITH A HIGH VIRAL LOAD

The third ‘90’ of the 90-90-90 targets demands that 90% of all patients on ART should be virologically suppressed. Throughout this report, a threshold of 1000 copies/ml has been used to define ‘suppression’. Knowing the proportion of patients found to have VL >1000 copies/ml is essential for four programmatic reasons:

- To assess the performance of the ART programme at district and site level
- To estimate enhanced adherence counselling workload each month
- To estimate future second line ART demands
- To estimate reagent needs for repeat testing

Rates of detectability ranged from 9%-40%. Reasons for the very high rates of virological failure in Mozambique are not clear, but may include the more frequent ART stock-outs that have occurred in the past.

DID TIME ON ART MAKE A DIFFERENCE?

Figure 2 shows the proportion of patients with VL >1000 copies /ml according to time on ART. With one exception (Nsanje, Malawi), there was no difference in rates of detectability by time on ART. Although there is a survivor bias, this data suggests that prioritising VL testing for patients who have been on ART longer may not be beneficial. It may be argued that intervening with patients who are identified as early poor adherers may have greater benefit in preventing development of future resistance.

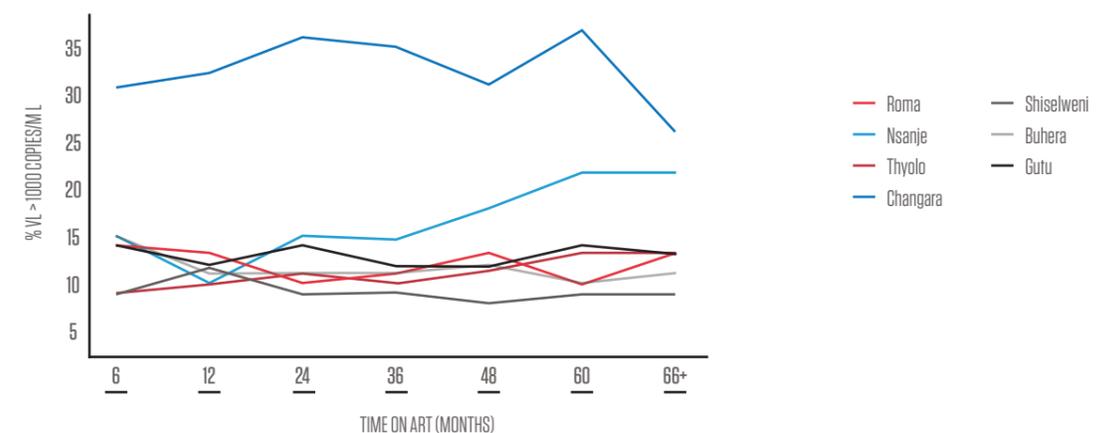
PAEDIATRIC OUTCOMES

Figure 3 shows the rates of virological failure (>1000 copies/ml) by age. Virological failure is consistently higher in children and adolescents. Increasing the frequency of VL testing for these sub-populations to every 6-months should be considered where resources permit.

Challenges identified by projects include:

- Lack of experienced personnel to implement paediatric disclosure counselling resulting in many children having delayed or no disclosure
- Lack of education of multiple care takers of younger children
- Limited time that healthcare workers have to explore psychosocial issues
- Lack of confidence to deal with sexual education for adolescents
- Lack of space to provide an adapted environment for children and adolescents
- Lack of an acceptable protease inhibitor formulation in treatment

FIG 2: PROPORTION OF VL > 1000 COPIES/ML BY TIME ON ART



Action points identified:

- Invest in training and mentorship in paediatric disclosure counselling
- Ensure a family approach is taken for these children: is the HIV and suppression status of the parents or siblings known?
- Link with community-based organisations for support for children who are failing
- Ensure the home environment has been assessed
- Advocate for improved paediatric formulations

RISK FACTOR ANALYSIS

A multivariate regression analysis to identify factors associated with having a viral load $\geq 1,000$ copies/ml among those aged 15 to 60 years, found that the risk was inversely related to age, being greater among those aged 15 to 19 years (adjusted risk ratio: 2.2; 95% CI: 2.1-2.3) or 20 to 24 years (adjusted risk ratio: 1.6; 95% CI: 1.5-1.7), compared to those aged ≥ 25 years. The risk of having a viral load $\geq 1,000$ copies/ml was also greater among men than women (adjusted risk ratio: 1.1; 95% CI: 1.1-1.2), and varied by country.

PREGNANT AND BREASTFEEDING WOMEN

Driven by the importance of identifying non-adherers early in PMTCT, MSF-supported projects in Zimbabwe performed the first VL test for pregnant and breast feeding women at month 3 on ART. Of those tested, 92% were suppressed at 3 months and 84% at 12 months on ART. In a multivariate analysis, the chance of suppression was similar for women in the PMTCT programme and for women not in the PMTCT programme: pregnant (RR 1.03) breastfeeding (RR 1.02). However, the chance of suppression was related to age, with younger women (15-25) less likely to be suppressed (6). In Swaziland, although uptake for VL

KHAYELITSHA, CAPE TOWN

In Khayelitsha, Cape Town, where VL has been available for many years, reflection on the high rates of paediatric failure and the lack of action being taken on the results resulted in a specific clinic being established to support failing children. The key intervention of this clinic was to provide a dedicated paediatric space where children are booked on the same day and where they are met by 'child-friendly' staff.

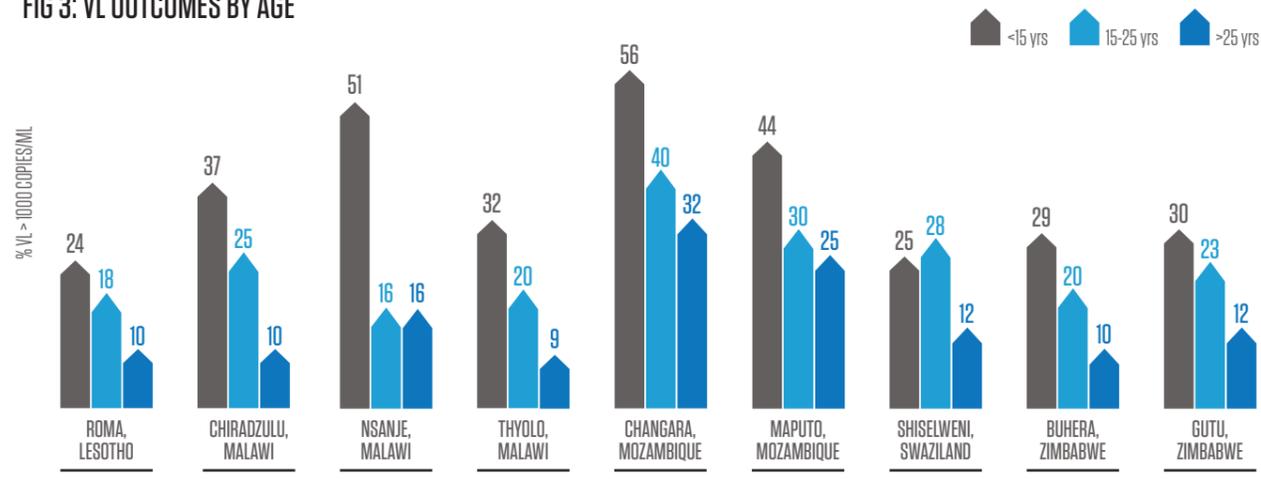
Staff were able to facilitate disclosure counselling in a timely manner and have time to explore in depth the psychosocial issues being faced by the child and their family. After an adherence intervention, 53% of those on a non-nucleoside reverse-transcriptase inhibitor regimen and 63% of those on a protease inhibitor regimen had suppressed.

testing in PMTCT B+ was low (<60% at 12 months), of those tested (223) between 3 and 12 months after ART initiation, 89% had a suppressed VL <1000 copies/ml (7).

PATIENTS INITIATED WITH HIGH BASELINE CD4 COUNTS

The 2015 WHO guidelines recommend ART initiation for all PLHIV regardless of CD4 count. Concerns have been raised that people with a high CD4, who do not feel sick may not adhere to treatment. In Swaziland, a test-and-start pilot study in non-pregnant adults showed that $\geq 95\%$ VL suppression (first VL 3-9 months after treatment initiation) was achieved in patients in the high CD4 strata (350-500 and >500 cells per μL), and was comparable to those within the CD4 <350 strata (90%) ($p=0.15$) (8).

FIG 3: VL OUTCOMES BY AGE



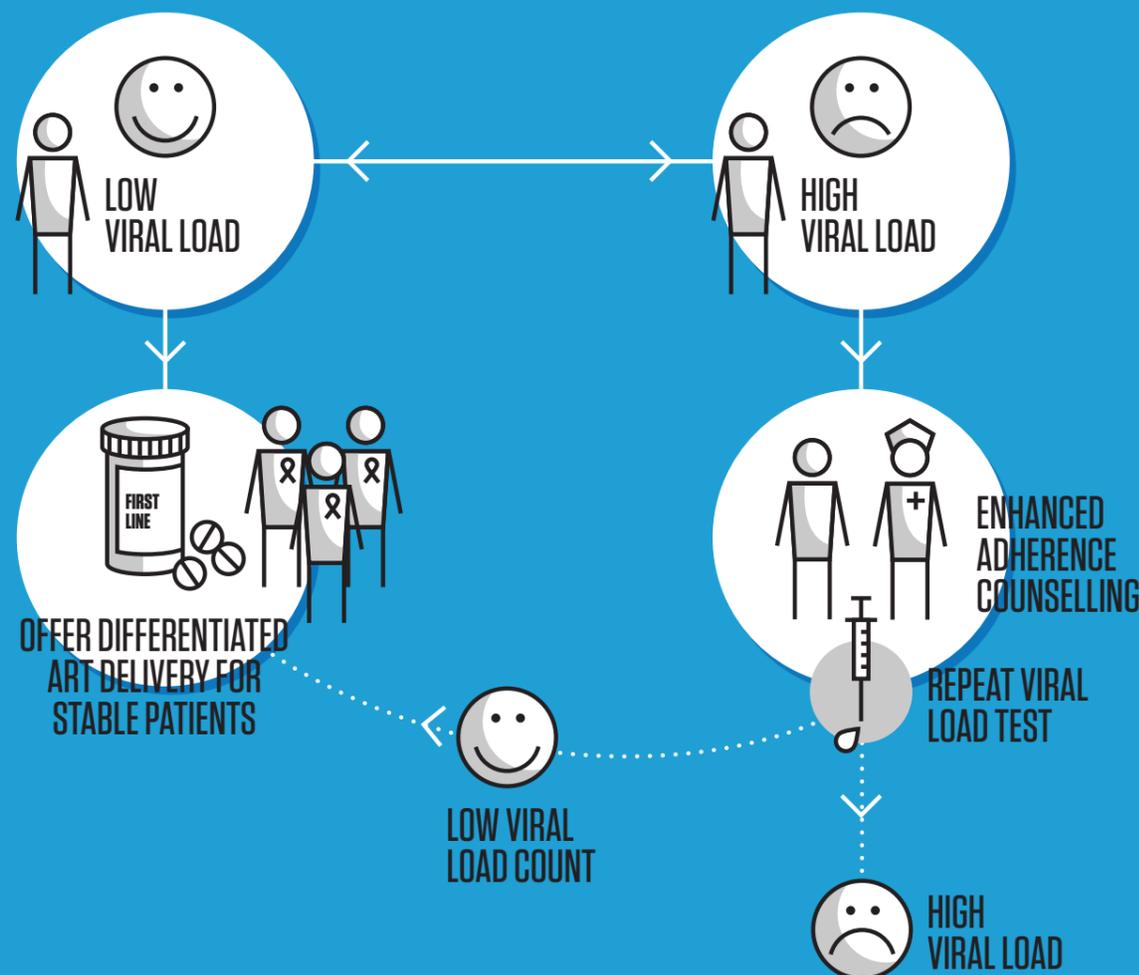
It came as a shock how many of our children and teenagers on ART were failing. We have now had a meeting at district level to see how we can work better with the social workers and schools to improve things. We also are going to run another training session on disclosure counselling for the primary counsellors who work in the clinic.

(Oniwel Nyekete, Counselling Supervisor, Gutu, Zimbabwe)

Susana Oñoro

STEP 2

ACTING ON THE RESULT



Enhanced Adherence Documented:



Repeat Viral Load Taken:



LESSONS LEARNED

ACTING ON A VL < 1000 COPIES/ML

- The positive impact of sharing a good result (<1000 copies/ml) on adherence should not be forgotten.
- A VL < 1000 copies/ml can be used as a criteria to differentiate ART delivery and reduce the burden of clinic visits for both the patient and health system.

ACTING ON A RESULT > 1000 COPIES/ML

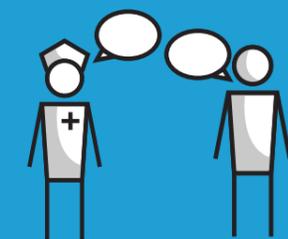
- The presence of a VL focal point (a dedicated staff member) to file results, complete the enhanced adherence register and actively identify those in need of adherence counselling and repeat VL testing facilitated action. Additional staff were not added to perform these tasks. Rather, job descriptions of existing lay cadres were formally adapted.
- Correct follow-up of a high VL result was more likely to occur if a triage system was in place.
- Flagging of results and automatic result lists (as described in the laboratory report) have facilitated identification of those with a high VL.
- Using the high VL summary form to flag the patient files for action at each visit and use of the enhanced adherence register facilitated tracing of defaulters.

PERFORMING ENHANCED ADHERENCE COUNSELLING (EAC)

- In most sites, EAC is performed by lay cadres who are not recognised within the MoH staff establishment lists. Funding for this cadre is not secured.
- Training and on-job support for lay cadres is needed to enhance their technical ability to deal with more complicated cases of treatment failure. In two sites, counsellors with formal qualifications were employed to review these cases. However, such personnel are rarely available in these contexts.

DATA

- Rates of documented EAC (evidence in EAC register or patient files) ranged from 56% to 82%, repeat VL testing from 23% to 71% and rates of suppression from 22% to 50%.
- The risk of persistent viraemia was:
 - » inversely associated with age
 - » strongly associated with the initial VL level, being highest among those with an initial VL $\geq 50,000$ copies/ml
 - » higher among males than among females



Funding for counsellors to perform enhanced adherence counselling must be assured

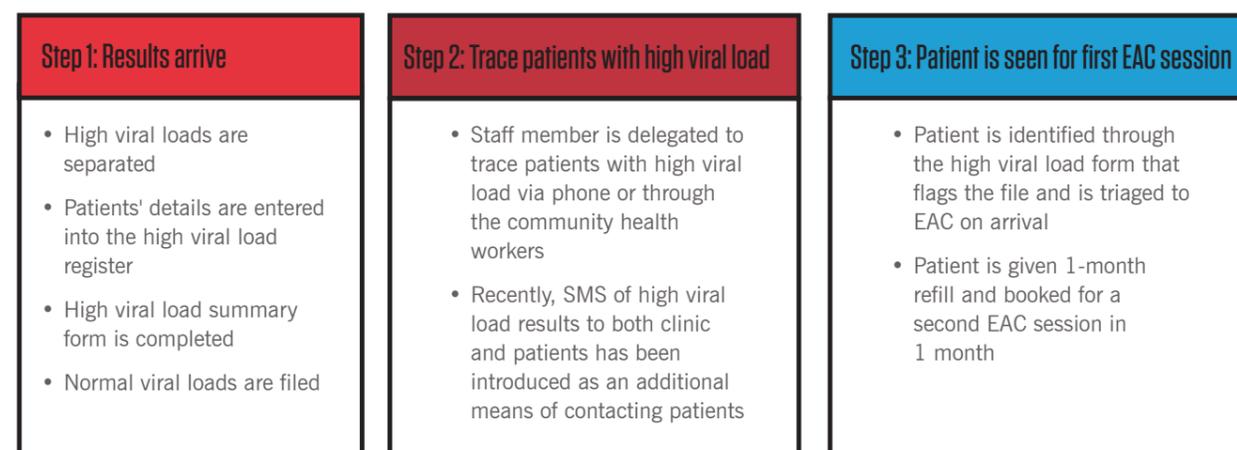
DOES A 'GOOD' RESULT MATTER?

Sharing the result of a suppressed VL with the patient is important. In Ndhiwa, Kenya, many sites reportedly only told patients when their VL result was high. As expressed in the qualitative work from Swaziland, being informed of a good result may act as an affirmation of success and lead to improved adherence. In addition, where a VL result <1000 copies/ml is used to differentiate ART delivery, this should affirm the use of VL as a way of decongesting the facility.

IDENTIFYING PATIENTS WITH HIGH VIRAL LOAD

When high VL results arrive in a clinic, whether by hard copy, SMS or email, prompt action is needed. Having a clear SOP and having someone delegated to act on and file results are priority interventions.

A **high viral load or enhanced adherence register** has been introduced across all sites to track patients with high VL through the remainder of the cascade. Completing this register is a challenge where there is not one dedicated cadre supervised to do this. In Zimbabwe and recently Nsanje, Malawi, a **high VL form** is completed when a high VL result is received. This form acts as a flag on the file and then later as a communication tool to inform switch decisions. In Zimbabwe, the SOP shown below was developed to assist the flow of results at clinic level.



APPROACHES TO ENHANCED ADHERENCE COUNSELLING (EAC)

Once a patient with a high VL is identified, WHO recommends an adherence intervention followed by repeat VL testing. However no specific content for this intervention has been defined. Likewise, at country level, apart from Zimbabwe and South Africa, there is no national level counselling toolkit for enhanced adherence. The enhanced adherence sessions defined in the VL toolkit aim to explore behavioural, socio-economic, cognitive and emotional barriers to adherence and to identify strategies to overcome these barriers (5).

In most MSF sites, **individual** approaches are used, as small numbers of patients are identified each month. The number of EAC sessions ranges from two to six; however, the number of sessions was generally reduced to the minimal number of two, to reduce transport burden on

“ Sometimes it is difficult for the patient to tell you that they have an adherence problem. When they come to see you for the first time with a high viral load, some say all is going well. It is only at the second EAC session that they open up and are able to tell us their problem. ”

(Counsellor, Maputo, Mozambique)

patients. Additional psycho-social support can be provided on a case-by-case basis. EAC sessions should ideally be matched with the clinical appointment and drug refill, as patients failed to come back for counselling alone.

In some sites (Khayelitsha, Cape Town) with a large number of high VL patients attending the same day for consultation, group approaches have been piloted. Patients pass through a **group** counselling session guided by a lay counsellor where adherence strategies are reviewed and common barriers discussed. In Tete, Mozambique, where community ART groups are widely established, a group counselling session is done with all Community ART group (CAG) members at the health facility or in the community to identify ways to support group members with a high VL. The impact of the group dynamics of differentiated ART delivery models on patients with high VL should be further explored.

“ We sat together with the Community ART Group (CAG) members of this patient with a high VL. The patient often forgot to take her drugs. One of the CAG members is a neighbour who decided to pass by every morning, so they could take their drugs together. ”

(Counsellor, Tete, Mozambique)

In all projects, the EAC intervention has been defined in specific session guides, accompanied by training and regular supervision, through file reviews and observation of sessions. As more experience was gained, a 'myth-buster' FAQ sheet was developed to address issues of taking ART and alcohol and the risks of re-infection being the cause of a high VL. These messages were integrated into the VL education tools (5).

“ One of my patients would never take drugs at the weekend. He said he was told he should not take ART and drink alcohol, but he always goes out with friends at the weekend. I clarified with him that it's better to take ART with alcohol than not taking them. Together we decided he would take his ARVs at the weekend a bit earlier, before leaving on a night out with friends. ”

(Counsellor, Khayelitsha, South Africa)

In Swaziland, Kenya and Zimbabwe, patients with a high VL are also screened for **depression and substance abuse**, using standardised screening tools (PHQ-9 and CAGE). This is mostly done on a case-by-case basis and only routinely done in Swaziland where patients with a positive screen can be referred to an MSF psychologist.

WHO IS PERFORMING EAC?

EAC is performed by lay counsellors in most sites. This is a health facility based cadre trained to educate and counsel patients but having no formal professional or para-professional certificate or degree in counselling/health education. These cadres are rarely recognised by Ministries of Health and in most cases are funded by partners such as MSF. The lack of official recognition and the insecure financing of this cadre is a clear threat to the continuation of not only EAC but also other adherence counselling interventions.

In some sites (Chiradzulu, Malawi and Kenya), EAC has been reallocated to professional counsellors due to quality concerns. Also, in Khayelitsha individual counselling for patients in need of being switched to second-line treatment has been allocated to nurses. The impact and feasibility of providing a more qualified counsellor to assess these clients should be further explored, as availability and funding for such personnel is limited.

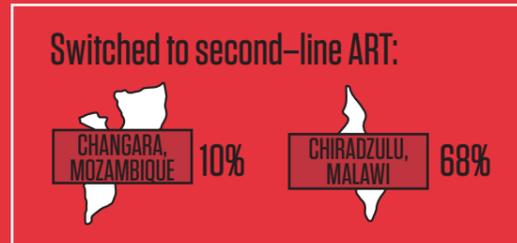
WHAT DID WE FIND?

In the cascade analysis performed, rates of documented EAC (evidence in EAC register or patient files) ranged from 56% to 82%, repeat VL testing from 23% to 71% and rates of suppression to <1000 copies/mL from 22% to 50%.

A multivariate regression analysis to identify factors associated with persistent viraemia of $\geq 1,000$ copies/ml, found that the risk was strongly associated with the initial viral load level, being greater among those with an initial viral load $\geq 50,000$ copies/ml (aRR: 2.4; 95% CI: 2.3-2.6), or 5,000 to 49,999 copies/ml (aRR: 2.0; 95% CI: 1.9-2.1), compared with those with an initial viral load of 1000 to 4,999 copies/ml. The risk of persistent viraemia was inversely related to age, being greater among those aged <15 years (aRR: 1.4; 95% CI: 1.4-1.5), or 15 to 24 years (aRR: 1.2; 95% CI: 1.1-1.3), compared to those aged 25 years or older. Persistent viraemia was weakly associated with gender, being more common among men than women (aRR: 1.1; 95% CI: 1.1-1.2).

STEP 3

SWITCHING TO SECOND-LINE ART



* LESSONS LEARNED

- Rates of switch to second-line ART remain low in most sites
- Where patients are well or where adherence is not optimal, clinicians are reluctant to switch and 'give more time' for adherence support
- The optimal duration to allow for suppression before switch is not clear but may depend on the first VL result
- Factors that facilitated switch to second-line ART included:
 - » Decentralisation of second-line initiation
 - » Task-shifting of second-line initiation to non-physician cadres
 - » M-health strategies to allow remote clinical decision support for switching
- Ensuring second-line drugs are available where the patient is accessing their first-line therapy should be a priority
- Ongoing adherence support following the switch to second-line ART is essential

TABLE 2: STRATEGIES FOR SWITCH TO SECOND LINE ART

| Sites | Who makes the switch decision? | Who can initiate second-line ART? | Is second-line initiation decentralised to primary care sites? | Is second-line follow-up decentralised to primary care sites? | Was switching as reported in cascade by MSF or MoH staff | Interventions to increase switch to second-line ART |
|-----------------------|---|-----------------------------------|--|---|--|---|
| BUHERA, ZIMBABWE | Doctor or nurse mentor in mobile team | Nurse or doctor | Yes, but mobile mentorship approach (1-2 times/month) for switch | Yes | MSF/MoH | M-health tools to share information of high VL form and to discuss cases for remote decision making; increasing the number of 'nurse mentors' or competent nurse switchers to task shift second-line ART initiation |
| GUTU, ZIMBABWE | Doctor or nurse mentor in mobile team | Nurse or doctor | Yes, but mobile mentorship approach (1-2 times/month) for switch | Yes | MSF/MoH | As per Buhera |
| THYOLO, MALAWI | Clinical officer or doctor. Only available at hospital sites on permanent basis | Clinical officer or doctor | No; second-line drugs only available at district hospital and few selected sites | Yes | MSF/MoH | Development of a national second-line examination: clinicians and nurses are required to pass before being certified |
| NSAMJE, MALAWI | Clinical officer or doctor. Only available at hospital sites on permanent basis | Clinical officer or doctor | No | Yes | MSF | As per Thyolo |
| CHIRADZULU, MALAWI | Clinical officer | Clinical officer or doctor | Move regularly (2-3 times/week) to the HC | Yes | MSF/MoH | As per Thyolo |
| ROMA, LESOTHO | National Committee | Doctor | Yes: mobile mentorship approach | Yes | MSF | Plans to train doctors at district level to make switch decision |
| CHANGARA, MOZAMBIQUE | National Committee | Clinical officer or doctor | No | No | MSF/MoH | Ongoing trainings, mentorship, facility-level ART committee |
| MAPUTO, MOZAMBIQUE | National Committee | Clinical officer or doctor | No | No | MSF/MoH | Ongoing trainings, mentorship, facility-level ART committee |
| SHISELWENI, SWAZILAND | Doctor | Doctor | Yes | Yes | MSF/MoH | MDs to have ongoing training on treatment switching. Integrate reporting on treatment switching into routine M&E to sensitise clinic staff: strengthen multidisciplinary approach to switching |
| ARUA, UGANDA | Clinical officer | Clinical officer | Yes | Yes | MSF | |

Rates of switch to second-line ART remain lower than expected across most sites, ranging from 10% to 68%. The highest rates were achieved in Chiradzulu, where results were available the same day and switching was fully decentralised. All sites in Chiradzulu had a clinician authorised to switch attending the clinic at least once a week and in some cases daily.

Despite these low rates, compared to before the introduction of VL, a significant increase in second-line initiations has occurred in some sites (Fig 4).

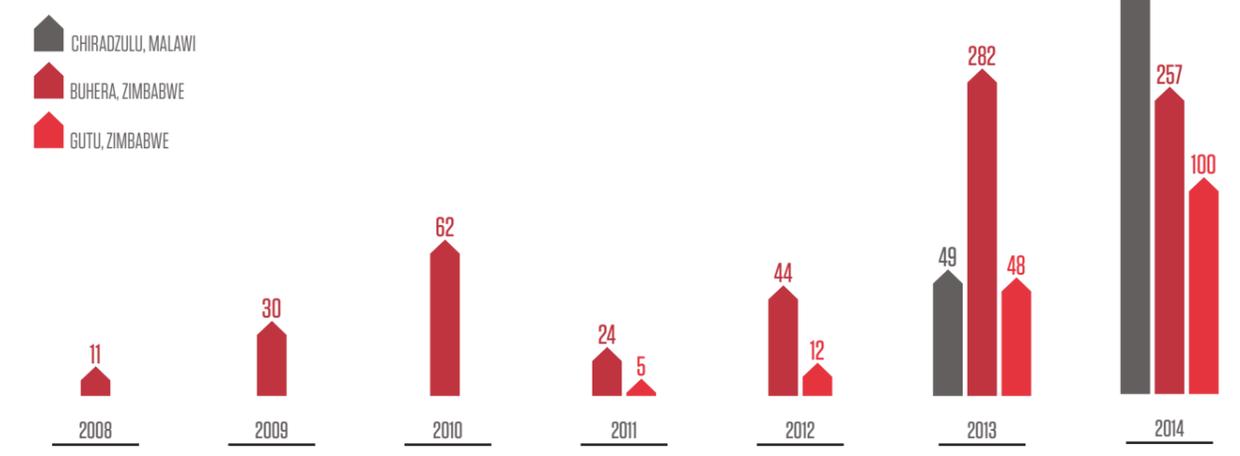
Barriers to switching and their solutions were identified across the sites and are summarised in Table 2. Lack of decentralisation and task-shifting recall the initial roll-out of first-line ART, where two decades ago lengthy centralised processes delayed ART initiation for sick patients. In addition to these challenges, supporting clinicians to feel confident to switch patient regimens will be an essential part of mentorship and supervision. When adherence is deemed 'not good enough', giving a 'bit more time' to suppress has become the norm in some sites, with patients having up to five high VL tests before a switch is authorised. An evidence-based and pragmatic approach to these cases is urgently needed.

In other sites, access to second-line drugs has been a challenge. For example, Thyolo, Malawi saw a significant shortage of second-line drugs due to lack of planning for the increased demands with the introduction of VL testing. Whether second-line regimens are still seen as the 'last resort' or perceptions of high drug costs deter switching are important issues to explore further.

Innovative ways of supporting second-line switching by MoH clinicians are being developed. In Buhera, Zimbabwe, MoH clinicians face challenges to visit all clinics (28 in one district) more than once a quarter. To overcome transport challenges, two strategies have been adopted:

- Copies of the high VL forms are photographed and sent using a smartphone to the responsible clinician at the district hospital. The clinician then interprets this, completes the high VL form and electronically sends back the decision
- Experienced nurses are selected and trained to switch. This group of nurses can then act as 'nurse second-line initiators' for a hub of local clinics.

FIG 4: SCALE UP OF SECOND LINE INITIATIONS: BUHERA AND GUTU, ZIMBABWE AND CHIRADZULU, MALAWI



MONITORING, EVALUATION AND SUPERVISION OF THE VIRAL LOAD CASCADE

QUESTION

Should the VL cascade be incorporated into routine monitoring and evaluation (M&E)?

ANSWER

Yes. Without monitoring the VL cascade, there is a high risk that:

1. Coverage of VL testing remains low
2. Patients do not receive the clinical care required based on their test result
 - » If VL is <1000 copies/ml, differentiated ART delivery is not offered
 - » When VL is >1000 copies/ml, an enhanced adherence intervention is not offered, VL is not repeated and appropriate switches are not performed
3. Sites with poor performance are not prioritised for mentorship and supervision
4. Money is wasted due to tests performed with no follow-up on results

From the cascade analyses carried out in Buhera, Zimbabwe, and Changara, Mozambique, the cost of inaction on a VL result is shown in Table 3. Not only is this a cost concern, but patients who remain unsuppressed will continue to transmit the virus.

Sites that have electronic medical records (EMRs) and the possibility to link directly with laboratory databases, give the best estimates of VL coverage. Otherwise, estimates using aggregate data of patients alive on ART and number of VLs performed can be used. In sites with paper-based M&E, a folder review may be necessary. In some sites, visits for enhanced adherence have also been included in patients' EMRs; otherwise, a separate analysis using the paper-based high VL registers and folder reviews may be needed to follow this step of the cascade.

A proposed approach to cascade analysis for routine VL testing is described in Annex 2. Clear guidance should be provided to Ministries of Health for performing this cascade analysis to standardise the approach across countries.

LINKING M & E WITH MENTORSHIP AND SUPERVISION

Across all sites, ongoing mentorship and feedback of the VL cascade at site level is essential. In Zimbabwe, where the cascade exercise has been performed twice in each district, the mentorship team used the analysis to feed

back to poorly performing sites. In Swaziland, VL cascade monitoring is being increasingly integrated into routine monitoring activities, and feedback meetings to the MoH and partners have been initiated.

WHAT ABOUT CD4 COUNT?

WHO has now recommended that in settings where routine VL monitoring is available, CD4 monitoring can be stopped in individuals who are stable on ART and virologically suppressed (1). During the period of the grant, CD4 monitoring was stopped in Zimbabwe. The cost savings of stopping CD4 for monitoring in Buhera district between 2011 and 2013, estimated to be \$94,212, was channelled towards VL testing.

However, CD4 counts at baseline and for assessment of clinically unwell or virologically failing patients will remain important. A 'late presenter' package of care should be offered to those presenting with a CD4 <100 cells/ μ l, including screening and treatment for Cryptococcus and TB. ART initiation should also be accelerated in these patients. In Buhera and Gutu, Zimbabwe, a triggered CD4 should be performed when a patient is found to have a VL >1000 copies/ml both to assess risk of opportunistic infections and immune reconstitution inflammatory syndrome for those switched to second-line ART. It also may act as an additional feedback mechanism to the patients on the effect the high VL has had on their immune system. Data on this intervention is not currently available.

| | BUHERA, ZIMBABWE | CHANGARA, MOZAMBIQUE |
|---|------------------|----------------------|
| VIRAL LOAD TESTS PERFORMED | 4331 | 1918 |
| VL > 1000 COPIES/ML | 606 | 767 |
| PATIENTS WITH NO REPEAT VL | 194 | 591 |
| COSTS OF VL > 1000 COPIES/ML PERFORMED, NOT ACTED ON (EST AT \$15/TEST) | \$2910 | \$8865 |

Table 3: Cost of inaction on a VL test in Buhera, Zimbabwe and Changara, Mozambique

THE WAY FORWARD

Five years ago, the technical challenges related to sample type and the cost of VL testing were the major barriers to VL scale-up. With the use of dried blood spots, near point of care technologies, and the significant cost reductions driven by competition, these barriers have been overcome. However, as the analysis of the cascade has demonstrated, having access to the test does not equate to its effective utilisation.

The next five years will hopefully start to reveal the programmatic 'how to' of VL implementation with the goals of:

- Using a VL <1000 copies/ml as a tool to differentiate ART delivery
- Completing the VL cascade for those with VL >1000 copies/ml

Major challenges remaining include:

- Improving the **knowledge and motivation** of healthcare workers to recognise the benefits of VL testing through mentorship, clinical governance mechanisms and adequate remuneration
- **Increasing awareness of patients and CSOs** to create demand and dispel myths around viral load testing
- Ensuring access to adequately trained and remunerated **HR to perform enhanced adherence counselling**

- **Strengthening the skills of clinic managers** to coordinate triage and patient flow
- **Decentralisation and task shifting of second line ART initiation and follow up, with continuous access to second line drugs**

Priority areas for future operational research include:

- understanding the impact of delaying the switch to second line after a repeat high viral load, both for the individual and from a public health perspective
- clarifying the direct impact of EAC on suppression
- extending the cascade analysis to assess if suppression is sustained
- and qualitative understanding of the reluctance of HCW to use viral load tests or to switch patients to second line treatments.

To overcome these challenges and answer these questions, Ministries of Health need to provide leadership and donors and implementing partners need to provide coordinated support. We hope the implementation tools and experiences described in this report will help to support future efforts for the scale up of VL, and that viral load monitoring will be truly routine by 2020.

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ANNEXES: AVAILABLE ONLINE OR ON USB

Annex 1: Activist Toolkit: Campaigning for routine VL monitoring
Annex 2: Monitoring and Evaluation of the Viral Load Cascade

Annex 3: MSF Viral Load Toolkit
Annex 4: MSF VL publications and conference abstracts

Once identified as failing we often see a reluctance by clinicians to switch, in some cases due to unfamiliarity with the process and the medicines, sometimes outdated beliefs about second line cost and overly conservative beliefs as to the level of adherence needed prior to switch. However once the clinician has decided to switch a patient to second line, the procedural barriers that are needed to pass through the national second line committee result in further delays. We need to give clinicians the confidence and knowledge to switch patients correctly and move away from systems that appear to ration access to second line rather than support patient management.

Dr Amir Shroufi MSF Medical Coordinator, South Africa and Lesotho





www.msfaaccess.org/makingviralloadroutine