Implementation Issues for Monitoring People on ART in Low-Income Settings in Sub-Saharan Africa

Bronte Hotel, Harare, Zimbabwe

11-12 March, 2015
Executive Summary

Background
Funded by the Bill and Melinda Gates Foundation, the HIV Modelling Consortium leads the coordinated interaction between modelling groups and policy makers, in conjunction with the targeted and responsive commissioning of new work. Its central objective is to help improve scientific support for decision-making by coordinating a wide range of research activities in the mathematical modelling of the HIV epidemic.

Further to the modelling analyses that the consortium undertook in support of the World Health Organisation (WHO) 2013 consolidated guidelines, new modelling analyses have been conducted for consideration in the development of the 2015 guidelines revision focusing on two key areas: 1) drivers of AIDS deaths and interventions to reduce AIDS-related mortality; 2) cost-effectiveness of alternative ways to monitor patients on ART.

From March 11-12, 2015, the HIV Modelling consortium hosted a meeting ‘Implementation Issues for Monitoring People on ART in Low-Income Settings in Sub-Saharan Africa’ in Harare, Zimbabwe. A total of 42 delegates from over 7 countries participated.

Objectives
Objectives of the meeting:
1) To obtain feedback on preliminary recommendations based on modelling and cost-effectiveness for patient monitoring – in the immediate term.
2) To discuss and document the issues programmes faces in implementing monitoring of patients on ART – now and in the future.

Main Outcome
The meeting provided a forum for consortium members to present modelling findings and delegates from international donors, ministries of health and implementing partners to share related information on guideline development and country implementation experiences under themes and session topics:

Theme: WHO HIV Treatment Guidelines and the role of modelling/cost-effectiveness analysis in informing policy
- Session 1: Modelling to support development of the WHO ARV guidelines on patient monitoring

Theme: Understanding where we currently are in the provision of HIV treatment and patient monitoring
- Session 2: Financing national HIV treatment responses and competing calls on limited resources
- Session 3 – Panel Discussion I: National HIV treatment programmes and policies (focus on patient monitoring policy); reasons for policy choices

Theme: Future directions for monitoring patients on ART
• Session 4 - Panel Discussion II: Investing in scale up of viral load measurement in the context of other healthcare needs
• Session 5: Panel Discussion III: Alternative options in scaling up viral load monitoring
• Session 6 – Panel Discussion IV: Ways to reduce costs and improve quality in patient monitoring; barriers to improvement
• Session 7: Reflections on workshop

Appendix III provides a condensed summary of presentations made during the two day workshop. More detailed summaries of presentation content and resulting key discussion points can be found in the main body of the report.
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7a: Allocating resources to patient monitoring to generate population health improvement: Collective Interpretation of Model Results and Data & Next Steps

Appendix I: Workshop Agenda

Appendix II: List of workshop participants

Appendix III: Condensed summary of session proceedings
Monitoring People on ART in Low-Income Settings in Sub-Saharan Africa

Acronyms

ASLM  African Society of Laboratory Medicine
CE    Cost effective
CHAI  Clinton Health Access Initiative
DALY  Disability-adjusted Life Year
DBS   Dried Blood Spot (sample)
EID   Early Infant Diagnosis
EPMS  Electronic Patient Monitoring System
GFTAM Global Fund to Fight AIDS, Tuberculosis and Malaria
ICL   Imperial College London
ILB   International Laboratory Branch
LSHTM London School of Hygiene and Tropical Medicine
LTFU  Loss to follow up
MOH   Ministry of Health
MOHCC Ministry of Health and Child Care (Zimbabwe)
PEPFAR United States President's Emergency Plan for AIDS Relief
PICO  Population; Intervention, Comparator; Outcomes (questions)
POC   Point of Care
PT    Proficiency Testing
SSA   Sub-Saharan Africa
TAT   Turnaround time
UCL   University College London
VL    Viral Load
VLM   Viral Load Monitoring
WHO   World Health Organisation
Day 1: Wednesday 11 March 2015
Theme: WHO HIV Treatment Guidelines and the role of modelling/cost-effectiveness analysis in informing policy

Welcome and introductions

Wla: Welcome and Introductions
Tsitsi Apollo, MoH Zimbabwe

Dr. Tsitsi Apollo, as representative of the Zimbabwean Ministry of Health and Child Care AIDS & TB unit, welcomed participants to Zimbabwe and to the Implementation Issues for Monitoring People on ART in Low Income Settings in Sub-Saharan Africa workshop. Participants representing many African Ministries of Health and international organisations in attendance (Appendix II) were acknowledged and welcomed to Zimbabwe. Dr. Apollo described looking forward to exploring how modelling can be used to inform national priority setting and how country experiences will inform modelling and subsequent guidelines over the course of the workshop.

Wlb: Overview of meeting and aims
Timothy Hallett, HIV Modelling Consortium, ICL

Prof. Hallett summarised the history of the consortium, with WHO 2013 guidelines described as a landmark for acknowledging the need to consider population perspectives and the role of mathematical modelling for supporting the decision making process of identifying programs with greatest potential impact across the population subject to available resources.

The HIV modelling consortium represents a large body of modellers seeking to support examination of questions for which trials or direct empirical measurements are not feasible or do not answer in full, while helping to shape priority questions arising from implementation of guidelines.

Two main questions the modelling consortium is looking at in support of the WHO 2015 guideline revision include:
1) What are the drivers of AIDS deaths and what interventions can reduce AIDS deaths?: Requires definition of care cascade in various settings and determination of where losses are having the greatest impact to guide interventions.
2) What ways of monitoring patients on ART can be recommended?: Focus of the current meeting, representing a milestone of a larger body of work in this area.

Based on the highlight focus upon monitoring of patients on ART, Prof. Hallett outlined 2 key objectives of the workshop:
1) To obtain feedback on recommendations based on preliminary modelling and cost-effectiveness for patient monitoring – in the immediate term.
2) To discuss and document the issues programmes face in implementing monitoring of patients on ART – now and in the future.
Session 1: Modelling to support development of the WHO ARV guidelines on patient monitoring

_Chair: Timothy Hallett, ICL_

1a: WHO Guidelines: CD4 and Viral Load Testing

_Jessica Markby, Diagnostics Adviser, HIV Department; Treatment and Care Unit, WHO_

Dr. Markby presented the foundation of evidence for current (2013) WHO guidelines on CD4 and viral load testing, highlighting diagnostic priorities for monitoring patients within the cascade of care as critical for achieving 90-90-90 goals. Consultative processes on CD4 and viral load resulted in the development of key PICO (Population; Intervention, Comparator; Outcomes) questions explored with the intention of guiding 2015 guideline revisions:

- **In individuals receiving ART, is initial viral load testing at 3 months more effective than at 6 months?**: Earlier testing (3mo vs. 6mo) for early detection of adherence problems.

- **In individuals with HIV who have been on ART for 12 months and have achieved viral suppression is measuring viral load every 6 months compared to every 12 months more effective?**: Priority sub-groups for enhanced monitoring including pregnant women, children, adolescents.

- **In individuals on ART is dried blood spot testing at VL threshold > 1000 cpm as effective as VL > 1000 cpm using plasma?**: questions about reduced sensitivity, meta-analysis by CHAI demonstrated ability of DBS to perform at equivalent capacity to plasma at 1000 copies/ml. DBS seen as crucial tool for increasing scale up of VL testing due to limitations of plasma-based VL testing beyond urban/centralised areas. Modelling will further inform impact of sensitivity at scale.

- **Is POC Early Infant Diagnosis (EID) and viral load performance equivalent to laboratory based methods?**: Point of Care (POC) VL monitoring technologies have great promise for improving access. Available technology in the immediate term indicates need for limited laboratory infrastructure for preparation of plasma. There will be a need for country-level mapping to understand where these technologies may be best placed.

- **In individuals with HIV who have achieved viral suppression on ART is CD4 count and VL annually more effective than VL annually?**: New 2015 guidelines will place emphasis on VL monitoring over CD4, though CD4 will likely continue to play an on-going role in initiation and monitoring in places where VL not available acknowledged.

Dr. Markby emphasised that in sub-Saharan Africa, substantial gaps exist between total need (defined in terms of patients on ART receiving routine VL testing) and total met need (5-10%) for VL testing (Figure 1). The value of Dried Blood Spot (DBS) testing for scaling up VL monitoring in the immediate term was emphasised.
Session 1a. WHO 2015 Guidelines; Summary Discussion Points:

- Lessons from EID indicate success of VL monitoring is to a degree predicated on short turnaround times (TAT) – this will be addressed in operational aspects of the revised guidelines and also linked to the timing of the first test after initiation.

- Systematic review of DBS conducted by LSHTM established different results can be linked to variety of methods used for DBS and not necessarily due to lab-based technologies. Primary factors include input volumes into lab assay, and different eluting procedures not optimised to platform. Need to work with manufacturers to know what optimised procedure for processing DBS is so that processes can be standardised.

- Research and systematic reviews on development of thresholds for POC are planned to determine if POC results in over-classification of failure due to specificity concerns. More evidence is required to better understand threshold levels to determine detectable VL and threshold for switching. For example, some POC in development uses whole blood and some plasma, so performance of assay will partly depend on this and will not be able to speak of common performance characteristics for VL POC.

- There is a role for modelling to understand the impact of factors such as reduced sensitivity and reduced access on cost-effectiveness of the strategy through sensitivity analyses.

- Understanding the critical factors for increasing met need for VL monitoring – operational guidelines provide interpretive guidance on how to translate guidelines at national level, though achieving coverage will require recognition of contextual factors influencing access and national level bottleneck analyses.

- While currently focusing on improving access to VL monitoring, there is need to establish effectiveness strategies for increased retention (proportion initiated on treatment 12 months later) and health outcomes. Modelling acts as a decision aid for guidelines in understanding the link between diagnostic and monitoring strategies and how these translate clinically to patient health.

1b: Allocating resources to patient monitoring to generate population health improvement: Evidence from modelling and economic analysis

Andrew Phillips, University College London

Prof. Phillips presented preliminary results of new cost-effectiveness (CE) modelling analyses with the intention of providing WHO advice to inform guideline revision. Results of three key questions modelled in the current analysis were summarised:

<table>
<thead>
<tr>
<th>Modelling Question</th>
<th>Preliminary Modelling Answer</th>
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<tbody>
<tr>
<td>1 For countries without access to viral load monitoring, what would be predicted to be the most cost-effective monitoring strategy?</td>
<td>In the lowest resource settings, clinical monitoring (with CD4 confirmation) appears cost-effective in some cases. If using CD4 count monitoring, the CD4 &lt; 200 strategy is likely to be cost effective compared to the current WHO strategy.</td>
</tr>
<tr>
<td>2 For countries scaling up viral load monitoring, what can modelling tell us about the pros and cons of plasma vs DBS vs POC?</td>
<td>VLM using DBS is likely cost effective if no POC. When POC becomes available, this is likely CE with assumptions that VLM results in less ART cost/clinic costs.</td>
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### Session 1b. Preliminary findings from recent modelling analyses; Summary Discussion Points:

- Current analysis assumes ‘all in’ costs based on available data; however validation of in-country costs for implementation of strategy is critical to understanding if assumptions modelled about costs are deliverable in country. In particular, establishing the cost effectiveness of POC VL will require additional input of implementers on total costs including human resources, infrastructure and consumables. This is an area where implementation can contribute to improved modelling: through collection of accurate and comprehensive costing data.
- With very low met need in most SSA countries, modelling provides useful information for Ministries making decisions for dedicated resource allocation among many competing needs (i.e., CE of use of DBS for increasing access to viral load measurement).
- The current model simulates an adult population in a low-income setting; however different VL monitoring strategies among sub-populations (pregnant women, young people, and children) are not done.
- Tiered facility-level characteristics that might impact effectiveness (i.e., POC in areas without electrification, seasonal transportation factors) were not independently modelled. Different probabilities linked to different approaches accounted for within the model that the test is actually done – and if not done, probability cost of test is being incurred. However, subtleties of mid-tier level stratification of model parameters will be something for consideration in future iterations as more accurate information about implementation of different VL monitoring strategies is gathered.

### 1c: The framework of analysis: assessing cost-effectiveness and summary of previous results

**Paul Revill, HIV Modelling Consortium, University of York**

Paul Revill led a session summarizing the framework of cost effectiveness analysis. Understanding assumptions that have gone into the analysis are important for determining how models can be adapted as contexts change, and enable better interpretation of results presented. The ultimate goal of modelling is to understand if the health gain from new intervention (such as change in VL monitoring guidelines) will be greater than the health foregone or displaced (Figure 2).
The use of Disability Adjusted Life Years (DALYs) to frame costs, and threshold of $500/DALY averted are used to interpret modelling results.

The HIV Modelling Consortium contributed to WHO 2013 guidelines through analyses using a common costing framework (inc. CD4 = $9, VL = $45) and 3 models provided results (HIV Synthesis, the Braithwaite model and the Estill model). These analyses demonstrated if ART coverage targets not met, resources allocated to increasing ART coverage would generate much greater benefits than if allocated to better patient monitoring (Figure 3). If high ART coverage, clinical monitoring delivers significant benefit compared to no monitoring or switching.

Session 1c. Framework analysis and 2013 Guidelines Results Summary; Summary Discussion Points:
- Setting an accurate cost-per-DALY-averted CE threshold for different settings was acknowledged as a limitation. Qualified assumptions are required in the absence of perfect information, which would allow us to clearly see what the marginal benefits are between competing strategies. As this is difficult to achieve in practice, each country, particularly those in lowest resources settings, is encouraged to critically reflect on the interpretation of threshold values for cost-effectiveness analyses.
- Assumptions regarding likelihood of ‘action’ following the taking of samples and receipt of VL monitoring results (proportion of patients switched who meet VL criteria) have a large effect on results and require additional implementation data. Such data could inform timing, scaling and resources required to realise greatest CE.
- Equity issues (e.g. how alternatives impact access to and the distribution of health gains across a population) are important when interpreting modelling results (focussing on patients in care vs. strengthening the continuum of care and ensuring individuals enter the cascade have a clear equity dimension).
- Sensitivity analyses to demonstrate impact of reductions in the costs of clinic visits (enabled through tiered care as a result of VLM) upon cost-effectiveness ratios were conducted.

1d: New considerations in modelling ART monitoring strategies

Andrew Phillips, University College London

Changes in monitoring landscape since 2013 analysis factored into current preliminary results presented were described by Prof. Phillips to contextualise current strategy attributes (Figure 4) and emphasise the continuously changing landscape of modelling input parameters.

Specific areas where changes have occurred:
- **Cost:** lower costs of VL (‘full loaded’-$22), 2nd line ART ($288 all in), sample transport leveraging from established EID
• **Relationship between VL monitoring and adherence**: VL as adherence measure requiring reduced clinic visits. Non-ART programme costs reduction with viral suppression (VL<1000) from $80 to $40.

• **Programmatic factors**: reduced TAT, improved knowledge on accuracy (sensitivity & specificity of DBS, plasma)

**Session 1d. New modelling considerations; Summary Discussion Points:**

- Assumptions regarding the capacity of POC (80% assumption VL done if patient needs; 70% for DBS) within the model are somewhat aspirational for what POC can achieve. Again, modellers emphasised the need to pair this with implementation data so that specifications can be adapted. Assumptions of standard deviation probably slightly over-estimated for probability of misclassification of VL being done using DBS* Probably best to be cautious where data isn’t available.

- Country implementers reported that the linkages between VL thresholds and switching are not as strong as they should be in many implementation settings.

- Similarly, modellers recognised need to understand in implementation going forward if VL measurement results in long-term or temporary increase in adherence, although as it stands this doesn’t seem to be a highly significant parameter.

- Within the current model as there is no 3rd line available, after switching to 2nd line assumption of no VL monitoring. Participants suggested monitoring within 2nd line might be approached as a strategy for adherence monitoring and tracking patient outcomes as a prevention measure for 2nd line failure. The use of other monitoring methods such as genotyping to determine whether failure to VL suppress is a resistance or adherence problem and avoid unnecessary switches were proposed. Recent analyses by Prof. Phillips have demonstrated individual level resistance testing is unlikely to be cost-effective and optimal outcomes for chronic poor adherence under 2nd line is more likely achieved by switching to boosted PI.

**1e: New modelling findings**

*Andrew Phillips, University College London*

Prof. Phillips provided a comprehensive presentation of the various monitoring strategies modelled to derive key modelling conclusions reviewed in Session 1b (Figure 5). Absolute values modelled to adult population in Zimbabwe. Sensitivity analyses to determine scenarios with and without tiered care under which VL monitoring measured as cost-effective threshold of $500/DALY averted:

i. Cost thresholds at which VL monitoring ceases to be most cost effective strategy (tiered care):

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• cost second line > $389
• VL > $51
• (no CD4 cost)
• reduction in non-ART program (visit) costs due to simplified visits < $10 per year

ii. Cost thresholds at which VL monitoring ceases to be most cost effective strategy (no tiered care):
• cost second line > $302
• VL > $23
• CD4 cost < $9

Session 1e. New modelling results; Summary Discussion Points:
• The implementation reality described by countries in attendance for the foreseeable future will involve a mix of plasma and DBS-based VL monitoring, rather than one all in strategy. Depending on value and key populations served at different tiers of care, the cost and clinical impacts of placing a POC vs. plasma vs. DBS labs-based sample processing, and impact upon increased TAT and loss to follow up (LTFU) will vary at different levels of care.
• As technological advancements occur, POC will become increasingly effective and more practical, especially among key populations where the impact will be marked (i.e., under B+ in high volume maternity settings). Models that enable simulation of impact of various strategies among key populations are of interest for guiding implementation and country plans. This would enable specific costing, program and health impact parameters and determining which monitoring strategy is cost-effectiveness at the given threshold.

1f: Morning Session – Key questions and discussion
Facilitated by Paul Revill, University of York

As a wrap up of the presentations regarding preliminary analyses and current guideline directions, Paul Revill presents 5 key questions to meeting delegates for discussion (Figure 6).

Q1: $500 an appropriate CE threshold?
• Countries acknowledge the rationale for setting a threshold for evaluating CE that reflects their budget constraints. Need for each country to critically interpret cost-effectiveness studies, particularly in very low-resource settings, based on what can be paid is important.
Q2. Attainability of low VL and 2nd line ART costs:

- From Global Fund perspective, pricing costs that have been used in the model are reasonable estimates. Working with manufacturers to get more complete costs would improve setting of accurate cost parameters in the future.
- It is important to recognise there are limits, to which costs can be pushed before strategies become unviable, i.e., there must be a price for economies of scale that you cannot go below. Stagnation in POC development may be due to the desire to reduce costs below which the manufacturing becomes unviable. Therefore, while costs can be expected to reduce, there will be a necessary floor.

Q3. Assumptions about rates of switching and interventions to improve:

- Country experiences regarding switching are as linked to skills-base and human resource capacity as technology. Example provided from Malawi, of low switching rates at start of VL monitoring. This was related to switch being centralised – so testing might be at lower level but 2nd line initiation only done at District or higher. Need to pace monitoring with treatment and care capacity and train ‘2nd line prescribers’ in rural health centres, so that switches can be decentralised and 2nd line initiation can match the VL testing.

Q4. Realisation of reduced costs with less frequent clinic visits, reinvestment of resources saved for health gains in other areas?

- Need to further explore ways to improve lab efficiencies and polyvalency of platforms, for example, GeneXpert availability increasing for increased access to TB testing, leverage VL test using technologies already being planned for roll-out in countries for further cost-savings.
- Role of country-level mapping and examination of tiered systems based on volumes, human and infrastructural capacity and structural factors will be important to realise cost-savings. Working within existing systems and increasing cost-effectiveness by changing of work flows without instrumentation changes are important areas of operational and implementation research for creating efficiencies. Models we are currently using are not structured to link probabilities to each and every operational influencer, though these are acknowledged to play a role in overall cost-effectiveness.
- Once a hub of instruments is established, countries can engage in exercises to define the radius around which DBS would work around centralised lab-based platforms. This will also require defining optimal throughput levels for different platforms in specific contexts.
- Infrastructural requirements for storage of consumables and medications will need planning to realise cost-effectiveness of fewer clinic visits from VL monitoring (i.e., extended pickups).
- While fewer clinic visits described as a cost-saving of VL monitoring, countries such as Zimbabwe, recommend clinical consultations for stable patients twice a year and monthly drug pick-ups. However to ensure retention in care and continuous adherence monitoring and support, health care workers prefer to see patients more frequently than every 6 months in the absence of widespread viral load availability. Medication stocks mean that 3 monthly-supplies of meds, a situation which is likely to continue for the foreseeable future with uncertainty in for countries to secure long-term ARV pipelines. This is an example of intersection between modelling/biology and system/patient implementation issues. Utility of these forums is to discuss practicality of what modelling analyses determine to be cost-effective and, relatedly, to inform issues of implementation.
Questions around how high-impact cost considerations such as quality assurance and health worker training and mentoring into costing in different settings highlight the need for greater involvement of Ministries of Health and implementers in comprehensive costing studies to support modelling, as these are not within the mandate of modellers. Modelling is bound by the availability and quality of evidence to set parameters and probabilities.

Emphasis that the current model takes a health system perspective, so that patient cost-savings of modelled strategies in terms of gains in productive time, savings on transport and health care costs from fewer clinic visits are not modelled or accounted for.

Q5. DBS investment vs. hold off until POC VL availability improves?

- General consensus among the group was that a ‘wait and see’ strategy for POC availability to increase is not advisable for SSA countries. Countries are currently positioned to leverage EID programs for VL DBS so this should move forward now. In addition, POC will not be appropriate for all settings (i.e., low volume, areas with insufficient infrastructural (electricity) and human resources), so a necessary mix will be required.

- Implementation experiences and improved efficiencies through expanding DBS and plasma platforms could be garnered in the interim, allowing for strategic placement and strengthened systems for POC placement and utilisation. Phased implementation of DBS was recommended as the most appropriate country-level strategy for increasing access to VL monitoring in the immediate term.

- Important to note that in areas with low ART coverage, previous analyses demonstrated that increasing treatment should be priority. In areas with high coverage, costs of finding remaining individuals not in care and investments into retention as a comparator to investing in VL monitoring are not known. Likely, countries will need to engage in a balance of trade-offs and the investment strategy will include elements intended to both increase ART coverage, and access to VL monitoring for those on ART.

- Country representatives described approaches for prioritising POC including: mapping patient volumes, TB/HIV burden, site-level capacity and commodity chain inventories, identification of ‘ideal clinic’ settings for POC for criteria setting. There is no one size fits all approach to POC. There is in-country need for strong forensic analysis about contextual factors regarding site characteristics and different implementation capacities. Modelling is not suitable to provide answers to these contextual factors at present, though algorithms at national level provide specifications for modelling.

Summary of Session 1 Key Messages

*Timothy Hallett, ICL*

Prof. Hallett provided the group with a condensed summary of the key message arising during group discussions during **Session 1: Modelling to support development of the WHO ARV Guidelines on Patient Monitoring**. The implications of these key messages for consideration by the HIV Modelling Consortium for alteration of the model under the current analysis are summarised.

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1. **Need approach to hybridize implementation of VL monitoring and phasing in a way that characterizes facility-based variation.** This is required to inform decision making for phased implementation approaches for optimising phasing of VL monitoring, but does not require a change within the current model structure which includes the tiered care analysis.

2. **Potential need to model scenarios for specific populations (pregnant women, adolescents, peds).** The model presented is designed as a general adult model, children aren’t currently modelled. However, it is possible to explore the potential value of disaggregating key parameters known to influence cost/effectiveness by age and see if these influence cost-effectiveness when modelled (i.e., adherence, CD4 monitoring in the Arrow trial). Potential to look at phasing, by key populations, by region.

3. **Determination of value of decentralising 2nd line, training/mentoring investment of health care workers so switching occurs, so that trade-offs complement perspective.** Based on preliminary experience of those reported at the meeting (MSF in Zim) currently implementing VL monitoring, it appears continued use of measuring CD4 doesn’t hold up as cost-effective strategy without a concrete action following receipt of result. Potentially hold off continued use of CD4 monitoring until better use of resources identified.

4. **Potential to interrogate impact of timing rather than frequency during first 6 months of care (i.e., @ 3 months after initiation).** If there is evidence upon influence of this strategy on future retention rates could be a justifiable implementation change to the VL monitoring strategy, however it won’t result in a difference in cost measuring at 3 months (just a change in timing of the test, not the number of tests conducted). If result of changed timing is an increase of effectiveness, then doesn’t require modelling to justify change in practice as cost would remain the same, with increased effectiveness.

5. **Need to model continued monitoring of patients on 2nd line ART.** Impression was there are benefits to continued monitoring of these patients in terms of adherence and effectiveness. Patients on 2nd line ART are not currently monitored on basis there is no 3rd line to model. If the model was going to be altered to accommodate this, there is a need for evidence that reports how adherence monitoring on 2nd line improves adherence or that 3rd line is available in practice in order to set values for input parameters.

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**Update on POC VL Landscape**

*Maurine Murtagh, UNITAID*

Prior to transition into Session 2, Maurine Murtagh from UNITAID provided a brief summary update on the VL pipeline and what is expected over the coming years (Figure 7). Considerations of use of different POC technologies at various system levels, current performance and expected advancements in the next one to two years were summarised.

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**Figure 7**
Theme: Understanding where we are in the provision of HIV treatment and patient monitoring

Session 2: Financing national HIV treatment responses and competing calls on limited resources
Chair: Lisa Nelson, GFATM

2a: HIV/AIDS Financial Landscape in Zimbabwe
Travor Mabugu, Health Economics and Policy Research Initiative (HEPRI-Zimbabwe), University of Zimbabwe, Clinical Research Centre

Mr. Mabugu, began his presentation with the recognition that national HIV budgets can only do “so much” and the trade-offs between various alternatives must be explored. Highlights on the Zimbabwean funding context from Mr. Mabugu’s presentation:

National HIV Funding Context:
- The HIV response in Zimbabwe includes funding flows from the AIDS&TB unit of the Ministry of Health and Child Care (MOHCC), private sector, MOHCC sectorial engagement and the National AIDS Council (NAC), which together through stakeholder engagement form the Zimbabwe National AIDS Strategic Plan III (ZNASP III) 2015-18
- 2 key sources of funding: external pool; domestic pool (AIDS levy, direct treasury funds, private sector).
- At presents, there are substantial gaps between mean need (479 mil) and mean available resource (257 mil) – a gap that is widening moving forward into the future (30% in 2014 to 60% to 2018).

Plans to increase VL monitoring access in Zimbabwe:
- Government of Zimbabwe has a commitment to building laboratory capacity and aggressively scaling-up VL testing to ensure access to VL testing services by at least 90% of people living with HIV (PLHIV) receiving ART by 2018.
- Coverage is intended to be achieved through a Four Phased approach (Figure 8) with initial plans to scale up DBS during Phase I and II with room for new technologies such as POC in III and IV.
Costs of VL monitoring in Zimbabwe:
- Cost per patient per year $250 direct treatment cost per year in Zimbabwe (2012), with ARV costs between $137-145.
- Comprehensive lab cost per person per year is that unit cost: CD4: $9.08 vs VL Test: $39.08. This is higher than the $22 modelled in the current analysis for reagents and consumables. (Figure 9)
- 45% of Zimbabwe cohort is rural, so likely target for VL POC; 41% district; 14% higher level.
- Financial implications of VL monitoring implementation through 2017 is approximately 26.8 million dollars, with the bulk in procurement and supply chain management as part of a activity based costing exercise.
- Available resources are currently $11 million for VL strategy (15.8 mil gap)
- As in many other countries, there are trade-offs in expanding laboratory capacity for VL monitoring with other currently underutilised labs for HIV positive individuals (urea, liver function).

Challenges to funding HIV services:
- Limited funding for basic HIV services: resulting in ART Care and treatment gaps (ARVs etc), Child ART coverage still remains low, despite improvements HTC need growing
- Shrinking formal sector: potential decline in NATF revenue (Main source of domestic pool)
- Lack of optimal resource allocation methodology that maximizes impact from available funding: requires more strategic resource allocation methods that maximise funding, and link funding to impact from a national strategy perspective. Modelling provides useful perspective for exploring long term impacts of investment decisions.
- HIV investment cases – front loading doesn’t make good investment case for HIV responses
- Need to develop a priority set is a gap

Paul Revill presenting on behalf of: Dominic Nkhoma, MOH Malawi

National HIV Funding Context:
- With a rapidly expanding population, largely agricultural, Malawi has faced difficulty in funding own health response with donor funding up to 70% in 2012 - exposing country to greater risk of programmatic disruption (Figure 10)
Health funding required estimated at 1.04 billion from 2015-2016, with 584mil secured, leaving a huge 458mil gap from planned spending.

HIV estimated to account for 38% of funding; 35% of DALYS in Malawi.

HIV/AIDS funding spent primarily on drugs and systems, with small proportion on programmatic efforts (2014 HSSP costing).

HIV/AIDS funding spent primarily on drugs and systems, with small proportion on programmatic efforts (2014 HSSP costing).

Funding Gaps for VL monitoring:

- Gap analysis has demonstrated very few HIV/AIDS funding areas without significant gaps (Figure 11)
- Malawi has prioritised DBS for VL monitoring at present following realisation during pilot scaling which starting with plasma that this was not feasible at scale. Now only using CD4 for eligibility and completely phased out monitoring for CD4 and only using DBS.
- Funding shortfalls compared to projected need under HIV programs under VL testing is 3.9million with 24 month testing), HTC (8mil), ART (84mil)
- VL testing comparable over funding required to HTC and VMC
- Take away: Financing pressure is acute in Malawi as in Zimbabwe.

Session 2: Open Discussion

Chair: Lisa Nelson, GFATM

- Acknowledgement that presentations do not factor in some recent and ongoing commitments from large donors such as GFATM.
- For many countries in SAA lack of predictability of funds in the midst of massive increases in scale and coverage targets of HIV programs has resulted in growing gap between aspirational targets and met costs.
- Scope to re-examine planning tools such as the World Bank optimizing banking operating models and increase testing and reporting of different models.
- Challenge faced by countries to conducting comprehensive and accurate gap analyses to develop funding requests as required by donors, and then donor division of the country by funding area, with some donors ring-fencing money for specific uses, often leaving both over-
funded and under-funded areas as demonstrated in the Malawi presentation. Expressed challenge for countries to align donor priorities and funding commitments with long-term national strategic plans.

- Emphasis of donor organisations of making strong investment cases for strategic goals such as increasing access to VL monitoring. Modelling is a useful tool for providing implication of cost-effectiveness of investment choices at one time into the future to inform trade-offs.

**Day 2: Thursday 12 March 2015**

*Continuing on Theme: Understanding where we are in the provision of HIV treatment and patient monitoring*

**Session 3: Panel Discussion I: National HIV treatment programmes and policies; reasons for policy choices**  
*Chair: Meg Doherty, WHO*

**3a: Zimbabwe National HIV Treatment Programme and Policies**  
*Tsitsi Apollo, Deputy-Director HIV/STIs, MOHCC Zimbabwe*

**Contextualizing HIV and ART in Zimbabwe**

- 1.1 million adults, 121K children in urgent need of ART in Zimbabwe (2014)
- 34% reduction in new HIV infections, in past 8 years
- Scaling of routine VL testing to cover central to district care
- 90-90-90; 66% of target of 1.26mil; 66% currently in need on ART
- HIV Testing and Counselling rates F: 51%; M: 40% (Multi Indicator Cluster Survey, MICS 2014) – need to target populations with greatest yield, with main challenges linking testing and care, self-testing, few counsellors and testers
- Major successes of program include PMTCT: nearing virtual elimination of new paediatric HIV
- Adult ART coverage high (69%) but paediatric coverage remains low (45.5%) – Accelerated Plan for Improving ART in Adolescents and Children

**Increasing access to VL Monitoring**

- Draft comprehensive phased approach to increasing VL coverage
- 4 phases (2014-2017), expected to reach 21% coverage by end 2015 (Figure 12)
- Implementation plan components include comprehensive systems and data considerations
- Goal to gradually reduce CD4, informed by implementation monitoring and evaluation
- Plan to standardise conventional testing platforms and limit them to a maximum of 2-3 different types; likely conventional plasma at higher level; POC lower level
- Challenges in securing adult and paediatric ART (Figure 13) highlight tensions in resource allocation between treatment and monitoring. These indicate potential need for targeted algorithms for VL testing among key populations (pregnant women, adolescents, and children).
- Modelling could be useful for prioritising funding within limited resources.

3b: National HIV treatment Programmes and policies- Policy choices

*Cordelia Katureebe, , MOH, Uganda*

As National coordinator Paediatric and Adolescent HIV services STD/AIDS Control Program at the Ugandan Ministry of Health, Dr. Katureebe provided the meeting with a summary of the process of guideline revision in Uganda towards VL monitoring with cost implications of implementing new guidelines.

**Increasing access to VL Monitoring in Uganda**

- 2014 revision of guidelines in Uganda to incorporate 2013 recommendations on VL monitoring.
  
  “VL testing is now WHO recommended for routine monitoring of ART patients as it helps identify cases of treatment failure early. Additionally, VL testing should be offered to patients who are suspected of treatment failure to enable urgent interventions and improve morbidity outcomes. If viral load is not routinely available, CD4 and clinical monitoring should be used to monitor response to ART”

- Together with donors and partners, government has negotiated price of $10/VL (consumables only)
- Populations prioritised for VL, Option B+, test and treat<15 yr
- VL monitoring being implemented with enhanced adherence counselling
- VL at 6 months after initiation and thereafter annually – if VL not routinely available, CD4 6 monthly
- Phased expansion of VL testing, with national coverage as future goal
- Sample transport/courier system leveraged from EID
- DBS primary sampling method, plasma at centralised (Figure 14)
- Adherence support intensive switch to 2nd at VL>5000; 1000-5000 continue treatment with annual VL testing
• Switching to new guidelines will save 1 million with gradual VL scale/CD4 mix per year (Figure 15)
• Doubling scale of VL every year 100K-200K-400K
• With huge expected increases in numbers on ART, VL monitoring strategies may face challenges including: sample transport volume, cold chain, capacity of the labs to process all samples and human resources.

Scale up requires caution and health system barriers should be identified and addressed in a continuous process.

Implementation of New Guidelines will increase ART costs by ~$32m or 15% for a 2 year period (2014, 2015). Pediatric costs during this period will increase by $11m, Adult by $23m.

<table>
<thead>
<tr>
<th></th>
<th>2014 USD $m</th>
<th>2015 USD $m</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ped ART</td>
<td>$11</td>
<td>$15</td>
</tr>
<tr>
<td>Adult ART</td>
<td>$89</td>
<td>$96</td>
</tr>
<tr>
<td>Total ART Costs</td>
<td>$100</td>
<td>$111</td>
</tr>
</tbody>
</table>

Comparative Monitoring Costs:

- CD4 (only) testing $10 VS.
- Gradual VL scale up/ CD4 mix $9 VS.
- VL testing (100% scale up $7

Figure 15

3c: Malawi National Treatment program
Zengani Chirwa, TA Care & Treatment, HIV & AIDS Department, MOH Malawi

Dr. Chirwa from the HIV and AIDS Department at Malawian Ministry of Health provided a summary presentation of the HIV landscape in Malawi and some preliminary experience in scaling VL monitoring.

Malawi HIV Context
• 1 million HIV infected population: 34,000 new infections; 48,000 AIDS deaths (2013)
• 521,319 (52%) on ART = 1/20 adults are on ART
• Has kept pace with guideline changes: Option B+ for PMTCT (2011), moved to 500 CD4 (2014), Universal access for children <5 years (2014)
VL monitoring in Malawi
- 2014 switch to VL monitoring, CD4 only used in Malawi to assess eligibility not monitoring
- First VL 6 months after initiation, then 2 year and bi-annual thereafter (Figure 16)
- Clients with VL>5000 with ‘good adherence’ can be switched to 2nd line
- Action taken following targeted or repeat VL testing if detectable VL depends on VL range (copies/ml)

Experiences and challenges in VL monitoring
- Early implementation started with plasma, barriers to achieving scale rapidly apparent, now DBS primary sampling method to enable rural reach – following validation DBS demonstrated high sensitivity/specificity
- January 2015 data indicates undetectable VL 84% routine; targeted 54% undetectable VL – indicating potential increase in cost-effectiveness thorough targeted VL monitoring (Figure 17)
- Riders for health sample transport in 7 districts, reduction of TAT 14 days, remainder of country average is 30 days.
- Absence of 2nd line providers at rural health facilities for switching, stock outs, breakdowns as challenges that also have cost and effectiveness implications of VL monitoring investments.

Data management systems for monitoring patients
- Data management between electronic patient monitoring (EPMS) and card-based patient records
- Combined requisition forms for EID and viral load = example of implementation efficiencies to improve CE and reduce overall program costs of guideline shifts
- ‘Pop up’ electronic monitoring system when client reaches milestone for VL monitoring, and if VL is high – system flashes continuously until resolution (either lower VL is entered or 2nd line switch documented).

3d: National HIV Treatment Programs and Policies: Kenya
Fred Sawe, Kenya Medical Research Institute/Walter Reed Project (KEMRI/WRP)

Dr. Sawe provided a review of the Kenyan context and HIV monitoring strategies currently being employed in Kenya, with plans for scale up.
Kenyan HIV context

- 2014 guideline revision
- 1,630,138 PLWHIV: 740,497 Current on ART; 45% ART coverage; 559,616 Unmet need (per national guidelines)
- Pediatrics: 179,793 LWHIV; 40% ART coverage
- PMTCT: 1,893,896 Expected pregnant women; 70% ARV coverage
- Emphasis that coverage remains important national target in conjunction with VL monitoring scale up (one should not move without other)

Clinical And Laboratory Follow Up of PLHIV

- CD4 for eligibility every 6 months, thereafter used based on clinical decision making (i.e., co-Is)
- Plasma preferred, DBS for rural/remote. National VL testing currently managed by 7 labs (Figure 19)
- VL monitoring algorithm indicates VL 6 months after initiation, then 12 months, then annually if suppression (Figure 19)
- VL>1000=failure criteria
- Kenya guidelines beginning to include 3rd line recommendations
- Main challenge between results and switching/action – resistance among HCWs to transition past first line
- Labs processing all research labs (less Mombasa) so have existing capacity to scale and absorb new technologies (personnel and infrastructure) building on EID capacity – possible to scale VL to 2400 facilities using same strategy for scale-up that has been successful (leveraging programme experience to save costs).
- 77% of VL in last 6 months done for routine monitoring

Session 3: Open Discussion Summary

- VL coverage levels among countries at present:
  - Kenya: Last 3 years 417K VL, expectation that numbers will increase;
  - Uganda: Very new, scale up in November 2014 so far only 50K tests as have just started. DBS for remote.
- **Malawi:** 15K/Q, which works to around 15% coverage, with coverage expected to increase tremendously in 2015. Failure to reach VL targets linked to staffing and training to support intervention limit transition to new VL monitoring guidelines. Delays in procurement and roll out of machines and commodities reduce level of performance.
- **Zimbabwe:** currently very low at 5%, phased scale-up planning rapid increases

- **Average TAT for different specimen types?:**
  - **Kenya:** Remains a challenge, worst case is 2-3 months to result receipt. Machine capacity a limitation (3 runs/day) so specimen processing is capped. Issue of bringing new machines is there is no infrastructure (Clinics taking consultation rooms over for labs)
  - **Uganda:** TAT between 2 weeks – 1 month as building upon EID systems.
  - **Malawi:** where doing plasma, 10-14 day turnaround. Sites with riders for health DBS TAT 10-14 days, no transport program up to 40 days. Districts with partners supporting have better TAT (i.e., transport support, SMS printers).

- **Funding gaps are a cyclical challenge for Ministries and highlight value of accurate costing exercises, as often working with estimates, may over/under-estimate requirements to cover gaps. These problems are compounded by limited growth in domestic funding. Challenge of knowing when to slow down to conserve resources in midst of ambitious goals for increasing HTC, ART and VL monitoring coverage.**

- **Discussion on what denominator countries should be using to calculate their 90-90-90 targets. WHO informed that definition clarification will be provided.**

- **Questions related to the rigidity of test timing within guidelines: countries described that during scale-up phases not being rigid in terms of pace of scale up and implementation flexibility to allows incorporation of lessons learned. ‘Catch up’ VL testing in Malawi currently encourages sites with capacity to test all above 6 months and then continue with routine after. Routine appointments are held every 3 months in Malawi, so can be expected to test within 3 months. Only re-test every two years is decision based on cost considerations and available resources (not on modelling or fixed cost-effectiveness analysis), an example of guideline recommendations based upon pragmatic choices based on available resources.**

- **There is a general impression among all presenting countries that there is a need to better understand and address adherence issues as a matter of priority, as there is a perception that low switching rates in those whose VL results qualify are a result of clinician hesitation to switch patients who are not true treatment failure, but non-adherent. Malawi reported results indicating adherence efforts can result in 50% re-suppression. Clinical judgements are seen by implementers as intention to filter out unnecessary switches, which could also have detrimental impact on cost-effectiveness with no 3rd line.**

- **If algorithm includes clinician judgement – this will result in reduced # of switches. If this is the implementation reality then accurate data on preliminary outcomes of early monitoring efforts will be critical for informing future algorithms and guidelines.**

- **With regards to whether guidelines should develop separate algorithms for key populations (which could then be modelled): Kenya: currently PMTCT guidelines cover VL monitoring for pregnant women (if none in past 6 months, then test if presenting in ANC). Otherwise, no separate guidance for key populations; Uganda: Option B+ in 2012, VL scale up in 2014. Initially in 2014, subpopulations were prioritised, now with scale up can be seen as VL for all PLHIV,**
therefore no specific emphasis. But now should re-examine to look at operational and cost issues related to targeted monitoring.

- What does ‘intensive or enhanced adherence counselling’ mean in different settings?
  - Adherence looked at in terms of pill counts, treatment supporters (criteria) then over time VL conducted to demonstrate if adherence or resistance resulting in detectable values.
  - Malawi: Increased appointment frequency, pill counts, treatment supporters, sending social worker for home visits, substance abuse issues.

**Theme: Future directions for monitoring patients on ART**

**Session 4: Panel Discussion II: Investing in scale up of viral load measurement in the context of health care needs**

*Chair: Joseph Murungu, MOHCC Zimbabwe*

**4a: Monitoring on ART**

*Diana Gibb, MRC CTU*

Professor Gibb provided a perspective on strategies for monitoring individuals on ART based upon evidence from Paediatric, adult and adolescent trials, the UK National Cohort (CHIPS) and over 25 years of experience in the clinical management of people living with HIV in UK. Key components of Prof. Gibb’s presentation included:

- Monitoring individuals on treatment has both individual (prevent resistance, improve health, switch if necessary, and possibly improve adherence) and population level (reduce community viral load and transmission) benefits.
- Immediate risk of clinical progression and death much better predicted by CD4, whereas VL is an independent predictor of disease progression before and on ART
- Monitoring trials have not shown clinical benefit of routine VL monitoring in adults (Thailand (PHP3), Uganda (HBAC), and Zambia) and children (Penpact1 Trial).
- Small but significant benefit of CD4/clinical vs clinical alone in DART and ARROW trials.
- “Using CD4 counts alone to monitor HAART in HIV treatment programs in resource-limited settings is an appropriate strategy to use” (PLoS Med Editorial)
- Importance of timing of monitoring in survival (Figure 20) of outcomes: if using early monitoring as gauge – need time to adjust to treatment (especially in children).
- Correlates between CD4
Monitoring People on ART in Low-Income Settings in Sub-Saharan Africa

and VL – are not useful comparators because they are measuring different things. Also CD4 monitoring doesn’t work as a monitoring tool perhaps because definitions are confusing and deserve consideration in future guidelines (thresholds or % from baseline?)

- In general, quality of evidence for additional benefit of VL monitoring is low at present - Need better evidence on adherence benefits of VL monitoring – cost and effectiveness issues of adding another monitoring system need to be better understood.
- Emphasis that in low resource settings both CD4 and VL could present barrier to switching patients who are clearly failing clinically (Figure 21)
- Value of modelling initial trial results in early implementing in South, countries that approach VL monitoring using public health approaches, to inform suitability of different strategies for scale based on switch rates and survival. Differential analyses will be required in countries with very high ART coverage.
- Question not only about what monitoring system is effective, but the implication of having 2 different monitoring systems on efficiency and the potential impact of this upon related patient care/outcomes.

**Session 4a. Monitoring on ART Trial Review; Summary Discussion Points:**

- Transmission piece not fully accounted in some trials presented which would be influenced by VL monitoring and add additional benefits to DALYs averted through prevention (although these benefits are expected to be low).
- VL much easier to implement and interpret for low resource countries, and provides an objective marker for switching. Also a good programmatic marker for success for large #s on treatment. Studies indicate as VL frequency increases, resistance drops. Practical concern of implementers is understanding if this can be afforded by countries.
- Possibility of future trials running both VL and CD4 together if labs are organised well to provide stronger evidence of CD4.
- Emphasis of whether knowing VL makes you better adherer is conditional and requires more evidence. For example, weekends off in adolescents showed effective to maintain VL suppression, social science evidence of self-reported ART holidays but still maintained suppression.
- In the scope of unlimited resources, combination approaches are best as each test has a different value. However, CD4 better immediate clinical predictor of risk of disease in the model and so conclusions are consistent with current structure. Modelling clinical decision making

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**Viral Load Failure & Switch to Second-line ART >10,000 children in Trials/Cohorts starting ART**

<table>
<thead>
<tr>
<th>Trials/Cohorts</th>
<th>ARROW Trial</th>
<th>CHAPAS Trial</th>
<th>CHER Trial</th>
<th>DeDEA S Africa</th>
<th>PHPT Thailand</th>
<th>Penpat1 Trial</th>
<th>EPP/CC Infants</th>
<th>CHIPS UK/Ireland</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>1206</td>
<td>475</td>
<td>415</td>
<td>5500</td>
<td>507</td>
<td>266</td>
<td>437</td>
<td>900</td>
</tr>
<tr>
<td>Monitoring strategy</td>
<td>Clinical or CD4 3m</td>
<td>Clinical &amp; CD4 3m</td>
<td>CD4 3m VL 12m</td>
<td>CD4 6m VL 12m</td>
<td>CD4 6m VL 6m</td>
<td>CD4/VL 3m VL 1000</td>
<td>CD4/VL 3m</td>
<td>CD4/VL 3m</td>
</tr>
<tr>
<td>% VL failure &gt;400c/ml at 2-5 yrs</td>
<td>15%</td>
<td>15%</td>
<td>16%</td>
<td>19%</td>
<td>23%</td>
<td>17%</td>
<td>23%</td>
<td>18% (rebound)</td>
</tr>
<tr>
<td>% switch at 3-6 yrs</td>
<td>5%</td>
<td>5%</td>
<td>2%</td>
<td>6.3%</td>
<td>17.8%</td>
<td>23%</td>
<td>17%</td>
<td>48% (rebound)</td>
</tr>
</tbody>
</table>

(ReBounds in red)


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Figure 21
(such as judgements on adherence) are not possible without better data on factors weighed in the clinical decision.

4b: Investing in scale up of viral load monitoring in the context of other health needs

George Abongomera, JCRC Uganda

Dr. Abongomera presented findings of the Lablite project population baseline survey that conducted cross-sectional mapping to evaluate usage of health services before and after ART provision at lower level facilities. Implication of these findings for investing in scale up of VL monitoring included:

- In Lablite context, VL monitoring preferred approach to confirm treatment failure, where VLM not available, CD4 count/clinical monitoring confirm treatment failure.
- Need to have realistic expectations for data management (how to do EPMS, real-time electronic monitoring when up to half all health sites in Uganda don’t have electricity?) – need to transfer paper-based to central levels for data entry and include data management costs.
- Prior to decentralisation found average 56km round-trip to collect ART – which has implications for making decisions about frequency and decentralisation of VL monitoring.
- Training needs assessment was a critical element of ensuring successful decentralisation of services (i.e., mentorship, data verification). Site-level training was huge part of ensuring confidence in HCWs to provide guideline concordant care (i.e., switching based on VL).
- Can expect variability of cost-effectiveness based on context such as human resources, integrated service delivery of HIV services, information systems, logistics and procurement, sustainable financing and governance.
- Barriers to optimal VL monitoring within implementation in context should be considered to retain cost-effectiveness (Figure 22)
- Revised guidelines of scale up of ART initiation without previous criteria for initiation, need to mobilise counselling and community volunteer linkages –adherence issues are anticipated with scaled ART. Greater emphasis on necessity of community linkage networks for patient follow up and tracking.
- Perception that basic needs at sites are attended to before VL scale-up. Very scaled approach that includes decentralisation, improved technologies including POC for cost-effectiveness.

4c: Viral load testing scale up initiative

Shirley Lecher, CDC USA

This presentation reviewed the status and activities involved in CDC’s viral load scale up initiative, like the HIV modelling consortium, a collaborative effort across agencies and working groups. Dr.
Lecher began the presentation by qualifying that the concept of VL cascade includes a multitude of considerations from demand creation through to patient management (Figure 23).

- The process of supporting country scale up from guideline recommendations (2013) to considerations for implementing VL testing (May 2014) and implementation workshop for identification of tools for VL scale up and development of country-level plans (Sept 2014) and country prioritisation of exercise by PEPFAR in Washington CD (Dec 2014).
- Key lessons and emerging evidence from this process include:
  - Presently countries are at various stages in sub-Saharan Africa in terms of viral load plans.
  - CDC International Laboratory Branch (ILB) engaged in operation research to develop new specimen types to be used in proficiency testing (PT) programs to transition to PEPFAR country programs and is currently supporting quality testing in 143 labs in 41 counties.
  - As countries increasingly participate in PT panel testing, their test results improve (Figure 24).
- Number of tools in development including training, patient education, costing and M&E frameworks.
- Now looking at high burden countries and high burden sites within countries for prioritising scale.

**Improved Performance of Laboratories Enrolled in PT for EID and VL**

![Image](Figure 24)

**4d: Investments in VL monitoring Vs Other Health care needs**

*Dzinkambani Kambalame, MOH Malawi*

Dr. Kambalame provided a presentation on the implementation reality of VL monitoring in one remote Northern region of Malawi. Challenge of obtaining complete data for the region for presentation at the meeting indicative of problems of coordinating transportation and logistics in remote areas. Based on data received:

- Approximately 4247 PLHIV alive and on treatment in the area, with an estimated ART coverage of 62%.
Only one facility in this region has appropriately skilled lab technician for CD4 to service this population and VL only done at central hospital 400km away from the District hospital.

Due to these constraints virologic failure still conducted using clinical monitoring and targeted VL for confirmation – underscoring the continued utility of CD4 in very low resource settings

Perceived benefits of VL monitoring outweigh challenges – improved detection of treatment failure, large existing workforce trained in DBS collection, transportation systems can be leveraged, negotiation power of consumables to bring cost down, and savings on limited HCW workforce (Figure 25) with reduced clinic visits.

There will be a need to merge benefits of VL scale up with ensuring 2nd line switches occur for cost-effectiveness to be maintained.

Session 4: Open Discussion Summary

- Dr. Gibb was asked if she believed if on trials using CD4 vs. no CD4, whether clinicians were better trained, and if this might indicate training for lower cadres of health care workers as a possible factor for improving effectiveness. She responded that a symptom checklist was developed and used by nurses at primary health care levels in the Lablite, and it is possible that this improved rapid identification of clinical failure and improved outcomes. Training is very likely to be important in all cases – both monitoring clinically and with laboratory monitoring.

- Regardless of monitoring strategy, is recommended to audit care given at primary health level and provide any required support for mentoring. Mentorship also provides parallel system for patient monitoring. Such interventions are however not easily monitored and part of improving program efficiencies.

- Noted that following adjudication of cases, CD4 monitoring less likely to have recorded WHO stage 3 and 4 events in the DART trial.

- Need for qualitative work to understand clinical approaches to adherence monitoring

Session 5: Panel Discussion III: Alternative options in scaling up viral load monitoring

Chair: Rosanna Peeling, LSHTM

5a: Alternative options in scaling up VL monitoring

Lugemwa Abbas, Head, JCRC-Mbarara Regional Centre of Excellence

Dr. Abbas described the experience of JCRC’s involvement
in the decentralisation of VL monitoring in Uganda.

- TATs greatly improved by linking VL with national DBS/EID program and introduction of leveraging of biker system for sample transport (Figure 26).
- Demand generation required with guideline changes, patient education required when decentralisation occurred, large numbers patients without record of VL – did not know to present to care for VL.
- Migration and conflict, communities with high mobility will require different strategies for ensuring effective monitoring.
- Increase in treatment hubs has reduced walking times, greatly increased patient volumes.
- Targeted VL stopped in 2014 with scale up plans – huge increases in total number of samples processed in past 6 months and also proportion of samples processed using DBS (Figure 27)
- Lessons for improving cost effectiveness: use EID DBS flow system for VL, need single national data system to minimise double testing and tracking patients between facilities, strategic assessment of structures with infrastructural capacity for expansion and mitigate impacts of breakdowns etc., community engagement, local systems to maximise implementation (i.e., seasonal transport), WHO chronic care model and mentoring for primary health care workers.

5b: Alternative ways to scale-up viral load monitoring (VLM) Plasma vs DBS vs POC

What’s in a number?

**Wendy Stevens, Department of Molecular Medicine and Haematology, University of the Witwatersrand and National Priority Programs, NHLS, Johannesburg, South Africa**

Prof Stevens provided a comprehensive presentation on the South African experience in implementing programs to increase access to VL monitoring.

- Scale of need and capacity required for
HIV monitoring is huge in South Africa - currently conducts approximately ~ 3.9 million CD4 tests annually, 2.8 million viral loads and currently 360 000 EID assays (2015) Figure 28.

- Need to revisit the data we view as evidence in view of rapidly changing guidelines and technological advances.
- POC should be multi-disciplined as if HIV positive patient, will require a number of different other tests, so multivalent platforms are strategic. For example, GeneXpert widely used multivalent platform to increase coverage. Likely further decentralisation with DBS.
- Critical choices around lab extension, replacement, multi-functionality or clinic-based service.
- Clinical laboratory interface is critical for determining effectiveness of systems and monitoring instrument performance: South African experiences with remote connectivity system (software as a service [SaaS]), GPS printers have shown promise.
- Appropriate use of POC technology indicate: appropriate controlled placement, total coverage model of tiered laboratory services, focussing on access to remote, low volume sites. However, Point of Treatment for all sites not affordable.
- Validation demonstrates changing landscape: validation to identify high performing machines with plasma, POC whole bloods look similar to DBS with whole blood (as specificity begins to decrease dramatically) Main concern now is misclassification at lower levels. More tests and modelling could inform cost implications.
- Costing exercises are demonstrating complete decentralisation with product niching as the solution to meeting demand with resources (labour wards, mobile labs).
- Only useful to put more patients on treatment if retained in care – role of VL monitoring in adherence.

5c: The Role of the African Society for Laboratory Medicine in Implementation Issues for Monitoring People on ART in Low Income Settings in Sub-Saharan Africa

Talkmore Maruta, ASLM

- The African Society for Laboratory Medicine (ASLM) introduced as a pan-African professional body launched in 2011 advancing laboratory services and guidelines in Africa
- 2013 ASLM VL meeting with recommendations feeding into the Diagnosis Access Initiative – to increase funding and price reductions to ensure high quality diagnostic
services: guiding pillars including advocacy, forecasting, financing, pricing, delivery, guidance and coordination.

- ASLM has developed a framework for viral load implementation to help guide country-level scale up and coordination activities and optimised use of available resources. Ensuring cost-effectiveness of strategies is a key element in the framework cascade and highlights role of modelling (Figure 29)
- September 2014 meeting resulted in the creation of a task force for viral load implementation – as presented by Dr. Lecher (CDC), at present countries are at various stages of VL implementation
- Key variables influencing scale up of VL by ASLM are consistent with those identified by partners during country presentations and provide a useful summary of factors for consideration (Figure 30)

### Key variables influencing the scale-up of viral load

Despite the VL price per test reduction, several key challenges have been highlighted by countries engaged to date

- Cost per test
- Cost of maintaining the system infrastructure
- Resources mobilization (GAVI, PEPFAR, etc.)
- Policies and algorithms
- SOPs
- Policy dissemination
- Product registration and regulatory requirements
- Patient education
- Service delivery models
- Public/Private partnerships
- Forecasting
- Procurement
- Distribution
- Sample referral network
- Return of results
- Some countries are still discussing when/how to adopt the WHO guidelines
- Some countries have decided to offer VL testing only for patients suspected of failing treatment
- Facilities do not currently offer VL testing due to poor patient and clinician awareness and education
- Countries are not requesting the funding needed to adopt the WHO guidelines
- The funding made available by donors and WHO are not adequate to meet countries' needs
- Sample transportation systems are:  
  - fragmented (regional partners led systems)
  - expensive (up to $5 per DBS envelope)
  - not integrated (e.g. HIV and TB have separate systems)

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**5d: Deployment of POC technologies: where, why and what impact?**

*Kara Palamountain, Kellogg School of Management*

Kara Palamountain’s presentation focused on the experience of mobilising commitment and resources for POC testing in resource-limited settings. Her presentation highlighted the results of infrastructural capacity surveys upon aggregate health outcomes if placed appropriately.

Findings of their analysis demonstrated:

- Many facilities should be immediately ruled out since they do not have the infrastructure to support the diagnostic instrument.
- The same number of identical devices can have different aggregate health outcomes

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Figure 30

5d: Deployment of POC technologies: where, why and what impact?

Kara Palamountain’s presentation focused on the experience of mobilising commitment and resources for POC testing in resource-limited settings. Her presentation highlighted the results of infrastructural capacity surveys upon aggregate health outcomes if placed appropriately.

Findings of their analysis demonstrated:

- Many facilities should be immediately ruled out since they do not have the infrastructure to support the diagnostic instrument.
- The same number of identical devices can have different aggregate health outcomes

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Figure 31

About half of the VL testing volume is expected to take place in facilities that will run fewer than 10 tests per day.
depending on the availability of services at the facilities they are placed in.

- The same number of identical devices can have different aggregate health outcomes depending on where patients present (or would present) for testing.
- High volume facilities may take first priority, but here are other variables to consider, including variations within the network.
- Impact of inappropriate placement of VL monitoring technology without consideration of site level factors clearly demonstrated by the differential sample processing volumes by tier of care (Figure 31).
- Development of placement algorithm (# processed/day) to eliminate majority of sites, then top-down decision analytic model based on a series of estimates used to examine the impact of different allocation schemas of Xpert device roll out on tuberculosis case detection rate in Uganda (Figure 32).
- Potential use VL monitoring as ‘swat team’ for strategic intervention at sites with noted high levels of detectable VL from programmatic data.
- Example of how placement of VL monitoring technologies could influence cost and effectiveness impact and placement model for VL testing roll-out.

5e Alternative options in scaling up viral load monitoring
Lara Vojnov, CHAI

Lara Vojnov’s presentation provided a regional perspective of use of VL testing technologies in SSA.

- Facility level ART patient numbers from Kenya, Uganda, Malawi and Zimbabwe indicate that majority of VL testing labs are in urban centres and large ART sites where patients seek care.
- Challenges exist to increase access to VL monitoring for the 52% who live beyond the 24 hr ‘radius of care’ to get to centralised labs.
- However the 52% access care at a large number of low volume sites, presenting challenges for use of plasma whole blood VL testing and indicating cost-effectiveness of DBS and POC solutions.
- In effort to understand DBS performance for VL – CHAI and collaborators conducted pooled data meta-analysis of primary data with combined >6500 data points: DBS thresholds to 1000 plasma threshold demonstrated variability in specificity at 1000 threshold; Fair bit of upward misclassification at 1000 threshold, but this is variable between technologies – what this means in terms of programmatic costs and patient outcomes is currently unknown. *Modelling of impact of lowered sensitivity and specificity upon cost and outcomes would be valuable.
• Analysis indicates need to include hybrid model as part of VL monitoring strategies – and to model the impact of optimal levels within such models.

Session 5: Open Discussion Summary
• Presenters were questioned about ability to engage with product developers in order to incentivize pricing structures based on demand:
  o Requirements depend on volume, so suggestion can be made to get under ‘$10’ as a peg, but this does not assure it will be met.
  o Good relationships in advising manufacturers. Generally they tend to come in at higher price than market demand and ability to pay warrants price adjustment.
  o Tenders with list of requirements is standard protocol, however for particular technologies (such as POC) there are small number of suppliers so direct negotiations are necessary.
  o Use of cost-effectiveness modelling is a useful way to demonstrate a range of feasible price setting.
• Any suggestions for different way of addressing sensitivity and specificity problem within models? Modelling takes into account how far you are misclassifying but must be careful with misclassification as if population clusters around threshold will have more misclassification and this can change.
  o Misclassification not measured with total pop as denominator which would skew – meta-analysis used numerator of those >1000 using DBS and denominator those <1000 using plasma. So can be used to apply that to your own setting in order to understand the number of misclassifications this represents in your context.
• Experience of presenters using pooled sampling?
  o Depending on how big pool is, would need certain % to be undetectable, which would require re-testing everyone in the pool. Currently this approach doesn’t work on a national scale.
  o So much time is spent unbundling pool in time and money, it ceases to be cost-effective (e.g. of blood bank – attempted 6 donor pool, but each pool positive for something). Therefore simpler to standalone.

Session 6: Panel Discussion IV: Ways to reduce cost and improve quality
Chair: Zengani Chirwa, MOH Malawi

6a: Ways to reduce costs and improve quality in patient monitoring: barriers to improvement
Lisa Nelson, Senior HIV Disease Advisor, The Global Fund

Dr. Nelson provided an overview of the new GFTAM funding and procurement models, intended to improve efficiencies of planning and application processes as well as increasing impact of funding. Key points of her presentation are below:
• New funding model – encouraging countries to articulate clear, ambitious vision, waves vs. years, new funding cycle, easier to re-program existing grant – intended to bring strategy of ‘investing for impact’ to life.
• Principles of new funding model include: bigger impact (high burden, low resource focus), predictable funding, ambitious vision, flexible timing (country schedules, context, and priorities); more streamlined processes.
• Bulk of countries submitting joint HIV/TB concept notes.
• ART cost projections: 2.6 billion for 2015-2017 cost projections (Figure 33) – wake-up call that there aren’t enough resources to cover all needs and highlight increasing importance of tools such as modelling for maximising resources through cost-effectiveness analyses.
• Procurement for Impact (P4i) – streamlining processes to eliminate activities and procedures that don’t add value.
• VL only represents 16% of diagnostic forecast spend for 2014 (Figure 34)
• Over 40% of global fund grants go to commodities (treatment, nets, etc.).
• GF engagement with manufacturers underscore multiple realities – that cost-effectiveness thresholds of producers and consumers (countries) don’t always match: Tender for VL published mid-April.
• Diff between high volume and low volume countries – desire to develop decision tree that assists in VL/EID procurement – noting that many platforms have polyvalency (TB, Hep C, HIV).
• Opportunity to not just drive down cost but also improve decision making.
• Funding model website provides guidance on funding process and steps, grant management platforms, application materials and support: theglobalfund.org/en/fundingmodel/

6b: Future directions for monitoring patients on ART: Ways to reduce costs and improve quality in patient monitoring, Uganda’s experience

Charles Kiyaga, National VL Coordinator, MOH Uganda

As National VL Coordinator for the Ugandan MOH, Charles Kiyaga provided Ugandan perspective on implementation of VL monitoring and indications for improving efficiencies for cost and quality improvements.

• After ART initiation, schedule of monitoring is drawn up for patients which includes:
  o 1st visit after 2 weeks to assess tolerance and adherence
  o Monthly visits for 1st 6 months and there after every 3 months
  o Monthly visits are synchronized with drug pick up and help to reinforce adherence
After 6 months it may not be possible to synchronize drug pick up and follow up visits

- Clinical guidelines for ART monitoring – include patient clinical monitoring, toxicity information, patient self-assessment of treatment effectiveness, adherence assessments by patient counsellor
- Clinical assessment takes 1 hr per patient (Sustain HR Assessment report 2012) resulting in long waiting times.
- Laboratory monitoring includes multiple tests upon pre-determined schedule (Figure 35)
- Switch only after 24 wks ART: VL as preferred approach (DBS VL> 5000 copies/ml in 2 consecutive occasions; or, Plasma VL>1000 copies/ml)
- Barriers to realising cost-effective savings of VL monitoring through reduced clinic visits: limited drug stocks, maintaining adherence, LTFU

6c: Ways to reduce costs and improve quality in patient monitoring: barriers to improvement, Buhera & Gutu district experience, Zimbabwe

Sandra Simons, MSF Zimbabwe

Dr. Simons reported on MSF experience implementing routine VL monitoring in 2 districts of Zimbabwe. The beneficial impact of dedicated VL monitoring upon increased access, improved switching rates and VL suppression in combination with Community Action support Groups (CAGs) and switching rates in comparison with previous mixed monitoring system was reported. A summary of key points from Dr. Simons’ presentation below:

- In 2012, monitoring of patients on ART done through resource intensive mixed monitoring system ART failure including 6 monthly cd4, weekly doctors visit, target VL – however switching rates remained low. Only once routine VL monitoring introduced in 2013 do switches begin to be seen.
- Algorithm for routine VL testing: month 3; annual thereafter. No CD4 except baseline and triggered CD4 if VL > 1000 (Figure 36)
A number of tools were developed in conjunction after high VL test so very clear procedures for switch (EAC Session guide, EAC Register, High Viral Load Form)

Among 14-15% with detectable VL, 57-76% enrolled in enhanced adherence counselling, 67-68% get switched. Continued reluctance of health care workers to place patients on 2nd line among clinicians emphasised need to reinforce switching guidelines.

Experience of VL monitoring: quality of consultations suffers with increased workload and administrative tasks.

In general, switch from mixed to VL monitoring outcomes very positive with 85% suppression rate – total of 15% in need of help, greater emphasis on younger groups for enhanced adherence counselling (more strategic approaches tailored to key populations).

Before VL monitoring 3 month visits – since 2013 drug pick up separated from clinical visits, key symptom checklist for all clients at drug pick if yes referral for clinic.

Community ART Groups (CAGs) composed of 6+ clients, enrolled when VL undetectable, collects 3 month supply, annual ‘group’ visit where all get VL taken – group goal being ‘undetectable VL’ – HCW embraced and groups rapidly established.

Now 250 CAGs in Gutu – 40% of clients on ART are part of this system. Preliminary evidence demonstrates improved VL suppression among CAG members (89%)

Session 6: Open Discussion Summary

For funders, are there any projections of what coverage might be like for VL monitoring in the coming years?
  o For tender process GF estimated funding procurement 500K-2mil VL tests over next 2 years. Each country has own plan for prioritised areas for applying.

Cost of 2nd line drugs can be negotiated at country-level, and cost savings can be applied to other priority areas.

Questions related to how the model simulates switches between CD4 vs. VL monitoring strategies:
  o Within current model existing guidelines under CD4 should lead to more switched then under VL monitoring. So increasing access to VL does not necessarily translate to more switches than CD4. Also, as noted by numerous presenters over past 2 days, costs and impact also depends if switches happens.

For VL monitoring in Zimbabwe, question was asked if people are chronically poorly adherent – do you switch or is there a wait and see approach to see if they will become adherent and only switch in the end? Is there any toxicity monitoring?
  o There is a wait and see approach used for a period of time, but if not improvement then switch is done. All toxicity and related levels are based on annual monitoring.

Great interest in the implementation methodology and encouraging results of the CAGs. Questions related to:
  o Effectiveness for reduced clinic visits: Keep 85% of patients out of clinic
  o How clinical monitoring is maintained: symptom screening checklist – if any symptoms that individual is group member who presents to clinic for check-up and med pick up
  o Cost of CAGs to treatment costs: need for comprehensive cost analysis to possibly model how community ARV management influences DALYs averted and cost-effectiveness of different monitoring strategies.
• Value of 3 month VL as potential too early to show suppression, depends on baseline and also between key population (children take longer to suppress): 3 month VL used to identify early non-adherers to enhance counselling process early, switch only after 1 year.

Session 7: Reflections on Workshop
Chair Maurine Murtagh, UNITAID

7a: Allocating resources to patient monitoring to generate population health improvement: Collective Interpretation of Model Results and Data & Next Steps
Tim Hallett, ICL

In this presentation, Prof. Tim Hallett, Director of the HIV Modelling Consortium, provided a summary to the workshop as an effort to close the gap between modelling and real world implementation experiences. Following a summary of guiding principles (Figure 37), Prof. Hallett presented 3 important qualifications that are difficult to set parameters for in a general adult model as their patterning will be different in each context. Although not modelled, these ‘things that go without saying’ should influence implementation of monitoring strategies in practice.

1. Under certain conditions, patients presenting with severe clinical symptoms should be switched even if VLM temporarily unavailable - with clinical caveat that those with very low CD4/high VL may initially deteriorate after initiation.
2. Schedule for patient monitoring can be different to the schedule for pick-up of medicines (pharmacy only visits).
3. There should be no barriers for patients that have disengaged from care to re-engaging.

9 key conclusions arising from session discussions were presented with the purpose of critical reflection of organisers and attendees of how stated experiences of implementers should inform model structure or parameters moving forward.

Conclusion 1: Training of practitioners is key to the success of any monitoring strategy.
• This influences quality of sampling methods, results interpretation and likelihood of switching – knock on costs and clinical effectiveness of strategies, and inputs of modelling impact of these.

Conclusion 2: From a clinical perspective, information on both VL and CD4 would be ideal; but the large cost of providing both makes it necessary in most settings to rely largely on one diagnostic.
• Role of modelling is to compare alternative monitoring strategies to identify most cost-effective option in context of competing needs and trade-offs.
Conclusion 3: There is clinical benefit and a population benefit in viral load monitoring over clinical-only or CD4 & clinical monitoring.

- While some trial results presented indicate value of CD4 there is general consensus among modellers and researchers that VL monitoring results in some aggregate clinical as well as transmission risk benefits over other methods.
- Benefits of VL monitoring include more rapid detection of the need to switch, somewhat reduced morbidity/mortality, and possible improved adherence) and reduce community viral load and transmission (including of drug resistant HIV) – many of these factors which are amenable to modelling and captured in the reported cost-effectiveness of VL monitoring.

Conclusion 4: If viral load monitoring for patients can be achieved at cost less than ~$50 per measurement, with patients monitored every 12 months, then that form of monitoring is probably the most cost-effective*. Otherwise, other forms of monitoring will be more cost-effective.

{Algorithm based on costs of different approaches.}

- Modelling provides useful targets for countries in working on target costing for components of their VL monitoring programs (and the associated reduction in visits in those with viral load <1000), together with country-level judgements about acceptable thresholds based on resource availability.

Conclusion 5: Application of simplified switch rule in use of CD4, “switch if CD4<200 | symptoms”.

- Modellers expressed openness to consider different modeling strategies, though no specific strategy with available data was proposed as being credible for inclusion in a future guideline recommendation.

Conclusion 6: Overall, it would be cost-effective to monitor patients with VL every 12 months or 24 months. There is a marginal benefit in monitoring every 12 months but a greater cost. More frequent monitoring would not be cost-effective, and is also expected to impose additional costs upon patients and losses in productivity.

- Benefits of efficient tiered care can be expected to increase productivity (i.e. through reducing indirect costs of patient time) though this is a benefit that is difficult to parameterize with existing data and has accordingly not been taken into account in the current analysis.
- As evidence increases on cohort outcomes for VL monitoring, perhaps further refine timing of VL monitoring parameters. For example, ‘Specified consecutive series of undetectable results’ might be language that clarifies monitoring changes if different thresholds of results are achieved. i.e., if they haven’t detectable viral load consecutively clinician would advise not to return if they don’t want to. At present, not possible to model what outcomes of making such recommendations would be.
- Moving forward, greater need to understand cost and clinical implications of improvements in adherence from different monitoring timings. Not possible to do within current context, but as strategies become widely available could be modeling work to enable optimization of current programs.

Conclusion 6a): There may be arguments for increasing the frequency of monitoring of particular patients (e.g. pregnant women; adolescents).
The model presented is an adult model, with no paediatric transmission, although influence of different adherence scenarios linked to specific populations (such as adolescents) can be modelled. For example, the age effect on adherence is modelled and will likely indicate greater benefit to target VL monitoring to under 35s, however recommending stratified services by age in public health guidelines is questionable for practical implementation.

Given the above, there was consensus that these groups will stand to have varying benefits and costs for VL monitoring and there is encouragement to develop more detailed evidence on what these are to inform modellers.

Many of the countervailing factors on age that would influence adherence and clinical benefits of differential monitoring timing (i.e., drug or alcohol dependency) will necessarily require clinical decision making that could not be captured within standardized monitoring guidelines, nor modelled in a general population model.

Consensus that much different implication of VL monitoring on groups such as pregnant women given transmission risks is valid, however is more a medical approach than public health approach (i.e., # of women who are virally suppressed at start vs. at the end of their pregnancy).

Best case scenario for development of effective monitoring guidelines would be to have one general algorithm, with caveats for specific populations as opposed to separate guidelines that would act to ‘de-consolidate’ guidelines. Accordingly, caveat for pregnancy within consolidated guidelines may be provided to ensure initiation on ART as a priority (B/B+) with emphasis that pregnant women without viral load should have one as a matter of urgency to ensure virally supressed in pregnancy as early as possible.

While 6a) remains a valid conclusion for implementation, such questions would be best addressed by population-specific models informed by evidence of VL timing on specific groups as opposed to attempting to accommodate within the parameters of a general adult model used for the current analysis.

Conclusion 7: In practice, the cost of VL measurement will vary by location; and achieving the necessary cost threshold will imply different strategies.

- Such strategies will be influenced by a multitude of factors (infrastructure, skilled workforce, transport networks, etc.). To accurately refine costs by location these different situations would ideally be informed by costing and operations studies of different situations.
- From a cost-effectiveness modelling perspective, current analysis indicates may be able to define and test general rules such as where you can implement VL monitoring for less than $x and with $y savings in clinic visit costs, do it; where you can’t (b) don’t, and do something else (CD4/clinical).
- Such an approach would present a potential issue of lack of equity.
- Based on information presented by implementers and existing evidence, it may be anticipated such locational groupings may include:

7a) Central, high density PLHIV areas: centralised laboratory testing using DBS and a threshold for indication of 1000 is likely to be cost-effective. (But this will depend on country geography etc.).
• The proportion dedicated to plasma/DBS alternatives will depend on country-context. Goal being to introduce VL at least using DBS and improve on it with POC and plasma in any places where this is possible.
• Implementation of such recommendations will depend on country geography so difficult to model accurately within a general model for all settings. As with cost-effectiveness thresholds, such recommendations would need to be interpreted within context.
• Implementation and costing data in specific context will inform country planning.
• Influence of sample stability on different sampling methods acknowledged, however performance characteristics in model based on assumption is package instructions have been followed, though the influence of variability on these could be examined through sensitivity analyses.

7b) Remote, low density of PLHIV areas: reliable centralised lab based on DBS may not be possible at low cost. A reliance of CD4 or clinical monitoring would be a cost-effective alternative strategy.
POC VL devices at Level II centres, may in the future provide a cost-effective alternative, if anticipated cost and performance characteristics are confirmed**
• The course of action for situation 7b) is likely to change over the next few years. POC VL devices at Level II centres may in the future provide a cost-effective alternative, if anticipated cost and performance characteristics are confirmed.
• Qualification of ‘may’ as changing prices in CD4 and POC may influence what will come out as cost-effective alternative.

7c) What factors most strongly determine these different situations would ideally be informed by costing, operations studies, costs falling on patients on different situations etc.

During final reflections on information discussed over the meeting and value of implementer perspectives on cost-effectiveness results of ART monitoring strategies (and vice versa), the following final key points were outlined in discussions:
1. To accrue benefits of implementing cost-effective monitoring strategies will require action on result, and clear guidance when and where to in switch, ensure switch is done and that 2nd line ARVs are available.
• As is not possible to model clinician judgement until data are available on the factors being considered and the weights attached, currently within the model 2 VL over 1000 then 50% chance of being switched. Acknowledged this rate will likely be different in context, model uses best available evidence for parameter setting.
• Bottleneck analysis in country context to identify and intervene on factors that may increase cost/reduce effectiveness of VL monitoring. For example, indications to only do monitoring if the patient will be able to access 2nd line. This is same rationale for not modelling 2nd line monitoring at present, with lack of 3rd line options, however implications on adherence and health outcomes may be factored in future once more evidence is available on impact of monitoring 2nd line patients.
2. Participants agreed that countries should ‘proceed with data’ when determining how to invest in monitoring strategies on the basis of modelling results because key uncertainties remain (e.g. actual costs of VL testing, costs savings associated with reducing clinic visits, successes with implementation) and are only likely to become resolved through time.
   - Research question modelled in current analysis does not produce a ‘slam dunk cost-effectiveness intervention for VL monitoring. This was supported by country-level implementation experiences and emphasis on impact of contextual factors upon outcomes that will influence cost-effectiveness.
   - Strength of existing data does not warrant holding off for new evidence to proceed with guideline recommendations. Rather than ‘proceed with caution’, ‘proceed with data’ so that evidence development is done at pace with increasing access to VL monitoring in SSA.
   - Slow scale of VL roll out likely best approach moving forward so that we can examine the impact of which implementation factors are most significant influencers of cost-effectiveness. Certainty of change over time of strategies also speaks to proceeding with caution to allow adaptation of strategies while avoiding undue opportunity costs of mass scale-up.

The workshop concluded with Prof. Hallett highlighting the value of the iterative process of reviewing modelling results over the course of the meeting. Reflecting on modelling results together with guideline directions, country-level policy and implementation experiences is novel and important for providing informed recommendations. HIV Modelling Consortium organisers thanked WHO, MOH representatives, funding and implementing partner perspectives for their active participation and contributions.
Appendix I: Workshop Agenda

Implementation Issues for Monitoring People on ART in Low-Income Settings in Sub-Saharan Africa

Bronte Hotel, Harare, Zimbabwe
11-12 March 2015
Agenda

Meeting objectives
- To discuss and document the issues MoH and other programmes face in implementing existing and potential new ART monitoring approaches.
- To obtain feedback on modelling/cost-effectiveness analyses of patient monitoring alternatives in order for such analyses to appropriately inform policy.

Day 1 – Wednesday 11 March 2015

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<tr>
<th>Time</th>
<th>Session</th>
<th>Speaker</th>
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<tr>
<td>09:00</td>
<td>Welcome coffee</td>
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<tr>
<td>09:30</td>
<td>Welcome and introduction</td>
<td>Tsitsi Apollo, MoH Zimbabwe</td>
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<td>• Welcome and introduction of attendees</td>
<td>Tim Hallett, ICL</td>
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<td>• Overview of meeting schedule and aims</td>
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<tr>
<td>10:00</td>
<td>Session 1: Modelling to support development of the WHO ARV guidelines on patient monitoring</td>
<td>Tim Hallett, ICL</td>
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<td></td>
<td>• The place of patient monitoring in the HIV treatment and care cascade</td>
<td>Jessica Markby, WHO</td>
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<td>• Questions to be considered for patient monitoring for 2015 Guidelines revision</td>
<td>Paul Revill, University of York</td>
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<td>11:15</td>
<td>Break</td>
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<td>11:45</td>
<td>Session 1 (continued): Modelling to support development of the WHO ARV guidelines on patient monitoring</td>
<td>Andrew Phillips, UCL</td>
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<td>• Preliminary findings from recent modelling analyses: the importance of understanding context and implementation</td>
<td>All (facilitated by Tim Hallett, ICL)</td>
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<td>• Q&amp;A session with the morning presenters / further investigation of the role of modelling studies informing guidelines and reflecting implementation challenges</td>
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<td>12:10</td>
<td>Lunch</td>
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<td>13:00</td>
<td>Theme for the afternoon: Understanding where we currently are in the provision of HIV treatment and patient monitoring</td>
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| 14:00 | **Session 2: Financing national HIV treatment responses and competing calls on limited resources**  
- Healthcare and HIV treatment financing in Malawi  
- Healthcare and HIV treatment financing in Zimbabwe  
- Open Discussion                                           | Paul Revil on behalf of Dominic Nkhoma, MOH Malawi  
Travor Mabugu, University of Zimbabwe  
All (facilitated by Lisa Nelson, GFATM) |
| 15:00 | Break                                                                   |                                                                         |
| 15:30 | **Session 3 – Panel Discussion I: National HIV treatment programmes and policies (focus on patient monitoring policy); reasons for policy choices**  
- Panellists (10 minutes presentation each)  
- Followed by open discussion  
**Panellists:**  
Cordelia Katureebe, MOH Uganda  
Fred Sawe, Kenya Medical Research Institute  
Tsitsi Apollo, MOH Zimbabwe | Chair: Meg Doherty, WHO |
| 17:00 | Day 1 close                                                             |                                                                         |
| 19:00 | Reception and dinner                                                    |                                                                         |

**Day 2 – Thursday 12 March 2015**

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<th>Time</th>
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<td>08:45</td>
<td>Welcome coffee</td>
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| 09:15 | **Session 4 - Panel Discussion II: Investing in scale up of viral load measurement in the context of other healthcare needs**  
- Panellists (10 minutes presentation each)  
- Followed by open discussion  
**Panellists:**  
George Abongomera, JCRC Uganda  
Shirley Lecher, CDC USA  
Diana Gibb, MRC CTU  
Dzikambani Kambalame, MOH Malawi | Chair: Joseph Murungu, MoH Zimbabwe |
| 11:00 | Coffee break                                                            |                                                                         |
| 11:30 | **Session 5: Panel Discussion III: Alternative options in scaling up viral load monitoring**  
- Panellists (10 minutes presentation each)  
- Followed by open discussion | Chair: Rosanna Peeling, LSHTM |
**Panellists:**
Abbas Lugemwa, MOH Uganda/JCRC
Lara Vojnov, CHAI
Wendy Stevens, National Reference Lab RSA
Talkmore Maruta, ASLM
Kara Palamountain, Kellogg School of Management

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<th>13:00</th>
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**Theme for the afternoon: Future directions for monitoring patients on ART (con’d)**

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<tr>
<th>14:00</th>
<th><strong>Session 6 – Panel Discussion IV: Ways to reduce costs and improve quality in patient monitoring; barriers to improvement</strong></th>
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<td>Panellists (10 minutes presentation each)</td>
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<td>Followed by open discussion</td>
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<td><strong>Chair:</strong> Zengani Chirwa, MOH Malawi</td>
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<td><strong>Panellists:</strong> Charles Kiyaga, MOH Uganda</td>
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<td>Sandra Simons, MSF Zimbabwe</td>
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<td>Lisa Nelson, GFATM</td>
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| 15:30 | Coffee break |

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<th>16:00</th>
<th><strong>Session 7: Reflections on workshop</strong></th>
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<td>Round the table reflections on discussions: Where now for ART patient monitoring policies?; Ensuring modelling/CEA is aligned with country needs and appropriately acts to inform policy; A future role for this group.</td>
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<td><strong>All (co-facilitated by Maurine Murtagh, UNITAID)</strong></td>
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| 17:30 | **Day 2 close** |

* **Speaker notes on financing of ART and patient monitoring, and competing calls on resources**
  ART financing issues – expenditure on HIV treatment, break downs between ARVs, diagnostics, healthcare infrastructure; future finance needs and anticipated finance availability (e.g. financial gap analyses). Financing issues in funding patient monitoring (e.g. who funds diagnostics, are there bottlenecks – such as transport of samples and results, levels of investments in community cadres and counsellors). What are the major gaps in funding HIV treatment and care? What about healthcare more generally? (i.e. make trade-offs between patient monitoring and other healthcare needs explicit)

** **Speaker notes for panel discussants**

1. **National policy environments**
   The ‘big picture’ of HIV treatment policies and provision (features of national ART Guidelines, numbers in need of and on ART, gaps and challenges (e.g. paediatrics), HTC situation, others (e.g. PMTCT, EID, key populations). National policy on use of CD4 (for staging and routine monitoring on ART; types of assays used; availability in different types
Monitoring People on ART in Low-Income Settings in Sub-Saharan Africa

2. Investments in VL monitoring versus other healthcare needs
Personal views on the desired speed of investment in VL monitoring scale-up versus other aspects of HIV treatment/healthcare delivery for countries in which VLM is not currently fully established. At what level of ART coverage should VL be scaled-up? Benefits of accelerated versus delayed scale-up. Frequency of VL monitoring at different stages of maturity in ART programme. Advantages/disadvantages of VL monitoring compared to CD4 or clinical monitoring (is 12-monthly VL better/worse than 6-monthly CD4 or clinical?). Complementarities and complexities in VL delivery in context of wider healthcare provision (e.g. coupling with EID; other parts of health system required but perhaps currently weak – e.g. transport). Is VLM a facilitator or barrier to switching to 2nd line? Fixing 2nd line ART availability first or proving VLM to support switching for patients virologically failing.

3. Alternative ways to scale-up VLM: Plasma vs DBS vs (waiting for) POC
Experiences in the use of VLM using plasma and dried blood spots (DBS). Transport requirements for different types of assays; by types of districts (urban, rural, semi-rural) and facilities (health centre IIIs; health centre IVs/district hospitals; central hospitals etc.). Transport networks currently in place. Ease of use and challenges – in sample collection, storage, transport and analysis; return of results to facilities (how frequently are samples/results lost?). Coupling with other transport networks (e.g. for EID). Current use within countries and personal views on desired future roles. Central laboratory requirements and capacity (e.g. available lab technicians). Investing in enabling VLM now, even in hard to reach facilities, or awaiting availability of future point-of-care alternatives. Sustainability of alternative approaches.

4. Ways to reduce costs and improve quality (feasibility of reducing clinic visits)
What is done at clinic visits - give as fine a breakdown as possible (perhaps split by patients recently started on ART or longer term on ART) including how clinical monitoring is implemented, who does it, how long it takes, waiting times, frequency of visits. Whether simplification of clinic visits is possible, particularly based upon whether patients are stable or at risk. The role of alternative monitoring approaches (clinical, CD4, VLM) in enabling clinic visit simplification. Does VLM have an advantage for reducing clinic visits? Translating lower frequency in clinic visit/time to HR savings and quality improvement. Barriers to reducing frequency of clinic visits (e.g. fragile drug supply leading to difficulties with providing patients drugs for a number of months; others).
Appendix II: List of workshop participants

Participant List

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## Implementation Issues for Monitoring People on ART in Low-Income Settings in Sub-Saharan Africa Meeting

**Theme:** WHO HIV Treatment Guidelines and the role of modelling/cost-effectiveness analysis in informing policy

### Session 1: Modelling to support development of the WHO ARV guidelines on patient monitoring

**Chair:** Timothy Hallett, ICL

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<tr>
<td>1a: WHO Guidelines: CD4 and Viral Load Testing</td>
<td>Jessica Markby, WHO</td>
<td>Dr. Markby presented the foundation of evidence for current (2013) WHO guidelines on CD4 and viral load testing, highlighting diagnostic priorities for monitoring patients within the cascade of care as critical for achieving 90-90-90 goals. Consultative processes on CD4 and viral load resulted in the development of key PICO (Population; Intervention, Comparator; Outcomes) questions explored with the intention of guiding 2015 guideline revisions.</td>
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<td>1b: Allocating resources to patient monitoring to generate population health improvement: Evidence from modelling and economic analysis</td>
<td>Andrew Phillips, UCL</td>
<td>Dr. Phillips presented results of new cost-effectiveness (CE) modelling analyses with the intention of providing WHO advice to inform guideline revision. Results of three key questions modelled in the current analysis were summarised for the following key findings: 1. <strong>Without access to VL:</strong> CD4 &lt; 200 strategy is likely to be more cost effective than the current WHO strategy. 2. <strong>Scaling to VL:</strong> a) No POC: VLM using DBS currently most cost effective approach if no POC.; b) With POC: most CE with assumptions that VLM results in less ART cost/clinic costs. 3. <strong>With VL monitoring:</strong> a) Most CE Schedule: Annual more CE than 6 months or 2 yrs; b) Threshold for failure: If it were possible to deliver a viral load result accurately at a 200 cpy/mL threshold, this would represent a more effective strategy but there is not currently evidence it would be more cost effective than the current 1000 threshold.</td>
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<td>1c: The framework of analysis: assessing cost-effectiveness and summary of previous results</td>
<td>Paul Revill, University of York</td>
<td>Dr. Revill led a session summarizing the framework of cost effectiveness analysis. Understanding assumptions that have gone into the analysis and important for determining how models can be adapted as contexts change, and enable better interpretation of results presented. The ultimate goal of modelling is to understand if the health gain from new intervention (such as change in VL monitoring guidelines) will be greater than the health foregone or displaced.</td>
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<td>1d: New considerations in modelling ART monitoring strategies</td>
<td>Andrew Phillips, University College London</td>
<td>Changes in monitoring landscape since 2013 analysis that have been factored into current preliminary results being presented were described by Dr. Phillips to contextualise current strategy attributes. Emphasis was placed on acknowledging on the continuously changing landscape of modelling input parameters based upon emerging evidence between guideline revisions.</td>
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<td>1e: New modelling findings</td>
<td>Andrew Phillips, UCL</td>
<td>Dr. Phillips provided a comprehensive presentation of the various monitoring strategies modelled to derive key modelling conclusions reviewed in Session 1b. Absolute values modelled to adult population in Zimbabwe. Sensitivity analyses to determine scenarios with and without tiered care under which...</td>
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VL monitoring measured as cost-effective threshold of $500/DALY averted.

1f: Morning Session – Key questions and discussion
Facilitated by Paul Revill, ICL

1. Is $500 an appropriate cost-effectiveness threshold to inform country policy (does it adequately reflect other calls on resources)?
2. Are low viral load testing and 2nd line ART costs really attainable by countries?
3. What should we assume about rates of switching given they are so low now? Can we really believe these will increase in future and can investments be made to support appropriate switching?
4. Will reduced costs associated with less frequent clinic visits really be realized and will released resources be used to achieve health gains cost-effectively in other ways?
5. Is it better to invest in DBS ‘now’ (despite current uncertainties over optimal VL measurement approach) or wait until the anticipated future availability of POC VL testing?

Summary of Session 1
Key Messages from Group Discussion
Tim Hallett, ICL

1. Need approach to hybridize implementation of VL monitoring and phasing in a way that characterizes facility-based variation.
2. Potential need to model scenarios for specific populations (pregnant women, adolescents, peds).
3. Determination of value of decentralising 2nd line, training/mentoring investment of health care workers so switching occurs, so that trade-offs complement perspective.
4. Potential to interrogate impact of timing rather than frequency during first 6 months of care (i.e., @ 3 months after initiation).
5. Explore need and ways to approach modelling of continued monitoring of patients on 2nd line ART.

Update on POC VL Landscape
Maurine Murtagh, UNITAID
Prior to transition into Session 2, Maurine Murtagh from UNITAID provided a brief summary update on the VL pipeline and what is expected over the coming years. Considerations of use of different POC technologies at various system levels, current performance and expected advancements in the next one to two years were summarised.

THEME: Understanding where we currently are in the provision of HIV treatment and patient monitoring

Session 2: Financing national HIV treatment responses and competing calls on limited resources
Chair: Lisa Nelson, GFATM

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<td>2a: HIV/AIDS Financial Landscape in Zimbabwe</td>
<td>Travor Mabugu, University of Zimbabwe</td>
<td>Mr. Mabugu, began his presentation with the recognition that national HIV budgets can only do “so much” and the trade-offs between various alternatives must be explored. Highlights on the current Zimbabwean funding context with specific emphasis on VL monitoring and challenges to funding HIV services in Zimbabwe were provided.</td>
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<td>2b: Overview of Malawi’s Health Financing Situation: HIV/AIDS Financing in a Limited Resource Setting</td>
<td>Paul Revill, University of York presenting on behalf of: Dominic Nkoma, MOH Malawi</td>
<td>Increasing demand in the midst of limited funding and increasing proportion of HIV services funded by donors in Malawi were highlighted. Funding shortfalls compared to projected need for HIV services with emphasis on VL monitoring.</td>
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For many countries in SAA lack of predictability of funds in the midst of massive increases in scale and coverage targets of HIV programs has resulted in growing gap between aspirational targets and met costs. Role of modelling for identifying cost-effective program directions as a tool for informing decision making.

**Session 3 – Panel Discussion I: National HIV treatment programmes and policies (focus on patient monitoring policy); reasons for policy choices**

*Chair: Meg Doherty, WHO*

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<td>3a: Zimbabwe National HIV Treatment Programme and Policies</td>
<td>Tsitsi Apollo, MOHCC Zimbabwe</td>
<td>Dr. Apollo’s presentation contextualised HIV and ART in Zimbabwe highlighting a reduction in new pediatric and adult infections, high adult ART coverage at 69% as program successes. Zimbabwe’s 4 phased plans for increasing access to VL monitoring were described.</td>
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<td>3b: National HIV treatment Programmes and policies- Policy choices</td>
<td>Cordelia Katureebe, MOH, Uganda</td>
<td>Dr. Katureebe provided the meeting with a summary of the process of guideline revision in Uganda towards VL monitoring with cost implications of implementing new guidelines. With huge expected increases in numbers on ART, the need to identify barriers to funding and implementing VL monitoring strategies was highlighted.</td>
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<td>3c: Malawi National Treatment program</td>
<td>Zengani Chirwa, MOH Malawi</td>
<td>Dr. Chirwa from the HIV and AIDS Department at Malawian Ministry of Health provided a summary presentation of the HIV landscape in Malawi and some preliminary experience in scaling VL monitoring. Lessons included changing primary sample strategy using plasma to DBS following recognition of obstacles of scaling access. A ‘pop up’ electronic patient monitoring system which is triggered when client reaches milestone for VL monitoring was of particular interest to participants.</td>
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<td>3d: National HIV Treatment Programs and Policies: Kenya</td>
<td>Fred Sawe, Kenya Medical Research Institute</td>
<td>Dr. Sawe provided a review of the Kenyan context and HIV monitoring strategies currently being employed in Kenya, with plans for scale up. Current algorithm being used to guide implementation of VL monitoring strategies was described, with current data indicating 77% of VL in last 6 months being done for routine monitoring.</td>
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**Session 3: Open Discussion Summary**

*Chair: Meg Doherty, WHO*

Funding gaps are a cyclical challenge for Ministries and highlight value of accurate costing exercises, as often working with estimates so may over/under-estimate requirements to cover gaps. Many countries are showing significant progress in rapid expansion of VL monitoring, though ensuring cost-effective approaches to scale will require accurate implementation and costing data.

**THEME: Future directions for monitoring patients on ART**

**Session 4 - Panel Discussion II: Investing in scale up of viral load measurement in the context of other healthcare needs**

*Chair: Joseph Murungu, MOHCC Zimbabwe*

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<td>4a: Monitoring on ART</td>
<td>Diana Gibb, MRC CTU</td>
<td>Dr. Gibb provided a perspective on strategies for monitoring individuals on ART based upon evidence from Paediatric, adult and adolescent trials, the UK National Cohort (CHIPS) and over 25 years of experience in the clinical management of people living with HIV in UK. Her presentation provided evidence regarding value of using CD4 to monitor patients on ART in low-resource settings and importance of timing for monitoring patients and the importance of clinical decision making for identifying and switching patients who are failing.</td>
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<td>Session 4: Open Discussion Summary</td>
<td>Chair: Joseph Murungu</td>
<td>Regardless of monitoring strategy recommended there is a need to audit care given at primary health level and provide any required support for mentoring. There is a need for qualitative work to understand clinical approaches to adherence monitoring.</td>
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### Session 5: Panel Discussion III: Alternative options in scaling up viral load monitoring

**Chair: Rosanna Peeling, LSHTM**

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<td>5a: Alternative options in scaling up VL monitoring</td>
<td>Lugemwa Abbas, Head, JCRC</td>
<td>Dr. Abbas described the experience of JCRC’s involvement in the decentralisation of VL monitoring in Uganda. Lessons for improving cost effectiveness included: use EID DBS flow system for VL, need single national data system to minimise double testing and tracking patients between facilities, strategic assessment of structures with infrastructural capacity for expansion and mitigate impacts of breakdowns etc, community engagement, local systems to maximise implementation (i.e., seasonal transport), WHO chronic care model and mentoring for primary health care workers.</td>
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<td>5b: Alternative ways to scale-up viral load monitoring (VLM) Plasma vs DBS vs POC What’s in a number?</td>
<td>Wendy Stevens, NHLS</td>
<td>Prof Stevens provided a comprehensive presentation on the South African experience in implementing programs to increase access to VL monitoring. Performance of different VL monitoring technologies was described and critical choices around lab extension, replacement, multi-functionality or clinic-based service for ensuring efficiency of VL monitoring strategies highlighted. Appropriate use of POC technology indicate: appropriate controlled placement, total coverage model of tiered laboratory services, focussing on access to remote, low volume sites. However, Point of Treatment for all sites not affordable.</td>
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<td>5c: The Role of the African Society for Laboratory Medicine in Implementation Issues</td>
<td>Talkmore Maruta, ASLM</td>
<td>Contributions of ASLM in advancing laboratory services and guidelines in Africa. A framework for viral load implementation to help guide country-level scale up and coordination activities and optimised use of available resources developed by ASLM</td>
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was presented. Key variables influencing scale up of VL and key common challenges including slow adaptation of VL policy, poor demand generation, insufficient funding and poor sample referral networks were described as key bottlenecks to scaling VL monitoring in African countries.

Kara Palamountain’s presentation focused on the experience of mobilising commitment and resources for POC testing in resource-limited settings. Her presentation highlighted the results of infrastructural capacity surveys upon aggregate health outcomes if placed appropriately. Ugandan experience involved successful development of placement algorithm (# processed/day) to eliminate majority of sites, then top-down decision analytic model based on a series of estimates used to examine the impact of different allocation schemas for rollout of GeneXpert for improved TB diagnosis. Experience provides a good example of how placement of VL monitoring technologies could influence cost and effectiveness impact and placement model for VL testing roll-out.

Lara Vojnov’s presentation provided a regional perspective of use of VL testing technologies in SSA. The majority of VL testing in SSA is performed in few countries (South Africa and Botswana) with large unmet need in other countries. Majority of VL testing labs are in urban centers and large ART sites where patients seek care. Challenge to increasing access for 52% of patients outside of the 24 hour ‘radius of care’ to access laboratory services indicate cost-effectiveness of DBS and POC solutions. Meta-analysis of DBS performance for VL indicates need to include hybrid model as part of VL monitoring strategies – and to model the impact of optimal levels within such models.

Experiences in engagement with product developers in order to incentivize pricing structures based on demand highlight competing needs for cost-effectiveness between purchasers and producers. Use of cost-effectiveness modelling is a useful way to demonstrate a range of feasible price setting.

Dr. Nelson provided an overview of the new GFTAM funding and procurement models, intended to improve efficiencies of planning and application processes as well as increasing impact of funding. ART cost projections and gap between available funds and projected need provide wake-up call that there aren’t enough resources to cover all needs. Such gaps highlight increasing importance of tools such as modelling for maximising resources through cost-effectiveness analyses. The Global Fund’s new funding model and Procurement for Impact (P4i) model were described as strategic efforts to streamline application and procurement processes and eliminate activities and procedures that don’t add value.

As National VL Coordinator for the Ugandan MOH, Charles Kiyaga provided Ugandan perspective on implementation of VL monitoring and indications for improving efficiencies for cost and quality improvements. Barriers to realising cost-effective savings of VL monitoring through reduced clinic visits include...
Uganda’s experience limited drug stocks, maintaining adherence, LTFU.

6c: Ways to reduce costs and improve quality in patient monitoring: barriers to improvement, Buhera & Gutu district experience, Zimbabwe

Sandra Simons, MSF Zimbabwe

Dr. Simons reported on MSF experience implementing routine VL monitoring in 2 districts of Zimbabwe. The beneficial impact of dedicated VL monitoring upon increased access, improved switching rates and VL suppression in combination with Community Action support Groups (CAGs) and switching rates in comparison with previous mixed monitoring system was reported.

Session 6: Open Discussion Summary

Chair: Zengani Chirwa, MOH Malawi

GF estimated funding procurement 500K-2mil VL tests over next 2 years as countries increase VL monitoring, with cost of 2nd line drugs negotiated at country-level, and cost savings can be applied to other priority areas in funding applications. Within current model existing guidelines under CD4 should lead to more switched then under VL monitoring. So increasing access to VL does not necessarily translate to more switches than CD4. Also, as noted by numerous presenters over past 2 days, costs and impact also depends if switches happens.

Session 7: Reflections on workshop

Chair Maurine Murtagh, UNITAID

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<td>7a: Allocating resources to patient monitoring to generate population health improvement: Collective Interpretation of Model Results and Data &amp; Next Steps</td>
<td>Tim Hallett, ICL</td>
<td>In this presentation, Prof. Tim Hallett, Director of the HIV Modelling Consortium, provided a summary workshop as an effort to close the gap between modelling and real world implementation experiences. Key conclusions resulting for the meeting session presentations and discussion: 1. Training of practitioners is critical to the success of any monitoring strategy. 2. From a clinical perspective, information on both VL and CD4 would be ideal; but the large cost of providing both makes it necessary in most settings to rely largely on one diagnostic. 3. There is clinical benefit and a population benefit in viral load monitoring over clinical-only or CD4 &amp; clinical monitoring. 4. If viral load monitoring for patients can be achieved at cost less than ~$50 per measurement, with patients monitored every 12 months, then that form of monitoring is probably the most cost-effective*. Otherwise, other forms of monitoring will be more cost-effective. (Algorithm based on costs of different approaches.) 5. Application of simplified switch rule in use of CD4, “switch if CD4&lt;200</td>
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monitoring of particular patients (e.g. pregnant women; adolescents).

7. In practice, the cost of VL measurement will vary by location; and achieving the necessary cost threshold will imply different strategies.

7a) Central, high density PLHIV areas: centralised laboratory testing using mix of hubs for plasma reaching predetermined geographical radius and DBS for remote and a threshold for indication of 1000 is likely to be cost-effective.

7b) Remote, low density of PLHIV areas: reliable centralised lab based on DBS may not be possible at low cost. In such cases POC servicing a remote radius, or CD4/clinical monitoring where POC unsuitable may be cost-effective alternative strategies.

8. To accrue benefits of implementing most cost-effectiveness monitoring strategies will require action on result, and clear guidance when and where to in switch, ensure switch is done and that 2nd line ARVs are available.

9. Current modelling results are consistent with guideline directions based on best available evidence; however countries should ‘proceed with data’.

Wrap up

Tim Hallett, ICL

The workshop concluded with Prof. Hallett highlighting the value of the iterative process of reviewing modelling results over the course of the meeting. Reflecting on modelling results together with guideline directions, country-level policy and implementation experiences is novel and important for providing informed recommendations. HIV Modelling Consortium organisers thanked WHO, MOH representatives, funding and implementing partner perspectives for their active participation and contributions.