# Assessment of laboratory test utilization for HIV/AIDS care in urban ART clinics of Lilongwe, Malawi

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## Abstract

### Background

The 2011 Malawi HIV guidelines promote CD4 monitoring for pre-ART assessment and considering HIVRNA monitoring for ART response assessment, while some clinics used CD4 for both. We assessed clinical ordering practices as compared to guidelines, and determined whether the samples were successfully and promptly processed.

### Methods

We conducted a retrospective review of all patients seen in from August 2010 through July 2011,, in two urban HIV-care clinics that utilized 6-monthly CD4 monitoring regardless of ART status. We calculated the percentage of patients on whom clinicians ordered CD4 or HIVRNA analysis. For all samples sent, we determined rates of successful lab-processing, and mean time to returned results.

### Results

Of 20581 patients seen, 8029 (39%) had at least one blood draw for CD4 count. Among pre-ART patients, 2668/2844 (93.8%) had CD4 counts performed for eligibility. Of all CD4 samples sent, 8082/9207 (89%) samples were successfully processed. Of those, mean time to processing was 1.6 days (s.d 1.5) but mean time to results being available to clinician was 9.3 days (s.d. 3.7). Regarding HIVRNA, 172 patients of 17737 on ART had a blood draw and only 118/213 (55%) samples were successfully processed. Mean processing time was 39.5 days (s.d. 21.7); mean time to results being available to clinician was 43.1 days (s.d. 25.1). During the one-year evaluated, there were multiple lapses in processing HIVRNA samples for up to 2 months.

### Conclusions

Clinicians underutilize CD4 and HIVRNA as monitoring tools in HIV care. Laboratory processing failures and turnaround times are unacceptably high for viral load analysis. Alternative strategies need to be considered in order to meet laboratory monitoring needs.

## Introduction

With increasing access to antiretroviral therapy for HIV-infected individuals in resource-limited settings, the need for establishing appropriate treatment monitoring strategies is required[1]. CD4 count analysis, a long-time determinant of antiretroviral therapy (ART) eligibility[2], has commonly been used for monitoring treatment failure, but immunological monitoring is poor at recognizing treatment failure compared to virologic monitoring[3].

Specifically in Malawi, with an estimated adult prevalence rate of 11%[4] and increasing population on ART, providing monitoring strategies presents an evolving problem. CD4 is used to determine need for ART for individuals in stage 1 and 2 and require reevaluation every 6 months before ART initiation. It has also been used for ART treatment monitoring in some centers as an established standard, even if not currently per the national guidelines. Meanwhile, HIV RNA for monitoring treatment failure is scheduled to be part of standard care by 2015[5].

However, limited data exist on how effectively current methods have been implemented, in terms of tests being ordered per schedule and results being returned on a clinically relevant timeline. As monitoring demands evolve, understanding whether appropriate testing was ordered and completed is necessary for evaluating effectiveness. Identifying barriers that prevented effective laboratory monitoring in the past will allow more successful implementation in the future.

Given the vital role laboratory tests play in providing quality HIV care, we aimed to quantify clinician laboratory ordering practices, as well as laboratory turnaround time for CD4 count and HIVRNA tests, so as to inform future laboratory monitoring activities.

## Methodology

### Study setting

Lighthouse Trust operates two urban HIV-care clinics based in Lilongwe, Malawi. Since 2004, both clinics have utilized 6-monthly CD4 monitoring for Pre-ART patients to determine ART eligibility and to monitor treatment for patients on ART. Lighthouse Clinic (LH) is located on the central hospital campus, with a neighboring research facility; Martin Preuss Centre (MPC) is located near a district hospital in central town. Both hospitals are Ministry of Health (MOH) facilities with access to laboratories expected to be able to do CD4 cell count and HIV RNA load analysis on a daily basis, as needed. Both clinics maintain electronic medical records (EMR) of all patient encounters including blood draws and lab results.

For each CD4 and HIVRNA sample ordered in clinic, nurses draw the blood in the clinic and the sample is sent to the MOH laboratory for processing. The results are delivered by hand to the clinic, and entered into the EMR by staff, to become available to clinicians. The clinic's monitoring and evaluation team follows up with the laboratory on samples if results are not returned.

## Study design, population, and data collection

We conducted a retrospective review from electronic medical records (EMR) of all registered patients seen in these two clinics from August 2010 through July 2011, and all laboratory orders for CD4 cell count and HIVRNA analysis. Permission to the data was granted by the Lighthouse Trust, Lilongwe, Malawi. This study was approved by the Malawi Institutional Review Board, the National Health Sciences Research Committee (NHSRC) as part of a program evaluation of Lighthouse Trust.

Exclusion criteria for patients included age below 18 years old, and being transferred into care during the period since information about previous laboratory evaluation was unknown. We excluded a small number of samples not processed by the Ministry of Health facility, as such samples

were ordered for research protocols by research clinicians, rather than regular care monitoring, and processed at a different research laboratory facility.

For each patient, we collected visit dates, when and if they were initiated on ART, and dates for when blood draws were completed for CD4 cell counts and HIVRNA analysis, using blood-draw as a proxy for ordering. Each sample is associated with a unique requisition number and electronically recorded date. Dates of blood draw, processing sample, and entering results in the EMR are all recorded in the EMR within 2 days of receipt by dedicated staff in the clinics, along with the sample result. For each result returned, we recorded the outcome (not returned, passed, failed, and voided), test value, date for lab processing, and date of result returned.

The MOH laboratory receiving all samples had 3 CD4 count analyzers (2 BD FACScount, 1 Beckman Coulter EPICS ) and one HIVRNA analyzer (Roche). The number of days machines were processing samples were confirmed by the laboratory's records of what days quality controls were completed per machine.

### Data analysis

Data was compiled from the EMR into a Microsoft Access database (2007) and analyzed in Stata (version 11.2). We calculated the percentage of patients on whom clinicians ordered CD4 or HIVRNA analysis per the schedule indicated by the standard of care. We determined rates of successful lab-processing, and the mean times to processing samples and returning results. We also looked for periods of time when no CD4 counts or viral loads were successfully processed, as a proxy for periods of time with equipment failure or shortage of reagents.

## Results

### Ordering

Between the two clinics, 20581 eligible patients were seen, of which 17737 (86.2%) were on ART, and 2844 (13.8%) were being followed before ART initiation. Based on the frequency of patient visits, 15924/20581 (76.6%) were seen at least once per six-month period during the 12 month study period, therefore eligible for two blood draws; the remaining 4657 patients were only seen within a six-month period, and therefore would be due for one blood draw.

Of the total patients, 8029/20581 (39.0%) had at least one blood draw for CD4 count analysis. Among pre-ART patients, 2668/2844 (93.8%) had CD4 counts performed for eligibility while among ART patients, only 5361/17737 (30.2%) received CD4 counts for monitoring. 1006/15924 (6.3%) had 2 or more blood draws for CD4 count analysis as per guidelines. Of the 8029 with CD4 analysis ordered, 4399/9043 (48.6%) patients were from LH; 3630/11538 (31.5%) were from MPC (p value < 0.0001).

Regarding HIVRNA ordering, 172/17737 of patients on ART (1.0%) had at least one blood draw for HIVRNA analysis; 30 patients had 2 or more blood draws. Of the 172 patients with HIVRNA analysis ordered, 155/9043 (1.7%) patients were from LH; 17/11538 (0.15%) were from MPC (p value < 0.0001).

### CD4 analysis

Of 9207 CD4 samples sent to the Ministry of Health laboratories, 8082 (89%) samples were returned as successfully processed (Table 1). Of those, mean time to processing was

1.6 days (s.d 1.5), whereas the internal laboratory standard is 2 days. However, mean time to results being available to clinician in the EMR was 9.32 days (s.d. 3.7). For both measures of time to processing and time to results available, there was statistical difference between the clinics (p value <.01) but no clinical difference (within 0.33 days for both). Of 365 expected days of processing, there were a total of 251 days when clinic samples were run, including weekend days, and 203 days when results were entered in the EMR. The laboratory processed samples on a total of 272 days. There were no gaps in processing samples longer than 4 days.

### HIVRNA analysis

Of 213 samples sent, only 118 (55%) samples were returned as successfully processed (Table 1). Among these 118 samples, mean processing time was 39.5 days (s.d. 21.9), with a wide range from 1 -132 days. Mean time to results being available to clinician was 43.1 days (s.d. 25.1). There was no statistical difference between the two clinics on either mean time (p value of 0.47 and 0.35 respectively). During the one-year evaluated, there were a total of 19 work days when the machine processed samples, with no regular interval and with 6 occurrences of breaks longer than 2 weeks in HIVRNA analysis. No samples were processed from May 2011 through July 2011.

*Table 1: Outcomes of samples sent to laboratory*

| | # samples | % total of ordered (N = 9107) | # samples | % total of ordered (N =213) |
|---|---|---|---|---|
| | | CD4 | | HIVRNA |
| | 217 | 2% | 68 | 32% |
| | 8890 | 98% | 145 | 68% |
| | 733 | 8% | 26 | 12% |
| | 8082 | 89% | 118 | 55% |
| | 75 | 1% | 1 | 0% |
| Of samples that returned as "pass" | | | | |
| | Mean days | Standard dev | Mean days | Standard dev |
| | 1.60 | 1.47 | 39.51 | 21.67 |
| | 9.32 | 3.67 | 43.13 | 25.13 |

## Discussion

Clinicians grossly underutilize CD4 and HIVRNA as diagnostic and monitoring tools. While CD4 count processing success is acceptable, the current 9 day availability to clinicians can be improved. Also, the 93.8% utilization reported for pre-ART monitoring is higher than for ART monitoring, as a large portion would be in newly diagnosed patients on an initial visit, as opposed to those being followed on an interval basis.

However, HIVRNA processing, lab availability, and turnaround time require marked improvement for effective monitoring. Notably, these are the identified problems in the most ideal of scenarios, where the two clinics have electronic medical records, access to laboratory equipment and staff

with transport mechanisms in place, and dedicated staff to follow up results (though we acknowledge it is possible that some samples were processed in the laboratory appropriately and not appropriately recorded by the clinic staff, but this number is not quantifiable and assumed to be small)

Uptake of both CD4 and HIVRNA testing differed according to clinic site, with LH ordering more tests than MPC. LH, a centre of excellence for the central region, maintains a more mature ART cohort, has more access to specialist physicians, and is closer to the primary lab. This may explain some differential in lab ordering, particularly with respect to HIVRNA testing. HIVRNA ordering is low at times of equipment failure, likely due to clinician knowledge of equipment status. Similarly, clinicians may not order CD4 for monitoring when processing capacity is low and decide to reserve resources for determining ART eligibility. Overall, laboratory ordering at both sites compared to country guidelines is suboptimal. Strategies to ensure adherence to monitoring guidelines can potentially be incorporated into the Electronic Monitoring Record through reminders at required lab draw dates.

Regarding rates of successful processing, the laboratory was able to provide a much more reliable service for CD4 than for HIVRNA. The two BD FACScount analysers were run almost daily, while the EPICS served as a back-up machine for when the BD machines needed service or reagents. This prevented large gaps in processing. However, the HIVRNA analysis was dependent on one analyser, which consistently had periods of machine failure and inability to run samples, delaying processing. The number of samples for CD4 analysis was also 100 fold of the number of HIVRNA samples, suggesting higher demand for consistent service. HIVRNA samples were run in batches collected over months, resulting in wide standard deviations of turnaround time.

Due to successful scale-up of antiretroviral therapy (ART) services over the past decade, almost 250,000 HIV-infected people were on ART as of December of 2010, and this number is expected to double by 2015[6]. The rate of finding HIVRNA above 1000 copies/ml in clinics across the country at comparable settings is 5.8%, with 7.4% at this clinic[7], suggesting approximately 1300 of the 17737 patients on ART in this study may be failing therapy, underscoring the potential benefit from routine HIV RNA analysis as proposed, compared to the 172 that received HIVRNA analysis under current conditions. As Malawi prepares to adopt scheduled HIVRNA analysis for all patients on ART[5], a clinic the size of Lighthouse would be expected to have the capacity to perform thousands of HIVRNA per year. Laboratory processing failures and turnaround times are unacceptably high to reach that goal and more effective maintenance of equipment is required to process samples more than 20 days out of a calendar year.

Alternative strategies may offer considerable improvement before successfully adopting these tests as standard-of-care. For CD4 analysis, point-of-care devices offer a practical alternative to providing lab results within a patient-visit, among other low-cost options[8]. When not available, SMS result reporting may improve the delay between processing and results being available to clinicians. For HIVRNA, improved equipment support, so the analyser is available to process samples more frequently, is needed. The use of dried blood spots would lengthen the life span of samples, so to adequately preserve them until the analyser is accessible.

## Conclusions

Compared to national and clinic guidelines, clinicians underutilize CD4 and HIVRNA as staging and monitoring tools, respectively. Laboratory processing failures and turnaround times are unacceptably high for viral load analysis. Alternative strategies need to be considered in order to meet laboratory monitoring needs.

## Competing interests

The authors declare that they have no competing interests.

## Authors' contributions

SP co-designed the database, performed the statistical analysis, and drafted the manuscript. HT acquired the data and co-designed the database. MH conceived the study, participated in its design and coordination, and reviewed the analysis for accuracy as compared to clinical experience. All authors read and approved the final manuscript.

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