Rapid, Real-Time Detection of Acute HIV Infection in Patients in Africa

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Background. We conducted a prospective study to evaluate methods of detecting clients with sexually transmitted diseases (STDs) who were acutely coinfected with human immunodeficiency virus (HIV) in Lilongwe, Malawi.

Methods. After informed consent was obtained, all clients with acute STDs were offered voluntary HIV counseling and testing by 2 rapid antibody tests. Samples from rapid test–negative or –discordant subjects were pooled (50:5:1) and tested for HIV RNA. Western blots were performed on all rapid test–discordant specimens with detectable HIV RNA. A subset of specimens received p24 antigen testing with standard and/or ultrasensitive methods. Patients with possible acute HIV infection were followed to confirm seroconversion.

Results. A total of 1450 clients (34% female and 66% male) agreed to testing, of whom 588 (40.55%) had established HIV infection and 21 (1.45%) had acute infection. Discordant rapid antibody tests identified 7 of 21 (33.3% sensitivity), standard p24 antigen identified 12 of 16 (75% sensitivity), and ultrasensitive p24 antigen identified 15 of 17 (88% sensitivity) acute cases. By definition, the sensitivity of the RNA assay was 100%.

Conclusions. Real-time pooled RNA testing for the detection of acute HIV infection is feasible in resource-limited settings. However, parallel rapid testing and p24 antigen testing are technologically simpler and together may detect ~90% of acute cases.

Compelling data suggest the potential importance of detecting acute HIV infection (AHI) both for public and individual patients’ health. In particular, people with AHI have high plasma and genital tract viral loads [1], increasing the probability of secondary transmission [2, 3]. Acutely infected persons may continue to engage in risky behavior, because they are typically unaware of their infections. Individuals must be identified as early in infection as possible to maximize the effectiveness of prevention measures [4, 5]. Furthermore, careful characterization of patients with AHI might create opportunities for basic HIV pathogenesis research, with implications for developing prophylactic vaccines. As a consequence, the detection of HIV has been deemed a priority by the World Health Organization (WHO), UNAIDS, the Centers for Disease Control and Prevention, and the National Institutes of Health [6, 7]. Unfortunately, diagnosis of AHI remains challenging. Routine antibody tests remain negative for the first 4–5 weeks of infection, necessitating diagnosis on the basis of clinical symptoms or the presence of HIV proteins or nucleic acids [8, 9]. Until recently, AHI had been diagnosed primarily in high-risk patients with acute retroviral symptoms, although only approximately half of patients develop typical mononucleosis-like symptoms [4, 10]. Given the absence of acute retroviral symptoms in many patients, detection of viral products, such as HIV RNA or p24 antigen, in antibody-seronegative subjects represents a more promising approach.
toward identifying patients with AHI [8, 10, 11]. In general, HIV RNA assays have been found to be more sensitive than p24 antigen assays but typically less specific [10, 11]. The potential usefulness of wide-scale testing for AHI has been demonstrated recently in North Carolina, where a pooling protocol is used to test antibody EIA–negative specimens for HIV RNA [3, 4]. Pooling increases the specificity of RNA assays because specimens are tested repeatedly during deconstruction of the pools.

However, the vast majority of HIV transmission occurs in resource-limited settings, where deficiencies in infrastructure and high equipment and reagent costs make large-scale application of specimen pooling and RNA testing unfeasible. Previous retrospective studies have suggested that sexually transmitted disease (STD) clinics in high-prevalence countries would be potentially important venues to screen for AHI [12, 13]. We describe here the feasibility and performance of using rapid tests and p24 assays to prospectively screen patients for AHI in real time at an STD clinic in Lilongwe, Malawi.

Figure 1. Flow chart of the study population of the Malawi Acute HIV Infection Study. STD, sexually transmitted disease; WB, Western blot.

PATIENTS, MATERIALS, AND METHODS

Study population. From February 2003 through October 2004, consecutive attendees to the Kamuzu Central Hospital (KCH) STD clinic (Lilongwe, Malawi) over the age of 17 years were invited to enroll in a study to assess methods for diagnosing AHI. Subjects who were too ill, had persistent STDs, or refused were excluded from the study. After informed consent was obtained, HIV counseling and testing as well as venipuncture were performed. All participants answered a brief questionnaire covering demographics, HIV infection risk factors, and acute retroviral syndrome symptoms in the past 4 weeks. Patients were given a brief physical exam, including a genital exam (with speculum for women), and were treated following the Malawian STD syndromic management guidelines. All patients were asked to return to the clinic the following week for follow-up of STD symptoms. The University of North Carolina School of Medicine and the Malawi Health Sciences ethics review boards approved this study.
Table 1. Demographic information.

<table>
<thead>
<tr>
<th>Infection status</th>
<th>Sex, no. (%)</th>
<th>Age, median (IQR), years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>AHI (n = 21)</td>
<td>16</td>
<td>5</td>
</tr>
<tr>
<td>EHI (n = 588)</td>
<td>354</td>
<td>234</td>
</tr>
<tr>
<td>Negative (n = 841)</td>
<td>581</td>
<td>258</td>
</tr>
<tr>
<td>All (n = 1450)</td>
<td>951</td>
<td>497</td>
</tr>
</tbody>
</table>

NOTE. AHI, acute HIV infection; EHI, established HIV infection; IQR, interquartile range.

* Two HIV-negative patients were missing data on sex and age.

HIV antibody testing. HIV testing followed the Malawi AIDS Counseling and Resource Organization scheme in use nationwide, supplemented with HIV antigen and RNA assays for the detection of AHI. Whole blood was tested in parallel with Determine (DT; Abbott Laboratories) and Unigold (UG; Trinity Biotech) rapid HIV assays at the STD clinic. Patients were informed of the results of these rapid tests during the initial visit. All patients with concordant positive rapid antibody results were counseled as HIV infected and were referred to HIV care at the KCH HIV clinic. Patients with discordant negative antibody results were counseled as HIV uninfected but were asked to return in 1 week for additional HIV results. Patients with discordant antibody results were counseled about the importance of returning in 7 days to obtain results from the additional tests.

HIV RNA. All negative and discordant rapid test plasma samples were screened for the presence of HIV RNA. Rapid test–negative/discardant samples were manually pooled using a 50:5:1 scheme initially. Briefly, 200 μL aliquots were pooled from 5 individual specimens to make an intermediate 5:1 pool. Then 200 μL from 10 intermediate pools were pooled to create a master 50:1 pool. The master pool containing plasma from 50 individuals was tested by the ultrasensitive Roche Amplicor Monitor HIV RNA assay (version 1.5) following the protocol on the manufacturer’s package insert. If the master pool was positive for HIV RNA, intermediate pools of samples and then individual specimens were tested using the standard Roche Monitor assay to identify the infected individual. Later, HIV antibody–negative or –discordant specimens collected during 1 week were pooled and tested for HIV RNA as described above. For a few patients, samples were not pooled and were tested using individual specimens only. The Lilongwe laboratory was certified by the NIH-sponsored Virus Quality Assurance Laboratory for Roche Monitor RNA testing.

HIV p24 antigen. Two versions of the Perkin-Elmer p24 antigen assay were used. In Malawi, we initially tested individual specimens from the first 703 rapid test–discordant or –concordant negative patients with the standard p24 antigen assay, following the manufacturer’s instructions. Patients received these assay results at the 1-week follow-up visit.

The sensitivity of the p24 assay can be increased by lysing the HIV virions in 30 mmol/L Tris/HCl (pH 7.2), 450 mmol/L of NaCl, 1.5% Triton X-100, 1.5% deoxycholic acid (sodium salt), 0.3% sodium dodecylsulfate, and 10 mmol/L of EDTA before boiling the plasma for 5 min to disrupt antigen-antibody complexes [14]. Additional sensitivity is achieved by signal amplification. We retrospectively tested a subset of plasma specimens with this heat-dissociated, signal amplified, ultrasensitive version of the assay (HIV-1 p24 amplified antigen assay; Up24) [14–18].

Western blot. Western blot testing was performed on all individuals with discordant rapid tests and detectable RNA, using a standard kit (Bio-Rad Laboratories) according to the manufacturer’s instructions. A positive test result was defined as at least 2 envelope bands (gp160, gp120, or gp41), in accordance with WHO criteria. A weakly positive result was defined as only 2 positive envelope bands, each with an intensity score of 1+; all other positive results were considered to be strongly positive. An indeterminate result was defined as any reactivity not meeting these definitions.

HIV status definitions. AHI was considered to be present if HIV RNA results were positive and 1 of the following conditions was met: (1) rapid antibody tests were both negative; (2) rapid antibody tests were discordant and Western blot results were negative or indeterminate; or (3) rapid antibody tests were discordant and Western blot results were weakly positive with subsequent band evolution. Fifteen of the 21 patients with AHI were followed up to confirm antibody seroconversion and positive Western blot; the other 6 subjects with AHI were lost to follow-up. Established HIV infection (EHI) was defined as either (1) 2 concordant positive rapid antibody tests or (2) discordant rapid antibody tests with a strongly positive Western.

Table 2. Sensitivity and specificity of rapid tests and p24 antigen assays for the detection of acute HIV infection.

<table>
<thead>
<tr>
<th>Test</th>
<th>True positive, no.</th>
<th>True negative, no.</th>
<th>False positive, no.</th>
<th>False negative, no.</th>
<th>Sensitivity, % (95% CI)</th>
<th>Specificity, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discordant rapid</td>
<td>7</td>
<td>827</td>
<td>14</td>
<td>14</td>
<td>33 (15–57)</td>
<td>98 (97–99)</td>
</tr>
<tr>
<td>Standard p24 antigen</td>
<td>12</td>
<td>682</td>
<td>3</td>
<td>4</td>
<td>75 (48–93)</td>
<td>99.6 (99–100)</td>
</tr>
<tr>
<td>Up24 antigen</td>
<td>15</td>
<td>82</td>
<td>0</td>
<td>2</td>
<td>88 (64–99)</td>
<td>100 (96–100)</td>
</tr>
</tbody>
</table>

NOTE. CI, confidence interval; Up24, ultrasensitive p24.
Figure 2. Probability of acute HIV infection (AHI) given discordant or concordant negative rapid test results (A), and probability of AHI given positive or negative standard p24 or ultrasensitive p24 (Up24) antigen test results (B). The X-axis represents a range of plausible prevalences for AHI, including the prevalence observed in the present study population (2.4%) after excluding those with established HIV infection. The Y-axis provides the probability of AHI based on the specific test result. For example, at a prevalence of 2.4%, the probability of AHI given discordant rapid test results is 33% (A). Note that the probabilities are equivalent to the positive predictive value for discordant rapid tests and positive p24 antigen tests and to 1 − the negative predictive value for concordant negative rapid test results or negative p24 antigen test results.

Blot. Individuals with negative or discordant antibody results and negative RNA were considered to be uninfected.

Statistical analyses. We examined the performance of discordant rapid tests, standard p24, and Up24 testing to detect 2 HIV outcomes: AHI and any HIV infection (AHI or EHI). In assessing the performance of the tests for AHI, persons with EHI were excluded. Sensitivity and specificity with 95% confidence intervals were calculated. Analyses were conducted using SAS (version 8.2; SAS Institute) and Stata (version 8.2; StataCorp).

To assess the potential value of these tests for the diagnosis of AHI, we calculated predictive values across a range of plausible prevalence values using Bayes’s theorem. We also examined the number of HIV cases, including EHI and AHI, that would be identified and missed, as well as the number of persons who would be misclassified with HIV infection by use of combinations of rapid tests and p24 assays in a hypothetical clinic population comparable to the study population.

We conducted Up24 testing in only 82 HIV-negative participants, a subset too small to produce reliable specificity estimates given the excellent performance of this assay (specificity of 100% in this subsample). Consequently, for purposes of
calculating predictive values and estimating performance in hypothetical populations, we assumed that the specificity of the Up24 assay was identical to the standard p24 assay. The difference in HIV RNA concentrations among persons with AHI and EHI was assessed using a Wilcoxon rank sum test.

**RESULTS**

**AHI.** We screened 1450 patients with STDs (34% female and 66% male) over a 21-month period (figure 1 and table 1). Of these, 588 (40.55%) had EHI, and 21 (1.45%) had AHI. Among persons without EHI, the prevalence of AHI was 2.4% (21/862).

**Performance of rapid antibody tests for the diagnosis of AHI.** Discordant rapid antibody tests identified 7 of 21 (sensitivity, 33.3%) cases of AHI (figure 1 and table 2). Of 841 clients negative for HIV RNA, 827 were rapid test negative (specificity, 98.3%). Two persons with discordant rapid test results had EHI. Among 15 individuals without EHI who had a positive DT result and a negative UG result, 6 (40%) were acutely infected. In comparison, only 1 of 6 individuals (17%) without EHI who had a negative DT and a positive UG result was acutely infected.

**Performance of standard and ultrasensitive p24 antigen assays for the diagnosis of AHI.** The standard p24 antigen assay was performed on specimens from the first 703 patients with discordant or concordant negative rapid test results. Of the 16 patients with AHI tested in this way, 12 were p24 positive (sensitivity, 75%) (table 2). Among the 685 persons without HIV infection for whom standard p24 antigen tests were performed, 3 false-positive p24 antigen results were obtained (specificity, 99.6%) (table 2). When we retrospectively used the Up24 antigen assay on a subset of specimens, we identified 15 of 17 cases of AHI (sensitivity, 88%) (table 2). All 82 HIV-negative subjects for whom we performed Up24 testing had negative results, corresponding to a specificity of 100%.

**Performance of HIV RNA testing on pooled plasma.** By definition, the sensitivity and specificity to detect AHI were 100% for the RNA testing. Median baseline viral load for the 21 patients with AHI was significantly higher (median, 1,409,218 copies/mL; range, 1008–198,387,097 copies/mL) than for the 114 patients with EHI (median, 75,313 copies/mL; range, 1275–588,733,491 copies/mL) (P = .0006).

**Predictive value for the diagnosis of AHI.** Given the 2.4% prevalence of AHI in our study population after exclusion of those persons with EHI, the positive predictive value of discordant rapid tests in detecting AHI was 33.3% (figure 2A). In a similar hypothetical population with a prevalence of 0.5%, the positive predictive value of discordant tests for identifying AHI would be 9.1%. At these same prevalences (2.4% and 0.5%), the probability of having HIV infection with 2 negative tests is 1.7% and 0.3%, respectively.

The positive predictive value of a positive standard p24 antigen test or Up24 test result in our population (prevalence, 2.4%) was 81.0% and 83.4%, respectively, for detecting AHI (figure 2B). At 0.5% prevalence, these values remained high at 46.3% and 50.3%.

**Detection of HIV infection (acute and established).** Considering 2 positive rapid test results as a joint positive rapid test result, only 96.2% (586/609) of persons with HIV infection were identified (table 3). All of these persons, by our definition, had EHI (specificity, 100%). Adding discordant results of rapid antibody tests to the definition of a positive test result, such that discordant or discordant results were considered to be positive, the sensitivity was increased to 97.7% (595/609), and the specificity was decreased to 98.3% (827/841).

Adding instead the p24 or Up24 assays to the definition of a positive test, such that discordant rapid test results or positive p24/Up24 result was considered to be a positive result, yielded a substantial increase in performance. With concordant rapid test results and the standard p24 assay, the sensitivity to detect any HIV infection was 99.0%, with a specificity of 99.6%. Using discordant rapid tests and the Up24 assay, the sensitivity was increased over the standard p24 assay to 99.5%, and the corresponding specificity was 100% in the small subset of HIV-negative specimens on which the Up24 assay was performed.
Table 4. Estimated cases of HIV infection, including established HIV infection (EHI) and acute HIV infection (AHI), by several test combinations in a hypothetical population of 10,000 sexually transmitted disease clinic patients.

<table>
<thead>
<tr>
<th>Category</th>
<th>Total cases</th>
<th>EHI cases</th>
<th>AHI cases</th>
<th>False positive</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Detected</td>
<td>Not detected</td>
<td>Detected</td>
<td>Not detected</td>
</tr>
<tr>
<td>In population with 42% prevalence (1.45% AHI + 40.55% EHI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concordant rapid</td>
<td>4041 (96.2)</td>
<td>159 (3.8)</td>
<td>4041 (99.7)</td>
<td>14 (0.3)</td>
</tr>
<tr>
<td>Discordant or concordant rapid</td>
<td>4103 (97.7)</td>
<td>97 (2.3)</td>
<td>4055 (100)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Positive Determine</td>
<td>4096 (97.5)</td>
<td>104 (2.5)</td>
<td>4055 (100)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Positive Unigold</td>
<td>4048 (96.4)</td>
<td>152 (3.6)</td>
<td>4041 (99.7)</td>
<td>14 (0.3)</td>
</tr>
<tr>
<td>In population with 46.86% prevalence (1.24% AHI + 45.62% EHI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concordant rapid or positive p24</td>
<td>4639 (99.0)</td>
<td>47 (1.0)</td>
<td>4546 (99.6)</td>
<td>16 (0.4)</td>
</tr>
<tr>
<td>In population with 46.90% prevalence (1.32% AHI + 45.58% EHI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concordant rapid or positive Up24</td>
<td>4667 (99.5)</td>
<td>23 (0.5)</td>
<td>4551 (99.8)</td>
<td>7 (0.2)</td>
</tr>
</tbody>
</table>

NOTE. Data are no. (%) of cases.

* Prevalence values in the study population used for estimation of p24 assay performance.

** Prevalence values in the study population used for estimation of Up24 assay performance.
Application of the assays in a hypothetical clinic population.

The STD clinic in Lilongwe sees ~10,000 persons each year. On the basis of the prevalences observed in this study, use of concordant rapid test results to define HIV positivity would miss ~145 cases of AHI and 14 cases of EHI (table 4). Including discordant rapid test results in the definition would miss 97 cases of AHI and no cases of EHI, but 97 persons would be mistakenly identified as being HIV positive.

Using the p24 assay and the prevalences of HIV infection observed in the subset of the study population tested with p24, only 31 of 124 cases of AHI and 16 cases of EHI would be missed, whereas 23 persons would be mistakenly identified as being HIV positive. With the Up24 assay, only 16 of 132 cases of AHI and 7 EHI cases would be missed. This difference is attributable to the standard p24 assay missing patients with early antibody responses.

DISCUSSION

Shortly after HIV was isolated, diagnostic HIV antibody testing using EIAs confirmed by Western blot was established. This procedure allowed the development of the voluntary counseling and testing strategy employed today and assured the safety of the blood supply. More recently, rapid antibody assays have been developed that allow patients to learn their HIV status before leaving the clinic [19, 20]. Protocols for paired testing using rapid tests with potentially different HIV antigens (either serially or in parallel) have been developed that have sufficient specificity to replace the Western blot for diagnosis [19, 20]. However, our results confirm that, in high-incidence settings, the sensitivity of a single test for HIV antibodies alone can be as low as 96%, due to the presence of significant numbers of previously unrecognized AHIs in the testing population. In this study’s high-risk population, we found that the sensitivity of a single rapid test could be substantially improved by adding a second (parallel) rapid test, by adding a pooled or individual HIV RNA test, or by adding a p24 antigen EIA test. Each of these alternative algorithms identified a substantial number of AHIs, creating new opportunities for HIV prevention, care, and research.

Our results directly contradict the conventional wisdom that truly acute infections will be rare in any clinic-based testing population. Under this assumption, the most recent WHO guidelines recommend serial rapid HIV tests, without additional, more sensitive tests, to save time and money. In this strategy, people with a negative initial test result are not tested further and only those with an initial positive test result are tested using a second confirmatory rapid test [21]. In either parallel or serial rapid testing, subjects with discordant results are asked to return for repeat testing in 6 weeks, by which time seroconversion should have occurred. However, because many clients fail to return, many clinics use a third rapid test as a “tiebreaker” test. In this study, a substantial number (35%) of individuals with a positive DT antibody test result and a negative UG test result had AHI. In an earlier study, Koblavi-Dème et al. [19] noted the ability of the DT assay to detect “early” HIV infection, although the biological basis for this result is unknown.

Although the serial approach suggested by the WHO aims to reduce costs by using fewer tests, according to our data this strategy will be less sensitive because most (70%–95%) cases of AHI will be missed, depending on the rapid test kit used. Specifically, had DT been used as the single screening test in our study, it would have detected 587 (99.8%) of 588 cases of EHI and only 6 (28.6%) of 21 cases of AHI; a single UG test would have detected 585 of 588 (99.5%) cases of EHI and 1 (4.8%) of 21 cases of AHI.

The current WHO guidelines are based primarily on assessments that used traditional antibody EIA and Western blot as the reference standard for the definition of HIV disease. Our results suggest that current WHO guidelines need to be reviewed as they pertain to testing in high-prevalence countries or clinics. Specifically, previous algorithm development and validation analyses may need to be repeated using HIV RNA detection as part of the reference standard for HIV infection. Furthermore, the cost-effectiveness of various testing approaches must be evaluated to consider the potential public health benefits specific to diagnosing HIV infection during AHI—the earliest and most contagious disease stage.

An approach that combines pooling of HIV antibody EIA–negative samples with HIV RNA detection has been used successfully in the United States to identify persons with AHI on a routine basis [3, 4]. However, nucleic acid testing in general is expensive and requires equipment, dedicated laboratory space, trained technologists, and rigorous quality assurance. Consequently, it is generally unsuitable for many resource-limited settings [22].

The ultrasensitive (heat dissociated and signal amplified) p24 antigen assay is an attractive alternative to HIV RNA testing in high-risk developing-world settings. This EIA-based assay is not prone to the contamination problems that plague nucleic acid amplification tests. It is a technologically simpler, high-throughput assay that is considerably less expensive than RNA tests. In our study, the Up24 assay had a high positive predictive value (83%) in the present setting, which had a high prevalence of AHI (2.4% among individuals without EHI). The high sensitivity of Up24 for early AHI is further supported by Pascual et al. [18], who tested samples from 4 seroconversion panels and found that Up24 assay results became positive within 3 days after the first detection of HIV RNA in all cases. However, it is unlikely that the Up24 assay would be useful in settings...
in which prevalence was very low, such as in population-based screening. In a hypothetical population with North Carolina’s 0.02% prevalence of AHI, we estimate that the positive predictive value of a p24 antigen or Up24 EIA would be only \(~3.5\)% on the basis of the sensitivity and specificity observed in this study.

Several logistical problems arose during the course of testing in Malawi. Our initial pooling strategy of 50:5:1 was not optimal, because it took too long to accumulate 50 negative clients and most of the 50-member pools were positive, thus defeating the reason for pooling. Later, we switched to a scheme of pooling all antibody-negative or discordant samples received during a week, which typically ranged from 10 to 20 specimens. This strategy allowed faster turn-around time and increased the sensitivity of the assay. Twelve patients did not have RNA testing done during the study period, and a recording error in 1 of the RNA pools required additional RNA testing to identify the true AHI case in the pool. It is crucial that the standard operating procedures and logistical details for rapid testing, pooling, RNA testing, and follow-up of suspected AHI cases be in place before testing and monitored closely during the conduct of testing.

The estimates for the sensitivity of the assays examined in this study are imprecise, because of the small number of persons with AHI. Consequently, these estimates should be considered with some caution. Furthermore, we assumed that all persons with concordant rapid test results had EHI. It is possible that a very small number of these persons actually had false-positive results. If so, the specificity estimates that we obtained would be overestimated. Finally, we did not perform the Up24 assay on all specimens from persons without HIV infection. We assumed that the specificity of the Up24 assay would be identical to the standard p24 assay for estimation of predictive values. This assumption is reasonable, but slight differences in specificity could affect these estimates. For example, if the Up24 specificity were 98.5%, the positive predictive value in a population with 2.4% AHI prevalence would be 59.5%, somewhat lower than the 83% positive predictive value we calculated. If, however, the Up24 specificity were 100% (as we observed in the small subset of samples on which we performed the Up24 test), the corresponding positive predictive value would be 100%.

In summary, we have confirmed the feasibility of screening for AHI in clinics in sub-Saharan Africa. Real-time identification of significant numbers of AHI cases is possible in resource-limited settings by use of either parallel rapid testing, Up24, or, when possible, RNA-based testing algorithms. Furthermore, the WHO guidelines for the use of rapid tests may require reconsideration and reevaluation with the use of a more complete reference standard that will identify persons with AHI.

MALAWI–UNIVERSITY OF NORTH CAROLINA PROJECT ACUTE HIV INFECTION STUDY TEAM

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References