# Diagnostic Performances of Three Rapid Diagnostic Tests for Detecting HIV Infections in Mali

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## Abstract

Diagnosis of HIV infections in resource-limited countries like Mali is based on Rapid Diagnostic Tests (RDTs). The RDTs are diagnostic assays designed for use at the Point-Of-Care (POC), which is quick, cost-effective and easy to perform. However, in these countries, the tests are commonly used without any initial evaluation or monitoring of their performance despite high levels of HIV strain diversity and rapid evolution of the virus. In this study, the reliability and accuracy of HIV RDTs (Determine™, Multispot™, SD Bioline™) used in Mali, where HIV-1 and HIV-2 co-exist, were evaluated from August 2004 to November 2017. A total of 1303 samples from new HIV-suspect patients in Bamako were tested for HIV-1 and HIV-2 using the RDT Determine™, followed by ELISA and Western Blot (WB). The Determine™ test showed a robust diagnostic sensitivity of 98.7% [CI 95: 97.59-99.37] and a diagnostic specificity of 99.2% [CI 95: 98.22-99.67]. The Multispot™ assay showed a diagnostic sensitivity of 98.77% [CI 95: 97.59-99.37] and a diagnostic specificity of 99.2% [CI 95: 98.22-99.67]. The diagnostic sensitivity and specificity of SD Bioline™ HIV-1/2 were 100% [CI 95:72.25-100] and 88.89% [CI 95: 56.50- 98.71], respectively. These data indicate excellent performance for HIV RDTs in Mali and we recommend the use of Determine™ HIV-1/2 for HIV screening and Multispot™ for discriminating HIV-2 from HIV-1 infections.

## Introduction

Human Immunodeficiency Virus (HIV), the causative agent of Acquired Immunodeficiency Syndrome (AIDS), is a retrovirus that was first isolated from men who had sex with men (MSM) in the 1980s and it still represents a global public health threat [1]. HIV infection leads to strong immuno-depression that promotes opportunistic infections in humans which could be prevented or reduced by early diagnosis and early treatment of the disease. In

June 2017, the United Nations HIV/AIDS Program (UNAIDS) estimated that 36.7 million people live with HIV [2]. From 2010 to 2016, there was an 11% decrease in the number of new infections among adults [2]. However, among people living with HIV/AIDS (PLWHA), only 53% [39-65%] have access to Antiretroviral Therapy (ART). The West and Central Africa regions are the most affected with 6.1 million cases. According to the last demographic and health survey (EDSM-V) conducted in 2012, the prevalence of HIV in Mali was 1.1% [3].

The current preventive measures against the disease and the antiretroviral therapy are effective; however, achieving the 90-90-

90 goals set by UNAIDS by 2020 remains challenging. The 90-90-90 program seeks to achieve 90% of infected people to know their status, 90% of those with HIV-positive results to have access to antiretroviral treatment and 90% of those on medication to have undetectable virus loads [4]. These goals are unachievable without easy, cost-effective and accurate screening tools for the most affected and under-resourced populations.

Diagnosis of HIV infections in Mali and most countries in Africa and other low and middle income countries is based on Rapid Diagnostic tests (RDTs) [5-7] which are based on immuno-chromatography or immuno-filtration principles [8]. However, the conventional gold standard diagnostic method (mostly used in developed countries) for HIV infection combines a specific antibody ELISA test followed by a confirmation test by Western blot (WB) of the positive cases [9]. This later strategy is difficult to implement in resource-limited countries as it requires well-trained staff, sophisticated laboratory equipment, longer experimental set-up and expensive reagents. These sophisticated tests may be unnecessary as RDTs have shown continuous improvements in diagnostic sensitivity and specificity and the current commercialized versions compare favorably to ELISA tests [10,11]. The WHO recommends the use of the RDTs in developing countries but they need to be evaluated and validated in each country [12]. Validation is important because of the inherent high genetic diversity of HIV and the continuous emergence of recombinant forms that might lead to serious diagnostic and therapeutic challenges. Also, the niche of HIV-2 is in West Africa, including Mali [13-16] although a few cases have also been found in Europe, India and the United States [17]. Since both HIV-1 and HIV-2 circulate in West Africa [15,18]. The diagnostic process in West Africa includes both HIV screening and HIV type discrimination/HIV confirmation [19].

This study was conducted in order to promote the screening for HIV with validated tests as widely as possible, with the aims of determining the performances of the rapid test Determine™ HIV-1/2 (which is the most frequently used HIV RDT in Mali) and other RDTs compared to ELISA and WB assays in the Laboratory of HIV and Tuberculosis Research and Training Center of the University Clinical Research Center (UCRC/SEREFO) of Bamako in Mali.

## Materials and methods

### Type of study and data collection

A cross-sectional study at the UCRC/SEREFO was conducted between June 2004 and November 2017. A total of 1303 patients were recruited and tested using a diagnostic regime as described in (Figure 1).
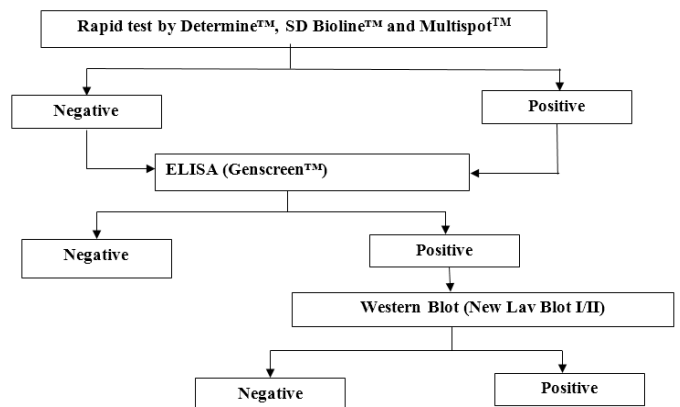


**Figure 1**: HIV diagnostic testing algorithm at the UCRC-SEREFO Laboratory.

### Study population

The target study population comprised suspected cases of HIV infection in the District of Bamako. The patients were aged 18 years or older who had consented to be tested for HIV and were either referred by one of the six reference health centers of Bamako or were from the HIV patient management center (CESAC) or the University Teaching Hospital Point-G of Bamako.

### RDTs, ELISA, Western blot and other assays

Whole blood was collected in 5 mL of blood separating tube (BD Vacutainer®, Becton Dickinson, Franklin Lakes, NJ, USA). HIV testing was performed as follows: A RDT was done on the study population using the Determine™ HIV-1/2 test (Abbott Laboratories, Matsudo-Shi, Chiba, Japan) (https://www.alere.com/en/home/product-details/determine-hiv-1-2.html) on all the participants (N=1303), on 56 patients using the Multispot™ HIV-1/HIV-2 test (Bio-Rad Laboratories, Redmond, WA, U.S.A.) (https://www.fda.gov/downloads/Biolog...remarketApprovalsPMAs/ucm091384.pdf) (N=56) and on 19 patients using the SD Bioline HIV-1/2 3.0 test (Standard Diagnostics, Inc 65, Borahagal-ro, Giheung-gu, Yongin-si, GYEONGGI-DO Gyeonggi-do, South Korea) (https://www.alere.com/en/home/product-details/sd-bioline-hiv-1-2-3-0.html) (N=19), with all RDT tests followed by a HIV ELISA test (Genscreen Ag-Ac Ultra HIV-1/2 version 2 Assay, Bio-Rad Laboratories, Marnes, France) (http://www.bio-rad.com/webroot/web/pdf/inserts/CDG/en/883605_EN.pdf). All the ELISA positive tests were further subjected to confirmation by WB assays (New Lav Blot I and Blot II, Bio-Rad Laboratories, Marnes, France) (http://www.bio-rad.com/webroot/web/pdf/inserts/CDG/en/883573_EN.pdf.). The diagnostic performances of all the RDTs were compared to the ELISA results. Patients with HIV positive

results were subjected to follow up confirmatory tests. CD4 and CD8 T lymphocyte counts were performed using a FacsCalibur flow cytometer (FASCalibur, BD, Biosciences, San Jose, CA, USA). Virus load was measured using the Roche COBAS® TaqMan® HIV-1 Test, v2.0. (Table 1) summarizes the properties of the HIV-1/2 RDTs, ELISA and WB assays that were used in this study.

| | Storage Temperature | Principle of the Test | Sample Type | Sample Volume (µL) Used for the Test | HIV typing detecting antibody | antigen tested | Presentation of Results |
|---|---|---|---|---|---|---|---|
| **Determine™ HIV-1/2** | +2 to +30°C | Immunochromatographic | Serum, Plasma, Whole blood | 50 | HIV-1 and HIV-2 | Recombinant and synthetic peptide antigens | Band |
| **Alere Determine™ HIV-1/2** | +2 to +30°C | Immunochromatographic | Serum, Plasma, Whole blood | 50 | HIV-1 and HIV-2 | HIV-1 gp41 and HIV-2 gp36, recombinants, surface antigens synthetic peptides | Band |
| **Alere Determine™ HIV-1/2 Ag/Ab Combo** | +2 to +30°C | Immunochromatographic | Serum, Plasma, Whole blood | 50 | HIV-1 and HIV-2, | HIV-1 gp41 and HIV-2 gp36, recombinants, surface antigens synthetic peptides; p24 antigen | Band |
| **SD Bioline™ HIV-1/2** | +2 to +30°C | Immunochromatographic | Serum, Plasma, Whole blood | 10; 20 | HIV-1 and HIV-2 | HIV-1 recombinant, antigen (gp41, p24) and HIV-2 (gp36); HIV-1 antigen p24 | Band |
| **Multispot™ HIV-1/2** | +2 to +30°C | Immuno- filtration assay | Serum, Plasma | 30 | HIV-1 and HIV-2 | Transmembrane antigens of HIV-1 and / or HIV-2 | Spot |
| **ELISA (Genscreen Ultra Ag-Ab)** | +2 to +8°C | Enzyme immunoassay based on the principle of the sandwich technique | Serum, Plasma | 75 | HIV-1 and HIV-2 | HIV-1 p24 antigen and detection of envelope antibodies associated with HIV-1 and/or HIV-2 virus | Absorbance measured |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Western Blot I (New Lav Blot I)** | +2 to +8°C | Indirect ELISA technique on a nitrocellulose strip containing all the HIV-1 constituent proteins and an internal anti-IgG control | Serum, Plasma | 20 | HIV-1 | The band corresponding to the internal control is localized on the strip end without any number, before the p16 reaction and allows to validate the addition of the sample | Band |
| **Western Blot II (New Lav Blot II)** | +2 to +8°C | indirect ELISA technique on a nitrocellulose strip containing all the HIV-2 constituent proteins and an internal anti-IgG control | Serum, Plasma | 20 | HIV-2 | The band corresponding to the internal control is localized on the strip end without any number, before the p16 reaction and allows to validate the addition of the sample | Band |

**Table 1**: Properties of the HIV-1/2 RDTs, ELISA and WB assays used in the study.

It should be noted that since 2005, our UCRC/SEREFO laboratory has been participating in External Quality Control (EQC) by the American College of Pathologists (CAP-Viral Marker) and showed satisfactory performance.

**Data analysis**

Patient records were entered into an electronic database in an Excel Sheet before being transferred and analyzed using the Epi-Info™ Statistical Software version 7.2. Frequency comparisons were done by the Chi-square and Fischer's tests. The diagnostic sensitivity, diagnostic specificity, and positive and negative predictive values were calculated to evaluate the performance of the three RDTs. Confidence Intervals (CI) at 95% were calculated for each of these estimates, assuming a binomial distribution for the values. A p value lower than 0.05 with an alpha risk of 5% was used to indicate statistical significance.

**Ethical considerations**

The study protocol was approved by the ethics committee of the Faculty of Medicine and Odonto-stomatology of the University of Sciences, Technics and Technologies of Bamako and the Institutional Review Board (IRB) of NIH-NIAID in the United States of America. Written informed consent was obtained from each subject before their participation in the study.

# Results

**Diagnostic performance of the HIV RDT Determine™**

Of the 1303 participants in the study, demographic data were available for 1165 individuals and biological data for 336. Most of the patients were male (60.6%) and most of them (36.8%) were between 30 and 35 years old. A total of 649 patients were confirmed to be HIV infected. (Table 2) summarized these and other data for all the participants.

| Parameter | % (n /N) |
|---|---|
| **Sex** | |
| Male | 60.6 (706/1165) |
| **Age (Years)** | |
| 18-24 | 19.4 (226/1165) |
| 30-35 | 36.8 (429/1165) |
| 35-44 | 24.8 (289/1165) |
| 45-54 | 13.3 (155/1165) |
| 55-64 | 3.7 (44/1165) |
| > 65 | 1.8 (22/1165) |
| **HIV-1 positive only** | 90.7 (589/649) |
| **HIV-2 positive only** | 2.0 (13/649) |
| **HIV-1 and HIV-2 coinfections** | 6.4 (42/649) |
| **CD4 absolute count (cells/μL) n=336** | 355 (164-572)* |
| **CD8 absolute count (cells/μL) n=336** | 860 (500-1232)* |
| **HIV Viral load absolute count (copies/mL) n=336** | 76281 (18991-175346)* |
| *Median (interquartile range) | |

**Table 2**: Demographic and biological characteristics of the study participants.

The prevalence of HIV detected by the Determine™ test was 49.42% (644/1303) while 49.8% (649/1303) were confirmed HIV-positive by the Genscreen™ ELISA test (Figure 2). The

Determine™ test failed to detect 1.23% of the ELISA HIV-positive cases (8/649) and these were deemed to be false negatives of the Determine™ test. From the 646 Determine™ positives, 0.77% (5/649) were deemed false positives when retested by ELISA. Testing the eight Determine™ false negatives by WB produced only three HIV-positives, two of which were positive for HIV-1 and one of which was positive for HIV-2, two indeterminate results and three negatives. Among all the 649 ELISA-positive samples, WB analysis determined that 90.75% (589/649) were of HIV-1 infections, 2% (13/649) HIV-2 and 6.47% (42/649) HIV-1/2 co-infections. In addition, 0.77% (5/649) of these WB tests were indeterminate (Figure 2). Among these five WB-indeterminate samples, three were positive and the two were negative when tested with Determine™.
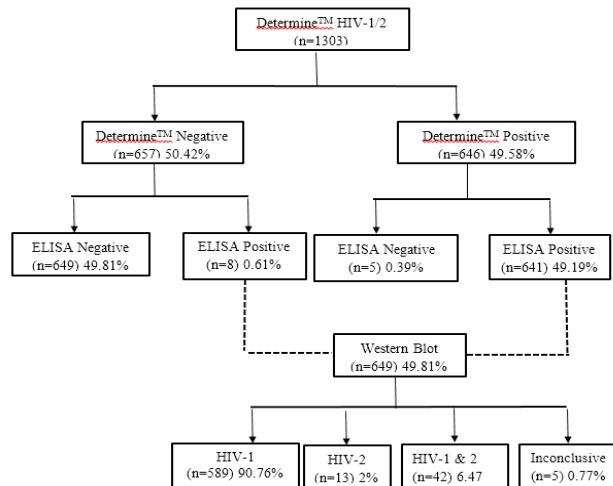


**Figure 2:** Flow Chart showing the diagnostic performance of the Determine™ HIV-1/2 RDT after confirmation using the ELISA and Western blot assays.

**Comparative diagnostic performances of the different HIV RDTs**

Taken together the Determine™ HIV test were positives for 49.19% (641/1303) of the samples tested, with apparent 0.77% (5/646) false-positives and 1.22% (8/657) apparent false-negatives according to the results obtained by the ELISA test. Also, on the basis of the ELISA results, the Determine™ test showed a diagnostic sensitivity of 98.77 % (641 ELISA-confirmed Determine™ positives/649 ELISA positives) and a diagnostic specificity of 99.23% (649 ELISA-confirmed Determine™ negatives/654 ELISA negatives). The predictive positive and negative values were 99.23% [CI 95: 98.20-99.67] and 98.78% [CI 95: 97.62-99.38], respectively (Table 3).

| Parameter (N=1303) | Determine™ HIV-1/2 Test<br>% (n/N) | Confidence interval 95% |
|---|---|---|
| **Diagnostic Sensitivity (%)** | 98.7 (641/649) | 97.6-99.4 |
| **Diagnostic specificity (%)** | 99.2 (649/654) | 99.2-99.7 |
| **Positive predictive value (%)** | 99.2 (641/646) | 98.2-99.7 |
| **Negative predictive value (%)** | 98.7 (649/657) | 97.6-99.4 |
| **Diagnostic accuracy (%)** | 99.0 | 98.3-99.4 |
| **Kappa** | 0.9 | 0.9-1.0 |

**Table 3**: Performance of the Determine™ HIV-1/2 test compared to the HIV ELISA Genscreen™ test.

Of the 1303 samples, the Determine™ test and the Genscreen™ test detected 646 and 649 positive samples, respectively. There were no significant differences between Determine™ HIV-1/2 and Genscreen™ ELISA ($p = 0.933$ and $0.934$) (Table 4).

| HIV Result | Determine™ HIV-1/2 Test<br>% (n/N) | ELISA (Genscreen™ HIV-1/2)<br>% (n/N) | *P* value |
|---|---|---|---|
| Positive | 49.58 (646/1303) | 49.81 (649/1303) | 0.933 |
| Negative | 50.42 (657/1303) | 50.19 (654/103) | 0.934 |
| Total | 100.00 | 100.00 | |

**Table 4**: Comparative diagnostic performances of the Determine™ HIV-1/2 test and the HIV ELISA Genscreen™ test.

Comparing the performance results obtained from the different versions of the Determine™ HIV-1/2 tests released over a period of time showed that the Determine™ test had improved with each new version. As shown in Table 5, the time periods shown represent when the tests were performed. All the versions were compared to the ELISA test The original Determine™ HIV-1/2 test, performed from 2004 to 2010, had a diagnostic sensitivity of 98.4 % [CI 95: 97.04-99.23] and a diagnostic specificity of 99.6 % [CI 95: 98.15- 99.94] (Table 5)., while the diagnostic sensitivity and specificity of the Alere Determine™ HIV-1/2 test, obtained from 2011 to 2014, were 100% [CI 95: 96.53-100] and 99% [CI 95: 97.10-99.66], respectively; and from 2015 to 2017, the Alere Determine™ HIV-1/2 Combo Assay produced 100% diagnostic sensitivity and specificity.

| Rapid diagnostic test | Performance parameters | | | |
|---|---|---|---|---|
| | Sensitivity (%) (95% CI) | Specificity (%) (95% CI) | PPV (%) (95% CI) | NPV (%) (95% CI) |
| Determine™ HIV-1/2 (n=831) | 98.4 (97.04-99.23) | 99.6 (98.15-99.94) | 99.8 (98.92-99.97) | 97.4 (94.99-98.69) |
| Alere Determine™ HIV-1/2 (n=407) | 100.0 (96.53-100) | 99.0 (97.10-99.66) | 97.2 (92.29-99.07) | 100.0 (98.72-100) |
| Alere Determine™ HIV-1/2 Combo (n=65) | 100.0 (79.61-100) | 100.0 (92.86-100) | 100.0 (79.61-100) | 100.0 (92.86-100) |
| SD Bioline™ HIV1/2 (n=19) | 100.0 (72.25-100) | 88.8 (56.50- 98.71) | 90.9 (62.26-98) | 100.0 (67.56-100) |
| Multispot™ HIV-1/HIV-2 (n=95) | 98.2 (90.55-99.68) | 100.00 (91.03-100) | 100.0 (93.47-100) | 97.5 (87.12-99.56) |
| PPV= Positive predictive value; NPV: Negative predictive value; CI= Confidence Interval | | | | |

**Table 5**: Comparative performances of the RDTs Determine™ HIV-1/2, Alere Determine™ HIV-1/2, Alere Determine™ HIV-1/2 Combo, SD Bioline™ HIV-1/2 and Multispot™ HIV-1/HIV-2.

Of the 1303 samples, 19 were also tested by the SD Bioline™ RDT and another 56 by the Multispot™ RDT (Table 4). These samples were also tested using the Determine™ tests. The diagnostic sensitivity and specificity of the SD Bioline™ HIV-1/2 test were 100% [CI 95:72.25-100] and 88.9% [CI 95: 56.50-98.71], respectively, compared to the benchmark ELISA test. The Multispot™ test had a diagnostic sensitivity of 98.2 % [CI 95: 90.55-99.68] and a diagnostic specificity of 100% [CI 95: 91.03-100] compared to the ELISA test. The ability of the Multispot™ HIV-1/2 test to discriminate between HIV-1 and HIV-2 infections was also evaluated using the WB New Lav Blot I and II assays as the gold standard. This resulted with a diagnostic sensitivity of 98.2 % [CI 95: 90.55-99.68] and a diagnostic specificity of 100% [CI 95: 43.85-100]. The 55 HIV positive samples identified by the Multispot™ HIV-1/2 RDT were all HIV-1. Positive and negative predictive values observed with the Multispot™ HIV-1/2 RDT were robust at 100% and 75%, respectively, with only one false negative for HIV-1 and no false positive was obtained when compared to the results of the Western Blot I benchmark (Table 6).

| Parameter (N=59) | Multispot™ HIV-1/2 test | Confidence Interval 95% |
|---|---|---|
| Diagnostic sensitivity (%) | 98.2 (55/56) | 90.6-99.7 |
| Diagnostic specificity (%) | 100.0 (3/3) | 43.9-100 |
| Positive predictive value (%) | 100.0 (55/55) | 93.5-100 |
| Negative predictive value (%) | 75.0 (3/4) | 30.1-95.44 |
| Diagnostic accuracy (%) | 98.3 | 91.0-99.7 |
| Kappa | 0.8 | |

**Table 6**: Performance of the Multispot™ HIV-1/2 test compared to the WB HIV-1 test.

## Discussion

All the HIV RDTs studied demonstrated an excellent performance with the Mali samples and are comparable to the performance of the complex and expensive ELISA and WB HIV assays when used in an area where HIV-1 and HIV-2 co-existed. This study with a large sample size that took place over a long period of time showed that the performance of the Determine™

HIV-1/2 RDTs improved over time. This proved the validity and the usefulness of these relatively cost-effective tests in low-resource settings, despite that the development of these assays were usually based on HIV strains circulating in high-income countries.

The Determine™ HIV-1/2 test and the Alere Determine™ HIV-1/2 test results obtained in this study are comparable to the 100% diagnostic sensitivity and 98.93% diagnostic specificity reported by the WHO for the recent version of Alere Determine HIV-1/2, version RoW [20]. The diagnostic sensitivity and specificity of the Alere Determine™ HIV-1/2 Combo test obtained are also consistent with those reported for other populations in similar studies [21,22]. However, discordant results on the diagnostic sensitivity of the Determine™ HIV-1/2 Combo test were also reported by other authors [23-25]. Additionally, some studies showed that the Alere Determine™ HIV-1/2 Combo could diagnose HIV-1 infection at earlier disease phases using plasma or serum than in whole blood [26,27]. The positive and negative predictive values obtained with the Determine™ test (average of all versions) were 99.23% [CI 95 : 98.20-99.67] and 98.78% [CI 95 : 97.62-99.38], respectively. These results are comparable to those reported in Cameroon [28] and Tanzania [29,30] surveys. A total of thirteen discordant samples, comprising eight false negatives and five false-positives, between the Determine™ tests (total of all versions) and the ELISA Genscreen™ test were observed. These results were lower than those of other studies from sub-Saharan Africa [31,32]. It is important to note that the performance of Determine™ had improved with the latest version as compared to HIV ELISA assay.

For the SD Bioline™ HIV-1/2 test, the diagnostic sensitivity obtained in this study (100%) is comparable to that reported in a Cameroon study (100%) [30,33,34]. However, the diagnostic specificity (88.89%) is lower than that reported in a study in the United States in 2017 (100%) [24]. In this study, only 19 samples were tested with the SD Bioline™ test which was not enough to provide an accurate diagnostic sensitivity and specificity for the assay. However, the results provided some preliminary data to be confirmed by a larger study. The SD Bioline™ test was reported by others to have a poor discrimination power of the HIV types [35,36]. Likewise, only 56 samples were tested by the Multispot™ HIV-1/2 test which was not enough to draw a strong conclusion on performance of the assay. The diagnostic sensitivity of the Multispot™ HIV-1/2 test compared to WB for HIV-1 detection observed in this study was 98.21% [CI 95: 90.55-99.68]. This data is comparable to the 99.9% reported by Lucia V. Torian *et al.* in the USA [37]. These apparent differences between populations may suggest a need to evaluate these assays for each specific area where they will be used. The high levels of genetic diversity and high mutation rates of the virus may also require continuous evaluation of these assays for each specific population. Further

molecular tests (sequencing) on the five indeterminate WB test results revealed two HIV-1 cases.

All the samples were tested by Determine™ but only a few were tested by Multispot™ and SD Bioline™, depending on their availability. In addition, PCR was not performed to further evaluate the indeterminate test results. It would be interesting to employ PCR followed by sequencing in the indeterminate samples in order to identify and characterize any HIV strains present, since these HIV RDTs were typically designed to detect HIV strains circulating in high-income countries. There were more HIV-1/2 dual positive samples in this study than HIV-2 only cases. This could be specific to this population or could indicate false HIV-1/2 dual positives. Problems with false HIV-1/2 dual positives were described in several studies, including a recent report from Guinea-Bissau [38]. A relevant future study would be to further analyze this type of samples by HIV PCR. Nevertheless, our study proved that RDTs have a very high diagnostic sensitivity and specificity for HIV diagnosis in our settings and should be used.

## Conclusion

Following the WHO's recommendation, the diagnostic performance of three rapid diagnostic tests for HIV detection in Mali were evaluated. All these tests showed excellent performance with the Alere Determine™ HIV-1/2 Combo assay scoring the highest detection rate. Also, the Multispot™ test had a good concordance with WB in discriminating HIV-1 from HIV-2 and could be used as an alternative to WB. Regular routine evaluation of these tests is also highly recommended.

## Acknowledgments

## Financial support and sponsorship

## Reference

1. Barré-Sinoussi F, Chermann JC, Rey F, Nugeyre MT, Chamaret S (2004) Isolation of a T-lymphotropic retrovirus from a patient at risk for acquired immune deficiency syndrome (AIDS). 1983 Rev Invest Clin 56: 126-129.

2. UNAIDS (2017) Fact Sheet_ Latest Statistics on the State of the AIDS Epidemic.

3. CPS (2014) Enquête démographique et de santé au Mali 2012-2013.

4. Onusida (2017a) En finir avec le sida - Progresser vers les cibles 90-90-90 Synthèse.

5. Kharsany ABM, Karim QA (2016) HIV Infection and AIDS in Sub-Saharan Africa: Current Status, Challenges and Opportunities. Open AIDS J 10: 34-48.

6. Lyamuya EF, Aboud S, Urassa WK, Sufi J, Mbwana J, et al. (2009) Evaluation of simple rapid HIV assays and development of national rapid HIV test algorithms in Dar es Salaam, Tanzania. BMC infectious diseases 9: 19.

7. White HL, Kristensen S, Coulibaly DM, Sarro YDS, Chamot E (2009) Prevalence and predictors of HIV infection amongst Malian students. AIDS Care 21: 701-707.

8. Chanteau S, Nato F, Migliani R (2003) Interest in rapid immunochromatography tests for surveillance of characteristic diseases epidemic in developing countries: the example of plague in Madagascar. Med Trop (Mars) 63: 574-576.

9. Hocini H, Andreoletti L (2009) Méthodes d'analyse et de suivi de l'infection par les virus de l'immunodéficience humaine. Revue Francophone des Laboratoires 2009: 39-48.

10. Alexander TS (2016) Human Immunodeficiency Virus Diagnostic Testing: 30 Years of Evolution. Clin Vaccine Immunol 23: 249-253.

11. Gautheret-Dejean A (2013) Actualités sur les tests rapides d'orientation diagnostique de l'infection à VIH : législation, performances, avantages et inconvénients. Immuno-analyse & Biologie Spécialisée 28: 8-17.

12. Global programme on AIDS (1992) Recommendations for the selection and use of HIV antibody tests. Releve epidemiologique hebdomadaire 67: 145-149.

13. Clavel F (1987) HIV-2 the West African AIDS virus. Editorial review. AIDS 1 : 135-140.

14. De Silva TI, Cotten M, Rowland-Jones SL (2008) HIV-2: the forgotten AIDS virus. Trends in Microbiology 16: 588-595.

15. Ekouevi DK, Balestre E, Coffie PA, Minta D, Messou E, et al. (2013) Characteristics of HIV-2 and HIV-1/HIV-2 Dually Seropositive Adults in West Africa Presenting for Care and Antiretroviral Therapy: The IeDEA-West Africa HIV-2 Cohort Study. PLoS ONE 8, e66135.

16. Romieu I, Marlink R, Kanki P, M'Boup S, Essex M (1990) HIV-2 link to AIDS in West Africa. J Acquir Immune Defic Syndr 3: 220-230.

17. Campbell-Yesufu OT, Gandhi RT (2011) Update on human immunodeficiency virus (HIV)-2 infection. Clin Infect Dis 52: 780-787.

18. Gilbert PB, McKeague IW, Eisen G, Mullins C, Guéye-Ndiaye A, et al. (2003) Comparison of HIV-1 and HIV-2 infectivity from a prospective cohort study in Senegal. Statistics in medicine 22 : 573-593.

19. WHO (2015) Consolidated Guidelines on HIV Testing Services: 5Cs: Consent, Confidentiality, Counselling, Correct Results and Connection 2015, Geneva.

20. World Health O (2016) WHO Prequalification of Diagnostics Programme PUBLIC REPORT.

21. Rosenberg NE, Kamanga G, Phiri S, Nsona D, Pettifor A, et al. (2012) Detection of acute HIV infection: a field evaluation of the determine® HIV-1/2 Ag/Ab combo test. J Infect Dis 205: 528-534.

22. Smallwood M, Vijh R, Nauche B, Lebouché B, Joseph L, et al. (2016) Evaluation of a Rapid Point of Care Test for Detecting Acute and Established HIV Infection, and Examining the Role of Study Quality on Diagnostic Accuracy: A Bayesian Meta-Analysis. PLoS ONE 11: e0149592.

23. Livant E, Heaps A, Kelly C, Maharaj R, Samsunder N, et al. (2017) The fourth generation Alere(TM) HIV Combo rapid test improves detection of acute infection in MTN-003 (VOICE) samples. Journal of clinical virology : the official publication of the Pan American Society for Clinical Virology 94: 15-21.

24. Stafylis C, Klausner JD (2017) Evaluation of two 4th generation point-of-care assays for the detection of Human Immunodeficiency Virus infection. PLoS ONE 12: e0183944.

25. Stekler JD, Ure G, O'Neal JD, Lane A, Swanson F, et al. (2016) Performance of Determine Combo and other point-of-care HIV tests among Seattle MSM. J Clin Virol 76: 8-13.

26. Masciotra S, Luo W, Westheimer E, Cohen SE, Gay CL, et al. (2017) Performance evaluation of the FDA-approved Determine HIV-1/2 Ag/Ab Combo assay using plasma and whole blood specimens. Journal of clinical virology : the official publication of the Pan American Society for Clinical Virology 91: 95-100.

27. Parker MM, Bennett SB, Sullivan TJ, Fordan S, Wesolowski LG, et al. (2018) Performance of the Alere Determine HIV-1/2 Ag/Ab Combo Rapid Test with algorithm-defined acute HIV-1 infection specimens. Journal of clinical virology : the official publication of the Pan American Society for Clinical Virology 104: 89-91.

28. Njouom R, Ngono L, Mekinda-Gometi DD, Nde CK, Sadeuh-Mba SA, et al. (2017) Evaluation of the performances of twelve rapid diagnostic tests for diagnosis of HIV infection in Yaounde, Cameroon. Journal of virological methods. 243:158-163.

29. Mayhood MK, Afwamba IA, Odhiambo CO, Ndanu E, Thielman NM, et al. (2008.) Validation, performance under field conditions, and cost-effectiveness of Capillus HIV-1/HIV-2 and determine HIV-1/2 rapid human immunodeficiency virus antibody assays using sequential and parallel testing algorithms in Tanzania. J Clin Microbiol 46: 3946-3951.

30. Njouom R, Ngono L, Mekinda-Gometi DD, Ndé CK, Sadeuh-Mba SA, et al. (2017) Evaluation of the performances of twelve rapid diagnostic tests for diagnosis of HIV infection in Yaounde, Cameroon. J Virol Methods 243 : 158-163.

31. Kosack CS, Shanks L, Beelaert G, Benson T, Savane A, et al. (2017a) HIV misdiagnosis in sub-Saharan Africa: performance of diagnostic algorithms at six testing sites. J Int AIDS Soc 20: 21419.

32. Kosack CS, Shanks L, Beelaert G, Benson T, Savane A, et al. (2017) Designing HIV Testing Algorithms Based on 2015 WHO Guidelines Using Data from Six Sites in Sub-Saharan Africa. J Clin Microbiol (10): 3006-3015.

33. Lodiongo DK, Bior BK, Dumo GM, Katoro JS, Mogga JJH, et al. (2018) Field evaluation of SD BIOLINE HIV/Syphilis Duo assay among pregnant women attending routine antenatal care in Juba, South Sudan. PLoS ONE 13: e0205383.

34. Shakya G, Singh DR, Ojha HC, Ojha CR, Mishra SK, et al. (2016) Evaluation of SD Bioline HIV/syphilis Duo rapid test kits in Nepal. BMC infectious diseases 16: 450.

35. Chaillet P, Tayler-Smith K, Zachariah R, Duclos N, Moctar D, et al. (2010) Evaluation of four rapid tests for diagnosis and differentiation of HIV-1 and HIV-2 infections in Guinea-Conakry, West Africa. Transactions of the Royal Society of Tropical Medicine and Hygiene 104: 571-576.

36. Honge BL, Bjarnason Obinah MP, Jespersen S, Medina C, Te Dda S, et al. (2014) Performance of 3 rapid tests for discrimination between HIV-1 and HIV-2 in Guinea-Bissau, West Africa. J Acquir Immune Defic Syndr 65: 87-90.

37. Torian LV, Forgione LA, Punsalang AE, Pirillo RE, Oleszko WR (2011) Comparison of Multispot EIA with Western blot for confirmatory serodiagnosis of HIV. Journal of clinical virology : the official publication of the Pan American Society for Clinical Virology 52 Suppl 1:S41-44.

38. Honge BL, Jespersen S, Medina C, Te DS, da Silva ZJ, et al. (2018) The challenge of discriminating between HIV-1, HIV-2 and HIV-1/2 dual infections. HIV medicine 19: 403-410.