Commentary | HIV Testing

Utilization of Rapid Diagnostic Testing in sub-Saharan Africa: Challenges and Effects on HIV Prevention

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ABSTRACT

The human immunodeficiency virus (HIV) remains a global threat to health. To prevent and control the disease caused by the virus, developed and developing countries continue to invest heavily in research and equipment so as to accurately detect the virus. The utilization of highly sensitive and effective rapid diagnostic tests (RDTs) have the potential to detect HIV in high-burden countries, especially those in sub-Saharan Africa (SSA). Yet, in SSA, challenges associated with HIV-RDT result inaccuracy, HIV misdiagnosis, poor tester capacity, and the improper storage of HIV-RDT kits have negatively impacted the benefits, and threaten to undermine HIV prevention. This paper focuses on the utilization of RDTs in HIV diagnosis in SSA, HIV-RDT challenges, and the effects of HIV-RDT challenges on HIV prevention. Subsequent to reviewing available literature, the authors found that although HIV-RDTs can negatively impact HIV-prevention efforts in SSA due to the likelihood of false positive HIV diagnoses, they generally provide quick results for people in resource poor settings, and do not require them to return to the testing sites to obtain their results. Obtaining accurate rapid HIV results means people who test positive can immediately seek care and take steps to prevent future transmission of the virus.

Key words: • HIV • Rapid HIV testing • HIV prevention • Sub-Saharan Africa

Introduction

In 2019, about 38 million people were living with the human immunodeficiency virus (HIV) globally. Of this population, 36.2 million were adults and 1.8 million were children (<15 years old). Accounting for only 11% of the world’s population, sub-Saharan Africa (SSA) continues to be the hardest hit region in the world, with an estimated 20.7 million people (54%) in East and Southern Africa, and 4.9 million (13%) in West and Central Africa, living with the virus. While SSA was able to reduce HIV incidence by 14% between 2010 and 2015 in East and Southern Africa, and by 8% in West and Central Africa due to a heightened focus on prevention, treatment, and care, challenges remain. SSA still accounts for two-thirds of the global HIV incidence.

Access to HIV testing services is crucial to HIV prevention. Knowing one’s HIV status is the
Recognizing the critical role of HIV testing in HIV prevention, the Joint United Nations Program on HIV/AIDS (UNAIDS) launched the 90-90-90 targets in 2015, with the goal that by 2020, “90% of all people with HIV will know their status, 90% will be diagnosed and receive sustained antiretroviral therapy (ART), and 90% of people receiving ART will achieve viral suppression.” In 2017, UNAIDS indicated that the greatest barrier to achieving the 90-90-90 targets will be access to HIV testing in SSA, where more than two-thirds of people living with HIV reside.

Prior to the introduction of rapid tests for HIV diagnosis, HIV tests were primarily done in advanced laboratories. The long wait times for the receipt of test results (1–2 weeks) contributed to low HIV testing uptake, the non-return of people for their results, and consequent missed opportunities for linkage of HIV positive persons to HIV treatment and care services. To address this problem, the World Health Organization (WHO) recommended that tests that relied solely on laboratories be replaced with simpler methods like rapid diagnostic tests (RDTs), as such tests provide same day results within an average of 10 minutes and can be performed by non-laboratory staff. The utilization of RDTs have made the delivery of HIV testing services in SSA much easier and faster. Globally, the WHO recommends an HIV testing system that comprises 2-3 RDTs (screening, confirmatory, tiebreaker) based on their clinical sensitivity and specificity (usually up to ≥99%).

In Ghana, the First Response® HIV1/2, OraQuick® HIV1/2, and INNO-LIA® HIV I/II Score are the RDTs used for HIV screening, confirmatory, and tiebreaker tests respectively. These tests are listed in the WHO prequalified RDTs for 2020. In Uganda, Determine™ HIV-1/2, HIV ½ Stat-Pak® Dipstick, and Uni-Gold™ HIV are the RDTs used and in South Africa, the GeneXpert cartridge-based platform is used to rapidly test for tuberculosis and HIV viral load. The choice of HIV RDT testing systems in many SSA countries usually depends on the decision of country ministry of health officials and the availability of funding from foreign donors.

HIV-RDT Challenges

HIV-RDT challenges associated with HIV prevention in SSA are due to several factors such as the inaccuracy of test results, HIV misdiagnosis, tester capacity, and the storage of kits at inappropriate temperatures.

Inaccuracy of RDT Results

A major issue with the utilization of RDTs in HIV diagnosis in SSA is their inaccuracy, poor sensitivity and specificity, and high rates of false HIV positive results. Sensitivity of RDTs is the probability of getting an HIV positive test result when the disease is truly present, and specificity is the probability of getting a negative test result when the disease is truly absent. The score of these variables range from 0-100%. According to the WHO, HIV- RDTs should
have a sensitivity of at least 99% and a specificity of at least 98%. The results of a study conducted by researchers on the utilization of Determine, a commonly used HIV-RDT in Cameroun, showed a sensitivity result of 100% and only a 91.5% specificity. However, when the samples were retested, 129 of the 295 people who were initially diagnosed as HIV-positive, were actually HIV-negative. A similar situation occurred in Uganda. In the Rakai district of Southwestern Uganda, an area with high HIV prevalence, three of the most commonly used HIV-RDTs (Determine™, STAT PAK®, and Uni-Gold™) revealed critical inaccuracies in results. About 45% of patients who received HIV positive results received them in error.

**HIV Misdiagnosis**

Results from HIV-RDTs can sometimes be difficult to interpret, especially when tests lines or bands are faint. In such cases, results are left to the subjective interpretation of testers, which most often leads to false positive HIV diagnosis. In a recent assessment of HIV-RDT administration in South Africa, issues with subjective interpretation of results were identified. This led to the misdiagnosis of some patients. In another incident that occurred between 2004 and 2005, Médecins Sans Frontières (MSF) staff offering HIV-RDTs in SSA, misdiagnosed 44 people in the Democratic Republic of Congo, Burundi, and Ethiopia with HIV.

**Tester Capacity**

Low staff capacity, coupled with high workload, and the lack of comprehensive quality management systems, have been found to contribute to HIV-RDT result errors. While the number of people receiving HIV-RDTs in SSA has significantly increased in the past few years, the number of health personnel available to administer these tests has not increased proportionally. Of those available to offer the service, several have not been adequately trained on how to adhere to standard operating procedures and to maintain quality assurance such as tester competency, pre-test preparations, quality control, and record keeping. Inadequate staff training in HIV-RDT methodology is costly. This is because it can negatively affect testing accuracy. The results of a study conducted in South Africa showed that the sensitivity and specificity of HIV-RDTs performed by lay nurses and counsellors were 92.5 – 97.3% and 97.6 – 98.2% respectively, while those performed by trained laboratory technicians showed a 100% performance. The researchers concluded that the inadequate training of lay nurses and counsellors may have contributed to the discrepancies and difficulties in the interpretation of RDT results. Several other HIV-RDT studies conducted in SSA identified lack of adequate tester testing capacity to be responsible for some of the false positive and negative HIV diagnosis.

**Poor HIV RDT Kit Storage**

HIV-RDTs are to be stored at ambient temperatures specified by manufacturers (36°- 86° F or 2-30°C) and used before their expiration dates. Yet, in some SSA countries, HIV-RDTs are stored in suboptimal conditions and those nearing expiration, are not discarded. This affects the quality and accuracy of test results. Researchers of a quality assurance study conducted to test the effects of higher than manufacturer-specified temperatures for three HIV-RDTs (OraQuick, Determine 1/2™ and Uni-Gold™) on 378 participants at Ndirande Health Centre in Blantyre, Malawi, found seven false HIV negative results among test kits that were stored at suboptimal temperatures. Facente et al also found a significant decline in test specificity of OraQuick ADVANCE® tests that were used a month after expiration.

**HIV-RDT Challenge Effects on HIV Prevention and Recommendations**

**Testing Credibility**

Poorly trained and inexperienced staff have the tendency to increase the likelihood of inaccurate interpretation of HIV-RDT results. Inaccurate results can lead to low HIV testing uptake, negate the goal and credibility of HIV-RDTs, and create missed opportunities for linking HIV positive people to care and prevention services. Inaccurate results can also cause the unintentional transmission of HIV to previously uninfected people. As HIV-RDT testing technology is rapidly evolving and is frequently
utilized in SSA, appropriate health personnel need to be trained, certified, and provided with routine support and supervision to ensure that testing procedures are followed correctly, and results are accurately interpreted. They also need to be trained in quality assurance, so they can ensure that expired kits are not used. Doing this will increase public trust and confidence in the technology.

To increase their efficacy and accuracy, HIV-RDT kits need to be stored at prescribed temperatures, and those nearing expiration need to undergo quality control checks before they are used. When it comes to temperature, it can be monitored by placing thermometers in storage areas where the kits are stored. This will enable site supervisors to surveil storage temperature ranges and to preserve kit quality. Temperature control logs can be posted outside storage areas so readings can be checked and recorded daily. Investing in proper storage protocols and facilities will ensure that manufacturer recommended instructions are observed. This will minimize false HIV diagnosis and wastage.

**Social, Emotional, and Economic Consequences**

The social and emotional consequences of a false HIV positive diagnosis can be severe and more difficult to handle than the physical effects of the infection. A false positive HIV result can put people at risk of physical and verbal abuse, abandonment, and ostracization by friends, family, and community members. These outcomes are disproportionately higher among women, as they are more likely than men to access health care facilities and to be tested for HIV. In addition to psychological trauma, an HIV misdiagnosis can also lead to unnecessary ART initiation and stigma. Some researchers who conducted studies on the effects of false HIV positive diagnosis on people found that it led to divorce, the incurring of unnecessary expenses due to clinical visits, and physical harm in some communities in the Democratic Republic of Congo, Burundi, Ethiopia, and Ghana.

To address the socio-economic and emotional consequences associated with the inaccurate interpretation of HIV-RDT results, health workers need to work with a “second-reader” to validate test results when they are unsure before pronouncing a diagnosis. Retesting also needs to be done as part of routine service prior to putting people on ART. This will help to save people falsely diagnosed from debt and financial ruin.

**Conclusion and Global Health Implications**

HIV-RDTs have proven to be of great benefit in SSA. Although these tests have the tendency to negatively impact HIV-prevention efforts due to the likelihood of false HIV positive diagnosis, they generally provide quick results and do not require a return to testing sites for results. Providing accurate HIV-RDT results means people who test positive can immediately seek care and take steps to prevent future transmission of the virus. The challenges caused by the inaccurate interpretation of HIV-RDT results have serious social, economic, and emotional consequences and thus, need to be addressed. With the need to scale-up HIV testing, diagnosis and linkage to care and treatment in SSA, a parallel push to improve the quality of HIV testing services and accurate diagnosis is essential.

**Key Messages**

- The utilization of RDTs have made the delivery of HIV testing services in SSA much easier and faster.
- A major issue with the utilization of RDTs in HIV diagnosis in SSA is their inaccuracy, poor sensitivity and specificity, and high rates of false HIV positive results.
- Providing accurate HIV-RDT results means people who test positive can immediately seek care and take steps to prevent future transmission of the virus.

**Compliance With Ethical Standards**

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References

1. U.S. Department of Health and Human Services. Global Statistics. The Global HIV/AIDS Statistics. HIV.gov. https://www.hiv.gov/hiv-basics/overview/data-and-trends/global-statistics. Published July 2020. Accessed August 02, 2020.

2. Martin J. Africa’s new strategies to defeat HIV/AIDS. Africa Renewal. https://www.un.org/africarenewal/magazine/december-2016-march-2017/africas-new-strategies-defeat-hiv-aids. Published March 2017. Accessed August 02, 2020.

3. World Health Organization. 90-90-90 An ambitious treatment target to help end the AIDS epidemic. Joint United Nations Programme on HIV and AIDS. http://www.unaids.org/sites/default/files/media_asset/90-90-90_en_0.pdf. Published October 2014. Accessed August 02, 2020.

4. Joint United Nations Programme on HIV/AIDS. Global AIDS Response Progress Reporting 2016 - Construction of core indicators for monitoring the 2011 United Nations Political Declaration on HIV and AIDS. https://www.slideshare.net/Ukraine_CDC/global-aids-response-progress-reporting-2016. Published January 2016. Accessed August 02, 2020.

5. Hutchinson AB, Branson BM, Kim A, Farnham PG. A meta-analysis of the effectiveness of alternative HIV counseling and testing methods to increase knowledge of HIV status. AIDS. 2006; 20(12): 1597-1604.

6. Sullivan PS, Lansky A, Drake A, HITS-2000 Investigators. Failure to return for HIV test results among persons at high risk for HIV infection: results from a multistate interview project. J Acquir Immune Defic Syndr. 2004; 35(5): 511-518.

7. World Health Organization. WHO recommends countries move away from the use of western blotting and line immunoassays in HIV testing strategies and algorithms. https://www.who.int/publications/i/item/move-away-from-western-blotting-and-line-immunoassays-in-hiv-testing. Published November 2019. Accessed August 02, 2020.

8. Mkwanazi NB, Patel D, Newell ML, et al. Rapid testing may not improve uptake of HIV testing and same day results in a rural South African community: a cohort study of 12,000 women. PLoS One. 2008; 3(10): e3501.

9. National Department of Health, South Africa. www.mchandaids.org

HIV and AIDS and STI National Strategic Plan for South Africa 2007–2011. Joint United Nations Programme on HIV/AIDS. https://gcwa.unaids.org/sites/womenandaidst/files/South-Africa-AIDS-National-Strategic-Plan-2007-2011-part1.pdf. Published March 2007. Accessed August 02, 2020.

10. World Health Organization. Guidelines for the management of sexually transmitted infections. www.emro.who.int/aiecf/web79.pdf. Published 2003. Accessed August 02, 2020.

11. Spacie L, Lutwama F, Shihab HM, et al. Diagnostic Accuracy of Ultrasensitive Heat-Denatured HIV-1 p24 Antigen in non-B Subtypes in Kampala, Uganda. Int J STD AIDS. 2011; 22(6): 310-314.

12. Crump J, Scott L, Msuya E, Morrissey A, Venter W, Stevens W. Evaluation of the Abbott M2000rt RealTime HIV-1 assay with manual sample preparation compared with the ROCHE COBAS AmpliPrep/AMPLICOR HIV-1 MONITOR v1.5 using specimens from East Africa. J Virol Methods. 2009; 162 (1-2): 218-222.

13. Murtagh M. HIV/AIDS Diagnostics Technology Landscape. https://marketbookshelf.com/publications/hiv/aids-diagnostics-technology-landscape-semi-annual-update-2012/. Published October 2012. Accessed August 01, 2020.

14. World Health Organization. WHO consolidated guidelines on HIV testing services. http://apps.who.int/iris/bitstream/10665/179870/1/9789241508926_eng.pdf?ua=1&ua=1. Published July 2015. Accessed July 31, 2020.

15. Delaney K, Branson B, Uniyal A, et al. Evaluation of the Performance characteristics of 5 rapid HIV antibody tests. Clin Infect Dis. 2011; 52(2): 257-263.

16. Tetteh AK, Agyarko E. Discordant HIV Test Results: Implications on Perinatal and Haemotransfusion Screening for HIV Infection, Cape Coast, Ghana. J Sex Transm Dis. 2017; 2017: 2857397.

17. World Health Organization.WHO list of prequalified in vitro diagnostic products. https://www.who.int/diagnostics_laboratory/evaluations/200507_prequalified_product_list.pdf?ua=1. Published May 2020. Accessed August 01, 2020.

18. Galiwango R, Musoke R, Lubayi L, et al. Evaluation of current rapid HIV test algorithms in Rakai, Uganda. J Virol Methods. 2013; 192(1-2): 25-27.

19. Karim QA, Abdool SS. COVID-19 affects HIV and
Tuberculosis care. Science. science.sciencemag.org/content/369/6502/366. Published July 2020. Accessed August 01, 2020.

20. World Health Organization and Centers for Disease Control and Prevention. Guidelines for appropriate evaluations of HIV testing technologies in Africa. https://apps.who.int/iris/bitstream/handle/10665/246182/GuiEvalHIV-eng.pdf. Published in 2002. Accessed August 01, 2020.

21. Acharya P. Sensitivity and specificity of a rapid test- what does it mean? Swasthyakhabar. https://swasthyakhabar.com/story/31819. Published April 2020. Accessed August 06, 2020.

22. World Health Organization. Diagnostics for HIV diagnosis of the Consolidated Guidelines on HIV testing services. https://www.who.int/hiv/pub/guidelines/hiv-testing-services/en/. Published July 2015. Accessed August 06, 2020.

23. Unite for Sight. Challenges and Failures of HIV Screening with Rapid Tests. http://www.uniteforsight.org/health-screenings/hiv. Published n.d. Accessed August 06, 2020.

24. Mwisongo A, Peltzer K, Mohlabane N, Tutshana B. The quality of rapid HIV testing in South Africa: an assessment of testers’ compliance. Afr Health Sci. 2016; 16(3): 646-654.

25. Wolpaw BJ, Mathews C, Chopra M, et al. The failure of routine rapid HIV testing: a case study of improving low sensitivity in the field. BMC Health Serv Res. 2010; 10(1): 1-4.

26. Shanks L, Klarkowski D, O’Brien DP. False positive HIV diagnoses in resource limited settings: operational lessons learned for HIV programmes. PLoS One. 2013; 8(3): e59906.

27. Grusky O, Roberts KJ, Swanson AN. Failure to return for HIV test results: a pilot study of three community testing sites. J Int Assoc Physicians AIDS Care (Chic). 2007; 6(1): 47-55.

28. Johnson CC, Fonner V, Sands A, et al. To err is human, to correct is public health: a systematic review examining poor quality testing and misdiagnosis of HIV status. J Int AIDS Soc. 2017; 20(6): 21755.

29. Shanks L, Siddiqui MR, Kliescikova J, et al. Evaluation of HIV testing algorithms in Ethiopia: the role of the tie-breaker algorithm and weakly reacting test lines in contributing to a high rate of false positive HIV diagnoses. BMC Infect Dis. 2015; 15:39.

30. Facente SN, Dowling T, Vittinghoff E, Sykes DL, Colfax GN. False positive rate of rapid oral fluid HIV tests increases as kits near expiration date. PLoS ONE. 2009; 4(12): e8217.