A Review of the Use of Rapid HIV Testing in Community Settings, With Specific Reference to Australia

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Abstract: Rapid HIV tests are used routinely as screening tests at the point of care in community settings in many developed and developing overseas countries, with reported clinical and operational benefits. In Australia, the uptake of rapid HIV testing has been limited to its use as a reference test in laboratories, but the 2011 National HIV Testing Policy now provides a quality-ensured framework for its use in community settings. Rapid HIV testing in Australia should be targeted where HIV prevalence rates are higher such as in men who have sex with men in urban settings, rather than rural, remote, or indigenous settings where HIV prevalence rates are lower. Barriers to uptake of rapid testing include current lack of testing rebates and high costs for registration of kits.

Key Words: point-of-care testing, HIV, AIDS, rapid HIV test, Australia

In 2009, more than 2.6 million people became newly infected with HIV worldwide, raising the total number of people living with HIV to an estimated 33.3 million.1 AIDS is now the leading cause of death among young adults globally.2 Because of the epidemic proportions of HIV/AIDS, particularly in Africa and Asia, major initiatives such as the Global Fund for AIDS, Tuberculosis, and Malaria; the World Health Organization’s (WHO’s) Three by Five Initiative; and the US Government’s Emergency Plan for AIDS Relief have been implemented to assist with HIV treatment and prevention.2 These initiatives mean that millions of HIV tests will need to be performed to identify HIV-positive individuals, allowing them to access treatment and encouraging them to change their behavior in a way that reduces the risk of transmitting HIV to others.2,3 However, performing such a large number of tests using conventional laboratory-based HIV blood testing is not practical in many settings because of limited access to laboratories and trained laboratory workers, the cost of laboratory testing, and a limited number of persons attending HIV testing clinics.4,5,6 Therefore, the introduction of rapid HIV tests is seen as a viable method for increasing HIV testing rates worldwide,4,5 a rationale that is supported by UNAIDS and WHO.6

In Australia, more than 21,000 people are currently living with HIV infection, with around 1000 new cases of HIV diagnosed annually.7 In 2006 to 2010, 66% of new HIV diagnoses in Australia occurred among men who have sex with men (MSM), 25% through heterosexual contact, and 3% due to injecting drug use.7 Notification rates of HIV and AIDS in Australia are similar for the indigenous and nonindigenous populations.8

Of the 5177 new diagnoses of HIV infection that occurred in Australia in 2006–2010, only 1481 had evidence of newly acquired infection. This means that as many as 70% may have been unaware of their HIV-positive status for more than a year.9 As early diagnosis is critical for controlling HIV infection and preventing HIV transmission, regular testing is essential among populations at increased risk of HIV infection, such as MSM.9 In Australia, clinical guidelines recommend HIV testing be performed at least once a year for MSM or every 3 to 6 months for higher-risk MSM including those who have multiple partners, attend sex-on-premises venues, or use recreational drugs.10

A recent study found that, despite these recommendations, less than 40% of MSM attending primary care clinics were retested after a year, whereas less than 20% of the higher-risk MSM were retested after 6 months.9

Australia’s Sixth National HIV Strategy for 2010–2013 states that although Australia maintains a high level of HIV testing, a continued pattern of late diagnosis implies that there is room for improvement.11 The priority actions in HIV testing are to increase the number of people who seek HIV testing and the rate of testing among higher-risk populations (thus decreasing the number of undiagnosed HIV cases in the community) and to promote HIV testing among gay men.11 Strategies to improve HIV testing rates in Australia include prioritized research of rapid HIV testing for use in clinical and community settings with high HIV prevalence and the assessment of programs that have successfully introduced rapid HIV testing to comparable countries.11 Recent reports suggest that the increased availability of rapid HIV testing has succeeded in attracting a high proportion of MSM who have never been previously tested for HIV, with very high positive yields being recorded from the tests performed.12

HIV TESTING IN AUSTRALIA

The 2011 National HIV Testing Policy lists a number of basic principles, which state that HIV testing in Australia must be confidential and voluntary and include prior informed consent. It must be of the highest possible analytical standard and timely, of benefit to the person being tested, and accessible to all at-risk persons. The policy also states that testing is critical to understanding the epidemiology of HIV infection in Australia.13

Current standard HIV diagnostic testing in Australia takes place in a laboratory setting using one of many commercially available Enzyme Immunoassays (EIAs) to screen for HIV by detecting HIV antibodies in a serum or plasma sample.6,14 Given the extremely high negative predictive values of these tests, negative samples are immediately diagnosed as “anti-HIV negative.”15 However, samples that give a reactive screening result must be retested using EIA, and any presumptive HIV-positive results are then confirmed by Western blot, a test that is more specific for HIV antibodies but is more expensive.5,14 New HIV diagnoses are often confirmed using a second blood
sample from the patient to ensure that sample misidentification did not occur during the testing process.\textsuperscript{15}

In addition to the large number of commercially available EIA tests approved for use in Australia by the Therapeutic Goods Administration (TGA), a small number of rapid HIV tests are also listed on the Australian Register of Therapeutic Goods (ARTG).\textsuperscript{14,16} These include the Determine HIV-1/2 Combo (Alere, Sinnamon Park, Queensland, Australia), Multispot HIV-1/HIV-2 (Bio-Rad Laboratories, Gladesville, New South Wales, Australia), and Serodia HIV (Siemens Healthcare Diagnostics, Bayswater, Victoria, Australia). However, until very recently, the use of these rapid HIV tests in Australia has been restricted to supplemental tests in diagnostic or confirmatory testing strategies in a laboratory setting, with their use as standard screening tests in community-based clinical settings not supported. The new Australian National HIV Testing Policy, published in 2011, approves the use of rapid testing for presumptive HIV screening in community settings, with a number of provisos that include staff performing rapid testing have received appropriate training, testing is conducted under the auspice of an accredited laboratory, quality assurance (QA) programs are in place, appropriate counseling services are available, and reactive results are sent for confirmatory testing at an accredited HIV testing laboratory.\textsuperscript{17}

GLOBAL EVIDENCE FOR AND AGAINST RAPID HIV TESTING

Despite Australia’s caution to take up rapid HIV testing, it has been effectively introduced in the United States, Canada, the United Kingdom, and many parts of Europe.\textsuperscript{6,17} The primary aim for the implementation of rapid HIV testing in these countries varied depending on the particular setting.\textsuperscript{18} In places where there was a low follow-up rate due to people presenting for standard HIV testing but not returning to collect their results, rapid HIV testing was introduced to increase the number of people aware of their HIV status.\textsuperscript{14,16,17} In areas of high HIV prevalence but low HIV testing rates, the aim of introducing rapid HIV testing was to increase testing rates and thus decrease the number of HIV-positive individuals unaware of their status so that appropriate care and support services could be arranged.\textsuperscript{16}

Individuals who are newly infected with HIV but remain undiagnosed contribute disproportionately to new HIV infections among MSM. In some countries, greater than 50% of new infections are due to transmission from MSM subjects who are undiagnosed, a large proportion of which are from people in primary stages of HIV infection where HIV viral load is extremely high and subjects are highly infectious.\textsuperscript{5,18,19} In Australia, estimates indicate that around 3% and 9% of HIV-infected MSM are in primary HIV infection or are undiagnosed, but they are responsible for 19% and 31% of new HIV infections, respectively.\textsuperscript{19} Acute or early HIV infection is the period from HIV acquisition to the completion of HIV seroconversion, when the body begins producing antibodies; this can take up to 2 months.\textsuperscript{18} During this period and for up to 6 months after infection, particularly high levels of the virus are present in the blood and genital secretions, increasing the person’s infectiousness.\textsuperscript{18,20} Therefore, it is critical to identify HIV-positive individuals early in their disease process, to encourage the modification of high-risk behavior and prevent forward transmission.\textsuperscript{5,18,21} Along with preventing HIV transmission, early diagnosis followed by appropriate patient management and the early initiation of antiretroviral therapy significantly benefits the individual’s quality of life and may lead to a near-normal life span.\textsuperscript{5,21} In addition, by providing HIV treatment in the early stages of disease when patients are asymptomatic, treatment costs may be reduced.\textsuperscript{22} Rapid HIV tests generally require a longer period following HIV infection to detect HIV antibodies (the “window period”) compared with the most sensitive laboratory tests. Whereas some specialist rapid HIV testing services recommend laboratory testing for people reporting recent risk exposures, others will offer rapid testing and laboratory testing.\textsuperscript{23}

In the United States, an estimated 25% of HIV-positive individuals are unaware of their HIV status.\textsuperscript{17,24,25} Because of these statistics, the Centers for Disease Control and Prevention recommended routine HIV screening for all patients between the ages of 13 and 64 years, regardless of risk,\textsuperscript{21} supporting the use of rapid HIV testing as a means to increase the number of tests performed.\textsuperscript{26} The feasibility of implementing routine hospital-wide HIV screening using rapid testing was found to be cost-effective through savings related to earlier HIV treatment and decreased HIV transmission.\textsuperscript{21} Another method of increasing testing rates is to take advantage of large numbers of people visiting hospital emergency departments, which has been identified as one of the most important potential HIV screening sites.\textsuperscript{27} It was noted that, in this setting, rapid HIV testing is more feasible than conventional testing and is able to generate results quickly enough to influence clinical management.\textsuperscript{22}

A further US study investigated the possibility of introducing rapid HIV testing into dental clinics and found that the patients’ acceptance rate to HIV counseling and testing in this setting was high (97.6%); this finding suggested that the introduction of rapid HIV testing in dental clinics could provide a further opportunity to test patients who may not otherwise access standard health care facilities for HIV testing.\textsuperscript{24}

In an attempt to increase testing rates, rapid HIV testing has been successfully implemented in countries such as the United States and the United Kingdom in a range of community settings such as community-based organizations,\textsuperscript{16,25,28} bars, public parks, homeless shelters, drug treatment facilities and syringe-exchange programs,\textsuperscript{29} and sex-on-premise venues and mobile vans.\textsuperscript{10} The rationale for this approach is that, by making HIV testing more accessible and attractive, people who have never been tested, do not visit primary care clinics, or are difficult to reach (ie, the homeless or drug addicts) will be encouraged to undergo HIV testing.\textsuperscript{6,16,29} In a US study where rapid HIV testing was offered in community-based organizations targeting high-risk populations such as MSM and migrants from high-prevalence regions, rapid HIV testing was found to be feasible and effective at reaching this target group, with more than 280 high-risk MSM being tested, of which 24% did not have a laboratory-confirmed positive HIV result.\textsuperscript{28} A separate US study offering rapid HIV testing in outreach and community settings (such as public parks, homeless shelters, and bars) targeted minority groups and those with a high risk of HIV.\textsuperscript{25} Of the 23,900 people tested, 30% had never been tested before, and 40% of those who had been tested previously had not been tested in the past year. Two hundred sixty-seven people were newly diagnosed with HIV infection, of which 76% were from racial/ethnic minority groups and 58% were MSM. Finally, 98% of the subjects tested indicated that they thought the venues were appropriate settings for testing.\textsuperscript{25}

Additional settings where rapid HIV testing has been advantageous include labor and delivery wards where a mother’s HIV status is critically needed to prevent mother-to-child vertical transmission or immediately after occupational exposure when a prompt decision must be made regarding antiretroviral prophylaxis.\textsuperscript{4,17,22,29}

With specific reference to the possible introduction of rapid HIV testing in Australia, a potentially relevant setting is in rural and remote regions, especially where there is limited access to
accredited laboratories. In these locations, it is often difficult to ensure that samples arrive at laboratories within an acceptable time frame and without exposure to environmental stressors that may compromise sample integrity. There may often be a lengthy turnaround time for test results and significant loss to follow-up when patients do not return to collect results. The delivery of results to a greater proportion of those who are tested is the key potential advantage of rapid HIV testing in rural and remote settings. However, there are other factors that may present barriers to the uptake and success of testing in these settings. The generally low prevalence of HIV in rural and remote Australia means that a higher proportion of initially reactive rapid test results will be false positives. This may create a burden on health services in managing anxious patients and require more confirmatory testing in laboratories. The chronic issue of high turnover in staff in rural and remote health services also makes it difficult to maintain workforce capacity and consistently deliver sustainable, quality-secured rapid HIV testing programs. The low prevalence of HIV in remote Aboriginal and Torres Strait Islander communities also limits the potential to use rapid HIV testing in these communities. Introducing rapid HIV testing for higher prevalence populations, such as MSM in inner-city areas in Australia's capital cities, may be more appropriate and result in detecting more underdiagnosed infections. Currently, there are urban-based trials of rapid testing occurring in Brisbane, Melbourne, and Sydney.

**ISSUES WITH IMPLEMENTING AND OPTIMIZING RAPID HIV TESTING**

**Sensitivity and Specificity**

Many studies have indicated that the sensitivity (number of true-positive results in HIV-positive patients) and specificity (number of true-negative results in HIV-negative patients) of rapid HIV tests are inferior to those of conventional laboratory HIV tests. However, whereas this was the case with early rapid HIV tests, some newer, rapid HIV tests now have 100% sensitivity and specificity. Currently, 6 rapid HIV tests are licensed for use in the United States, and all have been found to have high sensitivity (≈95%) and specificity (≈99%) compared with that of conventional laboratory EIAs in a recent field study. In specification sheets accompanying their kits, manufacturers often report specificities close to 100%. However, it is critical to note that the proportion of false-positive results is influenced by the prevalence of HIV in the population (with even the higher the HIV prevalence, the fewer the false-positive results for every true-positive result). This finding applies equally to laboratory EIA testing and rapid testing. Therefore, it is important that Western blot continues to be used for confirmatory testing. It is strongly recommended that, before the introduction of field testing, a rapid HIV test kit must be carefully validated in its intended nonlaboratory setting to ensure that the sensitivity and specificity claimed by the manufacturer are valid.

**Algorithms**

To address the need for a confirmatory test for initially reactive rapid test results in community settings where laboratory testing is unfeasible, the WHO recommends that a testing algorithm be used. A testing algorithm uses a combination of rapid HIV tests in sequence and is designed to achieve predictive values (number of positive or negative test results that are true positives or negatives) close to 100%. Algorithms may be either serial (the use of an alternate rapid HIV test to confirm an initial positive test) or parallel (2 rapid test kits performed concurrently). Serial testing is recommended for most settings as it is less expensive because a second test is required only when the initial test is positive. Many rapid HIV tests are based on the immunological detection of the same antigens and therefore may potentially share the same false reactivity. It is therefore essential that the combination of different rapid tests used in an algorithm must be verified for their differing antigenic specificities before field implementation. Algorithms based on rapid HIV testing as both screening and confirmatory tests are now used in most overseas countries as a cost-saving technique because of the inaccessibility to and the high cost of laboratory Western blot confirmatory testing.

Until recently in the Pacific Island countries and territories (PICTs), HIV testing was performed using a single rapid test followed by confirmatory testing of any reactive results in overseas laboratories in Fiji, Australia, or New Zealand. This often time-consuming method of confirmatory testing resulted in a major barrier to delivery of appropriate HIV care. In 2008, a study commissioned by the South Pacific Commission was devised to evaluate an HIV confirmatory testing algorithm to be implemented in the PICTs. The study resulted in the recommendation of the following rapid HIV testing algorithm: initial screening with Determine HIV-1/2 Combo (Alere) followed by confirmatory testing of any reactive specimens with parallel testing using UniGold (Trinity Biotech, Co. Wicklow, Ireland) and Insti HIV-1/HIV-2 (Biosyntech, British Columbia, Canada). This algorithm was found to have high specificity and sensitivity values (100% and 99.2%) as well as high positive and negative predictive values (100% and 99.8%). In 2010, following its validation, this rapid HIV testing algorithm was implemented in the PICTs, with a multicountry rollout following shortly after. The long-term results of this study may have implications for the possible implementation of rapid HIV testing algorithms for screening purposes in rural and remote Australia, which like the PICTs have low HIV prevalence and are remote from accredited laboratories. The future use of such algorithms in Australia would be dependent on the rapid tests being approved by the TGA for listing on the ARTG.

**Patient Loss to Follow-Up**

As conventional laboratory HIV testing requires a patient to wait for up to 2 weeks for results to be reported during a second visit to the clinic, patients often fail to return to the clinic to collect results. This leads to loss to follow-up, meaning that patients remain unaware of their HIV status. In rural areas, patients often have to travel for hours to visit a clinic, and if asked to return for results, many do not. While rapid HIV testing currently relies on confirmatory laboratory testing for any preliminary HIV-positive results, in most settings up to 99% of HIV test results will be negative, meaning that results can be reported to the patient immediately, and a second visit to the clinic is not required. This immediacy of results with negative rapid HIV tests has been found to prevent loss to follow-up. In addition, the high anxiety experienced by patients during the 1- to 2-week wait for conventional laboratory testing is reduced as negative results are available immediately. A recent study found that 65% of Australian MSM who had never been tested and 75% of those who had previously been tested would be more likely to undergo HIV testing if results were available in minutes. In a US study, all preliminary reactive patients were advised to return for a follow-up laboratory confirmatory test; however, only a quarter of patients returned for confirmatory testing, leading to many presumptive HIV-positive patients lost to follow-up. This problem was addressed by modifying the protocol to allow immediate on-site confirmation by the use of a rapid HIV testing algorithm, with confirmatory testing rates increasing to 100%.
Operator Training and Quality Management for Rapid HIV Testing

A fundamental premise of conducting rapid (or any form of point of care) testing both within laboratory and community-based settings is that testing must be supported by continuing operator training and competency assessment and that continuous quality management procedures must underpin such testing. The recently released 2011 National HIV Testing Policy outlines processes for operator training and competency assessment and that continuous quality management procedures must underpin such testing. The NRL provides both the QAAMS (Quality Assurance for Aboriginal Medical Services) and Northern Territory Point-of-Care Testing program are examples of national and state-based point-of-care testing programs, respectively, that have implemented long-term training and quality systems to underpin successful and sustainable models for community-based point-of-care testing in Australia. These have been based on cooperative partnerships between well-established specialist point-of-care testing units within tertiary institutions, professional bodies, and federal and territory governments. They also provide evidence-based working models for training and quality frameworks that could be adapted for use in future community-based rapid HIV testing programs in Australia.

As part of its training program, the National Serology Reference Laboratory (NRL) has studied the use of photographed rapid HIV test results to assess and compare the proficiency of operator interpretation. Evaluation of this scheme found that the operator’s accuracy of interpretation of the photographed test results improved from 75.8% to 94.6% after a brief tutorial on the subtleties of interpretation. Quality control and external proficiency or QA testing are 2 complementary tools used routinely by laboratories to monitor quality of pathology results. Most rapid HIV tests provide what are termed “on-board controls,” but in practice, these only check that the sample has migrated successfully; they do not test operator competence or strip reactivity. The NRL provides both quality control and QA materials for laboratory HIV testing, and the Royal College of Pathologists of Australasia Quality Assurance Programs Pty Ltd provides QA material. The QA products from the NRL and Royal College of Pathologists of Australasia QAP comprise a panel of specimens with both negative and a range of positive HIV loads, with testing frequencies ranging from 3 to 6 times a year. The potential to adapt this material for community settings exists; however, as with all biological materials, strict national and international guidelines regarding occupational health and safety would need to be complied with when distributing and handling potentially infectious samples.

Appropriate Counseling

Overall rapid HIV testing has been found to be popular with both patients and health care professionals. However, when implementing rapid HIV testing, it is essential that counseling also be offered on site. The 2011 Australian National HIV Testing Policy states that informed consent is required for HIV testing, except for rare occasions such as compulsory testing and in emergency settings. The person performing testing should use his/her clinical judgment in securing informed consent and base the discussion on the patient’s clinical presentation, risk exposure, epidemiology and prevalence, patient initiation, and the patient’s understanding of the HIV testing process and consequences of the result. The policy outlines processes for conveying HIV test results, which differ depending on whether the test was performed by conventional testing methods (ie, laboratory testing) or whether it was performed by point-of-care testing, in which case, if the test is initially reactive, a venous blood sample must be collected to enable reference laboratory confirmation. It is essential that operators are adequately trained for counseling as it forms an integral part of HIV testing.

CONCLUSIONS

Rapid HIV tests are used routinely in many developed and developing countries, and their use is supported by WHO and UNAIDS. Overall, rapid testing for HIV screening in overseas countries has reported benefits including successfully engaging different populations (notably those that are hard to reach and at high risk), increasing testing rates, enabling testing in nontraditional settings, reducing barriers to testing, reducing the time taken to deliver results, increasing patient and operator satisfaction, reducing costs for testing services, decreasing loss to follow-up, and increasing the proportion of newly diagnosed HIV-positive individuals referred to HIV treatment and care. In Australia, although HIV testing rates are high compared with overseas countries, they do not currently meet the guidelines for frequency of testing (once per year for high-risk individuals). As early diagnosis is necessary for optimal treatment and care of HIV-positive patients, any opportunity to improve testing frequency would be a positive change. The introduction of rapid HIV testing to community settings in Australia has the potential to reduce some of the barriers to testing by making HIV testing quicker, less invasive, and more accessible. In particular, because of the high sensitivity of available tests, patients with a negative result could be given their result on the spot, significantly reducing both rates of loss to follow-up and the level of anxiety felt during the waiting period for the result. There would also be substantial reduction in the number of samples sent to the laboratory as only initially reactive samples would need to be sent for confirmatory laboratory testing.

In practice, rapid HIV testing in Australia should be targeted at groups and locations in which prevalence rates are highest such as MSM in urban settings, rather than most rural, remote, or indigenous settings, where prevalence rates are comparatively lower. A future possibility for remote settings could be the use of testing algorithms using a combination of rapid HIV tests; these are being trialed in the PICTs, but the test kits for such a purpose would require TGA approval and ARTG listing before field implementation. Currently, this registration process is a very costly exercise and, given the relatively small size of the Australian market and the generally low prevalence of HIV in this country, manufacturers may feel it is not financially viable for them to undertake this arduous registration process. As well as the cost of kit registration, other economic and operational barriers to the uptake of rapid HIV testing by community-based health practitioners and health services include the current lack of Medicare rebate for rapid tests, the need for staff to undertake specific training programs and maintain competency standards, and the need to participate in external QA testing programs. At the time of writing, new rapid testing technologies based on nucleic acid amplification are being developed and/or implemented in some countries. The potential improved diagnostic capabilities of these technologies may significantly alter the future field applications and uptake of rapid HIV testing. As a result, the changing face of community-based rapid HIV testing will continue to be the subject of challenging debate.

REFERENCES


