Title: New Initiatives to develop self-testing for HIV

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Abstract

Purpose of the review: The purpose is to describe the most recent literature associated with HIV self –testing (HIVST).

Recent findings: HIVST is acceptable to a range of populations in a variety of contexts, particularly if users values and preferences are taken into account in intervention development. Approaches being explored in on-going and planned studies are the efficacy of HIVST to increase diagnosis of longstanding prevalent infections and to reduce the interval between HIV transmission and diagnosis, particularly in high incidence groups. Though there is little evidence of harms related to HIVST, this remains a potential issue. Concerns remain about the reliability of currently available HIVST kits, which have lower sensitivity than testing options available in clinical settings, particularly in early HIV infection. Evidence on linkage to care for confirmatory testing after a reactive HIVST result and the cost effectiveness of HIVST to increase rates of HIV diagnosis is currently limited.

Summary: HIVST is relatively new innovation that appears acceptible to key populations and which could increase HIV testing rates and rates of HIV diagnosis especially in at-risk groups. Concerns remain about test sensitivity, particularly in early HIV infection, and linkages to care for confirmatory testing after a reactive HIVST.

Scope of this review

The field of literature surrounding HIVST is evolving rapidly. While some key literature has been formally published, much of the most up to date and relevant evidence comes from conference abstracts. Understanding key elements of HIVST, including values and preferences in key populations most impacted by HIV is crucial. In terms of HIVST outcomes; feasibility studies, pilot HIVST projects and non-RCT intervention studies have occurred in a variety of settings, as have several randomised controlled trials (RCTs). Both RCTs and non-RCTs typically focus on interventions to detect prevalent infections, or increase testing frequency. Evidence on harm is limited, but important work is emerging. Economic evidence including cost-effectiveness analysis is very much in the nascent stages of development.

The purpose of this review is to describe the most recent literature on outcomes and issues associated with HIVST.

HIV testing rates

A high proportion of people living globally with HIV remain undiagnosed. Despite intensive interventions to increase testing over the past decade, 17.1 million of the estimated 36.9 million people living with HIV worldwide in 2014 remained undiagnosed (1). This has implications not just for individual health, with the results of the START trial in 2015 indicating antiretroviral therapy (ART) is beneficial at any CD4 count, but also for onward transmission of HIV, with 60-80% of transmission thought to occur from those as yet undiagnosed and often in the early stages of infection where risk of onward transmission is greater (2-5).

The 'Test and Treat' approach has been enshrined in the UNAIDS global 90-90-90 targets, which aim by 2020, to achieve 90% of people with HIV being diagnosed, 90% taking ART and 90% of those treated achieving virological suppression (6). The first '90' is the largest gap with only 53% of those living with HIV currently being diagnosed. Efforts to increase testing rates has led to expansion of testing opportunities and testing interventions to meet the needs of a range of different groups in a variety of contexts (see Table 1) (7-10). HIV self-testing (HIVST) is simply the latest iteration of testing modalities.

HIV self-testing

Regulatory approval and policy

We define HIVST as when an individual takes their own sample, processes it and interprets their own result. A reactive result from an HIVST is not a diagnosis; this requires the individual to subsequently attend a testing facility for confirmatory HIV testing and linkage to care. Self-tests for a variety of other conditions are already available to the general public. HIV has long been viewed as an exceptional disease by policy makers and clinicians, and this exceptionalism meant that early in the epidemic, HIVST was banned in many countries, due to concerns over the potential for self-harm in the absence of effective treatments and the potential for coercive use (11). In recent years, the shift in HIV to a chronic manageable disease with near normal life expectancy (12, 13) through highly effective ART has led to changing attitudes towards of the impact of HIV diagnosis among clinicians and populations affected by HIV. These changes have led to a more permissive policy environment, with increasing numbers of countries enacting laws or repealing legislation making rapid diagnostic tests (RDTs) for self use available. The UK for example legalised HIVST on April 1st 2014, with the first commercially available test released the following year (Biosure^{TM}). HIVST is permitted with regulated tests available from the private sector in other countries such as the US, France, Belgium and Brazil (14). Other countries such as Australia have policies permitting HIVST, but no tests are as yet approved by the necessary regulatory agencies. Many more nations have no official policies on the technology, but unregulated HIVSTs and RDTs intended for clinical use are often available either online or through pharmacies, raising concerns about quality (14).

In efforts to continue expanding HIV testing, HIVST has been officially adopted on a global policy level, with the World Health Organisation (WHO) incorporating HIVST into their Consolidated Guidelines on HIV testing services in July of 2015 (15).

Potential benefits

HIVST has been promoted as a low cost alternative to facility based testing, potentially reducing barriers such as stigma and opportunity cost while boosting patient choice and enhancing autonomy, thereby potentially expanding testing to new groups and enabling increased testing frequency in those at highest risk (16). HIVST also has applications in intensive combination HIV prevention initiatives such as the targeted expansion of testing, treatment and pre-exposure

prophylaxis (PrEP) (16, 17). HIVSTs are available using both a whole blood sample, usually from a finger prick, or using oral fluid.

Understanding implementation contexts: values and preferences

In general studies, which seek to understand how populations might accept HIVST, tend to include participants who have not actually experienced HIVST themselves and the intervention is therefore hypothetical. Understanding this evidence remains worthwhile because it provides an indication of how populations are likely to engage with the technology, and how interventions should be delivered to ensure they are acceptable.

MSM (and to a lesser extent trans gender women and female sex workers [FSW]) in high and middle income settings are well represented in literature around HIVST acceptability as well as values and preferences, though there is little data as yet from Europe. General populations are less well represented in available data, although there is some evidence emerging from East and Southern Africa (18, 19). Recent studies report high acceptability for HIVST across a range of settings and populations. Emerging evidence from Peru (20, 21), Scotland (22), the USA (23, 24), Vietnam (25) and Mexico (26) report that MSM find HIVST highly acceptable, with moderate acceptability observed in Hong Kong (27). In a recent cross-sectional study in England, HIVST was the second most preferred location for future HIV testing and tended to have greater popularity amongst MSM less likely to test at a frequency in line with national guidelines (28).

Confidentiality, convenience, immediacy and the opportunity to increase testing frequency are commonly cited benefits of HIVST (22-25, 29-32). Barriers tend to be concerns around dislocation from care pathways, the possibility of coercive testing practices, and perceived issues with self-efficacy as well as kit accuracy (31, 33, 34).

A systematic review conducted by Figueroa, Johnson (29) provides an excellent analysis of the relative preferences of various intervention components among key populations. Evidence suggests that oral fluid RDTs are marginally preferred over finger stick or whole blood tests, although this tends to vary across country income settings and population (29). For example, a recent UK study found that MSM preferred HIVST kits using a blood sample due to concerns around accuracy with oral fluid HIVST (31). In a study in Vietnam MSM and female sex workers (FSW) preferred oral fluid HIVSTs, while injection drug users (IDU) preferred blood based kits (25). In work from the US conducted with an ethnically diverse group of high risk MSM, more frequent testers preferred blood based testing, whereas men who tested less frequently preferred oral fluid HIVSTs (35).

Demonstrating impact of HIVST: outcomes from pilot projects and RCTs

A range of feasibility studies, pilot projects and trials have provided data on the feasibility and impact of providing HIVST to different groups through an array of intervention designs. While the aims for each study vary (as does quality, particularly in feasibility and pilot studies), intervention designs tend to fall into one of two categories. The first is to detect longstanding prevalent infections among groups who have never tested or who test sub-optimally. The second is to increase frequency of testing to decrease the time between acquiring HIV infection and diagnosis, particularly in risk groups with high incidence. Evidence surrounding linkage to care in RCTs remains limited. Table two presents key RCTs planned, on-going and completed.

Detection of prevalent infections

Feasibility and pilot HIVST studies provide some evidence that HIVST will likely detect undiagnosed prevalent infections in individuals who test sub-optimally or have never tested, although it remains unclear if HIVST is more efficacious than other testing options to meet this aim. Projects in the US which focussed on reaching groups who have not previously tested or have difficulty accessing services seem to be successful in reaching MSM online (36, 37) and to an extent in sex on premise venues (38). In Vietnam, community distribution was successful in reaching MSM, FSW and IDUs in urban and rural settings (25).

Of particular interest is a cohort study conducted in Kenya which provided women with a varying number of HIVSTs to distribute to their sexual partners (39). Of 58 women recruited in antenatal care, 91% (53) distributed a kit to their partner, as did 86% (91) of 106 women in postpartum care and 75% (64) of 85 female sex workers (39). In an RCT distributing HIVSTs to pregnant women and their partners in Kenya, a significantly greater proportion of those in the HIVST arm tested for HIV compared to those randomised to SoC facility based testing. More male partners of women in the intervention group tested (90.8% vs 51.7%) and higher levels of couples testing also occurred in those in the intervention arm (75.4% vs 33.2%) (40). It is important to note that figures in both studies are based on participants' reports of their partners' testing behaviour and must therefore be interpreted with caution.

Reducing interval between infection and diagnosis

Efforts to increase the frequency with which at risk groups with high HIV incidence test are central to aspirations around the expansion of HIVST, and increased frequency of testing is a key benefit often

repeated in values and preferences studies conducted with key populations. Non-RCT projects which have provided participants with a number of HIVSTs with instructions to test frequently have shown that distribution in line with this intervention approach is feasible amongst trans gender women in San Francisco (32), and MSM in Brazil and Peru (21).

RCT evidence in this area is not strong, largely because studies have been underpowered to assess rates of diagnosis and therefore frequency of testing has been used as a proxy measure. In Seattle, MSM tested significantly more frequently when provided with multiple HIVSTs compared to SoC (5.3 tests compared with 3.6 over 15 months) (41). The study was too small (n=230) to show an effect on increasing HIV diagnosis (41). These findings were repeated in MSM in Australia which showed increased testing frequency among the self-testing group, which did not reduce attendance in STI clinics indicating that men in this study used HIVST largely as a supplementary option (42). Encouragingly, in both these RCTs testing frequency was increased in both frequent and infrequent testers.

Linkage to care

Linkage to care for confirmatory testing is critical following a reactive result from a HIVST. A cluster randomised trial in Malawi reported that 56.3% (524/930) of people who had a reactive HIVST subsequently linked to care for confirmatory testing (43). Similar results have been seen in other observational studies in sub Saharan Africa (39). There is as yet very limited evidence from high income settings of linkage rates after HIVST, though a planned trial as detailed below, aims to provide data in this area.

Planned studies

Two planned studies are worth noting. The HIV Self-Testing Africa Project – Research (STAR project) is a $23 million four-year study taking place in Malawi, Zambia and Zimbabwe which will be the largest investigation of HIVST to date. This project will evaluate accuracy, uptake, case finding and linkage to care through a variety of models of HIVST delivery in these three countries.

The planned SELPHI study in the UK will be the first RCT which attempts to address questions on both the ability of HIVST to detect prevalent infections and also to reduce the time between infection and diagnosis and aims to recruit 10 000 MSM in England and Wales from early 2017. The primary outcome is rates of HIV diagnosis as determined through confirmatory testing and linkage to care. This RCT will provide vital evidence for future policy makers in high-income settings and those

working with key populations on the efficacy and cost effectiveness of HIVST in increasing rates of HIV diagnosis.

Technological issues: Sensitivity of HIVST, particularly in early HIV infection

Reliable use of HIVST kits has been reported as highly variable in observed studies (25-99.2%) (18, 44, 45), though groups used in these studies are not necessarily reflective of those likely to need or use HIVST, which makes critical assessment of these results complex. However sensitivity and specificity estimates for HIVST when used by self-testers are high, though would appear to be higher for whole blood based HIVST compared to oral fluid based tests (96.2-100% compared to 80-100%) (46). Promisingly, repeated exposure to and use of HIVST seems to increase the confidence and ability of individuals to perform the tests correctly (19, 23, 47).

Perhaps a more pressing concern, reflected by policy makers, commissioners and patients, is that HIVST kits have a lower sensitivity (and specificity) than those currently available in clinical settings, in particular in the period of early HIV infection known as the window period. The time from initial HIV infection to detection of infection (window period) depends on the properties of the test used. Figure 1 demonstrates the range of window periods before detection of HIV infection depending on whether antibody, antibody/antigen combination or HIV RNA tests are used. Currently available HIVST products are classed as second generation tests (antibody tests that are not laboratory run through tests), highlighting that HIVST is an innovation using older generation assays.

Manufacturers of current blood based and oral test fluid based HIVST give window periods of up to 3 months for their products. Oraquick™ also reports data indicating 95-98% detection of new HIV infection at 6 weeks and 99% by week 12 (48). Blood based antibody tests are likely to have slightly shorter window periods. In high risk populations the window period of current tests is particularly troubling, with mathematical modeling suggesting that widespread use of oral HIVST in high risk populations could potentially increase prevalence due to the long window period prior to detection of infection, and potentially a false sense of security from non-reactive HIVST results leading to greater sexual risk-taking (49).

One of the potential utilities of HIVST is for those who require frequent HIV testing such as people taking PrEP. There is concern however that using an oral based HIVST in particular may lead to an increased rate of false negative tests in early infection. During the Bangkok Tenofovir Study, staff reported non-reactive monthly oral fluid HIVST (Oraquick™) results for 8 participants (20% of all seroconversions in the study) for more than 3 months (84 days) after HIV

infection. Participants receiving Tenofovir in this study took longer to develop a reactive OraQuick™ HIVST (191.8 days) than participants receiving placebo (16.8 days) (p = 0.02) (50). This may be due to the fact that the OraQuick™ test contains only a single glycoprotein antigen (anti-gp41), so it will not identify HIV-infected individuals who fail to mount a substantial antibody response to that particular antigen, perhaps due to the presence of ART. It is likely however that HIVST kits, particularly blood based products, will improve in time with antigen detection, thus increasing sensitivity and specificity.

Potential for social harms from HIVST

When considering implementation of HIVST the potential for harm among the self-tester and the broader population are often iterated concerns. A systematic review in 2014 of a variety of self-diagnostics (including 49 papers on HIVST) found very little evidence of any harm occurring in self-testing (51) . However ongoing vigilance is required for any potential negative effects as HIVST is expanded in at risk populations.

A further concern around HIVST remains is the potential for intimate partner violence (IPV) and coercive testing though there is little current evidence in this area. In a recent study involving 600 women in Kenya in which pregnant women were given HIVSTs for themselves and their partner; low and equal rates of IPV was observed in both the HIVST and SoC arms (1 incident in each) (40). However women who felt they were at risk of IPV were excluded from this study. Coercive testing has been described in Malawi, with more men than women reporting having been coerced (33, 52), but evidence suggests that this did not impact on intervention acceptability. In some cases coercion was felt to be beneficial in that it reduced personal barriers to testing indicating that 'coercion' conceptually must be understood in the social context within which it occurs (33).

Further avenues of exploration: economic evaluation

Evidence that HIVST will save costs to health services is currently lacking, particularly in resource rich settings though planned studies aim to fill this gap.

In sub-Saharan Africa, in a sub-study from the cluster RCT in Malawi, the mean society cost of HIVST compared with facility based testing has been estimated to be US$9.2 (95% CI: US$9.1-US$9.3) versus US$11.8 (95 % CI: US$10.8-12.9). The cost per infection detected was higher through HIVST (US$97.5) than for facilities, which ranged between US$25.2-US$76.1 (53).

Recently published evidence from Cambiano, Ford (54) assessed the potential impact and cost-effectiveness of HIVST in Zimbabwe estimating two models where HIVST was not introduced, and one where it was. They estimated that the introduction of HIVST alongside existing testing interventions would save $75 million while averting 7000 disability-adjusted life-years over 20 years. This work also found however that should linkage to cascades of care be significantly impacted, ART CD4 thresholds lowered or if HIVSTs cost significantly more than the scenario estimated cost of $3 then scenarios could emerge where HIVST was not cost effective when compared to the reference scenario.

Conclusions

Based on a review of the current of evidence HIVST is clearly acceptable and feasible to deliver to a range of populations in a variety of settings. In addition, HIVST has a role alongside other existing service provision, but it's imperative to understand this in particular demographic, cultural and health systems contexts as well as the values and preferences of the intended end users. While HIVST seems able to encourage testing in individuals who test sub-optimally and can increase the frequency at which some individuals test, it is less clear whether it is more efficacious or cost effective at detecting prevalent infections or reducing the interval between HIV infection and diagnosis for those in high incidence groups than current testing provision. Rates of linkage to care, an essential step following a reactive result with HIVST, are unclear particularily in resource rich settings.

Improvements in kit sensitivity with shorter window periods, potentially with Ab/Ag combinations are vital to serve the needs of individuals particularily those from key populations with high incidence of infection. It is presently uncertain to what degree harms, if any, occur from HIVST and what form these harms may take. Social sciences should be key in responding to questions about harms so that these are understood from the perspective of those utilising the intervention. Economic evaluation of HIVST is in nascent stages and should be a key priority area moving forward.

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Conflicts of interest

The authors have no conflicts of interest.

Papers of particular interest, published within the annual period of review, have been highlighted as:

* of special interest

** of outstanding interest

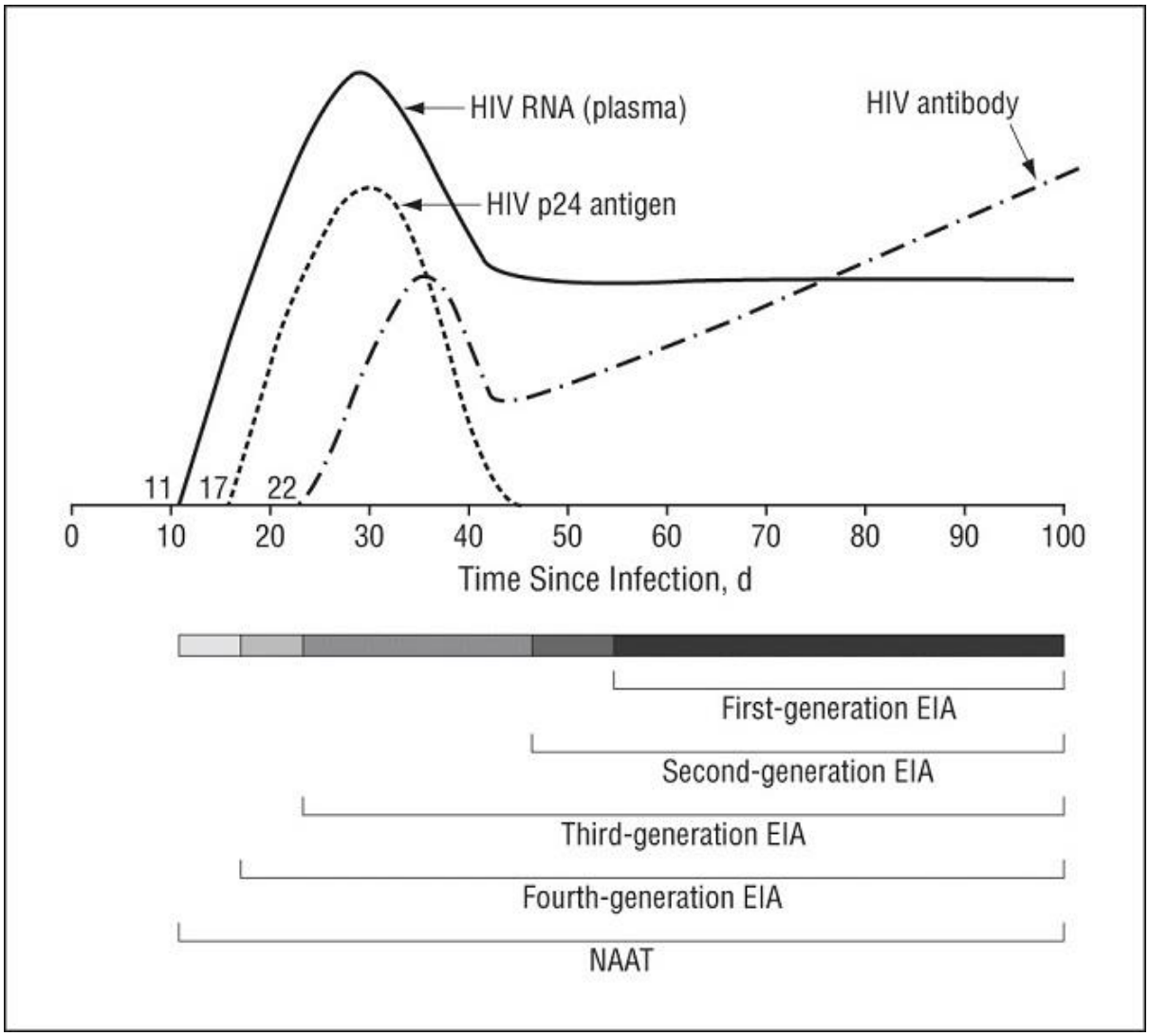
References

1. UNAIDS. AIDS by the numbers: 2015. 2015.
2. Attia S, Egger M, Muller M, Zwahlen M, Low N. Sexual transmission of HIV according to viral load and antiretroviral therapy: systematic review and meta-analysis. AIDS. 2009;23(11):1397-404.
3. Granich RM, Gilks CF, Dye C, De Cock KM, Williams BG. Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model. . The Lancet. 2009;373:48-57.
4. Rodger AJ, Cambiano V, Bruun T, Vernazza P, Collins S, van Lunzen J, et al. Sexual Activity Without Condoms and Risk of HIV Transmission in Serodifferent Couples When the HIV-Positive Partner Is Using Suppressive Antiretroviral Therapy. JAMA. 2016;316(2):171-81.
5. Group ISS, Lundgren JD, Babiker AG, Gordin F, Emery S, Grund B, et al. Initiation of Antiretroviral Therapy in Early Asymptomatic HIV Infection. N Engl J Med. 2015;373(9):795-807.
6. UNAIDS. 90-90-90: An ambitious treatment target to help end the AIDS epidemic. 2014.
7. Matovu JK, Makumbi FE. Expanding access to voluntary HIV counselling and testing in sub-Saharan Africa: alternative approaches for improving uptake, 2001-2007. Trop Med Int Health. 2007;12(11):1315-22.
8. Musheke M, Bond V, Merten S. Couple experiences of provider-initiated couple HIV testing in an antenatal clinic in Lusaka, Zambia: lessons for policy and practice. . BMC Health Services Research. 2013;13(97).
9. Rayment M, Thornton A, Mandalia S, Elam G, Atkins M, Jones R, et al. HIV testing in non-traditional settings--the HINTS study: a multi-centre observational study of feasibility and acceptability. PLoS One. 2012;7(6):e39530.
10. Burns F, Edwards SG, Woods J, Haidari G, Calderon Y, Leider J, et al. Acceptability and feasibility of universal offer of rapid point of care testing for HIV in an acute admissions unit: results of the RAPID project. PLoS One. 2012;7(4):e35212.
11. Frith L. HIV self-testing: a time to revise current policy. The Lancet. 2007;369(9557):243-5.
12. Nakagawa F, May M, Phillips A. Life expectancy living with HIV: recent estimates and future implications. Curr Opin Infect Dis. 2013;26(1):17-25.
13. Teeraananchai S, Kerr SJ, Amin J, Ruxrungtham K, Law MG. Life expectancy of HIV-positive people after starting combination antiretroviral therapy: a meta-analysis. HIV Med. 2016.
14. HIVST.org. Policy & Regulations for HIVST 2016 [cited 2016]. Available from: http://www.hivst.org/policy-regulations-for-hivst-1/.
15. Organisation WH. Consolidated guidelines on HIV testing services. 5cs: consent, confidentiality, counselling, correct results and connection. . Geneva, Switzerland.: 2015.
16. Johnson C, Baggaley R, Forsythe S, van Rooyen H, Ford N, Napierala Mavedzenge S, et al. Realizing the potential for HIV self-testing. AIDS Behav. 2014;18 Suppl 4:S391-5.
17. Punyacharoensin N, Edmunds WJ, De Angelis D, Delpech V, Hart G, Elford J, et al. Effect of pre-exposure prophylaxis and combination HIV prevention for men who have sex with men in the UK: a mathematical modelling study. The Lancet HIV. 2016;3(2):e94-e104.
18. Peck RB, Lim JM, van Rooyen H, Mukoma W, Chepuka L, Bansil P, et al. What should the ideal HIV self-test look like? A usability study of test prototypes in unsupervised HIV self-testing in Kenya, Malawi, and South Africa. AIDS Behav. 2014;18 Suppl 4:S422-32.

19. Kurth AE, Cleland CM, Chhun N, Sidle JE, Were E, Naanyu V, et al. Accuracy and Acceptability of Oral Fluid HIV Self-Testing in a General Adult Population in Kenya. AIDS Behav. 2016;20(4):870-9.
20. Bustamante MJ, Konda KA, Joseph Davey D, Leon SR, Calvo GM, Salvatierra J, et al. HIV self-testing in Peru: questionable availability, high acceptability but potential low linkage to care among men who have sex with men and transgender women. Int J STD AIDS. 2016.
21. Volk JE, Lippman SA, Grinsztejn B, Lama JR, Fernandes NM, Gonzales P, et al. Acceptability and feasibility of HIV self-testing among men who have sex with men in Peru and Brazil. Int J STD AIDS. 2016;27(7):531-6.
22. Flowers P, Riddell J, Park C, Ahmed B, Young I, Frankis J, et al. Preparedness for use of the rapid result HIV self-test by gay men and other men who have sex with men (MSM): a mixed methods exploratory study among MSM and those involved in HIV prevention and care. HIV Med. 2016.
23. Brown W, 3rd, Carballo-Dieguez A, John RM, Schnall R. Information, Motivation, and Behavioral Skills of High-Risk Young Adults to Use the HIV Self-Test. AIDS Behav. 2016;20(9):2000-9.
24. Hurt CB, Soni K, Miller WC, Hightow-Weidman LB. Human Immunodeficiency Virus Testing Practices and Interest in Self-Testing Options Among Young, Black Men Who Have Sex With Men in North Carolina. Sex Transm Dis. 2016;43(9):587-93.
25. Green K. In the hands of the community: Accelerating key population-led HIV lay- and self-testing in Vietnam. . 21st International AIDS Conference; 18-22nd July.; Durban, South Africa.2016.
26. Oldenburg CE, Biello KB, Perez-Brumer AG, Rosenberger J, Novak DS, Mayer KH, et al. HIV testing practices and the potential role of HIV self-testing among men who have sex with men in Mexico. Int J STD AIDS. 2016.
27. Wong HT, Tam HY, Chan DP, Lee SS. Usage and acceptability of HIV self-testing in men who have sex with men in Hong Kong. AIDS Behav. 2015;19(3):505-15.
28. Witzel TC, Melendez-Torres GJ, Hickson F, Weatherburn P. HIV testing history and preferences or future tests among gay men, bisexual men and other MSM in England: results from a cross-sectional study BMJ Open. 2016;6.
29. ** Figueroa C, Johnson C, Verster A, Baggaley R. Attitudes and Acceptability on HIV Self-testing Among Key Populations: A Literature Review. AIDS Behav. 2015;19(11):1949-65.
30. Schnall R, John RM, Carballo-Dieguez A. Do High-Risk Young Adults Use the HIV Self-Test Appropriately? Observations from a Think-Aloud Study. AIDS Behav. 2016;20(4):939-48.
31. Witzel TC, Rodger AJ, Burns FM, Rhodes T, Weatherburn P. HIV Self-Testing among Men Who Have Sex with Men (MSM) in the UK: A Qualitative Study of Barriers and Facilitators, Intervention Preferences and Perceived Impacts. PLoS One. 2016;11(9):e0162713.
32. Lippman SA, Moran L, Sevelius J, Castillo LS, Ventura A, Treves-Kagan S, et al. Acceptability and Feasibility of HIV Self-Testing Among Transgender Women in San Francisco: A Mixed Methods Pilot Study. AIDS Behav. 2016;20(4):928-38.
33. Lora W, E. C, Desmond N. Understanding coercion in the context of semi-supervised HIV self-testing in urban Blantyre. . AIDS 2016; 18-22nd July 2016.; Durban, South Africa.2016.
34. Bilardi JE, Walker S, Read T, Prestage G, Chen MY, Guy R, et al. Gay and bisexual men's views on rapid self-testing for HIV. AIDS Behav. 2013;17(6):2093-9.
35. Balán I, Frasca T, Ibitoye M, Dolezal C, Carballo-Dieguez A. Fingerprick Versus Oral Swab: Acceptability of Blood-Based Testing Increases If Other STIs Can Be Detected. AIDS Behav. 2016.
36. Gibson W, Challenor R, Warwick Z. HIV home/self-testing: a pilot project and service evaluation. 22nd Annual Conference of the British HIV Association; 19-22nd April 2016. ; Manchester2016.
37. Rosengren AL, Huang E, Daniels J, Young SD, Marlin RW, Klausner JD. Feasibility of using GrindrTM to distribute HIV self-test kits to men who have sex with men in Los Angeles, California. Sex Health. 2016.
38. Woods WJ, Lippman SA, Agnew E, Carroll S, Binson D. Bathhouse distribution of HIV self-testing kits reaches diverse, high-risk population. AIDS Care. 2016;28 Suppl 1:111-3.

39. ** Thirumurthy H, Masters SH, Mavedzenge SN, Maman S, Omanga E, Agot K. Promoting male partner HIV testing and safer sexual decision making through secondary distribution of self-tests by HIV-negative female sex workers and women receiving antenatal and post-partum care in Kenya: a cohort study. The Lancet HIV. 2016;3(6):e266-e74.
40. Thirumurthy H, Masters S, Obonyo B, Mavedzenge SN, Maman S, Omanga E, et al. Promoting male partner and couples HIV testing through secondary distribution HIV self-tests: a randomized trial. . AIDS 2016; 18-22nd July, 2016. ; Durban, South Africa. 2016.
41. Katz DA, Golden MR, Hughes JP, Farquhar C, Stekler JD. HIV Self-Testing Increases HIV Testing Frequency among High Risk MSM: A Randomized Controlled Trial. . IAS 2015; Vancouver, Canada. .
42. * Jamil MS, Prestage G, Fairley CK, Grulich AE, Smith KS, Chen M, et al. Access to HIV self-testing doubles the frequency of HIV testing among gay and bisexual men at higher risk of infection: a randomised controlled trial. . AIDS 2016; Durban, South Africa. : 18-22nd July, 2016. ; 2016.
43. * MacPherson P, Lalloo DG, Webb EL, Maheswaran H, Choko AT, Makombe SD, et al. Effect of optional home initiation of HIV care following HIV self-testing on antiretroviral therapy initiation among adults in Malawi: a randomized clinical trial. JAMA. 2014;312(4):372-9.
44. Gras G, Le Bret P, Daillous JF, Le Moal G, Raoult A, Fajole G, et al. Low Feasibility Rate of Self Testing with a Finger-Stick Whole Blood Test. Conference on Retroviruses and Opportunistic Infections; 3-6 March 2014. ; Boston2014.
45. Prazuck T, Karon S, Gubavu C, Andre J, Legall JM, Bouvet E, et al. A Finger-Stick Whole-Blood HIV Self-Test as an HIV Screening Tool Adapted to the General Public. PLoS One. 2016;11(2):e0146755.
46. Figueroa C, Johnson C, Verster A, Dalal S, Baggaley R. Systematic review on HIV self-testing (HIVST) performance and accuracy of results. 21st International AIDS Conference; 18-22nd July. ; Durban, South Africa. 2016.
47. Yan H, Yang H, Raymond HF, Li J, Shi LE, Huan X, et al. Experiences and correlates of HIV self-testing among men who have sex with men in Jiangsu province, China. AIDS Behav. 2015;19(3):485-91.
48. Food and Drug Administration. Vaccines BB. Information Regarding the OraQuick In-Home HIV Test. 2014 [cited 2016 03 October]. Available from: www.fda.gov/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/PremarketApprovalsPMAs/ucm311895.htm.
49. Katz DA, Cassels SL, Stekler JD. Replacing clinic-based tests with home-use tests may increase HIV prevalence among Seattle men who have sex with men: evidence from a mathematical model. Sex Transm Dis. 2014;41(1):2-9.
50. Suntharasamai P, Martin M, Choopanya K, Vanichseni S, Sangkum U, Tararut P, et al. Assessment of Oral Fluid HIV Test Performance in an HIV Pre-Exposure Prophylaxis Trial in Bangkok, Thailand. PLoS One. 2015;10(12):e0145859.
51. Brown AN, Djimeu EW, Cameron DB. A review of the evidence of harm from self-tests. AIDS Behav. 2014;18 Suppl 4:S445-9.
52. Choko AT, Desmond N, Webb EL, Chavula K, Napierala-Mavedzenge S, Gaydos CA, et al. The uptake and accuracy of oral kits for HIV self-testing in high HIV prevalence setting: a cross-sectional feasibility study in Blantyre, Malawi. PLoS Med. 2011;8(10):e1001102.
53. Maheswaran H, Petrou S, MacPherson P, Choko AT, Kumwenda F, Lalloo DG, et al. Cost and quality of life analysis of HIV self-testing and facility-based HIV testing and counselling in Blantyre, Malawi. BMC Med. 2016;14:34.
54. * Cambiano V, Ford D, Mabugu T, Napierala Mavedzenge S, Miners A, Mugurungi O, et al. Assessment of the Potential Impact and Cost-effectiveness of Self-Testing for HIV in Low-Income Countries. J Infect Dis. 2015;212(4):570-7.

Figure 1: Window of Detection for HIV, Based on the Test Used



Legend: Nucleic acid amplification testing (NAAT) is performed to detect HIV RNA. Enzyme immunoassay (EIA) is performed to detect HIV antibody (second- and third-generation EIA) or HIV antibody/antigen (fourth-generation EIA).

Note: Figure was reproduced from 'Diagnosis and Management of Acute HIV Infection'. This material was accessed on [16/09/2016] on the HIV Clinical Resource website (www.hivguidelines.org). The HIV Clinical Guidelines Program is a collaborative effort of the New York State Department of Health AIDS Institute and the Johns Hopkins University Division of Infectious Diseases.

Table 1: HIV testing intervention types

Voluntary testing and counselling: Facility-based HIV testing and counselling.

Community based HIV testing: Voluntary testing and counselling undertaken in a community setting such as in a van or in a commercial venue.

Home-based voluntary testing and counselling: Testing undertaken in a domestic setting by a trained healthcare worker.

HIV self-sampling: HIV testing whereby an individual takes their own sample and returns it to a lab which processes it and returns a result.

HIV self-testing (HIVST): Testing where a person carries out an HIV rapid test on themselves. They take their own sample, process is and interpret their own result.

Supervised HIV self-testing: HIVST conducted in the presence of a healthcare worker.

Table 3: Completed, ongoing and planned HIVST RCTs.

Investigator	Year	Population/ location	HIVST kit	Study Design	Outcomes
LSHTM, UNITAID/PSI, UCL, LSTM, CRP, WHO. HIV Self-testing Africa (STAR). Multiple studies planned.	2016-18	General population, Malawi	OraQuick	Cluster Randomized Trial to SOC or HIVST or HIVST+ home HIV care initiation (n=5000)	Uptake of testing in each group [12 mths]. Disclosure of a positive HIV result. ART initiation rates
MacPherson, Corbett, Choko, Wellcome Trust. (43)	2010-2012	General population, Malawi	OraQuick	Cluster Randomized Trial community areas (n=14, pop 16, 660) to facility-based HIV care or home HIV care. HIV-ST promoted in all clusters.	Uptake HIV-ST high (76%), 75.8% shared results with counselors. Positive HIVST reporting to CHW was higher in home HIV care cluster compared to facility (6% vs 3.3%) as was ART initiation (2.2% vs 0.7%)
Merchant et al, Rhode Island Hospital	2015-16	Young Adult MSM Rhode Island, US	OraQuick	Randomized to ST or blood based SS or standard of care (n=450 total)	Uptake of testing in each group [12 mths]
MacGowan et al. The eSTAMP Study, CDC/Emory	2015-16	Internet-recruited MSM, US	OraQuick & Sure Check	Randomized to 4 ST (2 oral, 2 blood) or standard of care (n=3200 total)	Frequency of testing (12 mths). Linkage to care. Risk behaviour. Testing of partners and social networks
The FORTH Study, Kirby Institute, Australia (42)	2013-15	MSM, Australia	OraQuick	Randomized to 4 ST (all oral) or standard of care	Frequency of testing (12 months). STI test frequency, acceptability, use of tests

				(n=350)	
Thirumurthy, et al. University of North Carolina, Chapel Hill (40).	June – October 2015	Women in ANC or PPC in Kisumu, Kenya	OraQuick	Randomised to receive 2 HIVSTs or a referral voucher to attend testing in VCT clinic.	Male partner testing: 148 (51.7%) in SoC vs (90.8%) of HIVST group. Difference 39.1 (ci 32.4 to 45.8) Couples testing: 95 (33.2%) in SoC vs 214 (75.4%) HIVST. Difference 42.1 (34.7 to 49.6). Disclosure 145 (50.7) in SoC vs 255 (89.8) HIVST diff 39.1 (32.3 to 45.9) 1 case of IPV in each arm (women who felt at risk of IPV were excluded).
Stekler & Katz, University of Washington (NIH). The iTest Study (41)	2012-14	MSM, Seattle, US	OraQuick	Randomized to ST (any number) or standard of care (n=230)	Number of HIV tests during follow-up (15 mth): 5.3 ST versus 3.6. STI diagnosis (5% ST versus 12%). CL AI at 12 months (21% ST versus 22%) and 15 months (29% ST versus 24%)
Rodger et al, SELPHI study	2017-2020	MSM, England and Wales, UK	BioSure	Randomisation A: from 10 000 MSM, 40% SoC, 60% one HIVST Randomisation B: 3 000 eligible MSM. 50% receive SoC, 50% receive HIVST every 3 months.	Primary outcome: diagnosis of HIV infection confirmed through linkage to UK national HIV surveillance database of all diagnosed infections. Secondary outcomes include HIV and STI testing behaviours, sexual activity and cost effectiveness of HIV ST in increasing HIV diagnosis.