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# Realizing the potential of HIV self-testing for Africa: lessons learned from the STAR project

**Guest Editors:** Vincent J Wong, Nathan Ford, Kawango Agot
**Supplement Editor:** Anna Grimsrud


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## Acknowledgements

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EDITORIAL

# To thine own test be true: HIV self-testing and the global reach for the undiagnosed

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Globally, we are at an inflection point in achieving UNAIDS' 95-95-95 goals for 2030. A recent *Lancet* editorial observed that "the last big shared challenge remaining is testing—in every region the number of undiagnosed HIV infections remains a substantial barrier to achieving UNAIDS targets and ending AIDS by 2030" [1]. While UNAIDS estimates we are at 75% diagnostic coverage globally, within this figure is great variation: between men and women, younger and older individuals, rural and urban populations, among key populations and between countries [2,3]. After 18 years of expansive programming in global health for HIV testing through a multitude of modalities in communities and facilities, reaching the remaining undiagnosed individuals with flat-lined donor funding will require new efforts [3]. Many of the remaining undiagnosed individuals are presumably not engaging with HIV services, and novel avenues to HIV testing services (HTS) that overcome both stigma and structural barriers are needed: a new HIV testing paradigm is urgently needed to reach these remaining undiagnosed individuals and effectively link them to treatment.

HIV self-testing (HIVST) has developed substantially in recent years and is now considered a new and critical HIV response strategy in controlling the epidemic. In 2012, the US FDA approved the OraQuick® HIV Self-Test Kit introducing the first HIV rapid test kit intended for use by the general population and available for purchase over-the-counter in the United States. Building on a history of public health interventions aimed at self-screening for health conditions that includes home pregnancy tests, breast self-examinations for cancer screening and blood-glucose monitoring, access to HIVST permits individuals perceiving themselves to be at-risk of infection to test independently and privately. Global attention to the potential of HIVST took root in 2013 following the OraQuick FDA approval, with UNAIDS and the World Health Organization (WHO) holding an initial consultation on the ethical and public health implications of HIVST. At that time, no HIVST kits were publicly available in low- and middle-income countries (LMIC) (outside a small number of studies and "grey market" test kits), no normative guidelines had been established and only a small body of LMIC-focused evidence around HIVST existed. Within a year, a full HIVST journal supplement had been published exploring early issues in HIVST introduction: regulation and policy, optimal product profiles, ethical considerations and both positive and negative potential impacts of rollout [4-6]. This led, in 2015, to Unitaid's catalytic investment in the five-year HIV Self-Testing Africa (STAR) initiative. The first two-year phase, which included Malawi, Zambia and Zimbabwe, aimed to generate evidence on the feasibility and acceptability of HIVST as well as how to distribute self-test products effectively, ethically and efficiently, with adequate post-test support. Evidence from this phase supported country policy development, and studied impacts and cost-effectiveness of various delivery models, addressed structural barriers and assessed consumer demand. Findings from these and other studies led to the WHO guidance on HIVST in 2016 (also strategically paired with the HTS) Partner Notification guidelines [7]. A separate but concurrent process resulted OraQuick being the first WHO prequalified HIVST kit. In 2017, the Bill and Melinda Gates Foundation provided financial support to bring the unit cost of the OraQuick self-test kit down to US$2 in selected sub-Saharan African and other low-income countries, removing a critical cost barrier to HIVST expansion [8].

These initial supportive efforts established the foundation needed for HIVST expansion across countries. The second three-year phase of STAR added Lesotho, Eswatini and South Africa, and aimed to create a market for HIVST and evaluate optimal distribution models for increasing access to testing among those unwilling or unable to utilize traditional testing venues and ensuring linkage from a preliminary positive HIVST result to confirmatory testing and treatment. By the end of the programme, Unitaid, the STAR programme's commodities funder, will have provided five million HIVST kits to the six project countries. Building on STAR's momentum and their own smaller scale pilot programmes in 2016, PEPFAR

expanded its HIVST programming and will have delivered 2.3 million HIVST kits across 11 countries in 2017 to 2018. Similarly, the Global Fund is expanding HIVST support across 18 countries, estimated to cover about 12% of the global HIVST volume [9]. With 59 countries having, or developing, national HIVST policies, there is global acceleration towards the expansion of HIVST access and programmes and, with good linkage, increased diagnostic coverage [9]. However, these numbers remain small relative to the overall number of people tested; PEPFAR alone accounted for roughly 85 million HIV tests in 2017 [10]. But HIVST deployed strategically within programmes, and made available through multiple avenues, is anticipated to amplify the impact of current HIV programming by reaching the critical remaining at-risk populations with needed testing and treatment.

The articles collected for this *Supplement* present a diverse range of the key findings from the first phase of STAR, and provide a basis for needed programmatic action to accelerate expansion. Presently, in sub-Saharan Africa, there are 15 countries that have HIVST policies in place or under consideration and multiple products available with some type of certification [9,11]. However, products of unknown quality have been available on the unregulated market, posing risks and underscoring the need for further quality and consumer protection regulations [6,11]. Dacombe *et al*. explore the regulatory environment in Malawi, Zambia and Zimbabwe [12]. Using key informant interviews which included laboratory staff and policymakers, they consulted 66 individuals from the three countries. Interviews showed that in these countries, there was a need for regulation of *in vitro* diagnostic tests in general, and HIVST kits were no exception. The authors call for a regional collaboration to spread the regulatory burden across countries and facilitate the passing of required legislation to support more codified regulation of diagnostics.

WHO prequalified test kits have gone through quality assurance evaluations aimed at ensuring "global standards of quality, safety and efficacy" to support Ministries of Health and the introduction of quality diagnostics [13]. However, product performance includes not just quality standards of the test kit itself, but also usability by the target population and the successful insertion of HIVST into the clinical cascade. Early studies showed some challenges in following instructions for use (IFU) [5,14], but as kits have been refined, results have improved. A recent review demonstrated general agreement between results of HIVST kits and facility testing algorithms [15]. However, challenges relating to literacy remain, underscoring the need for clear and simple language in package inserts [15-17] and IFUs that are adapted to local contexts. In this *Supplement*, Simwinga *et al*. present findings from Malawi and Zambia evaluating an IFU translated into the local language and evaluated for clarity and ease of use [18]. Investigators used feedback from testers to optimize the IFU, concurring with previous findings that the educational level of the tester correlates to the ability to follow the IFU. In response, they suggest that in certain contexts community demonstrations of how to use HIVST kits could overcome this barrier.

In another study, given that programmes have proposed late reading of returned kits to determine HIV positivity, Watson *et al*. evaluated the OraQuick HIV-1/2 antibody test kits for result stability post-testing. They showed that while strongly reactive HIVST remained stable, 29% of initially non-reactive kits converting to be weakly reactive false positive when read at least four days later, countering previous work which indicated OraQuick test kits were stable for up to a year [19,20]. Re-reading may be problematic and result in artificially inflated positivity rates; this finding led the WHO to recommend *against* any delayed readings of kits [21].

Eaton *et al*. model how HIVST and other "test for triage" strategies might impact national algorithm performance [22]. Considering modelled high- and low-prevalence scenarios, as well as using data from Malawi, a high-prevalence country with high rates of diagnosis [23], the authors show that the addition of triage testing before the national algorithm increases the positive predictive value and decreases the number of false-positive diagnoses, possibly eliminating the need for verification testing at initiation of antiretroviral therapy (ART).

Methodologies for HIVST distribution will be a critical aspect of programme effectiveness. Various delivery modes have been considered: vending machines, over-the-counter at pharmacies, secondary distribution when an HIVST is distributed to one person for use by another, and facility- and community-based distribution [11,15,24-26]. In this *Supplement*, Sibanda *et al*. began with the clients, investigating preferences for access to HIVST in rural Zimbabwe through discrete choice assessments, finding respondent preferences for door-to-door distribution, kits free-of-charge, access by telephone to help in using kits and linkage to confirmatory testing, and that programmes use patient reminders and outreach to enhance effectiveness [27]. For confirmatory testing and ART initiation, respondents also preferred these to be free, located near their home and that ART could be initiated immediately [27]. This study supports previous findings on user preferences emphasizing ease of access, usability and privacy [11].

Also in this *Supplement*, Hatzold *et al*. reviewed STAR data from Malawi, Zambia and Zimbabwe that assessed the integration of HIVST tools into HIV programming [28]. They found that by having clients perform HIVST in outpatient settings, they were able to decongest clinical testing facilities because healthcare workers could focus only on those that screened positive. They also demonstrated the ability to reach men through community distribution and in particular workplaces, and explored male attitudes to HIVST, noting that the briefer counselling messages, privacy and convenience appealed to them [28].

Advantages of HIVST, such as the ability to test privately, may also be misused or abused and potential social harms should not be ignored. Previously in Kenya, low rates of physical and verbal abuse have been reported with the introduction of HIVST kits by women for their male partners to test themselves [29]. In this *Supplement*, Kumwenda *et al*. provide new evidence on social harms from projects in Malawi, summarizing data from six HIVST projects from 2011 to 2017 where a combination of qualitative and quantitative methods were used [30]. Coercion was reframed to have both negative and positive aspects, and the concept of compassionate coercion was introduced to describe instances when family members encourage a member who is ill to test. Overall, they report 25 serious adverse events through the active reporting systems from all six studies with a total of 178,833 self-tests distributed. The most common event was marriage breakdown in serodiscordant relationships though verbal abuse, and physical and economic intimate partner violence were infrequently also observed [30]. The potential for social harms is not unique to

HIVST, but the present work elucidates the need for intimate partner violence screening when considering HIVST secondary distribution and partner testing, and the need for ongoing monitoring of social harms within existing systems.

In the context of HIVST, linkage to care refers not just to the initiation of ART, but first to confirmatory testing after a positive HIVST [31]. Since using an HIVST kit in private is often preferred by testers, the onus to link to care is firmly placed in the hands of the tester. As such, linking testers to care and estimating linkage rates can be a challenge. Some HIVST research studies have estimated linkage rates to be between 36% and 78% with a variety of methodologies as there is no standard process to measure linkage [24,29,31,32]. In this *Supplement*, Neuman *et al*. reflect on the difficulties in estimating linkage as HIVST is brought to scale [33]. They note the limited metrics available – HIVST kit distribution totals and self-reported data, neither of which is optimal to estimate linkage rates accurately [33]. The investigators present a summary of study protocols estimating linkage from published STAR studies. These estimate HIVST linkage by using ecological indicators such as comparisons of ART initiation rates in areas with HIVST campaigns versus in areas without HIVST campaigns. Taken on its own, it is only correlative; however, when considered in addition to other information it can be used to create a body of evidence regarding linkage to care.

Costing HTS is highly contextual with considerable variation, but important to programme planning and bringing HIVST to scale. In this *Supplement*, Mangenah *et al*. performed a cost analysis of community HIVST kit distribution in Malawi, Zambia and Zimbabwe as well as a sensitivity and scenario analysis to project future costs [34]. The average cost per kit distributed (i.e. not only the commodity cost) ranged from US $ 7.23 to US$ 14.58 with variation by site location, but still comparable to previously published values [35]. In a second article, Cambiano *et al*. use this data to present a modelling analysis comparing community distribution to three priority populations in Zimbabwe and Malawi: women having transactional sex (WTS), youth and adult men [36]. The model showed that distribution to men averted the most deaths, but distribution to WTS was the most efficient as measured in number of tests per death averted. Cambiano *et al*. have added to cost-effectiveness research, considering the trade-offs between investing in HIVST and other HIV programmes, they estimate that HIVST is cost-effective when the mean cost per disability adjusted life year averted is below US$ 500. According to their models, this occurs when HIVST kits were distributed to WTS and men but not to youth.

Offering commentary on the use of HIVST, Ingold *et al*. focus on the broader policy environment in LMIC, market development for HIVST kits, the STAR programme experience and its positioning for HIVST scale-up [37]. As part of the intervention, the STAR programme engaged with manufactures and stakeholders at the country and multilateral levels to create demand, assess viability of HIVST as a route to diagnosis and research delivery methods. The overall goal being to pave the way for increased access to quality HIVST kits to mobilize more people living with HIV to know their status. The authors highlight the progress that has been made in addressing these barriers, including amassing a sufficient evidence base for WHO guidance and a more enabling policy environment in general, prequalification of two types of HIVST kits and a more robust product pipeline. Pilot studies have demonstrated the ability of HIVST to reach populations that have traditionally been refractory to other testing strategies and viability for priority populations. Ingold *et al*. also touch on outstanding challenges to be addressed and present a call to action to maintain momentum in bringing HIVST to scale [37].

Since 2012, substantial progress has been made on HIVST programmes, policy and products – but few countries are implementing HIVST at scale, with many still conducting smaller volume pilot programmes. Recent HIV response framings have declared that "what got us here won't get us there" [38]; for HIV testing, the rapid expansion of voluntary counselling and testing, provider-initiated approaches and community-based campaigns have achieved a global 75% diagnosis rate. The final reach to the remaining undiagnosed individuals, including early diagnosis of decreasing numbers of newly infected persons, will depend critically on an evolution of new approaches: HIVST, expansions of index testing and partner notification as a new minimum standard of care, and programmatic improvements of existing HTS access points. The evidence to date has demonstrated the potential of HIVST to reach both the unreached and those at high risk, which is key in achieving the 95-95-95 goals and controlling the epidemic.

However, operational questions remain. Intentional misuse, accuracy and performance of secondary distribution, more effective leveraging of public–private sector collaborations to reach high-risk populations, programmatic use of blood-based HIVST kits, use of HIVST as a demand generation tool for Pre-exposure prophylaxis (PrEP), volume procurement approaches to reduce unit pricing and the use of mobile technology and other methods to estimate linkage post-HIVST, could all benefit from more operations research to guide programming.

The body of evidence produced in this *Supplement* adds significantly to the field of HTS, exemplifying the potential public health role of this new technology to critically increase coverage. Still, HIVST access will not reach the scale needed to impact the epidemic without both leveraging existing health programmes and developing new and innovative avenues of access. The integration of HIVST should work to amplify existing HIV programming to achieve multiple purposes that serve public health goals: reaching unreached and high-risk individuals at an early disease stage, reducing testing burdens on taxed health systems, and critically identifying the most effective avenues to linking persons screening positive to onward testing and treating or linking persons screening negative to prevention services. All are outcomes of critical importance to controlling the HIV epidemic. And novel avenues such as private sector delivery will continue to need to be explored. While we find ourselves at the "last big shared challenge" of HIV testing, in the race towards control of the HIV epidemic, this *Supplement* strongly illustrates that a new testing paradigm based in part on HIVST is key to the next decade of the HIV response and achieving 95% diagnosis rates everywhere.

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## COMPETING INTERESTS

VW, EJ, NF and HI declare no competing interests.

## AUTHORS' CONTRIBUTIONS

VW and EJ drafted the initial manuscript. All authors critically reviewed the manuscript, suggested revisions and editorial changes, and approved the final version.

VW is a member of the Unitaid HIVSTAR Technical Advisory Group.

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## REFERENCES

1. The Lancet HIV. Divergent paths to the end of AIDS. Lancet HIV. 2017 [cited 2019 January 11];4(9):e375. Available from: http://linkinghub.elsevier.com/retrieve/pii/S2352301817301571
2. PHIA. PHIA Project: A drop that counts [Internet]. 2018 [cited 2019 January 11] ICAP at Columbia University. Available from: https://phia.icap.columbia.edu/
3. UNAIDS. Global AIDS Update 2018: Miles To Go Closing Gaps Breaking Barriers Righting Injustices [Internet]. 2018[cited 2019 January 11]. Available from: http://www.unaids.org/sites/default/files/media_asset/miles-to-go_en.pdf
4. Brown AN, Djimeu EW, Cameron DB. A review of the evidence of harm from self-tests. AIDS Behav. 2014;18 Suppl 4:S445–9.
5. 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.
6. Wong V, Johnson C, Cowan E, Rosenthal M, Peeling R, Miralles M, et al. HIV self-testing in resource-limited settings: regulatory and policy considerations. AIDS Behav. 2014;18 Suppl 4:S415–21.
7. WHO. Guidelines on HIV Self-Testing and Partner Notification. 2016.
8. Orasure. OraQuick HIV Self-test [Internet]. 2017 [cited 2019 January 11]. Available from: http://www.orasure.com/products-infectious/products-infectious-oraquick-self-test.asp
9. WHO/UNITAID. HIV rapid diagnostic tests for HIV self-testing. 2018.
10. PEPFAR. PEPFAR 2017 Annual Report to Congress. 2017.
11. Indravudh PP, Choko AT, Corbett EL. Scaling up HIV self-testing in sub-Saharan Africa: a review of technology, policy and evidence. Curr Opin Infect Dis. 2018;31(1):14–24.
12. Dacombe R, Watson V, Nyirenda L, Madanhire C, Simwinga M, Chepuka L, et al. Regulation of HIV self-testing in Malawi, Zambia and Zimbabwe: a qualitative study with key stakeholders. J Int AIDS Soc. 2019;22(S1):e25229.
13. WHO. Prequalification of *in vitro* diagnostics [Internet]. *In vitro* diagnostics and laboratory technology. 2018 [cited 2018 Apr 9]. Available from: http://www.who.int/diagnostics_laboratory/evaluations/en/
14. Pant Pai N, Sharma J, Shivkumar S, Pillay S, Vadnais C, Joseph L, et al. Supervised and unsupervised self-testing for HIV in high- and low-risk populations: a systematic review. PLoS Med. 2013;10(4):e1001414.
15. Figueroa C, Johnson C, Ford N, Sands A, Dalal S, Meurant R, et al. Reliability of HIV rapid diagnostic tests for self-testing compared with testing by health-care workers: a systematic review and meta-analysis. Lancet HIV. 2018 [cited 2019 January 11];5(6):e277–90. Available from: https://doi.org/10.1016/s2352-3018(18)30044-4
16. Grésenguet G, de Longo J D, Tonen-Wolyec S, Mboumba Bouassa R-S, Belec L. Acceptability and usability evaluation of finger-stick whole blood HIV self-test as an HIV screening tool adapted to the general public in the Central African Republic. Open AIDS J. 2017[cited 2019 January 11];11(33):101–18. Available from: http://www.ncbi.nlm.nih.gov/pubmed/29290887%0Ahttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC5730956
17. Tonen-Wolyec S, Batina-Agasa S, Muwonga J, N'kulu FF, Bouassa RSM, Bélec L. Evaluation of the practicability and virological performance of finger-stick whole-blood HIV self-testing in French-speaking sub-Saharan Africa. PLoS One. 2018;13(1):1–22.
18. Simwinga M, Kumwenda MKRD, Kayira L, Muzumara A, Johnson C, Indravudh P, et al. Ability to understand and correctly follow HIV self-test kit instructions for use: applying the cognitive interview technique in Malawi and Zambia. J Int AIDS Soc. 2019;22(S1):e25253.
19. Choko AT, Taegtmeyer M, Macpherson P, Cocker D, Khundi M, Thindwa D, et al. Initial accuracy of HIV Rapid test kits stored in suboptimal conditions and validity of delayed reading of oral fluid tests. PLoS One. 2016;11(6):6–13.
20. Watson V, Dacombe RJ, Williams C, Edwards T, Adams ER, Johnson C, et al. Re-reading of OraQuick HIV-1/2 rapid antibody test results: quality assurance implications for HIV self-testing programmes. J Int AIDS Soc. 2019;22(S1):e25234.
21. WHO. HIV Self-Testing Strategic Framework a Guide for Planning, Introducing and Scaling Up. Geneva; 2018.
22. Eaton JW, Terris-Prestholt F, Cambiano V, Sands A, Baggaley R, Hatzold K, et al. Optimizing HIV testing services in sub-Saharan Africa: cost and performance of verification testing with HIV self-tests and tests for triage. J Int AIDS Soc. 2019;22(S1):e25237.
23. ONUSIDA. Unaids Data 2018. 2018 [cited 2019 January 11];370. Available from: http://www.unaids.org/sites/default/files/media_asset/unaids-data-2018_en.pdf
24. Choko AT, MacPherson P, Webb EL, Willey BA, Feasy H, Sambakunsi R, et al. Uptake, accuracy, safety, and linkage into care over two years of promoting annual self-testing for HIV in Blantyre, Malawi: a community-based prospective study. PLoS Med. 2015;12(9):e1001873.
25. Kojima N, Klausner JD. Accelerating epidemic control: the role of HIV self-testing. Lancet HIV. [cited 2019 January 11];2018;5(6):e266–7.
26. Choko AT, Kumwenda MK, Johnson CC, Sakala DW, Chikalipo MC, Fielding K, et al. Acceptability of woman-delivered HIV self-testing to the male partner, and additional interventions: a qualitative study of antenatal care participants in Malawi. J Int AIDS Soc. 2017;20(1):1–10.
27. Sibanda EL, D'Elbée M, Maringwa G, Ruhode N, Tumushime M, Madanhire C, et al. Applying user preferences to optimize the contribution of HIV self-testing to reaching the "first 90" target of UNAIDS Fast-track strategy: results from discrete choice experiments in Zimbabwe. J Int AIDS Soc. 2019;22(S1):e25245.
28. Hatzold K, Gudukeya S, Mutseta M, Chilongosi R, Nalubamba M, Nkhoma C, et al. HIV self-testing: breaking the barriers to uptake of testing among men and adolescents in sub-Saharan Africa, experiences from STAR demonstration projects in Malawi, Zambia and Zimbabwe. J Int AIDS Soc. 2019;22(S1):e25244.
29. 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. Lancet HIV [Internet]. 2016 [cited 2019 January 11];3(6):e266–74. Available from: https://doi.org/10.1016/s2352-3018(16)00041-2
30. Kumwenda M, Johnson C, Choko A, Lora W, Sibande W, Sakala D, et al. Exploring social harms during distribution of HIV self-testing kits using mixed-methods approaches in Malawi. J Int AIDS Soc. 2019;22(S1):e25251.
31. Cambiano V, Mavedzenge SN, Phillips A. Modelling the potential population impact and cost-effectiveness of self-testing for HIV: evaluation of data requirements. AIDS Behav. 2014;18 Suppl 4:S450–8.
32. Macpherson P, Lalloo DG, Webb EL, Choko AT, Makombe SD, Anthony E, et al. Effect of optional home initiation of HIV care following HIV self- testing on antiretroviral therapy initiation among adults in Malawi. JAMA. 2014;312(95):372–9.
33. Neuman M, Taegtmeyer M, Hatzold K, Johnson C, Weiss HA, Fielding K. Challenges in measurement of linkage following HIV self-testing: examples from the STAR Project. J Int AIDS Soc. 2019;22(S1):e25238.
34. Mangenah C, Lawrence M, Sande L, Ahmed N, D'Elbee M, Chiwawa P, et al. Economic cost analysis of door-to-door community-based distribution of HIV self-test kits in Malawi, Zambia and Zimbabwe. J Int AIDS Soc. 2019;22(S1):e25255.
35. 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 [Internet]. 2016 [cited 2019 January 11];14(1):1–12. Available from: https://doi.org/10.1186/s12916-016-0577-7
36. Cambiano V, Johnson C, Hatzold K, Fern T-P, Maheswaran H, Thirumurthy H, et al. The impact and cost-effectiveness of community-based HIV self-testing in sub-Saharan Africa: a health economic and modelling analysis. J Int AIDS Soc. 2019;22(S1):e25243.
37. Ingold H, Mwerinde O, Ross AL, Ross L, Corbett E, Hatzold K, et al. The Self-Testing AfRica (STAR) Initiative: accelerating global access and scale-up of HIV self-testing. J Int AIDS Soc. 2019;22(S1):e25249.
38. El-Sadr WM, Harripersaud K, Rabkin M. Reaching global HIV/AIDS goals: what got us here, won't get us there. PLoS Med. 2017 [cited 2019 January 11];14(11):e1002421. Available from: http://dx.plos.org/10.1371/journal.pmed.1002421

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RESEARCH ARTICLE

# Regulation of HIV self-testing in Malawi, Zambia and Zimbabwe: a qualitative study with key stakeholders

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## Abstract

**Introduction:** HIV self-testing (HIVST) is being introduced as a new way for more undiagnosed people to know their HIV status. As countries start to implement HIVST, assuring the quality and regulating *in vitro* diagnostics, including HIVST, are essential. We aimed to document the emerging regulatory landscape and perceptions of key stakeholders involved in HIVST policy and regulation prior to implementation in three low- and middle-income countries.

**Methods:** Between April and August 2016, we conducted semi-structured interviews in Malawi, Zambia and Zimbabwe to understand the relationships between different stakeholders on their perceptions of current and future HIVST regulation and the potential impact on implementation. We purposively sampled and interviewed 66 national-level key stakeholders from the Ministry of Health and the regulatory, laboratory, logistical, donor and non-governmental sectors. We used a thematic approach to analysis with an inductively developed common coding framework to allow inter-country comparison of emerging themes.

**Results:** In all countries, the national reference laboratory was monitoring the quality of HIVST kits entering the public sector. In Malawi, there was no legal mandate to regulate medical devices, in Zambia one regulatory body with a clear mandate had started developing regulations and in Zimbabwe the mandate to regulate was overlapping between two bodies. Stakeholders indicated that they had a poor understanding of the process and requirements for HIVST regulation, as well as lack of clarity and coordination between organizational roles. The need for good collaboration between sectors, a strong post-market surveillance model for HIVST and technical assistance to develop regulators capacity was noted as priorities. Key informants identified technical working groups as a potential way collaboration could be improved upon to accelerate the regulation of HIVST.

**Conclusion:** Regulation of *in vitro* diagnostic devices, including HIVST, is now being recognized as important by regulators after a regional focus on pharmaceuticals. HIVST is providing an opportunity for each country to develop similar regulations to others in the region leading to a more coherent regulatory environment for the introduction of new devices.

**Keywords:** quality assurance; policy; *in vitro* diagnostics; post market; implementation; harmonization

Additional Supporting Information may be found online in the Supporting information tab for this article.

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## 1 | INTRODUCTION

The World Health Organization (WHO) defines HIV self-testing (HIVST) as "a process in which a person collects his or her own specimen (oral fluid or blood) and then performs a test and interprets the result, often in a private setting, either alone or with someone he or she trusts" [1]. HIVST has been put forward as an innovative tool for reaching the remaining 23% (33% to 12%) of people with HIV who do not know their status [2]. The number of HIVST kits accessible through the public sector in Africa is increasing rapidly in response to the global scale-up [3]. The regulation of kits has been identified as an important emerging area to protect the consumer from harm [4].

HIVST kits are classed as *in vitro* diagnostic (IVD), that is tests on specimens taken from the body, and thus are considered medical devices by the International Medical Device Regulation Forum [5]. Medical devices are classified according to the hazard the device presents based on its intended use and the expertise of the user and the impact of the result. Due to the potentially severe outcomes of an incorrect result and its use by lay persons, regulators would likely consider HIVST kits as a Class D (highest risk) medical device and therefore subject to the greatest degree of regulation [6]. For an HIVST kit to meet

the stringent regulatory standards of the International Medical Device Forum, it must not only demonstrate the stability and accuracy required for device registration, but also take into account mechanisms for ensuring the kit performs optimally in the hands of intended users. HIVST kits approved for use by regulatory authorities in high-income countries, such as the United States Food and Drug Administration, may take several years to evaluate and test performance in their specific population [7,8]. To speed up this process and make the evaluation more focused on low- and middle-income countries, in 2016, the WHO released the technical specifications series for the pre-qualification (PQ) of HIVST kits [9] and in 2017 the OraQuick® HIV Self-Test was the first device to be given PQ approval [10].

Surveys of regulation across Africa have identified IVD regulation as a neglected area [11,12]. In the majority of countries, including those with generalized HIV epidemics planning to use the HIVST approach as part of their strategic response, HIVST remains unregulated [4,12]. Many low- and middle-income countries and donors use WHO PQ as a pre-requisite or substitution for device registration. However, PQ does not cover all monitoring of device performance undertaken once a device is on the market (post-market surveillance) though an adverse event reporting system is in place [13]. For professional use HIV rapid diagnostic tests (RDTs), programmes for external quality assurance (EQA) have been developed for resource-limited settings to compare testing performance between sites [14]. In Africa, EQA programmes are largely run by the tertiary HIV referral laboratories or national reference laboratories and act as a post-market surveillance system in the absence of or, where available, in collaboration with IVD regulators. These approaches require adaptation to work for HIVST. However, at present many of these EQA programmes are not working due to insufficient funding [15].

We set out to determine the current regulatory status of HIVST in Malawi, Zambia and Zimbabwe and document the perceptions and suggestions of key stakeholders regarding current and future HIVST regulation in each country. These countries had been selected for the Unitaid/PSI HIV Self-Testing in AfRica (STAR) project based on their high HIV prevalence (Malawi 9.2%, Zimbabwe 13.5% and Zambia 12.4%), established community-based HIV testing services, availability of data from pilot studies on HIVST and importantly, local government support for HIVST [16-19]. The STAR project aims to catalyse the market for high quality HIVST. Appropriate effective regulation is required to meet this aim.

## 2 | METHODS

We used qualitative and policy analysis methods to understand the relationships between different stakeholders, their perceptions of current and future regulation and its links to potential scale-up [20,21]. We sought to document the current understanding and knowledge of HIVST regulation and to explore sensitive areas around how the development of regulation for HIVST can be influenced by context and individual stakeholders. Individual semi-structured interviews with key informants were conducted at the convenience of the key informants [22]. The consolidated criteria for reporting qualitative research were used when preparing this manuscript to ensure all relevant information was included [23].

### 2.1 | Selection of study participants

The study took place in Malawi, Zambia and Zimbabwe. We considered stakeholders likely to give in-depth information on regulation in each country and/or who were likely to play a key role in HIVST scale-up. We developed lists of participants with input from country research teams using both relevant policy and regulatory documents and local knowledge. We further supplemented this list by snowball sampling.

### 2.2 | Data collection

We developed topic guides informed by literature on regulation, global and national policies on HIV testing and HIVST and implementation experience related to HIVST and based on the policy triangle framework. The policy triangle is a framework developed to examine not only the content of policy but also why is it needed (context), the stakeholders involved (actors), and how it is developed and implemented (the process). The topic guides focused on questions considered to be important in HIVST including key informants' perceptions on the current and future processes for regulation of HIVST, key stakeholders in regulation and policy and their relationships and views on the context of scale-up of HIVST in each country (Data S1). Additional questions were added iteratively after interim analysis of emerging themes. Participants gave written consent to be interviewed. Interviews were conducted in English between April and August 2016, by RD, VW, LN and CM. Interviews were digitally recorded and emerging themes discussed within the research team to triangulate findings.

### 2.3 | Data analysis and trustworthiness

Audio recordings of the interviews were transcribed verbatim and NVivo qualitative data analysis Software (QSR International Pty Ltd. Version 11, 2017) was used to manage the data. VW and RD independently coded a subset of ten transcripts each and then met to determine consensus and minimize inter-coder variability for quality control purposes [24]. A thematic approach for data analysis was used which generated themes inductively based on what emerged from the data [25]. In order to ensure trustworthiness, initial analysis was discussed and refined by all the interviewers. Findings were then presented to a wider audience of researchers, regulators, WHO staff and policymakers from the three countries at a STAR consortium meeting in Lusaka in October 2016 and an international HIVST workshop held in Nairobi in March 2017, with the subsequent feedback and discussion further informing the analysis [26].

### 2.4 | Ethical considerations

We obtained ethical approval from the Liverpool School of Tropical Medicine(Ref: 15.030, University of Zambia (Ref: 013-11-15) and Medical Research Council of Zimbabwe (Ref: MRCZ/A/180) and the Malawian College of Medicine Research Ethics Committee (Ref: P.01/16/1860).

## 3 | RESULTS

We purposively sampled a total of 66 national-level key informants across the three countries (Table 1). Three main themes emerged from the interviews: (1) the limited capacity for IVD regulation, (2) the need for improved coordination for IVD regulation, and (3) a desire for international and regional harmonization. These are summarized in Table 2.

### 3.1 | Limited capacity for IVD regulation

Across all three countries, knowledge and understanding of IVD regulation and HIVST was limited. Few key informants were clear on what regulation for HIVST would entail. Both Zambia and Zimbabwe medicines regulatory authorities (Zambia Medicines Regulatory Authority (ZAMRA) and The Medicines Control Authority of Zimbabwe (MCAZ), respectively) reported that they were starting to develop regulations for IVDs, though not specific to HIVST. While most participants in Zambia identified ZAMRA as having the mandate for IVDs, several others thought HIVST regulation would be handled by the Central Medical Stores or the laboratory technical working group. A small number of laboratory staff thought other authorities would need to be involved, such as the Bureau of Standards.

In Zimbabwe, respondents from two authorities reported that they considered themselves to be mandated to regulate HIVST kits (MCAZ and the Medical Laboratory and Clinical Sciences Council of Zimbabwe (MLCSCZ)). However, at the time of the interviews neither had started regulating HIVST kits and it was unclear to respondents who had the regulatory mandate: "No, actually I have just assumed that they do go through MCAZ [Medicines Control Authority of Zimbabwe] but I am not sure. It is very unclear" (Zimbabwe KII23 Male). The majority of respondents reported it was either the MLCSCZ or MCAZ with an approximately equal proportion suggesting it was both. However, some respondents also mentioned the need to have regulatory approvals from the Health Professions Association and the Standards Association of Zimbabwe.

In Malawi, the majority of policymakers and laboratory staff identified that there were no regulated HIVST kits in Malawi. Most identified the national reference laboratory as the responsible body for regulating IVDs, with a few laboratorians and NGO staff respondents reporting that they thought Pharmacy, Medicines and Poisons Board (PMPB) was responsible for regulating IVDs. While respondents indicated that legal mandates for IVDs regulations were unclear, they were aware of a process to provide more clarity, such as the PMPB seeking the mandate to regulate through an Act of Parliament: "In fact, they [parliament] are reviewing their Act [of Parliament] at present to include medical devices" (Malawi KII20 Male). While most identified the national reference laboratory as responsible for IVDs, the majority of respondents felt that regulations of professional use, as well as HIVST kits, should move to the PMPB in the future: "The issue of regulation is different because the reference laboratory is not a regulator. The Pharmacy, Medicines and Poisons Board is a regulator. That is one of their roles" (Malawi KII18 Female).

Regulators in all countries expressed a need for more support to develop IVD regulations. None of the countries had regulations that entirely covered the regulation of IVDs or any specific guidance on HIVST regulation. In Zambia, regulators said they were focusing on getting guidelines developed for the pre-market registration of products. In Zimbabwe, they were focusing on import and export regulations. In Malawi, regulators were focused on product registration, but noted that they needed support to develop IVD regulations: "Definitely we have to have the capacity and indeed so in the process of our capacity building, we have to actually develop those skills [in IVD regulation]" (Malawi KII14 Male).

**Table 1. Key informant characteristics**

| | Number of participants interviewed | | |
|---|---|---|---|
| **Participant constituency** | **Malawi** | **Zambia** | **Zimbabwe** |
| Ministry of Health Policymaker | 6 | 3 | 4 |
| Regulator | 3 | 1 | 4 |
| Laboratory | 4 | 3 | 2 |
| Pharmacy/stores | 1 | 1 | 3 |
| NGOs | 3 | 6 | 7 |
| WHO/UN | 2 | 2 | 4 |
| Donors | 4 | 0 | 3 |
| **Total** | **23** | **16** | **27** |

WHO, World Health Organization.

### 3.2 | The need for improved coordination for IVD regulation

In all countries, significant potential to support HIVST regulation existed between the Ministry of Health HIV department, national reference laboratory and the IVD regulator. Key informants consistently recognized that links between policymakers, regulators and laboratorians were weak: "I think the link is quite weak, we don't really have much interaction" (Malawi KII12 Male). Some regulatory key informants in Zimbabwe and Malawi reflected that greater collaboration maybe useful considering that medical devices were new: "Medical devices would be a new thing, that's why probably we are doing the regulations. Perhaps then we cannot be exclusive" (Zimbabwe KII10 Female).

The lack of an effective regulation system and of a coordinated approach was a concern for all respondents in all countries. A key concern was the potential entry of unregulated and poor quality HIVST kits into the domestic market and was regarded as a risk for all countries. All key informants in Malawi and Zambia indicated that they had not seen HIVST in the private sector. However, in Zimbabwe the majority of policymakers thought that HIVST was available in the private sector, indicating that regulation was urgently required: "We hear people are already selling, kits are out there" (Zimbabwe KII21 Female).

The quality of HIVST kits, particularly their performance in the hands of intended users, was a concern for the majority of key informants across all countries as illustrated by a respondent from Zambia: "If somebody has a false negative, it could be a real issue because they suddenly don't think they

**Table 2. Main themes emerging from interviews**

| Theme | Country | Category | Supporting Quote | Source |
|---|---|---|---|---|
| Limited capacity for IVD regulation | Malawi | No authority with legal mandate for IVD regulation | "In fact, they [parliament] are reviewing their Act [of Parliament] at present to include medical devices" | Malawi KII20 |
| | Zimbabwe | Two authorities considered mandated to regulate IVDs | "No, actually I have just assumed that they do go through MCAZ [Medicines Control Authority of Zimbabwe] but I am not sure. It is very unclear" | Zimbabwe KII23 |
| | All | Support required to develop regulations | "Definitely we have to have the capacity and indeed so in the process of our capacity building, we have to actually develop those skills [in IVD regulation]" | Malawi KII14 |
| The need for improved coordination for IVD regulation | All | Weak coordination between ministries of health, regulators and national reference laboratories | "I think the link is quite weak, we don't really have much interaction" | Malawi KII12 |
| | Zimbabwe and Malawi | Need for greater collaboration by regulator | "Medical devices would be a new thing, that's why probably we are doing the regulations. Perhaps then we cannot be exclusive" | Zimbabwe KII 10 |
| | All | Regulator not part of HIV self-testing technical working groups/task forces | "At the moment we are in what is called drug and medical supplies [technical working group]" | Malawi KII14 |
| International and regional harmonization | All | WHO pre-qualification an important mechanism for ensuring the quality of test kits | "For now, we are happy to look at what WHO has recommended as a bare minimum, then we will add additional prerequisites ourselves, but it must have a recommendation from WHO. If they are fully pre-qualified that's even better" | Zambia KII12 |
| | All | Coordination between countries seen as benefit for developing regulations | "It's a matter of trying to get Malawi at the table to see how other countries are doing so they can set up something similar" | Malawi KII13 |

IVD, *in vitro* diagnostic.

have HIV" (Zambia KII4 Male). There was concern from the majority of key informants around the type of post-market surveillance model to be used for HIVST as it would not be performed by professionals in facilities. The majority of laboratorians and policymakers across countries were concerned with how to monitor false non-reactive results: "Most likely we will see the positives in the test facility. [The concern is] The ones who come out with a negative and they don't come to the facility" (Zambia KII17 Female).

Technical working groups with a mandate to focus on HIVST were seen as a way of coordinating the development of policy and regulation. In Malawi, most key informants felt the scale-up of HIVST should be coordinated by the HIV Testing and Counselling Technical Working Sub-group and a minority of laboratorians thought it should be coordinated through the laboratory technical working group. Notably, neither group included PMPB. They instead belonged to a different technical working group: "At the moment we are in what is called drug and medical supplies [technical working group]" (Malawi KII14 Male).

In Zambia, there was no regulatory involvement in the HIV counselling and testing technical working groups though one policymaker indicated that ZAMRA initiated some *ad hoc* meetings with the Ministry of Health. Some policymakers indicated that approval by the national reference laboratory would be part of HIVST regulation but the ZAMRA were considering outsourcing to a different laboratory: "The best outsourced reference lab that I might point out is the Bureau of Standards" (Zambia KII6 Female).

Memoranda of understanding were identified as a possible mechanism by which different organizations could work together. However, regulatory key informants in Zimbabwe thought split mandates needed to be addressed in a way that the mandate rests with one regulator only: "How we team up with them is through MOUs" (Zimbabwe KII10 Female). "So, let's work together you as medicine laboratory scientists,

evaluating controlling regulating kits for us but not the other way around" (Zimbabwe KII27 Female).

### 3.3 | International and regional harmonization

WHO pre-qualification was recognized by key informants from all sectors, across all countries, as an important mechanism for ensuring the quality of test kits from manufacturers. Most also stated that it was a procurement requirement from donors as illustrated by this commonly held view: "For now, we are happy to look at what WHO has recommended as a bare minimum, then we will add additional prerequisites ourselves, but it must have a recommendation from WHO. If they are fully pre-qualified that's even better" (Zambia KII12 Female).

There was little mention of the existence of any regional bodies or other inter-country interactions other than with the WHO for IVD regulation, but participants from all sectors were aware of the benefits of a shared approach and were open to the possibility. One regulatory key informant indicated they were using other countries' regulations to base their own draft IVD regulations on: "you see, we pick it up from different countries and then we sort of custom make our own" (Zimbabwe KII10 Female). Similarly, ZAMRA were reported to be looking at regional collaboration: "We will sit down as regulators and say fine how are we going to look at this because I know Zimbabwe had some guidelines" (Zambia KII6 Female). Recognition of regional efforts for collaboration was also seen amongst laboratorians and regulators as indicated by this key informant: "It's a matter of trying to get Malawi at the table to see how other countries are doing so they can set up something similar" (Malawi KII13 Male).

## 4 | DISCUSSION

HIVST is a relatively new technology, especially in the context of regulations in low- and middle-income countries [27]. Our research found that the development of regulation for IVDs ranged from none in one country to the drafting of guidelines for pre-market regulation in the other two countries. We found lack of clarity of roles and responsibilities across different organizations and regulatory authorities making it difficult to determine who was responsible for HIVST regulations in country. We also found that overlapping mandates for regulating *in vitro* diagnostics may be a significant factor in delaying the development of regulations and could result in stalemate or the development of conflicting regulations. Key informants we interviewed were particularly concerned about the performance of HIVST in the hands of intended users and the implications for post-market surveillance despite evidence to the contrary [28].

The potential role of HIV National Reference Laboratories who are already monitoring HIV kits for professional use, in post-market surveillance of HIVST had not been recognized by most regulators. There is a clear, recognized need for strengthened regulatory capacity for medical device regulators, HIV departments and National Reference Laboratories and clarity on their roles in HIVST regulation, so policy and regulation can be properly aligned and the experience of reference laboratories in checking HIV kits can be properly utilized.

HIVST regulation and implementation is a rapidly evolving field. A study conducted in 2013 involving similar constituents, and in the case of Malawi some of the same individuals, showed that few participants had come across HIVST in practice [29]. Concerns were voiced about the need for counselling and the potential for coercive testing and to a lesser extent about kit accuracy. In contrast, we found widespread familiarity with HIVST as an approach and more focus on concerns over test performance and systems for quality assurance. The development of post-market surveillance systems able to detect false non-reactive results is of concern in other studies too [29,30] but we are not aware of any programmes that have successfully addressed this. Current HIV quality assurance approaches are designed for facility-based rapid testing, where testing is conducted by trained testers who record results and where kit storage and lot numbers can be traced [31]. Alternative approaches to monitoring HIVST performance, such as the visual stability of kits for re-reading, digital photography and direct observation need further investigation [32,33].

HIVST regulation has failed to keep pace with the scale-up of HIVST and IVD regulation in general and is underdeveloped in many countries [11,12]. Globally, only one HIVST device has been pre-qualified by the WHO and the process to gather the evidence required for dossier submission can take many years [34]. Our findings of poor national-level coordination and capacity have implications for both manufacturers trying to enter these local markets and for end users. For manufacturers, the fragmented and uncertain regulatory environment creates barriers that mean they are reluctant to take the financial risks associated with the development of high quality HIVST products. Manufacturers lack incentives to innovate further product development and prices for existing products remain high due to lack of competition [35]. For end users, the delays could result in the proliferation and use of unregulated low quality tests and ultimately incorrect HIV screening results and loss of consumer confidence [36].

The current lack of IVD regulation in many African countries presents an opportunity for regulatory convergence between countries. Regional groups, such as the Pan African Harmonization Working Party [37] and the African Society for Laboratory Medicine [38], already exist with this aim but lack adequate resourcing and political prioritization. Regional coordination can develop capacity, save time and effort and speed up costly, cumbersome and duplicative processes. Four key areas to aid convergence are: common pre-market registration; joint manufacturing site inspections; joint data review and evaluation protocols and the establishment of laboratory networks for post-market surveillance [12,39]. Our findings indicate WHO pre-qualification is likely to be an important component of any common pre-market HIVST registration system in the African region provided manufactures buy into the process [40]. Collaborative regulatory procedures (e.g. reviews of dossier submissions) make a more attractive regulatory environment for manufacturers who would no longer need to submit different dossiers to multiple regulatory authorities [41].

National leadership links HIVST to the wider HIV testing strategy and brings key stakeholders under a common vision.

A single coordinated approach that establishes roles and responsibilities from an early stage, will allow a complete picture of HIVST situation within the country, linking HIV testing policymakers, regulators and laboratory stakeholders. Experience from policy development elsewhere reveals that power, inclusive of funders, politics and patronage can play as much of a role in delaying or pushing through policy as evidence and need [42]. The current fragmented approach risks exacerbating this situation when there is a lack of direction, convergence within intra-country constituencies and strong leadership.

The study shares limitations of qualitative approaches in general, principally the non-generalizability of study findings. However, the qualitative approach insisting on depth rather than breadth was suitable for our study since it enabled us to explore, describe and analyse sensitive issues related to a new testing approach. Though we interviewed a wide range of participants across seven different sectors, the small number of respondents in some categories made comparison across groups difficult. Due to a limited number of possible respondents, countries rather than constituencies have been used for attribution of illustrative quotations to protect individual's anonymity. Some areas related to regulation such as government procurement processes and supply chain were not explored in depth during the interviews to try and focus more on the barriers and opportunities to developing regulations.

## 5 | CONCLUSIONS

The recognition of the role of regulation in the scale-up of HIVST is important to ensure the market only has high quality test kits that can be used correctly and confidently by intended users. Programmes should establish clear lines of communication with IVD regulators early to allow for the alignment of policy and regulation and ensure all voices are heard in their respective development. The expertise of HIV National Reference Laboratories should be used to assist in the evaluation of HIVST kits and the development of post-market surveillance systems.

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### COMPETING INTERESTS

None of the authors have any conflicts of interest.

### AUTHORS' CONTRIBUTIONS

RD was involved in the concept, design, data collection and management, analysis of study data and led the writing of the manuscript. VW was involved in the concept, design, data collection and management of the study and contributed to the writing of the manuscript. LN was involved in the design and data collection portion of the study and contributed to the writing of the manuscript. CM, LC ad MS were involved in the data collection portion of the study and reviewed the manuscript. CJ, ELC and KH were involved in the concept and design of the study and reviewed the manuscript. MT was involved in the concept, design and analysis of the study and contributed to the writing of the manuscript.

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### REFERENCES

1. World Health Organisation. March 2014 supplement to the 2013 consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. 2014.
2. UNAIDS. UNAIDS Data 2018. 2018.
3. Indravudh PP, Choko AT, Corbett EL. Scaling up HIV self-testing in sub-Saharan Africa: a review of technology, policy and evidence. Curr Opin Infect Dis. 2018;31(1):14–24.
4. Wong V, Johnson C, Cowan E Rosenthal M, Peeling R, Miralles M, et al. HIV self-testing in resource-limited settings: regulatory and policy considerations. AIDS Behav. 2014;18 Suppl 4:S415–21.
5. Study Group 1 of the Global Harmonization Task Force. Definition of the Terms 'Medical Device' and 'In Vitro Diagnostic (IVD) Medical Device. 2012.
6. The Global Harmonization Task Force. Principles of Medical Devices Classification. 2012.
7. US Food adn Drug Administration. OraQuick In-home HIV Test. US Food and Drug Administration: Premarket Approvals. 2012.
8. Myers JE, El-Sadr WM, Zerbe A, Branson BM. Rapid HIV self-testing: long in coming but opportunities beckon. AIDS. 2013;27(11):1687–95.
9. World Health Organisation, TSS-1. Human Immunodeficiency Virus (HIV) rapid diagnostic tests for professional use and/or self-testing, in Technical Specification Series for submission to WHO Prequalification - Diagnostic Assessment. 2016.
10. World Helath Organisation. WHO Prequalification of In Vitro Diagnostics Public Report. 2017.
11. McNerney R, Peeling RW. Regulatory in vitro diagnostics landscape in Africa: update on regional activities. Clin Infect Dis 2015;61 Suppl 3:S135–40.
12. Rugera SP, McNerney R, Poon AK, Akimana G, Mariki RF, Kajumbula H, et al. Regulation of medical diagnostics and medical devices in the East African community partner states. BMC Health Serv Res. 2014;14:524.
13. World Health Organisation. Post-market surveillance of in vitro diagnostics. 2015.
14. Parekh BS, Kalou MB, Alemnji G, Ou CY, Gershy-Damet GM, Nkengasong JN. Scaling up HIV rapid testing in developing countries: comprehensive approach for implementing quality assurance. Am J Clin Pathol. 2010;134 (4):573–84.
15. Zungu LI, Magombo T, Chikaonda T, Thomas R, Mwenda R, Kandulu J, et al. A national quality assurance programme for point-of-care testing in Malawi. Afr J Lab Med. 2016;5(2):540.
16. Choko AT, Desmond N, Webb EL, Chavula KNapierala-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.
17. 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.
18. Buzdugan R, Watadzaushe C, Dirawo J, Mundida O, Langhaug L, Willis N, et al. Positive attitudes to pediatric HIV testing: findings from a nationally representative survey from Zimbabwe. PLoS One. 2012;7(12):e53213.
19. Zachary D, Mwenge L, Muyoyeta M, Shanaube K, Schaap A, Bond V, et al. Field comparison of OraQuick ADVANCE rapid HIV-1/2 antibody test and two blood-based rapid HIV antibody tests in Zambia. BMC Infect Dis. 2012;12:183.
20. Walt G, Shiffman J, Schneider H, Murray SF, Brugha R, Gilson L. 'Doing' health policy analysis: methodological and conceptual reflections and challenges. Health Policy Plan. 2008;23(5):308–17.

21. Pope C, Mays N. Reaching the parts other methods cannot reach: an introduction to qualitative methods in health and health services research. BMJ. 1995;311(6996):42–5.
22. Houston MJ, Sudman S. A methodological assessment of the use of key informants. Soc Sci Res. 1975;4(2):13.
23. Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. Int J Qual Health Care. 2007;19(6):349–57.
24. Baxter P, Jack SM. Qualitative case study methodology: study design and implementation for novice researchers. The Qualitative Report 2008;13 (4):544–59.
25. Braun V, Clarke V. Using thematic analysis in psychology. Qual Res Psychol. 2006;3(2):77–101.
26. STAR. HIV Self-Testing Workshop, Nairobi. 2017 [cited 2018 Feb 20]. Available from: http://hivstar.lshtm.ac.uk/st_events/
27. Johnson C, Baggaley R, Forsythe S, Van Rooyen H, Ford N, Mavedzenge SN, et al. Realizing the potential for HIV self-testing. AIDS Behav. 2014;18 Suppl 4:S391–5.
28. Figueroa C, Johnson C, Ford N, Sands A, Dalal S, Meurant R, et al. Reliability of HIV rapid diagnostic tests for self-testing compared with testing by health-care workers: a systematic review and meta-analysis. Lancet HIV 2018;5 (6):e277–90.
29. van Rooyen H, Tulloch O, Mukoma W, Makusha T, Chepuka L, Knight LC, et al. What are the constraints and opportunities for HIVST scale-up in Africa? Evidence from Kenya, Malawi and South Africa. J Int AIDS Soc. 2015;18:19445.
30. Makusha T, Knight L, Taegtmeyer M, Tulloch O, Davids A, Lim J, et al. HIV self-testing could "revolutionize testing in South Africa, but it has got to be done properly": perceptions of key stakeholders. PLoS One. 2015;10(3):e0122783.
31. World Health Organisation. Consolodated guidelines on HIV testing services 2015. 2015.
32. Choko AT, Taegtmeyer M, MacPherson P, Cocker D, Khundi M, Thindwa D, et al. Initial accuracy of HIV rapid test kits stored in suboptimal conditions and validity of delayed reading of oral fluid tests. PLoS One. 2016;11(6):e0158107.
33. Watson V, Dacombe R, Williams C, Edwards T, Adams E, Johnson C, et al. Determination of OraQuick® HIV self-test result stability with delayed visual re-reading: an external quality assurance analysis, in IAS 2017. Paris: France; 2017.
34. Johnson CF, C:Cambiano V, Phillips A, Sands A, Urassa W, Perez Gonzalez I, et al. A cinical untility risk-benefit analysis for HIV self-testing, in IAS2017. Paris France; 2017.
35. Population Services International, Expanding access to HIV self-testing: A market development approach. Washington DC. 2016.
36. Williams OD, Dean JA, Harting K, Bath K, Gilks CF. Implications of the online market for regulation and uptake of HIV self-testing in Australia. AIDS Care. 2017;29(1):112–7.
37. Asian Harmonization Working Party. Asian Harmonization Working Party Playbook for Implementation of Medical Device Regulatory Frameworks. Asian Harmonization Working Party. 2014.
38. African Society for Laboratory Medicine. ASLM 2020 Vision. 2015 [cited 2018 Feb 20]. Available from: http://www.aslm.org/who-we-are/aslm2020-vision/
39. McNerney R, Sollis K, Peeling RW. Improving access to new diagnostics through harmonised regulation: priorities for action. Afr J Lab Med. 2014;3 (1):123.
40. Morin S, Bazarova N, Jacon P, Vella S. The manufacturers' perspective on world health organization prequalification of in vitro diagnostics. Clin Infect Dis. 2018;66(2):301–5.
41. Ndomondo-Sigonda M, Miot J, Naidoo S, Dodoo A, Kaale E. Medicines regulation in Africa: current state and opportunities. Pharmaceut Med. 2017;31 (6):383–97.
42. Erasmus E, Gilson L. How to start thinking about investigating power in the organizational settings of policy implementation. Health Policy Plan. 2008;23 (5):361–8.

## SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

**Data S1.** Interview Guide for Key National Stakeholders: HIVST regulatory and policy.

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RESEARCH ARTICLE

# Ability to understand and correctly follow HIV self-test kit instructions for use: applying the cognitive interview technique in Malawi and Zambia

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## Abstract

**Introduction:** The ability to achieve an accurate test result and interpret it correctly is critical to the impact and effectiveness of HIV self-testing (HIVST). Simple and easy-to-use devices, instructions for use (IFU) and other support tools have been shown to be key to good performance in sub-Saharan Africa and may be highly contextual. The objective of this study was to explore the utility of cognitive interviewing in optimizing the local understanding of manufacturers' IFUs to achieve an accurate HIVST result.

**Methods:** Functionally literate and antiretroviral therapy-naive participants were purposefully selected between May 2016 and June 2017 to represent intended users of HIV self-tests from urban and rural areas in Malawi and Zambia. Participants were asked to follow IFUs for HIVST. We then conducted cognitive interviews and observed participants while they attempted to complete the HIVST steps using a structured guide, which mirrored the steps in the IFU. Qualitative data were analysed using a thematic approach.

**Results:** Of a total of 61 participants, many successfully performed most steps in the IFU. Some had difficulties in understanding these and made errors, which could have led to incorrect test results, such as incorrect use of buffer and reading the results prematurely. Participants with lower levels of literacy and inexperience with standard pictorial images were more likely to struggle with IFUs. Difficulties tended to be more pronounced among those in rural settings. Ambiguous terms and translations in the IFU, unfamiliar images and symbols, and unclear order of the steps to be followed were most commonly linked to errors and lower comprehension among participants. Feedback was provided to the manufacturer on the findings, which resulted in further optimization of IFUs.

**Conclusions:** Cognitive interviewing identifies local difficulties in conducting HIVST from manufacturer-translated IFUs. It is a useful and practical methodology to optimize IFUs and make them more understandable.

**Keywords:** HIV self-test; performance; *in vitro* diagnosis; instructions for use; Zambia; Malawi

Additional Supporting Information may be found online in the Supporting information tab for this article.

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## 1 | INTRODUCTION

HIV self-testing (HIVST) is increasingly being introduced as a testing approach recommended by the World Health Organization (WHO) to reach those who may not otherwise test [1,2]. Key advantages of HIVST are its high acceptability among men, young people and key populations, who often prefer the privacy and convenience of self-testing over other HIV testing options [3]. Without the ability to perform the test and interpret the results correctly, many of the potential benefits of HIVST are lost [4].

During development and for regulatory approvals, manufacturers provide the results of a process of evaluation that includes studies on ease of use and comprehension of test kit materials. An assessment of how the kit (device plus supporting materials) performs among untrained self-testers is part of the standard regulatory approval process. Manufacturers' pre-submission enquiries [5] and full product dossiers undergo

comprehensive assessment before site inspection and laboratory evaluations of performance are conducted. Approval implies that resource-limited settings can have confidence that self-use products have been rigorously evaluated [6]. At the time of writing, one product has been prequalified by WHO with four approved for procurement with donor funds on an interim basis by the Global Fund's Expert Review Panel for Diagnostics [7].

The results of HIVST by untrained users have been shown to be relatively accurate though variable. Both oral fluid- and blood-based HIVST have shown acceptable accuracy [8], especially when conducted with additional support in small-scale assessments in sub-Saharan Africa [9-15]. External packaging, instructions for use (IFU) and any supplementary materials can impact the ability of users to correctly perform a self-test and interpret the results. In Zimbabwe, overly wordy instructions were shown to result in poor outcomes in rural settings [15]. In South Africa, poor self-test outcomes were reported among healthcare workers who did not receive clear instructions on how to use and interpret the results of oral fluid-based tests [13]. A study comparing the usability of different prototypes of oral fluid- and blood-based tests found participants confused by IFUs, even when the instructions had been specifically adapted for self-test use [8]. Video evaluation showed multiple errors in specimen collection, use of buffer, read times and interpretation of results, regardless of whether the kit was oral fluid based or blood based [16]. Errors persisted even after self-test prototypes were further adapted [9,10,12,14,17]. Blood-based self-tests have been shown to be more sensitive than oral fluid-based tests, but evidence suggests that invalid results among self-testers may be also be higher [18-21]. Such variability presents a dilemma to potential implementers and to country regulatory authorities, and defeats the purpose of HIVST.

Cognitive interviewing has often been used to identify likely sources of response error in survey questionnaires. Using verbal probing to guide "thinking out loud," it evaluates people's comprehension of specific words and phrases, assessing relevance and acceptability in a particular context [22,23]. We aimed to estimate the utility of cognitive interviewing in optimizing the local understanding of manufacturers' IFUs to achieve an accurate HIVST result. To do this, we adapted cognitive interviewing techniques to include not only verbal comprehension but also in-depth qualitative interviews and the observation of the ability to follow instructions. We tested the use of this adapted approach to cognitive interviewing for IFU optimization in two African countries with low literacy levels – Malawi and Zambia.

## 2 | METHODS

This study was nested within the Self-Testing Africa (STAR) consortium, a large-scale evaluation of HIVST in Malawi, Zambia and Zimbabwe [24]. Before conducting the cognitive interviews, professional translators hired by the manufacturers had translated the IFUs into the local languages (Chichewa in Malawi, and Bemba, Nyanja and Tonga in Zambia). The translated IFUs are available at: https://www.psi.org/star-hiv-self-testing-africa/.

Participants were purposefully selected to represent intended users of HIV self-tests. We included adult men and women aged ≥18 years; 44 participants in Malawi (May 2016 to June 2017) and 17 participants in Zambia (May to August 2016). They were recruited from primary health facilities when they presented for HIV testing, and were eligible for inclusion if they demonstrated functional literacy when asked to read a short text in the local language and self-reported that they were HIV negative or of unknown status and were not on antiretroviral therapy (ART). Participants were from six communities – two rural and two urban communities in Malawi, and one rural and one urban community in Zambia. We included both rural and urban communities as literacy levels and comprehension of IFUs was likely to vary between these [25]. Cognitive interviews were conducted with them; in Malawi, we used three iterations, with each stage informing further refinement and adaptation of IFUs; 20 participants used the first iteration, 12 used the second iteration and 12 used the third iteration. Changes made at each stage in the interactive process were communicated to the manufacturer through e-mails. In Zambia, we additionally recruited participants who received an HIVST at their home to ensure that the context (e.g. lighting) in which HIVST was conducted was considered. In Zambia, one iteration of the IFU was used and evaluated by all participants, and suggested changes communicated to the manufacturer through email.

Trained research assistants recruited participants. A structured guide that mirrored the steps depicted in the IFUs illustrated in Figure 1 informed the interviews. All participants were then given an OraQuick HIV Self-Test kit, which contained this manufacturer's original IFU. They were asked to (1) read the instructions, (2) reflect on the pictorial and word instructions and explain these to the social scientist, (3) perform the actions depicted, and (4) reflect on how easy or difficult other members of their community would find the word and pictorial instructions. Scripted probes were included in the guide to ensure better understanding at each step, and research assistants were also trained to use spontaneous probes. Daily debriefing of field experiences was done to enhance the rigour of the cognitive interviewing process.

In Malawi, research staff took detailed observation notes at each step of the process. In Zambia, interviews were recorded, transcribed, translated into English and saved on password-secured computers at the research offices. Data from both countries were analysed deductively and we used a thematic approach based on the various steps in the testing process. The comparative analysis presented here uses data from the second Malawian iteration and the single Zambian iteration, as these very closely matched the early feedback incorporated by the manufacturer from the first Malawian iteration. This involved researchers familiarizing themselves with the data, developing codes and then merging the codes into broader themes.

Readers should note that there were fewer steps in this manufacturer's original IFU than those in the final iteration included in our Table S1 that can be found in the supplementary materials submitted with this paper, because additional steps were added to the IFU as a result of early iterations.

### 2.1 | Ethical considerations

In Malawi, we obtained ethics approvals from the College of Medicine Research Ethics Committee [Ref: P.01/16/1861] and


**Figure 1. Manufacturer's original instructions for use. This figure is reproduced from OraQuick HIV Self-Test instructions for use item number 3001-XXXX rev.10/15 with permission from OraSure Technologies Inc.**

the London School of Hygiene and Tropical Medicine (LSHTM) Ethics Committee [Ref: 10566]. In Zambia, the study was approved by the University of Zambia Biomedical Research Ethics Committee [Ref: 013-11-15] and LSHTM Ethics Committee [Ref: 10632]. All study participants provided informed consent.

## 3 | RESULTS

A total of 61 participants were included in this study. Over half of the participants in both countries understood the text and pictures used in the IFUs and could correctly conduct the self-test and interpret the results. Performance errors, however, were identified at each of the 15 steps outlined in the manufacturer's original IFU, including unanticipated difficulties with opening the packet through to kit disposal. We present the results thematically and provide illustrative quotations. A summary table in the supplementary materials presents participants' experiences at each step of following the IFU and compares results by country.

Over half of the participants found the textual and pictorial instructions to be complementary. Participants with lower literacy levels reported that the pictorial instructions improved their comprehension of the written instructions. When pictures were too difficult to understand, participants indicated that they used the textual instructions instead, such as the picture(s) in a step on when to start "timing the test." Other factors that limited participants' understanding and performance of certain instructions included translation errors, use of complicated terms, use of unfamiliar images and symbols, and the order in which the text and pictures describing the steps were presented.

### 3.1 | Language (use of complicated terms) and low literacy

Translations and the use of complicated terms led to some misunderstanding of the IFUs and user errors. Sometimes these issues arose from translation errors in the IFUs themselves, and at other times it was lack of familiarity with certain terms. For example, some participants in Zambia found the translated word for "pouch" in the instructions too difficult to understand.

> *Two pouches? Someone would get confused, yes. At least put simpler words because someone would ask, "what are pouches?" and may be guess that these are pouches (female, 29 years, Kanakantapa, rural, Zambia).*

The translation of "flat pad" in instruction 7 was also difficult for some people in Malawi and failure to understand the meaning of the local word resulted in a few participants touching the "flat pad" as illustrated by this quote: *Both sides are flat pads. The instruction should read, "gwirani kwakukuluko osati kwakung'ono" [touch the large side and not the smaller side] (female, 44 years, Madziabango, rural, Malawi).* Participants also found words and phrases like "swab," "press the pad firmly" confusing. This resulted in some participants doing odd things like pressing the pad hard "so that it could accumulate an adequate specimen" or placing the pad on their teeth and gums.

A related challenge was the variation in languages and dialects used within countries. Rural areas tended to use the original languages while urban areas tended to use colloquial versions. In Malawi, the Chichewa translation of the word gum was *usinini* but some participants from rural Malawi said this was a confusing translation and suggested *nkhama* instead. Thus, rural populations with poor literacy were more likely to struggle with understanding the messages in the IFUs and thereby made more errors. Rural participants who did comprehend IFUs and completed the self-test correctly indicated that they relied on the pictorial instructions rather than the text.

### 3.2 | Unfamiliar images and symbols

Images and pictorial illustrations in the IFU were meant to enhance understanding and performance of the instructions when used individually or complementarily with the word instructions. However, participants did not understand the

meaning of some images that were not familiar to their local context. Over half the participants in both countries incorrectly interpreted the cutlery symbol in the directions at the top of the IFU (see Table S1) due to lack of familiarity with using cutlery for eating:

> *. . . the picture does not make sense. What does the cutlery mean? Use a toothbrush and Colgate and put in mind that most Malawians do not use forks [male, 20 years, Zingwangwa urban, Malawi].*

Instead, participants from both countries interpreted the image to mean "avoid cutting oneself," "do not eat or drink contents of the test-kit" and "do not use a knife or fork to open the test kit." The fact that over half of the participants performed this and other instructions successfully points to the fact that pictorial and word instructions complemented each other and common sense prevailed.

A red line was drawn through images/pictures to warn participants not to carry out certain actions such as not to pour out the liquid (instruction 5). However, over half the participants preferred crossed red lines as used in warning signs in Malawi and Zambia.

> *If this picture was like this (makes a gesture with crossed hands to make an X) it would show that you should not do this . . . (female, 35 years, Mtendere, urban, Zambia).*

### 3.3 | Presentation of images and instructions

Circumstances that made interpretation difficult included information that was clustered within an instruction. Instruction number one contained images of a wristwatch, a digital watch and a phone to illustrate the importance of having a timing device. Some participants felt that having several images talking about one thing was misleading: *It is not clear. Is it a time or a date? (male, 29 years, Limbe, urban, Malawi).* Indeed, over half the participants did not have timing devices; a potential challenge for ensuring correct reading times even if the instruction was clearly understood.

Different font types, sizes and colours also created confusion. Some participants observed that the instruction about removing the test device from the pouch was written in a small font and therefore difficult to see. Other participants said that the presentation of instructions in different font sizes and colours could prompt users to think that the instructions in question were not important.

Some word instructions did not have corresponding pictorial instructions and vice versa. For instance, the written statement that users should not use "mouth cleaning products 30 minutes before you start the test" did not have a corresponding picture/image. This affected the participants' understanding of the instructions.

### 3.4 | Order, clarity and adequacy of instructions/messages

The order or positioning of instructions was critical to avoid confusion. The red capitalized instruction "IF YOU READ BEFORE 20 MINUTES, RESULTS MAY NOT BE CORRECT" came after the user had tested and had been told to "leave the test device in the tube for 20 minutes before reading the results" without telling the user the implications of reading the results earlier than 20 minutes or after 40 minutes. According to the participants, presenting the implications earlier could have enhanced understanding of and adherence to instructions.

Inadequate information was also a source of poor cognition of the instructions. For example, a warning that being on ART may lead to incorrect (false-negative) results was included, because retesting to confirm a previously known positive status has previously been reported and can lead to a false-negative self-test result [15,26,27]. However, participants found this message to be confusing and did not understand how someone who is infected with HIV could obtain negative results when the intention of the test-kit was to detect HIV: *How does one that is HIV positive get negative results? (female, 22 years, Mpemba, rural, Malawi). I don't understand, how can you get a false-negative result? (female, 29 years, Kanakantapa, rural, Zambia).*

## 4 | DISCUSSION

Our study aimed to evaluate the utility of cognitive interviewing in optimizing the local understanding of manufacturers' IFUs to achieve an accurate HIVST result. This study was nested within the STAR consortium, a large-scale evaluation of HIVST in Malawi, Zambia and Zimbabwe. We used cognitive interviewing in Malawi and Zambia, two African countries with low literacy levels, to rapidly identify how well users of oral fluid-based HIV self-test kits were able to understand IFUs and their ability to obtain accurate results.

The use of cognitive interviewing in the iterative creation and improvement of questionnaires and health promotion materials has been described elsewhere, particularly for exploring how survey questions are understood by research participants and how these require significant contextual adaptation [28-30]. Results from cognitive interviews often show that some survey questions are appropriately interpreted by respondents, and others show significant differences between what the researchers intended them to measure and what they actually do [31,32]. We found the same with IFU with some instructions being easy to understand and conduct as intended by the manufacturers and others not. We adapted these methods by combining the step-by-step drill down on each IFU instruction with qualitative data capture and observed the errors. This allowed us to gain additional insights on how to best tailor support materials, which was not possible from less targeted interviews, even when supported by video observation [16]. We found the principle of cognitive interviewing to be an essential element, i.e. taking time to explore the understanding of each instruction, statement or question.

While systematic reviews and evaluations have shown that HIVST can be successfully conducted by the intended users without in-person demonstrations [8], we feel that additional support materials such as checklists, videos and in-person demonstrations are likely to be particularly important for rural and urban populations with low literacy [33-35]. Viewing a demonstration video increased adolescents' and adults'

confidence in their ability to self-test in Zambia [36]. Providing an in-person demonstration resulted in high sensitivity of oral fluid self-testing in KwaZulu Natal [17], which did not happen when the oral fluid test was conducted unsupervised in similar settings [12]. Demonstrations of how to use the kit are an integral part of our studies in Malawi, Zambia and Zimbabwe [10,11,37,38]. Demonstration materials do, however, need to be tailored to the context. Men who have sex with men in South Africa preferred fingerstick self-testing but were better able to perform the oral fluid tests resulting in the need for additional instructional resources for blood-based testing in this context [39]. Ortblad et al. reported that when peer educators working with female sex workers in Uganda gave an HIVST demonstration based on materials developed without detailed knowledge of common misunderstandings, the sex workers struggled to correctly interpret the test results [40]. In Zimbabwe, on the other hand, where female sex workers were shown a video based on findings from cognitive interviews, they were able to correctly perform and interpret oral fluid-based HIVST [38]. Training lay people, including women with untested male partners, on how to demonstrate a self-test may be another option. In Malawi and Kenya, HIVST delivered to the male partners of pregnant women resulted in high uptake and increased couples' testing [41-43]. Over time, as knowledge and awareness of HIVST increases, the need for cognitive interviewing is likely to decline.

Our findings were used to provide feedback to the manufacturer and resulted in further optimization of IFUs as well as the development of demonstrations used in the STAR project to further improve performance. However, iterations and adaptation of the actual IFUs are neither possible nor desirable for every community, every key population or subgroup. They are also not possible from a regulatory point of view, since regulators and WHO prequalification regard only the IFUs in the final prequalified product as approved package inserts, allowing only simple changes for clarification and translation [44]. The onus is thus on programmes to ensure appropriate introduction of HIVST. A practical toolkit aimed at programmes wishing to introduce HIVST is now being developed to provide further guidance on how to optimize HIVST implementation, including guidance on how to conduct and interpret findings from cognitive interviews exploring IFUs.

Our study had several limitations, such as different data collection techniques. Data collection in Malawi was captured using an observational checklist while a digital audio recorder was used in Zambia. However, the differences in data capturing techniques did little to influence our analysis, since the focus of data synthesis was on how each client understood each instruction, and how they practically translated word and pictorial instructions when performing an HIVST. Malawi conducted three iterations with the aim of improving the IFUs at each iterative stage while Zambia only had a single iteration and fewer participants, and this might have influenced our findings, although the comparison used the same IFU iteration and the same principles of cognitive interviewing methods. Professional translations done by the manufacturers had several problems and required revisions by researchers within the study team in both countries. Finally, similar cognitive interviews conducted in Zimbabwe a year before this study informed the development of study tools in Malawi and Zambia; however, as the team iteratively changed the IFUs several times, there was no version that exactly matched the ones used in Malawi and Zambia. We felt that the methods did not overlap sufficiently to include them, limiting the potential for comparison in a third context.

## 5 | CONCLUSIONS

Cognitive interviewing provided an excellent methodological approach to assessing IFU but required some adaptation to include direct observation of test performance. The adapted cognitive methodology we used highlighted several errors that were common across both countries and helped us to determine the nature of support users might need and to pre-empt common test performance problems, through improved translations and adaptation of manufacturers' IFUs. Efforts to further optimize performance may not always be feasible through IFUs alone but may require the addition of demonstrations and support tools in settings and populations with low education and literacy levels.

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### COMPETING INTERESTS

No potential conflict of interest is reported by the authors.

### AUTHORS' CONTRIBUTIONS

MS and MK wrote first draft and led the entire writing process. LK and AM were the principal data collectors and contributed to the first draft. PI, ES, LN and RD also contributed to first draft and reviewed subsequent iterations. CJ, KH, ELC and HA provided a thorough review of the drafts and contributed to the second draft. MT contributed to all the iterations and provided technical guidance to MS and MK.

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### REFERENCES

1. World Health Organization. Guidelines on HIV self-testing and partner notification: supplement to consolidated guidelines on HIV testing services. Geneva, Switzerland: World Health Organization; 2016.
2. 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. https://doi.org/10.1007/s10461-014-0832-x.
3. Indravudh PP, Sibanda EL, d'Elbee M, Kumwenda MK, Ringwald B, Maringwa G, et al. "I will choose when to test, where I want to test": investigating young people's preferences for HIV self-testing in Malawi and Zimbabwe. AIDS. 2017;31(Suppl 3):S203–12. https://doi.org/10.1097/qad.0000000000001516
4. 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. https://doi.org/10.1371/journal.pone.0059906.

5. World Health Organization. Technical specifications series for submission to WHO prequalification – diagnostic assessment: human immunodeficiency virus (HIV) rapid diagnostic tests for professional use and/or self-testing. Geneva: World Health Organization; 2016. Licence: CC BY-NC-SA 3.0 IGO. 26 p.
6. World Health Organization. WHO prequalification of in vitro diagnostics public report. Product: OraQuick HIV self-test. WHO reference number: PQDx 0159-055-01 (version 2.0). Geneva, Switzerland: World Health Organization; 2017 [cited 2018 Mar 10]. Available from: http://www.who.int/diagnostics_laboratory/evaluations/pq-list/170720_final_amended_pqdx_0159_055_01_oraquick_hiv_self_test_v2.pdf
7. The Global Fund to Fight AIDS, Tuberculosis and Malaria. List of HIV diagnostic test kits and equipments classified according to the Global Fund Quality Assurance Policy (version 17). Geneva, Switzerland: The Global Fund; 2017 [cited 2018 Mar 10]. Available from: https://www.theglobalfund.org/media/5878/psm_productshiv-who_list_en.pdf
8. Figueroa C, Johnson C, Ford N, Sands A, Dalal S, Meurant R, et al. Reliability of HIV rapid diagnostic tests for self-testing compared with testing by healthcare workers: a systematic review and meta-analysis. Lancet HIV. 2018;5(6):e277–90. https://doi.org/10.1016/s2352-3018(18)30044-4.
9. Asiimwe S, Oloya J, Song X, Whalen CC. Accuracy of un-supervised versus provider-supervised self-administered HIV testing in Uganda: a randomized implementation trial. AIDS Behav. 2014;18(12):2477–84. https://doi.org/10.1007/s10461-014-0765-4.
10. 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. https://doi.org/10.1371/journal.pmed.1001102.
11. Choko AT, MacPherson P, Webb EL, Willey BA, Feasy H, Sambakunsi R, et al. Uptake, accuracy, safety, and linkage into care over two years of promoting annual self-testing for HIV in Blantyre, Malawi: a community-based prospective study. PLoS Med. 2015;12(9):e1001873. https://doi.org/10.1371/journal.pmed.1001873.
12. 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. https://doi.org/10.1007/s10461-015-1213-9.
13. Pant Pai N, Behlim T, Abrahams L, Vadnais C, Shivkumar S, Pillay S, et al. Will an unsupervised self-testing strategy for HIV work in health care workers of South Africa? A cross sectional pilot feasibility study. PLoS ONE. 2013;8(11):e79772. https://doi.org/10.1371/journal.pone.0079772.
14. Smith P, Wallace M, Bekker LG. Adolescents' experience of a rapid HIV self-testing device in youth-friendly clinic settings in Cape Town South Africa: a cross-sectional community based usability study. J Int AIDS Soc. 2016;19(1):21111. https://doi.org/10.7448/ias.19.1.21111.
15. Mavedzenge SN, Sibanda E, Mavengere Y, Hatzold K, Mugurungi O, Ncube G, et al. Supervised HIV self-testing to inform implementation and scale up of self-testing in Zimbabwe. 8th IAS Conference on HIV Pathogenesis, Treatment and Prevention (IAS 2015); 2015 Jul 19-22; Vancouver. [cited 2018 May 4]. Available from: http://hivst.org/tools/2016120supervised-hiv-self-testing-to-inform-implementation-and-scale-up-of-self-testing-in-zimbabwe
16. 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. https://doi.org/10.1007/s10461-014-0818-8.
17. Martinez Perez G, Steele SJ, Govender I, Arellano G, Mkwamba A, Hadebe M, et al. Supervised oral HIV self-testing is accurate in rural KwaZulu-Natal, South Africa. Trop Med Int Health. 2016;21(6):759–67. https://doi.org/10.1111/tmi.12703.
18. Gaydos CA, Hsieh Y-H, Harvey L, Burah A, Won H, Jett-Goheen M, et al. Will patients "opt in" to perform their own rapid HIV test in the emergency department? Ann Emerg Med. 2011;58(1 Suppl 1):S74–8. https://doi.org/10.1016/j.annemergmed.2011.03.029.
19. Ibitoye M, Frasca T, Giguere R, Carballo-Diéguez A. Home testing past, present and future: lessons learned and implications for HIV home tests. AIDS Behav. 2014;18(5):933. https://doi.org/10.1007/s10461-013-0668-9.
20. Lee VJ, Tan SC, Earnest A, Seong PS, Tan HH, Leo YS. User acceptability and feasibility of self-testing with HIV rapid tests. J Acquir Immune Defic Syndr. 2007;45(4):449–53. https://doi.org/10.1097/QAI.0b013e318095a3f3.
21. de la Fuente L, Rosales-Statkus ME, Hoyos J, Pulido J, Santos S, Bravo MJ, et al. Are participants in a street-based HIV testing program able to perform their own rapid test and interpret the results? PLoS ONE. 2012;7(10):e46555. https://doi.org/10.1371/journal.pone.0046555.
22. Willis GB. Cognitive interviewing: a "how to" guide, from the short course "reducing survey error through research on the cognitive and decision processes in surveys."Meeting of the American Statistical Association, Dallas (TX); 1999.
23. Willis GB, Artino AR Jr. What do our respondents think we're asking? Using cognitive interviewing to improve medical education surveys. J Grad Med Educ. 2013;5(3):353–6. https://doi.org/10.4300/jgme-d-13-00154.1.
24. HIV Self-Testing Africa. The STAR Initiative [Internet]. Washington, DC: PSI [cited 2018 Dec 28]. Available from: https://www.eatright.org/]; https://www.psi.org/star-hiv-self-testing-africa
25. Zhang Y. Urban-rural literacy gaps in Sub-Saharan Africa: the roles of socioeconomic status and school quality. Comp Educ Rev. 2006;50(4):581–602. https://doi.org/10.1086/507056.
26. Johnson CC, Sands A, Urassa W, Baggaley R. Alert, but not alarmed – a comment on "Towards more accurate HIV testing in sub-Saharan Africa: a multisite evaluation of HIV RDTs and risk factors for false positives." J Int AIDS Soc. 2017;20(1):22042. https://doi.org/10.7448/ias.20.1.22042.
27. Moore A, Cassidi T, Steele SJ, Shroufi A, Ntuli N, Ndani L, et al. Self-testing: an effective means of increasing HIV-testing and status awareness. 9th IAS Conference on HIV Science (IAS 2017); 2017 July 23-27; Paris, France. [cited 2018 Mar 10]. Available from: http://www.ias2017.org/Portals/1/Files/IAS2017_LO.compressed.pdf
28. Egger-Rainer A. Enhancing validity through cognitive interviewing. A methodological example using the Epilepsy Monitoring Unit Comfort Questionnaire (EMUCQ). J Adv Nurs. 2019;75(1):224–33. https://doi.org/10.1111/jan.13867.
29. Vreeman RC, Nyandiko WM, Ayaya SO, Walumbe EG, Inui TS. Cognitive interviewing for cross-cultural adaptation of pediatric antiretroviral therapy adherence measurement items. Int J Behav Med. 2014;21(1):186–96. https://doi.org/10.1007/s12529-012-9283-9.
30. Drennan J. Cognitive interviewing: verbal data in the design and pretesting of questionnaires. J Adv Nurs. 2003;42(1):57–63. https://doi.org/10.1046/j.1365-2648.2003.02579.x.
31. De Silva MJ, Harpham T, Tuan T, Bartolini R, Penny ME, Huttly SR. Psychometric and cognitive validation of a social capital measurement tool in Peru and Vietnam. Soc Sci Med. 2006;62(4):941–53. https://doi.org/10.1016/j.socscimed.2005.06.050.
32. Bowden A, Fox-Rushby JA, Nyandieka L, Wanjau J. Methods for pre-testing and piloting survey questions: illustrations from the KENQOL survey of health-related quality of life. Health Policy Plan. 2002;17(3):322–30. https://doi.org/10.1093/heapol/17.3.322.
33. Tonen-Wolyec S, Batina-Agasa S, Muwonga J, N'kulu F, Bouassa RSM, Belec L. Evaluation of the practicability and virological performance of finger-stick whole-blood HIV self-testing in French-speaking sub-Saharan Africa. PLoS ONE. 2018;13(1):e0189475. https://doi.org/10.1371/journal.pone.0189475.
34. Tonen-Wolyec S, Mboup S, Gresenguet G, Bouassa RB, Belec L. Insufficient education is a challenge for HIV self-testing. Lancet HIV. 2018;5(7):e341. https://doi.org/10.1016/s2352-3018(18)30141-3.
35. Wei C, Yan L, Li J, Su X, Lippman S, Yan H. Which user errors matter during HIV self-testing? A qualitative participant observation study of men who have sex with men (MSM) in China. BMC Public Health. 2018;18(1):1108. https://doi.org/10.1186/s12889-018-6007-3.
36. Zanolini A, Chipungu J, Vinikoor MJ, Bosomprah S, Mafwenko M, Holmes CB, et al. HIV self-testing in Lusaka Province, Zambia: acceptability, comprehension of testing instructions, and individual preferences for self-test kit distribution in a population-based sample of adolescents and adults. AIDS Res Hum Retroviruses. 2017;34(3):254–60. https://doi.org/10.1089/aid.2017.0156.
37. Kapaku KN, Neuman M, Maluzi K, Sigande L, Nalubamba M, Taegtmeyer M, et al. Is OraQuick®HIV-self-testing valid among intended users? Analysis from a clinical performance study in Lusaka, Zambia. 9th IAS Conference on HIV Science (IAS 2017); 2017 July 23-27; Paris, France. [cited 2018 May 4]. Available from: http://www.ias2017.org/Portals/1/Files/IAS2017_LO.compressed.pdf
38. Sibanda EL. Usability and validity of oral fluid self-tests among intended users: experiences from Malawi, Zambia and Zimbabwe. 9th IAS Conference on HIV Science (IAS 2017); 2017 July 23-27; Paris, France. [cited 2018 May 4]. Available from: http://programme.ias2017.org/Programme/Session/76
39. Lippman SA, Gilmore HJ, Lane T, Radebe O, Chen Y-H, Mlotshwa N, et al. Ability to use oral fluid and fingerstick HIV self-testing (HIVST) among South African MSM. PLoS ONE. 2018;13(11):e0206849. https://doi.org/10.1371/journal.pone.0206849.

40. Ortblad KF, Musoke DK, Ngabirano T, Nakitende A, Haberer JE, McConnell M, et al. Female sex workers often incorrectly interpret HIV self-test results in Uganda. J Acquir Immune Defic Syndr. 2018;79(1):e42–5. https://doi.org/10.1097/QAI.0000000000001765.
41. Masters SH, Agot K, Obonyo B, Napierala Mavedzenge S, Maman S, Thirumurthy H. Promoting partner testing and couples testing through secondary distribution of HIV self-tests: a randomized clinical trial. PLoS Med. 2016;13(11):e1002166. https://doi.org/10.1371/journal.pmed.1002166.
42. Gichangi A, Wambua J, Gohole A, Mutwiwa S, Njogu R, Bazant E, et al. Provision of oral HIV self-test kits triples uptake of HIV testing among male partners of antenatal care clients: results of a randomized trial in Kenya. 21st International Aids Conference (AIDS 2016); 2016 Jul 18-22; Durban, South Africa; 2016 [cited 2018 May 4]. Available from: http://www.aids2016.org/Portals/0/File/AIDS2016_Abstracts_LOW.pdf
43. Choko AT, Kumwenda MK, Johnson CC, Sakala DW, Chikalipo MC, Fielding K, et al. Acceptability of woman-delivered HIV self-testing to the male partner, and additional interventions: a qualitative study of antenatal care participants in Malawi. J Int AIDS Soc. 2017;20(1):21610. https://doi.org/10.7448/ias.20.1.21610.
44. World Health Organization. Reportable changes to a WHO prequalified in vitro diagnostic medical device. Geneva, Switzerland: World Health Organization; 2016.

## SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

**Table S1:** Results (participants' experiences).

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SHORT REPORT

# Re-reading of OraQuick HIV-1/2 rapid antibody test results: quality assurance implications for HIV self-testing programmes

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## Abstract

**Introduction:** Scale-up of HIV self-testing (HIVST) will play a key role in meeting the United Nation's 90-90-90 targets. Delayed re-reading of used HIVST devices has been used by early implementation studies to validate the performance of self-test kits and to estimate HIV positivity among self-testers. We investigated the stability of results on used devices under controlled conditions to assess its potential as a quality assurance approach for HIVST scale-up.

**Methods:** 444 OraQuick® HIV-1/2 rapid antibody tests were conducted using commercial plasma from two HIV-positive donors and HIV-negative plasma (high-reactive n = 148, weak-reactive n = 148 and non-reactive n = 148) and incubated them for six months under four conditions (combinations of high and low temperatures and humidity). Devices were re-read daily for one week, weekly for one subsequent month and then once a month by independent readers unaware of the previous results. We used multistage transition models to investigate rates of change in device results, and between storage conditions.

**Results and discussion:** There was a high incidence of device instability. Forty-three (29%) of 148 initially non-reactive results became false weak-reactive results. These changes were observed across all incubation conditions, the earliest on Day 4 (n = 9 kits). No initially HIV-reactive results changed to a non-reactive result. There were no significant associations between storage conditions and hazard of results transition. We observed substantial statistical agreement between independent re-readers over time (agreement range: 0.74 to 0.96).

**Conclusions:** Delayed re-reading of used OraQuick® HIV-1/2 rapid antibody tests is not currently a valid methodological approach to quality assurance and monitoring as we observed a high incidence (29%) of true non-reactive tests changing to false weak-reactive and therefore its use may overestimate true HIV positivity.

**Keywords:** HIV self-testing; Quality assurance; Delayed re-reading; Visual stability; False reactive; Misdiagnosis; HIV testing

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## 1 | INTRODUCTION

HIV self-testing (HIVST) is being scaled-up using a variety of distribution models throughout Africa, the Americas, Asia and Europe [1-4]. No clear monitoring and evaluation or external quality assurance (EQA) systems exist for HIVST devices and this raises concern for national reference laboratories, regulators and policymakers [5-7].

While previous studies report acceptable sensitivity and specificity when HIVST is conducted by intended users [8,9], it is unclear whether this will be maintained once HIVST programmes are implemented at scale. Observation and in-depth interviews reveal that without a demonstration, operator errors are common in both conducting and interpreting self-tests [10,11]. Scale-up will have to be accompanied by a robust quality assurance system.

A reactive HIVST indicates that HIV antibodies are present in the oral or fingerstick/blood sample of the user. Further testing to confirm a positive diagnosis following linkage to care acts as an active system for detecting false-reactive results and ensures individuals are not incorrectly started on antiretroviral therapy (ART). In most contexts, however, the prevalence of false-reactive results prior to ART clinic enrolment (whether or not individuals came from HIVST) is not tracked and rates of linkage remain highly variable and can be very low without active support [12-14]. Self-testers with non-reactive results, unless linking to voluntary male medical circumcision or pre-exposure prophylaxis services, would not typically seek or receive further testing and confirmation, meaning a false non-reactive result would not be detected.

Methods that detect incorrect results and misinterpretation are required for individual care as well as for quality

assurance. One approach, which has been utilized in early HIVST implementation studies, is for self-testers to return used devices for delayed re-reading by trained staff in parallel with self-reported interpretation of results [15,16]. However, delays between device use and re-reading, and environmental storage conditions during this period could impair the validity of this method. We therefore set out to investigate the stability of OraQuick® HIV-1/2 rapid antibody test (OraQuick HIV) results with delayed re-reading stored under controlled incubation conditions for prolonged periods. We selected the OraQuick® HIV-1/2 rapid antibody test kit, which is the same product (in different packaging) as the OraQuick® HIV Self-Test which is prequalified by the World Health Organization (WHO) [17].

## 2 | METHODS

### 2.1 | Materials and equipment

Two different batches (HIVCO-4308 and HIVCO-4309) of OraQuick® HIV-1/2 rapid antibody test kits (assembled in Thailand for OraSure Technologies, Inc. Bethlehem, PA, USA) were obtained from the manufacturer. Human HIV seroconversion panel plasma samples from two donors (Donor No. 73695 panel number 12007-08 and 09, [18] and 75018 panel number 9077-24 and 25 [19]) were purchased from Zepto-Metrix Corporation (Buffalo, NY, USA). Human plasma negative for HIV, hepatitis B, C, E and syphilis was purchased from the National Blood Service (Liverpool, UK).

### 2.2 | Sample preparation

The OraQuick® HIV-1/2 Rapid Antibody Test is WHO prequalified for use with oral fluid, whole blood, serum or plasma. The matrix of the sample (i.e. plasma rather than an oral crevicular fluid sample) was not a crucial factor in this investigation, as we were not investigating specificity or sensitivity. What was important was the basis of the immuno-chromatographic stability of the test. The use of HIV antibody-positive and -negative plasma allowed us to investigate this.

Four panel samples from two donors were combined to produce an HIV-reactive "mini-pool" of stock serum. This was checked to ensure the correct result and intensity of test line on the OraQuick HIV device. From this stock, an HIV-reactive sample was prepared with the addition of HIV-negative plasma (1:8 dilution factor). An HIV weak-reactive sample was prepared with a 1:16 dilution factor.

### 2.3 | Sample size calculation

To estimate sample size, we assumed that 0.2% of all used tests would change over six months. To estimate accuracy of rate of change within ± 1% with 95% confidence, 77 tests were required to be read for each condition, with a total of four conditions, giving a minimum sample of 308 kits. With available resources, were able to include more samples (444 total).

### 2.4 | Conducting the tests

The study was conducted in the laboratory under controlled conditions rather than using actual patient-used HIVST devices. This eliminated the risk that the test had not been performed correctly which could have influenced the study results.

A total of 444 OraQuick HIV tests were conducted in the laboratory following the manufacturer's instructions for use (IFU). Five microlitres of the prepared samples (HIV reactive n = 148, HIV weak-reactive n = 148 or HIV non-reactive n = 148) was delivered into the developer solution before mixing gently. The test device was labelled with an identification number on the back and inserted "pad end" into the developer solution. Devices were read within the 20- to 40-minute reading window (measured using a digital timer) by three different laboratorians, trained in the reading of the devices and blinded to each other's interpretation.

### 2.5 | Read definitions/interpretation

On the test device there is a window next to which there is a letter "T" for test line and a "C" for control line. As per the IFU, a non-reactive result was recorded when only a single quality control line was visible adjacent to the letter "C" on the test device. A weak-reactive was recorded when there were two visible lines on the test device, the first adjacent to the letter "C" (control) and the second adjacent to the letter "T" (test) but the test line was not as intense as the control line. A reactive test was recorded when both "C" and "T" lines were visible and the "T" line was at least as intense as the "C" line. An invalid result was defined as no line present adjacent to the letter "C."

### 2.6 | Incubation conditions

Following initial reads, devices were placed in one of four laboratory benchtop incubators (Benchmark Scientific), each set to a different incubation condition: (a) control temperature (30°C) with high humidity (70%); (b) control temperature (30°C) with low humidity (20%); (c) high temperature (40°C) with high humidity (70%); (d) or high temperature (40°C) with low humidity (20%). Each condition had 37 HIV non-reactive, 37 HIV weak-reactive and 37 HIV reactive devices allocated to it (Figure 1).

### 2.7 | Re-reading intervals

Devices were re-read by either two or three blinded and independent readers daily for one week, weekly for one subsequent month and then once a month for the following five months, giving a total of 13 reads over the 6-month study period (November 2016 through to April 2017). Each of the laboratorians interpreted the test face up, recorded the test result (check box non-reactive, weak-reactive or reactive) on the data log sheet and then turned the test over to record the test identification number along with any additional comments. Data were input onto a blinded (of previous re-read result) electronic log. Data were unblinded and analysed after 6 months.

### 2.8 | Data analysis

Two laboratorians had to be in agreement for a "final" test result interpretation. We compared agreement between readers at each time point using the kappa statistic with bootstrapped 95% confidence intervals for three readers and Scott's pi for two readers. To estimate the hazard of transition between device states (non-reactive, weak-reactive, and

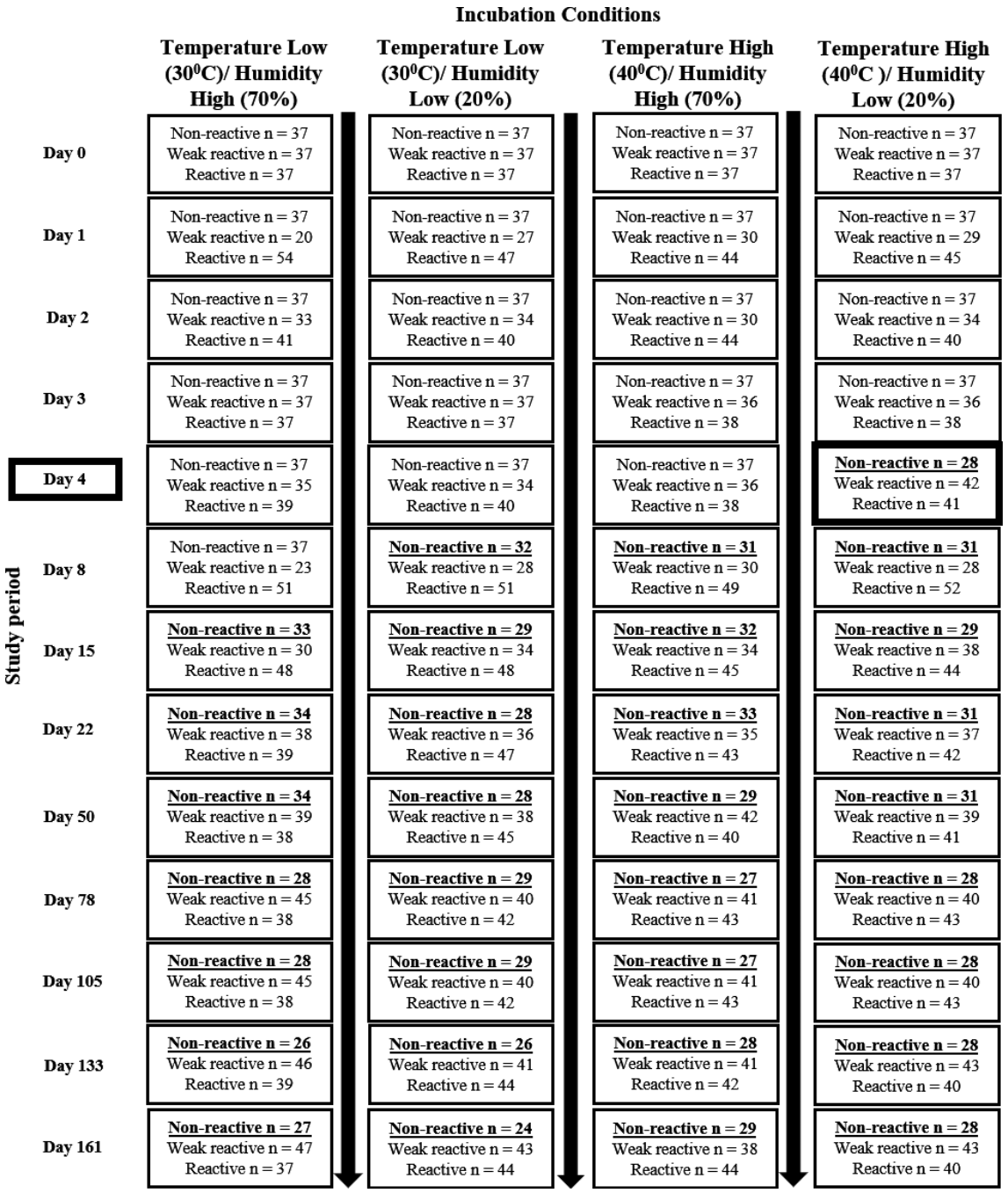


**Figure 1. Flow diagram of sample allocation and re-read results over time.**
The flow chart shows the allocation of non-reactive, weak reactive and reactive test devices to the four different incubation conditions on Day 0 and the re-read results for Day 0 to Day 161. Changes in non-weak reactives are underlined and highlighted in bold. The first changes observed "non-reactive" transitioning to "weak reactive" was on Day 4 in the incubation condition of high temperature and low humidity.

reactive) over time, and the effects of incubation storage conditions, we fitted a multistage transition model using a hidden Markov process. Model fit was evaluated by visually comparing the fitted hazard function within each condition over time with observed transition events. In the final model, terms for piecewise intensities were fitted at Day 1 to 2, Day 2 to 3; Day 3 to 4; Day 8 to 15; and Day 15 to 181 to account for the high intensity of transition. Analysis was done using R version 3.3.2 (R Foundation for Statistical Computing, Vienna).

## 3 | RESULTS AND DISCUSSION

Devices were first read following the manufacturer IFU, after 20 minutes and within 40 minutes of conducting the test

(Day 0) for control purposes. On Day 0, all reactive devices gave the expected dilution results (reactive or weak-reactive) and a following masked re-read showed all three independent readers in agreement (100%). Statistical agreement between independent readers over the six-month period ranged from 0.70 (95% confidence interval (CI): 0.66 to 0.74) to 0.96 (95% CI: 0.94 to 0.98) [20].

There was a high incidence of OraQuick HIV result transition between states over time (Figure 2). A total of 43 of the 148 true non-reactive devices (29%) changed to a false weak-reactive result with the earliest change observed on Day 4 (n = 9 kits) incubated at high temperature and low humidity (Figure 1). Transition between states over time was also observed, with tests changing from true non-reactive to false weak-reactive and then back to true non-reactive (77 instances out of a total of 1776) and weak-reactive results changing to strong reactive and then back to weak-reactive (135 instances). The majority of these true reactive transitions occurred early (from Day 1) with the greatest intensity of transition occurring up to Day 15. Transitions continued to occur throughout the six-month follow-up period. No devices with an initial reactive result changed to a weak-reactive or non-reactive result over the six-month period. The test control line showed 100% stability throughout the study.

Changes occurred across all controlled incubation conditions with the earliest transition from a true non-reactive to a false weak-reactive occurring under high temperature and low humidity conditions on Day 4. However, in our final model, there was no significant association between the incubation condition under which devices were stored and the hazard of transition between stages (Table 1).

Our key finding shows the OraQuick HIV device can have a result change from a true non-reactive to a false weak-reactive result when reading is extended beyond the manufacturer reading time window. The reasons underlying our finding are not clear and we did not find any association with different temperature and humidity conditions. Explanations for the appearance of the false weak-reactive lines may be due to nonspecific antibody binding at the HIV antigen test site on the devices nitrocellulose test strip [21] or nonspecific binding of protein-A gold conjugate which the test uses as the colorimetric indicator or perhaps a lateral back flow or "settling effect" over time and further investigation into these hypotheses is required.

The observed change in result raises concerns over the use of delayed re-reading of devices for monitoring HIVST interpretation, as well as for programmatic monitoring, evaluation and EQA. Research studies utilizing delayed re-reading of returned OraQuick® HIV Self-Test for establishing positivity may overestimate the true HIV positivity amongst a self-testing population.

A previous study conducted in Malawi examined the pre-use stability of OraQuick® HIV test kits [16]. 371 optimally stored and 375 pre-incubated used devices were re-read over a 12-month period. A 0.2% change from an initial reactive result to a later non-reactive was observed (one in the pre-incubated and one in the optimally stored group). These results suggested that HIVST device results remained stable over time. However, the focus of this study was its effect on pre-use storage conditions. Post-use storage conditions were not rigorously monitored and so cannot be reliable compared with the results from our study.

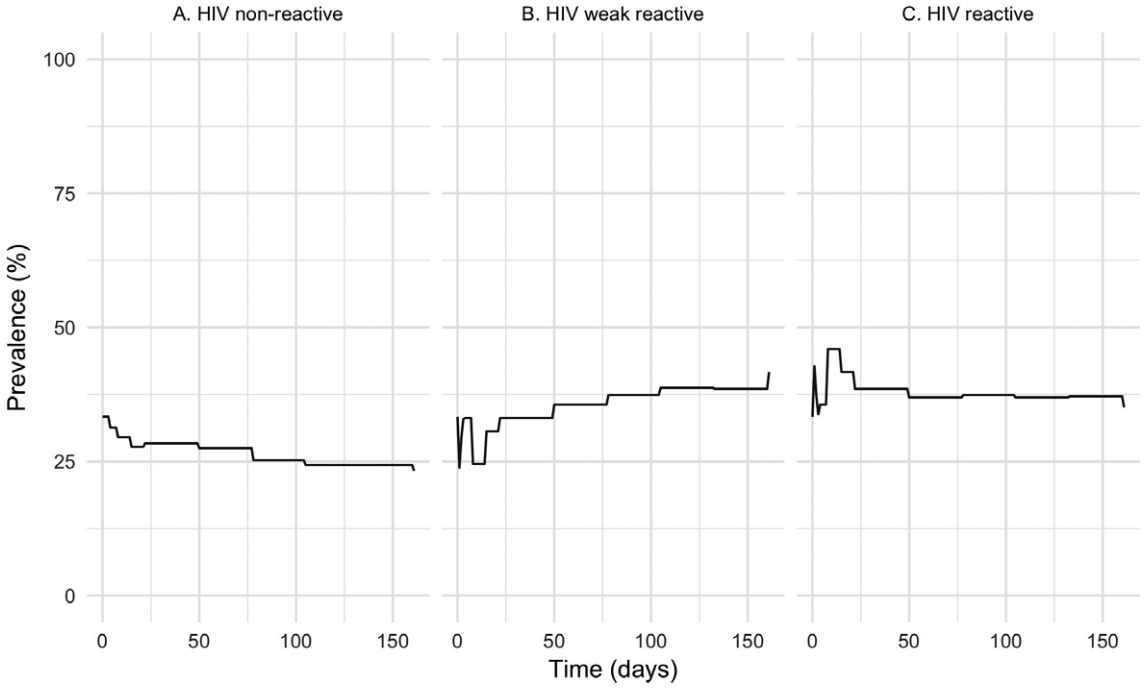


**Figure 2. Observed transitions between HIV re-read results over the study period.**
(A) Decrease in true HIV non-reactive inoculated test devices as they transit to "false" HIV weak reactive. (B) Increase in the number of test devices re-read as HIV weak reactive. (C) Increase in the number of test devices re-read as reactive which then transition back to weak reactive over time.

**Table 1. Hazard of transition between HIV test read stage over six months**

| Incubation condition and transition stage (From → To) | Hazard ratio for transition intensity (vs. cool/dry incubation condition) | 95% confidence interval |
|---|---|---|
| Cool/humid | | |
| HIV non-reactive → HIV weak-reactive | 0.88 | 0.47 to 1.64 |
| HIV weak-reactive → HIV non-reactive | 0.95 | 0.33 to 2.71 |
| HIV weak-reactive → HIV reactive | 1.27 | 0.80 to 2.03 |
| HIV reactive → HIV weak-reactive | 1.41 | 0.87 to 2.28 |
| Warm/humid | | |
| HIV non-reactive → HIV weak-reactive | 0.81 | 0.43 to 1.56 |
| HIV weak-reactive → HIV non-reactive | 1.27 | 0.47 to 3.42 |
| HIV weak-reactive → HIV reactive | 0.87 | 0.53 to 1.44 |
| HIV reactive → HIV weak-reactive | 0.94 | 0.56 to 1.59 |
| Warm/Dry | | |
| HIV non-reactive → HIV weak-reactive | 1.06 | 0.57 to 1.95 |
| HIV weak-reactive → HIV non-reactive | 1.24 | 0.46 to 3.35 |
| HIV weak-reactive → HIV reactive | 0.94 | 0.58 to 1.52 |
| HIV reactive → HIV weak-reactive | 1.15 | 0.69 to 1.89 |

Estimated by fitting multistage transition model for each test read condition with hidden Markov process, and with terms for incubation condition and piecewise transition intensities between Day 1 to 2, Day 2 to 3, Day 3 to 4, Day 8 to 15 and Day 15 to 181.

During this controlled study, our trained laboratorians could correctly distinguish false weak-reactive test lines from true weak-reactive test lines as they have a greyish appearance compared with the pinker true-reactive. Implementation of this more nuanced approach may however prove challenging in programmatic settings where previous reports show that providers struggle to identify and interpret weak reactives [22] and other factors, such as interferents, and tests used among people with HIV using ART can cause weak reactives [23].

In addition to a false weak-reactive line causing uncertainty to an EQA model, when testing a population, it is likely that more "true negative" samples will change to "false weak reactive" and delayed re-reading by self-testers themselves could lead to individual misinterpretation and misunderstandings. Our study showed that the OraQuick HIV device was stable up to four days after the sample was applied, suggesting that the risk of this is low but nevertheless self-testers need clear messages about the read window and the importance of reading the device according to manufacturer instructions.

A limitation of this study was that on some re-read days only two individual re-reads were conducted (23%) and therefore a third "tie breaker" re-read was not available. The very nature of self-testing (conducting the test privately at home) means conventional facility/laboratory-based QA systems of test devices are eluded, and an alternative approach is required. Digital photography and immediate re-reading are two other options that are being further explored for QA during HIVST scale-up, but these also have their limitations. National reference laboratories should play an integral role in external quality control measures by conducting batch testing at the actual sites of distribution of HIVST to ensure that the integrity of the devices is not compromised during transport and storage.

## 4 | CONCLUSIONS

The use of re-reading used OraQuick HIVST devices as an approach to quality assurance and monitoring test results is not advised. The instability observed in true non-reactive tests changing to false weak reactive test results in our study demonstrates that re-reading is not a reliable method to assess user interpretation of the OraQuick HIVST and measurement of HIV positivity rates among self-testers.

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### COMPETING INTERESTS

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### AUTHORS' CONTRIBUTIONS

VW, RD and MT formulated and designed the experiments. VW, RD, CW, TE and EA performed the experiments. VW, PM and RD analysed the data. VW, RD, CW, TE, EA, CJ, MM, EC, FC, HA, KH, PM and MT wrote the concise communication.

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## REFERENCES

1. Thirumurthy H, Masters SH, Napierala Mavedzenge S, Maman S, Omanga E, Agot K. Promoting male partner testing and safer sexual decision making through secondary distribution of HIV self-tests by HIV uninfected female sex workers and women receiving antenatal and postpartum care in Kenya: a cohort study. Lancet HIV. 2016;3(6):266–74.
2. Marlin R, Young S, Bristow C, Wilson G, Rodriguez J, Ortiz J, et al. Feasibility of HIV self-test vouchers to raise community-level serostatus awareness, Los Angeles. BMC Public Health. 2014;14:1226.
3. Green K, Thu H. In the hands of the community: accelerating key population-led HIV lay and self-testing in Viet Nam. [Abstract THSA1804] 21st International AIDS Conference 18-22 July 2016.
4. Brady M. Self-testing for HIV: initial experience of the UK's first kit. [Abstract 19] 22nd Annual Conference of the British HIV Association 21 April 2016.
5. Makusha T, Knight L, Taegtmeyer M, Tulloch O, Davids A, Lim J, et al. HIV self-testing could "revolutionize testing in South Africa, but it has got to be done properly": perceptions of key stakeholders. PLoS One. 2015;10(3):e0122783.
6. Van Rooyen H, Tulloch O, Mukoma W, Makusha T, Chepuka L, Knight LC, et al. What are the constraints and opportunities for HIVST scale-up in Africa? Evidence from Kenya, Malawi and South Africa. J. Int AIDS Soc. 2015;18:19445.
7. Dacombe RJ, Watson V, Sibanda E, Nyirenda L, Simwinga M, Cowen E, et al. A Baseline Assessment of the Policy and Regulatory Environment for HIV Self-testing in Malawi, Zimbabwe and Zambia. [Oral poster] African Society for Laboratory Medicine 3rd International Conference 3-8 December 2016.
8. Johnson C, Figueroa C, Cambiano V, Phillips A, Sands A, Meurant R, et al. A clinical utility risk-benefit analysis for HIV self-testing. [Abstract TUPEC0834]. 9th IAS Conference on HIV Science 23-26 July 2017.
9. Figueroa C, Johnson C, Ford N, Sands A, Dalal S, Meurant R, et al. Reliability of HIV rapid diagnostic tests for self-testing compared with testing by healthcare workers: a systematic review and meta-analysis. Lancet HIV. 2018;5(6):277–290.
10. Gotsche CI, Simwinga M, Muzumara A, Kapaku KN, Sigande L, Neuman M, et al. HIV self-testing in Zambia: User ability to follow the manufacturer's instructions for use. [Abstract MOPED1167]. 9th IAS Conference on HIV Science 23-26 July 2017.
11. Mwau M, Achieng L, Bwana P. Performance and usability of INSTI, a blood-based rapid HIV self test for qualitative detection of HIV antibodies in intended use populations in Kenya. [Abstract MOAX0106LB] 9th IAS Conference on HIV Science 23-26 July 2017.
12. Ortblad K, Musoke DK, Ngabirano T, Nakitende A, Magoola J, Kayiira P, et al. Direct provision versus facility collection of HIV self-tests among female sex workers in Uganda: a cluster-randomized controlled health systems trial. PLoS One. 2017;14(11):e1002458.
13. 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):372–379.
14. Choko AT, Feilding K, Stallard N, Maheswaran H, Lepine A, Desmond N, et al. Investigating interventions to increase uptake of HIV testing and linkage into care or prevention for male partners of pregnant women in antenatal clinics in Blantyre, Malawi: study protocol for a cluster randomised trial. Trials. 2017;18:349.
15. Unitaid PSI HIV STAR Consortium. Zambia clinical performance study protocol. 2016; Available from: http://hivstar.lshtm.ac.uk/files/2016/11/STAR-Protocol-for-Zambia-Clinical-Performance-Study-web.pdf
16. Choko AT, Taegtmeyer M, MacPherson P, Cocker D, Khundi M, Thindwa D, et al. Initial accuracy of HIV rapid test kits stored in suboptimal conditions and validity of delayed reading of oral fluid tests. PLoS One. 2016;11(6):e0158107.
17. WHO Prequalification of *In Vitro* Diagnostics. Public Report. Product: OraQuick HIV Self-Test WHO reference number: PQDx 0159-055-01. 2017 [cited 2018 Aug 08]. Available from: http://www.who.int/diagnostics_laboratory/evaluations/pq-list/170720_final_amended_pqdx_0159_055_01_oraquick_hiv_self_test_v2.pdf
18. Zeptometrix. HIV Seroconversion Panel Donor No. 73695. Zeptometrix. 2019; URL:https://www.zeptometrix.com/media/documents/PIHIV12007.pdf. Accessed: 2019-01-04. http://www.webcitation.org/75Ajt4f0y (Archived by WebCite® at http://www.webcitation.org/75Ajt4f0y)
19. Zeptometrix. HIV Seroconversion Panel Donor No. 75018. Zeptometrix. 2019; URL: https://www.zeptometrix.com/media/documents/PIHIV9077.pdf. Accessed: 2019-01-04. http://www.webcitation.org/75AjSCRd9. (Archived by WebCite® at http://www.webcitation.org/75AjSCRd9)
20. Hartling L, Hamm M, Milne A, Vandermeer B, Santaguida P, Ansari M, et al. Validity and Inter-Rater Reliability Testing of Quality Assessment Instruments. [Internet]. Rockville, MD: Agency for Healthcare Research and Quality (US); 2012[cited Accessed October 2016]. Table 2, Interpretation of Fleiss' kappa (κ) (from Landis and Koch 1977) Available from: https://www.ncbi.nlm.nih.gov/books/NBK92295/table/methods.t2/
21. Klarkowski D, O'Brien DP, Shanks L, Singh KP. Causes of false-positive HIV rapid diagnostic test results. Expert Rev Anti Infect Ther. 2014;12(1):49–62.
22. Johnson CC, Fonner V, Sands A, Ford N, Obermeyer CM, Tsui S, 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 (Suppl 6):21755. doi: 10.7448/IAS.20.7.21755.
23. Fogel JM, Piwowar-Manning E, Debevec B, Walsky T, Schlusser K, Laeyendecker O, et al. Brief report: impact of early antiretroviral therapy on the performance of HIV rapid tests and HIV incidence assays. J Acquir Immune Defic Syndr. 2017;75(4):426–430.

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RESEARCH ARTICLE

# Optimizing HIV testing services in sub-Saharan Africa: cost and performance of verification testing with HIV self-tests and tests for triage

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## Abstract

**Introduction:** Strategies employing a single rapid diagnostic test (RDT) such as HIV self-testing (HIVST) or "test for triage" (T4T) are proposed to increase HIV testing programme impact. Current guidelines recommend serial testing with two or three RDTs for HIV diagnosis, followed by retesting with the same algorithm to verify HIV-positive status before anti-retroviral therapy (ART) initiation. We investigated whether clients presenting to HIV testing services (HTS) following a single reactive RDT must undergo the diagnostic algorithm twice to diagnose and verify HIV-positive status, or whether a diagnosis with the setting-specific algorithm is adequate for ART initiation.

**Methods:** We calculated (1) expected number of false-positive (FP) misclassifications per 10,000 HIV negative persons tested, (2) positive predictive value (PPV) of the overall HIV testing strategy compared to the WHO recommended PPV ≥99%, and (3) expected cost per FP misclassified person identified by additional verification testing in a typical low-/middle-income setting, compared to the expected lifetime ART cost of $3000. Scenarios considered were as follows: 10% prevalence using two serial RDTs for diagnosis, 1% prevalence using three serial RDTs, and calibration using programmatic data from Malawi in 2017 where the proportion of people testing HIV positive in facilities was 4%.

**Results:** In the 10% HIV prevalence setting with a triage test, the expected number of FP misclassifications was 0.86 per 10,000 tested without verification testing and the PPV was 99.9%. In the 1% prevalence setting, expected FP misclassifications were 0.19 with 99.8% PPV, and in the Malawi 2017 calibrated setting the expected misclassifications were 0.08 with 99.98% PPV. The cost per FP identified by verification testing was $5879, $3770, and $24,259 respectively. Results were sensitive to assumptions about accuracy of self-reported reactive results and whether reactive triage test results influenced biased interpretation of subsequent RDT results by the HTS provider.

**Conclusions:** Diagnosis with the full algorithm following presentation with a reactive triage test is expected to achieve PPV above the 99% threshold. Continuing verification testing prior to ART initiation remains recommended, but HIV testing strategies involving HIVST and T4T may provide opportunities to maintain quality while increasing efficiency as part of broader restructuring of HIV testing service delivery.

**Keywords:** HIV; HIV testing; HIV self-testing; Retesting; ART initiation; Quality

Additional Supporting Information may be found online in the Supporting information tab for this article.

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## 1 | INTRODUCTION

Substantial scale-up of HIV testing services (HTS) has contributed to tremendous progress towards global targets to diagnose 90% of people with HIV by 2020. In 2017, PEPFAR alone conducted more than 85 million HIV tests [1]. Despite this scale-up, an estimated 25% of people with HIV remain unaware of their status [2].

Striving for these ambitious targets for HIV diagnosis, while also seeking increases in the efficiency and effectiveness of services, has stimulated innovative approaches to providing HTS. Recent forecasts suggest the HIV response is not on track to achieve the 90-90-90 testing and treatment targets unless significant investments are made [3], and there are increases in effectiveness and efficiency of services. The expanded volume of HIV testing and depletion of undiagnosed

persons has increased the marginal testing cost per HIV-positive person identified. Static donor investment has also added pressures to implement more "cost-effective" testing approaches. As a result, many countries are looking for innovative ways to continue to scale-up HIV testing, while maximizing effectiveness and efficiency and maintaining quality.

To establish a diagnosis of HIV infection, WHO Guidelines recommend using multiple independent serological assays (rapid diagnostic tests (RDTs) and enzyme immunoassays) [4]. Each assay must demonstrate at least 99% sensitivity and 98% specificity. In settings where the prevalence among HTS clients is above 5%, guidelines recommend reactive results from two consecutive assays conducted serially to establish HIV infection, and three consecutive assays in settings with HIV prevalence below 5% (Figure 1A), ensuring a positive predictive value (PPV) of above 99% in all settings [4]. If the results of the assays are discrepant, both assays are repeated. In the high prevalence setting (≥5%), if still discrepant, a third assay is applied. If the third assay is non-reactive, the result is reported as HIV negative, while if reactive the result is reported as inconclusive to be retested in 14 days. In the low prevalence setting, all three assays must be reactive to establish HIV infection; if the first two are reactive and the third non-reactive, the result is reported as inconclusive for re-testing in 14 days.

Recent reports have described suboptimal quality of HIV testing and cases of HIV misdiagnosis [5], highlighting the importance of ensuring reliable and accurate HIV testing, alongside scale-up. A recent systematic review identified the main reason for false-positive (FP) HIV diagnosis was the use of incorrect or suboptimal testing strategies and algorithms in facilities [6]. To mitigate misclassification of HIV status (often due to human error), WHO recommends re-testing with the full diagnostic algorithm by an independent provider to "verify" HIV-positive status immediately prior to anti-retroviral therapy (ART) initiation (Figure 1B) [4]. Recent analyses estimated that additional verification testing prior to ART initiation is highly cost-saving [6,7], in addition to being good public-health practice, but many countries are yet to implement this approach [8].

HIV self-testing (HIVST) and "test for triage" (T4T) are two testing modalities that both involve provision of a single HIV RDT, referred to as an "A0" (assay 0) test, either by oneself (HIVST) or a lay-provider in a community-based setting (T4T). Clients with reactive A0 RDT results are linked to the health system for testing with the full national testing algorithm to

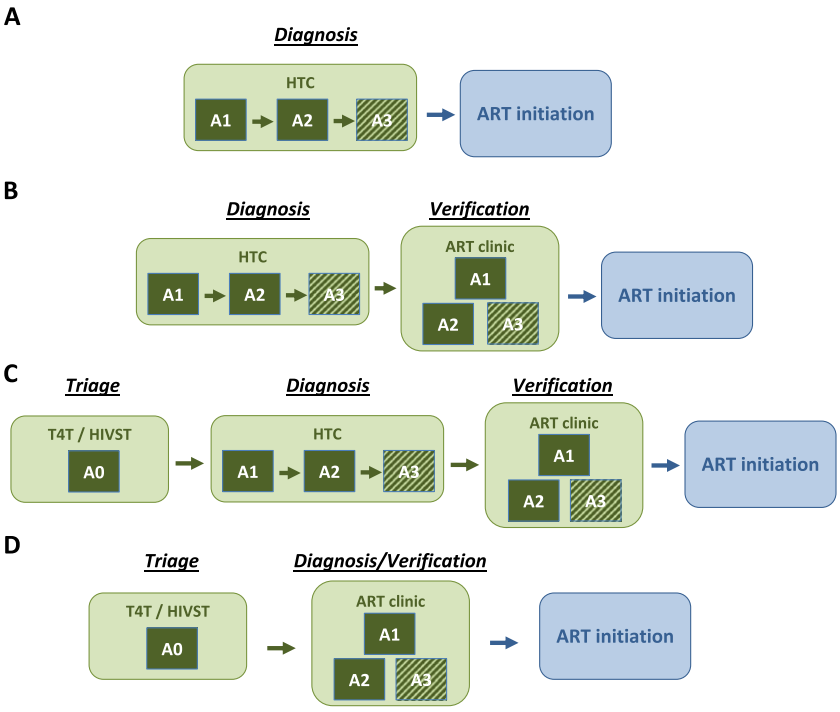


**Figure 1. Simplified flow diagram for alternative HIV testing and diagnosis strategies prior to ART initiation.**
(**A** and **B**) represent current "status quo" HIV testing strategies without and with verification testing prior to ART initiation, respectively. (**C** and **D**) illustrate potential testing strategies for clients presenting to HIV testing services (HTS) following a single reactive RDT through HIV self-testing or test for triage modalities. In (**C** and **D**), the "A0" assay represents a single RDT, either HIVST or T4T, applied before referral to HIV testing services for testing and diagnosis with the full diagnostic algorithm. Assays "A1," "A2," and "A3" represent HIV antibody rapid diagnostic test (RDT) conducted in serial comprising a testing algorithm in a setting using a 2-test strategy or 3-test strategy. The "A3" assay is shaded to indicate that this assay is only applied in a setting using a 3-test strategy for HIV diagnosis (recommended for prevalence <5%). HIV diagnosis is established only if all two/three serial RDTs are reactive. Discordant results (A1 reactive/A2 non-reactive) should be re-tested using the same two assays; if they remain discrepant, the result is reported as HIV-inconclusive and the client is retested in 14 days. Full details of the flow and reporting of results in the case of discrepant results are described in [4]. In our simplified simulation, it is assumed that discrepant results will be adjudicated correctly upon retesting, and thus FP misclassification only occurs if the results of all two or three assays are misclassified as reactive in serial. ART, anti-retroviral therapy; HIVST, HIV self-testing; HTC, HIV testing and counselling; RDT, rapid diagnostic test.

confirm HIV-positive status. Such strategies offer opportunities to reach those with a single RDT who may not otherwise test and then promote to further testing and treatment linkage for those with a reactive test result [4,9]. HIVST has been highlighted as an effective way to increase uptake and frequency of testing in high risk populations [10]. These approaches offer the opportunity to improve quality and efficiency in the health system, including fast-tracking those with reactive results to care and those who are negative to prevention [4,9]. In the light of evidence suggesting suboptimal specificity of HTS [6] and recent evidence that HIVST is highly specific [11], many countries rolling out HIVST are considering whether additional verification testing is still required before ART initiation for people presenting to care following a reactive HIVST result.

This analysis considers whether patients with a single reactive A0 RDT, from either HIVST or T4T, must undergo the full testing strategy twice (1) for diagnosis and (2) for verification testing prior to ART initiation, or if is it adequate to initiate ART following an initial reactive A0 result followed by a diagnosis with the full testing strategy alone (i.e. without additional verification of HIV status at ART initiation, hereafter verification testing).

## 2 | METHODS

We used a simple probability model to calculate the expected levels of FP misclassification arising from HIV testing strategies that included an A0 RDT prior to presenting for HTS compared to current HIV testing strategies that do not include an A0 test. The model extends a previously developed model of WHO recommended HIV testing strategies, including verification testing, to incorporate a single RDT as an A0 T4T [6]. All analyses were conducted in R version 3.5.0. An R script reproducing all analyses is provided as Data S1.

### 2.1 | Testing strategies considered

Figure 1 presents the four testing strategies considered. The first two (A and B) are "status quo" HIV testing strategies without or with verification testing before ART initiation (Figures 1A and 1B respectively); WHO HTS Guidelines recommend testing including verification (Figure 1B). The HTS client is considered "diagnosed" following reactive results on two independent RDTs (A1 + A2) in a setting with prevalence above 5% or three independent RDTs (A1 + A2 + A3) in a setting with prevalence below 5%. Following diagnosis, the client is referred for HIV care and treatment at which point the full two-test or three-test HIV testing strategy is repeated to verify the HIV status (Figure 1B), followed by ART initiation if the HIV diagnosis is confirmed.

In the third strategy (Figure 1C), we considered that clients underwent an A0 test with a reactive result prior to presentation at HTS. Following this they proceed through the full diagnosis and verification before initiating ART. In the fourth strategy, we considered combining the "diagnosis" and "verification" stages for clients presenting for HTS following a reactive A0 test (Figure 1D). That is, they are initiated to ART following a single sequence of two or three reactive RDTs per the validated national testing algorithm.

### 2.2 | Modelled scenarios and assumptions about RDT performance in diagnostic settings

As base scenarios, we considered a "high-prevalence" setting using a two-test strategy with 10% HIV prevalence among testing clients and a "low-prevalence" setting employing a three-test strategy with 1% HIV prevalence. Consistent with previous application of our model [6], we assumed 98% specificity of each RDT in the algorithm, which is the minimum specificity required for WHO prequalification [12]. We further assumed a 20% probability that a FP misclassification on one RDT would also be misclassified on the subsequent independent RDT [6]. This is due to potential correlated exogenous factors that might influence correlated FP classification errors, such as environmental conditions or user errors affecting the outcome of both tests. The specificity for the overall testing algorithm (A1 + A2 or A1 + A2 + A3) is calculated as one minus the probability that both or all three assays are reactive given the true status is HIV negative:

$$\text{spec}_{2-\text{test}} = 1 - (1 - \text{spec}_{A1}) \cdot (c + (1 - c) * (1 - \text{spec}_{A2}))$$

$$\text{spec}_{3-\text{test}} = 1 - (1 - \text{spec}_{A1}) \cdot \big(c + (1 - c) \cdot (1 - \text{spec}_{A1}) \cdot (c + (1 - c) \cdot (1 - \text{spec}_{A3}))\big)$$

where $\text{spec}_{Ax} = 0.98$ is the specificity for each individual assay and $c = 0.2$ is the additional probability that a FP misclassification one on RDT results in a misclassification on the next RDT in the algorithm. These assumptions imply overall testing algorithm specificity of $\text{spec}_{2\text{-test}} = 99.57\%$ for the two-test strategy and $\text{spec}_{3\text{-test}} = 99.91\%$ for the three-test strategy.

We considered a third scenario indicative of the performance of the national HIV testing programme of Malawi in 2017. Malawi currently uses a two-test strategy and has conducted verification testing prior to ART initiation since 2011. The national HIV prevalence among adults in 2017 was 10% [13], the positivity among HTS clients was 4% across all testing modalities including health facilities, non-health facility venues, mobile testing, and community-based testing [14]. According to 2017 verification testing records, of the 174,078 clients testing positive and undergoing verification, 1481 (1%) were subsequently found to be HIV negative of the 174,078 testing HIV positive and undergoing verification [14]. The prevalence among testers of 4% and PPV of 99% imply that the specificity for the two-test algorithm is 99.96%.

### 2.3 | Assumptions about performance of A0 tests

We assumed a specificity of 98% for A0 tests conducted via HIVST or T4T modalities as a base assumption and varied specificity from 90% to 100% in sensitivity analyses [11]. In our base analysis, we assumed that the outcome of the A0 test does not affect accuracy of subsequent diagnostic testing conducted by an HTS provider. However, in sensitivity analysis we considered the potential effect of knowledge of the A0 test result influencing reader error resulting in FP misclassification by the HTS provider. In sensitivity analysis, we modelled a probability ranging from 0% to 20% that the A1 test

would be misclassified for an HIV-negative individual presenting for HTS following a FP A0 triage test result. We report results focused on 0% and 5% probability of reader error.

### 2.4 | Cost assumptions

We assumed a cost of $7 per client for verification retesting with the three-test strategy and $5 per client for verification retesting with the two-test strategy, informed by HIV testing cost data typical for sub-Saharan Africa [15]. We estimated the discounted lifetime ART cost of $3000. This was based on an annual cost of $150 per year in sub-Saharan Africa including ARV commodities, diagnostics, and clinical monitoring, and service delivery for stable ART patients [16] over 30 years life expectancy discounted at 3% per annum [17] assuming no loss to follow-up. All costs were considered in 2016 US dollars.

### 2.5 | Analysis

For each testing strategy and scenario ("high prevalence"—10%, "low prevalence"—1%, "Malawi 2017"—4%), we calculated three outcomes of interest:

(1) The expected number of FP misclassifications per 10,000 HIV-negative persons tested.
(2) The expected PPV for the overall testing strategy, that is, the probability that a person initiated on ART is truly HIV positive.
(3) The expected cost per FP person identified through verification re-testing compared to the expected lifetime cost of ART.

For the calculation of PPV, we conservatively assumed a sensitivity of 90% among HIV-positive clients, such that:

$$\mathrm{PPV} = \frac{\mathrm{sens} \cdot \mathrm{prev}}{\mathrm{sens} \cdot \mathrm{prev} + (1 - \mathrm{spec}_{\mathrm{strgy}}) \cdot (1 - \mathrm{prev})}$$

where $\mathrm{spec}_{\mathrm{strgy}}$ is the specificity of the overall testing strategy including any A0 test or verification testing. We considered testing strategies "acceptable" if the PPV for the overall testing strategy was above the 99% threshold defined by the WHO Guidelines [15].

We considered additional verification testing "cost-efficient" if the cost per FP misclassification identified was less than the expected lifetime ART cost of $3000. The total cost of verification testing was the cost per client for verification testing ($5 or $7 depending on 2-test or 3-test algorithm) times the number of clients classified as HIV positive before verification testing:

$$[\text{verification cost}] = [\text{cost per verification client}] \cdot (\mathrm{sens} \cdot \mathrm{prev} + (1 - \mathrm{spec}_{\mathrm{no-verif}}) \cdot (1 - \mathrm{prev}))$$

The expected number of false positive cases identified through verification testing was calculated as the number of negative clients testing times the specificity of the strategy with verification testing minus the specificity of the same strategy without verification testing:

$$[\text{FP identified}] = (1 - \mathrm{prev}) \cdot \left(\mathrm{spec}_{\mathrm{w/verif}} - \mathrm{spec}_{\mathrm{no-verif}}\right)$$

The cost per FP identified was the ratio of total verification cost divided by the number of FP identified.

## 3 | RESULTS

### 3.1 | Rates of false positive misclassification

#### 3.1.1 | *Scenario 1: High prevalence (10%)*

In scenario 1, with 10% HIV prevalence and using the two-test strategy, the "status quo" scenario of HIV diagnosis following reactive A1 and A2 RDTs without additional verification testing (Figure 1A) resulted in 43.2 FP misclassifications per 10,000 HIV-negative persons tested (Table 1). Implementing verification testing by retesting using the full testing strategy (Figure 1B) reduced the number of misclassifications to 0.64. The PPV increased from 95.9% to 99.9%.

When HTS clients had a reactive A0 triage test prior to full diagnosis at HTS, the expected number of misclassifications was only 0.86 and the PPV was 99.9% without additional verification testing (Figure 1D). Additional verification testing (Figure 1C) reduced the number of misclassifications to 0.01. When we assumed that a false-reactive A0 RDT may induce a 5% probability of reader error of the A1 RDT at HTS, the expected number of FP for the diagnosis without additional verification increased to 3.0, but the PPV was 99.7%, remaining well above the 99% target threshold.

#### 3.1.2 | *Scenario 2: Low prevalence (1%)*

In scenario 2, with 1% HIV prevalence and using the a three-test strategy, the expected number of FP misclassifications was lower for all strategies due to the inclusion of the third RDT, but the PPV was also slightly lower due to the lower prevalence (Table 1). The number of FP for HIV diagnosis following a single application of the three-test algorithm was 9.3 and the PPV was 90.7%. For clients presenting with a reactive A0, the number of FP reduced to 0.2 and the PPV was 99.8%. Assuming a 5% error for the A1 test following a false-reactive A0 changed the expected FP to 0.6 and the PPV to 99.3%, still above the 99% threshold.

#### 3.1.3 | *Scenario 3: Malawi 2017 (4% positivity; 99% PPV)*

In the scenario based on programmatic data from Malawi in 2017, in which HIV positivity among HTS clients was 4% and the two-test strategy performed with a 99% PPV, the expected number of FP misclassifications was 4.2 per 10,000 HIV-negative persons tested. The number of FP reduced to 0.08 with a 99.98% PPV for clients presenting with a reactive A0, or 2.1 FP and a 99.5% PPV when we assumed a 5% reader error for the A1 RDT.

### 3.2 | Cost per false positive identified

Without A0 triage testing before presentation for HTS ("status quo" scenario), additional verification testing was clearly

**Table 1. Results for number of false positive misclassifications, PPV, and cost per FP identified for alternative scenarios and testing strategies**

| | 10% prevalence | | | 1% prevalence | | | Malawi 2017[a] | | |
|---|---|---|---|---|---|---|---|---|---|
| | Status Quo | With A0 | A0, 5% A1 error | Status Quo | With A0 | A0, 5% A1 error | Status Quo | With A0 | A0, 5% A1 error |
| Testing Strategy | Two-test | | | Three-test | | | Two-test | | |
| Algorithm specificity | 99.57% | | | 99.91% | | | 99.96% | | |
| Verification testing cost | $5 | | | $7 | | | $5 | | |
| False positive misclassifications per 10,000 HIV negative persons tested | | | | | | | | | |
| No verification[b] | 43.2 | 0.86 | 2.98 | 9.3 | 0.19 | 0.64 | 4.18 | 0.08 | 2.10 |
| With verification[c] | 0.64 | 0.01 | 0.04 | 0.03 | 0.001 | 0.002 | 0.04 | 0.001 | 0.02 |
| PPV | | | | | | | | | |
| No verification[b] | 95.86% | 99.91% | 99.70% | 90.69% | 99.80% | 99.30% | 98.90% | 99.98% | 99.44% |
| With verification[c] | 99.94% | >99.99% | >99.99% | 99.97% | >99.99% | >99.99% | 99.99% | >99.99% | 99.99% |
| Cost per FP identified[d] | $123 | $5,880 | $1,708 | $75 | $3,428 | $999 | $460 | $22,743 | $909 |

FP, false-positive; PPV, positive predictive value.
[a]Prevalence among HIV testing clients was 4% in Malawi in 2017. HIV prevalence among all adults was approximately 10%.
[b]"No verification" corresponds to strategy in Figure 1A under "status quo" scenario and Figure 1D for "with A0" scenarios.
[c]"With verification" corresponds to Figure 1B under "status quo" scenario' and Figure 1C under "with A0" scenarios.
[d]Cost per FP identified through verification testing compared to no verification testing. Cost is calculated as the expected number of verification tests conducted (sens × prev + (1 − spec) × (1 − prev)) times the cost per verification test divided by the number of FP cases identified through verification testing.

cost-efficient. The estimated cost per FP misclassification identified was $123, $75, and $460 for the "high prevalence," "low prevalence" and "Malawi 2017" scenarios respectively (Table 1), which compared very favourably to the $3000 expected lifetime cost had the misclassified client been initiated on ART. When clients presented for HTS following a reactive A0 RDT, the cost per FP identified was $5880 in the base case 10% prevalence setting, $3428 in the 1% prevalence setting, and $22,743 for the Malawi 2017 HTS assumptions. The cost per FP identified was lower when assuming 5% reader error in the A1 RDT at $1708, $999, and $909 respectively, but still markedly higher than the cost per FP identified associated with verification testing in the absence of the A0 triage test.

### 3.3 | Sensitivity analysis of A0 specificity

Figure 2 considers the sensitivity of these conclusions to assumptions about the specificity of the A0 triage test, assumed to be 98% in the base-case analysis in Table 1. For specificity values ranging between 90% and 100%, the expected number of FP cases is higher and PPV lower for lower A0 specificity, but in all cases the PPV is well above the 99% PPV target threshold. Figure 3 considers the sensitivity to the assumed probability of reader error misclassification of the A1 test following attendance with a reactive A0 triage test, which was assumed to be 0% or 5% in Table 1. Higher probabilities of reader error associated with a FP A0 result reduced the performance of the overall testing strategy, and at high levels of error additional verification testing may be needed to meet the 99% PPV target threshold. In the Malawi 2017 scenario, in which the specificity of the A1 test was higher than the 98% assumed in the baseline scenario, HTS performance could be worse than the status quo without verification testing if a FP A0 test resulted in greater than 10% reader error in A1 test results, and this threshold would vary depending on the attained specificity of the A0 test.

## 4 | DISCUSSION

The recommendation for verification of HIV status before ART initiation has been increasingly adopted to ensure the fidelity of the HIV testing and ART programmes and avoid future costs and ramifications associated with inadvertently initiating HIV-negative persons on lifelong ART. Previous studies have highlighted that retesting may be particularly important considering reports of poor quality testing and low uptake of WHO-recommended HIV testing strategies and algorithms [5,18-21]. Policy analysis from 2015 suggested fewer than 20% of reporting countries had a national testing strategy and algorithm that was in full alignment with WHO guidelines [8].

In this analysis, we considered whether such additional verification testing is required and cost-efficient for clients who already underwent diagnostic testing to confirm their HIV status in HTS following a reactive triage test. Taken together, our analysis suggests triage test approaches, including HIVST, can potentially result in lower FP HIV misclassification in settings not implementing verification testing prior to ART. We find that the rate of FP misclassification is expected to be very low for persons presenting with a reactive HIVST confirmed by diagnostic testing and the PPV is expected to be well above 99% without additional verification testing. This is the case even with base assumptions about the accuracy of HTS that appear conservative compared to programmatic data about the current performance of HIV testing in programmatic settings. Given the very small number of clients

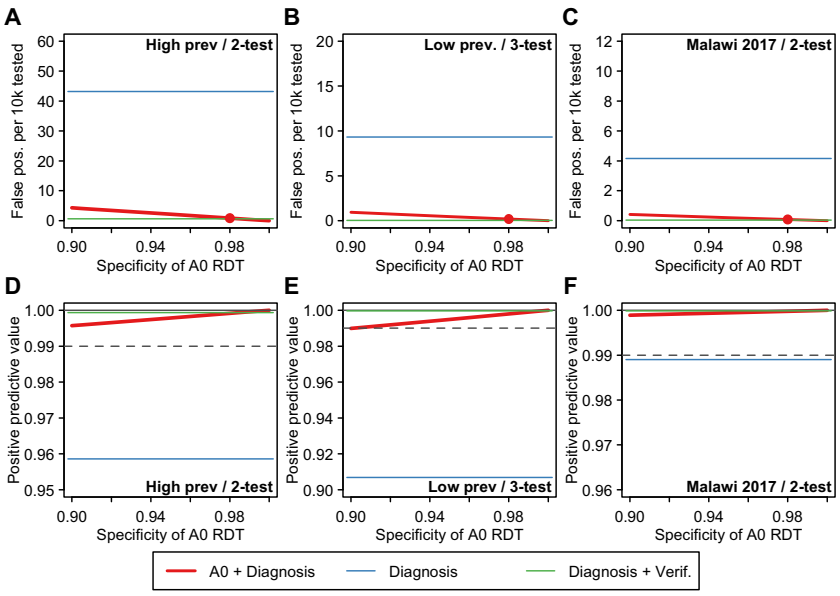


**Figure 2. Sensitivity analysis of assumptions the specificity of the A0 RDT on the expected number of false positive misclassifications per 10,000 HIV negative persons tested (A to C) and the positive predictive value (PPV) of the overall testing strategy, conservatively assuming 90% sensitivity (D to F).**

Red line illustrates scenario in which clients present to HTS following a reactive test and undergo the national HIV testing algorithm once (Figure 1D). Red points mark the assumed 98% specificity assumed in the base-case analysis. For benchmarking, the blue horizontal line indicates the results for status quo HIV testing without verification testing (Figure 1A) and the green line indicates status quo testing with verification testing (Figure 1B). For PPV results (**D** to **F**), the grey dashed line indicates the 99% PPV threshold recommended by WHO Consolidated HIV Testing Guidelines. RDT, rapid diagnostic test.

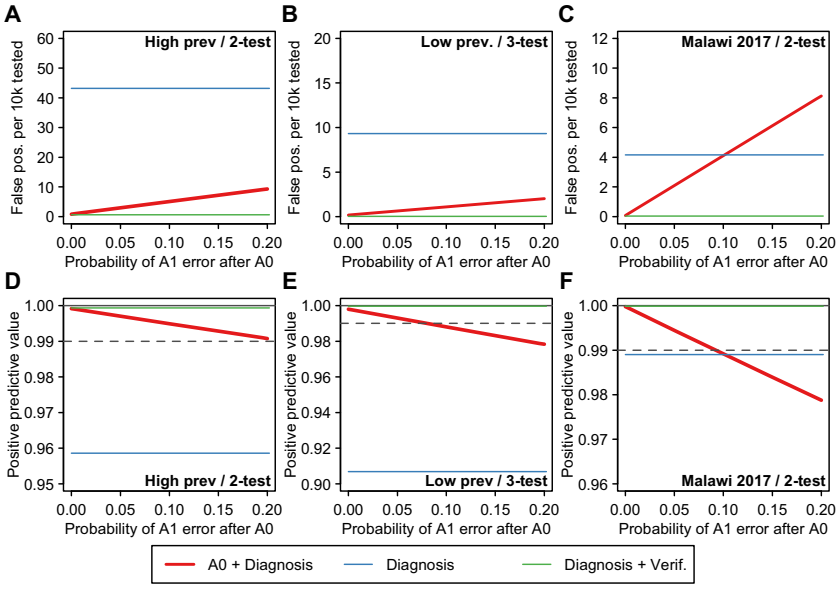


**Figure 3. Sensitivity analysis about the probability of excess reader error for A1 test if presenting following a false-reactive result of the A0 RDT. (A to C) illustrate the effect on the expected number of false positive misclassifications per 10,000 HIV negative persons tested and (D to F) illustrate the positive predictive value (PPV) of the overall testing strategy, conservatively assuming 90% sensitivity.**

Red line illustrates scenario in which clients present to HTS following a reactive A1 test and undergo the national HIV testing algorithm once (Figure 1D). For benchmarking, the blue horizontal line indicates the results for status quo HIV testing without verification testing (Figure 1A) and the green line indicates status quo testing with verification testing (Figure 1B). For PPV results (**D** to **F**), the grey dashed line indicates the 99% PPV threshold recommended by WHO Consolidated HIV Testing Guidelines. HTS, HIV testing services; RDT, rapid diagnostic test.

expected to be identified as FP, verification testing may not be cost-efficient relative to the lifetime costs of ART for FP persons.

Even with imperfect specificity of HIVST, the expected number of FP among persons presenting for HTS following a reactive HIVST is far lower than would be expected amongst a population of HTS clients who had not undergone triage testing. Most basically, this conclusion reflects the difference in the prior probability that a client is truly HIV positive before presenting to HTS. In the absence of triage testing, with a true HIV positivity of 5% among those testing, 95% of clients will be truly HIV negative, leaving a large pool among which a FP misclassification could occur. Among 100 HTS clients presenting following a reactive HIVST with 98% specificity, only 2% would be truly HIV negative, a much smaller group among whom a FP misclassification could occur.

Our analysis has several limitations and the findings should be considered in the light of important uncertainties about key assumptions. First, findings were sensitive to whether we assumed that presenting with a reactive A0 test might bias the provider in interpreting results of subsequent A1 RDT results. Currently, even in relatively high HIV prevalence settings, the large majority (>95%) of HTS clients are classified as HIV negative following a single RDT. This would change for a provider seeing a large number of clients referred to care following a reactive HIVST or T4T. This could change the prior expectations of the provider about the likely outcome of the test and subtly bias the interpretation of inconclusive test results. However, to our knowledge, evidence is not yet available to evaluate whether this occurs. We consider this a high priority evidence gap for further research as HIVST scales up.

Second, our analysis takes a narrow perspective on the potential costs and consequences of FP misclassification by considering only the costs to the health system associated with lifetime ART for a misdiagnosed client. Costs and adverse consequences born by clients may be substantially greater, including unnecessary care and treatment, consequences for family, marriages, and relationships, potential adverse effects of ART. Without capturing the full health and quality of life consequences of HIV misclassification, we are not able to undertake cost-effectiveness analysis to benchmark investments in verification testing against other potential allocation of health resources. More broadly, cases of FP misclassification may serve to undermine confidence and engagement in the health system outstripping the economic costs of unnecessary treatment.

Third, we considered only the risk of false positive diagnosis amongst HIV-negative clients. Ensuring highly accurate HIV diagnosis is paramount for HIV testing services. Evidence suggests that rates of false negative misclassification in both traditional HTS and HIVST are also higher than would be expected given 99% sensitivity required for WHO prequalification [11,22]. Quantifying the rates, reasons, and consequences of false negative diagnosis is an important area for further implementation research and modelling.

These modelling results need to be considered in the light of practical implementation issues. Although the expected number of FP misclassifications identified through verification testing was low for persons presenting following HIVST, it is not recommended to discontinue verification testing for these clients in settings where verification testing is already in place, working well, and achieving results. It will be important to review data from settings where this new testing strategy is used before suggesting changing current recommended practice. For example, in 2015, Malawi was one of few countries implementing WHO recommended testing strategies and verification testing among people with HIV prior to starting ART [4,8]. These efforts combined with updated guidelines and retraining of testers, decreased HIV-negative test results following an initial HIV-positive diagnosis from 7% to 1% between 2014 and 2016 [14]. Additional studies have highlighted the role of retesting, alongside validation of national algorithms, to ensure quality [18,20].

The HIV testing resources required for verification testing is a small proportion of the overall HIV testing resources, considering that the very large majority of HTS clients will be classified as HIV negative from the first assay in the HIV testing algorithm [6]. This will especially be the case as positivity and number of new diagnoses decline as a share of all those tested. Currently HIVST is not available at national scale in most settings, and proposing different models for diagnosis, verification, and treatment initiation for these few HIVST clients may potentially increase fragmentation of HTS, which could increase opportunities for errors. Broader changes in future HTS delivery may reconsider the role of verification *vis-à-vis* the "test-for-triage" model in which a single RDT is applied at the first engagement with HIV testing services, following which clients are referred to HIV care and treatment facilities for full diagnostic testing with the full national HIV testing algorithm. For example, embracing the "test-for-triage" model across all HIV testing modalities, whether facility-based or community-based may simplify and streamline the provision of HTS, and harmonize client flow for HIVST clients with those engaging through other modalities. Such approaches should be considered and evaluated in programmatic settings.

Programmatically, it may be most advantageous to promote T4T and HIVST as simplified initial screening tests on a large scale and deliver quality-assured verification testing directly before ART initiation at health facilities, cutting out the need for parallel "intermediate" confirmation testing at peripheral testing sites.

## 5 | CONCLUSIONS

Following WHO testing strategies with verification testing prior to ART initiation is recommended and should be continued. T4T and HIVST approaches could potentially improve accuracy and quality of HTS in settings not implementing diagnostic testing followed by repeated verification testing prior to ART. T4T followed by diagnosis with full national testing algorithm is expected to deliver accurate results above WHO benchmarks for PPV of at least 99%, so long as the quality and specificity of HTS remains similar to current programmatic performance. While HIVST scale-up may render verification testing before ART less necessary in high quality programmes, selectively discontinuing full diagnosis with the national testing algorithm before verification testing for a subset of clients who present following reactive A0 test must be considered agains the risk risks of additional complexity and potential for increased user and provider error. T4T and HIVST may provide an opportunity to restructure HTS delivery and quality assurance systems which should be explored further and evaluated in programmes to guide future policy.

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## COMPETING INTERESTS

We have no competing interests to declare.

## AUTHORS' CONTRIBUTIONS

JWE and CJ drafted initial manuscript with inputs from all authors. All authors contributed to the final manuscript.

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## DISCLAIMER

The funder did not have any role in the design and analysis of the study.

## REFERENCES

1. PEPFAR 2018 Annual Report to Congress. 2018.
2. UNAIDS. Miles To Go: Global AIDS Update. 2018.
3. Stover J, Bollinger L, Antonio Izazola J, Loures L, DeLay P, Ghys PD, et al. What is required to end the AIDS epidemic as a public health threat by 2030? The cost and impact of the fast-track approach. PLoS One. 2016;11:e0154893.
4. World Health Organization. Consolidated guidelines on HIV testing services. 2015 https://apps.who.int/iris/bitstream/handle/10665/179870/9789241508926_eng.pdf; accessed 13 February 2019.
5. Johnson CC, Fonner V, Sands A, Ford N, Obermeyer CM, Tsui S, 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(Suppl 6):21755. doi: 10.7448/IAS.20.7.21755.
6. Eaton JW, Johnson CC, Gregson S. The cost of not retesting: human immunodeficiency virus misdiagnosis in the antiretroviral therapy "Test-and-Offer" era. Clin Infect Dis. 2017;65:522–5.
7. Hsiao N, Zerbe A, Phillips TK, Myer L, Abrams EJ. Misdiagnosed HIV infection in pregnant women initiating universal ART in South Africa. J Int AIDS Soc. 2017;20(Suppl 6):21758. doi: 10.7448/IAS.20.7.21758.
8. Flynn D, Johnson C, Sands A, Wong V, Baggaley R. Annex 2: an analysis of 48 national HIV testing and counselling policies. Consolidated guidelines on HIV testing services. 2015 https://apps.who.int/iris/bitstream/handle/10665/180208/WHO_HIV_2015.19_eng.pdf; accessed 13 February 2019.
9. World Health Organization. Guidelines of HIV Self-Testing and Partner Notification. 2016 [cited 2018 Nov 15]. Available from: http://apps.who.int/iris/bitstream/handle/10665/251655/9789241549868-eng.pdf?sequence=1
10. Johnson CC, Kennedy C, Fonner V, Siegfried N, Figueroa C, Dalal S, et al. Examining the effects of HIV self-testing compared to standard HIV testing services: a systematic review and meta-analysis. J Int AIDS Soc. 2017;20(1):21594. doi: 10.7448/IAS.20.1.21594.
11. Figueroa C, Johnson C, Ford N, Sands A, Dalal S, Meurant R, et al. Reliability of HIV rapid diagnostic tests for self-testing compared with testing by health-care workers: a systematic review and meta-analysis. Lancet HIV. 2018;5:e277–90.
12. WHO Prequalifications Team: Diagnostics. Technical specification series for submission to WHO prequalification—diagnostic assessment: TSS-1: human immunodeficiency virus (HIV) rapid diagnostic tests for professional and/or self-testing. 2016 [cited 2018 Nov 15]. Available from: http://apps.who.int/iris/bitstream/handle/10665/251857/9789241511742-eng.pdf
13. Ministry of Health Malawi. Malawi Population-based HIV Impact Assessment (MPHIA) 2015-16: First Report. 2017 [cited 2018 Nov 15]. Available from: https://phia.icap.columbia.edu/wp-content/uploads/2017/11/Final-MPHIA-First-Report_11.15.17.pdf
14. Government of Malawi Ministry of Health. Integrated HIV Program Report (October-December 2017). Lilonwe: Government of Malawi Ministry of Health; 2018.
15. Clinton Health Access Initiative. ARV market report: the state of the antiretroviral drug market in low- and middle-income countries, 2015-2020. 2016.
16. UNAIDS. Fast-Track Update on Investments Needed in the AIDS Response. 2016 [cited 2018 Nov 2018]. Available from: http://www.unaids.org/sites/default/files/media_asset/UNAIDS_Reference_FastTrack_Update_on_investments_en.pdf
17. Edejer TT-T, Baltussen R, Adam T, Hutubessy R, Acharya A, Evans D, et al. Making choices in health: who guide to cost effectiveness analysis. Geneva: World Health Organization; 2003 [cited 2013 Feb 13]. Available from: http://www.who.int/choice/publications/p_2003_generalised_cea.pdf
18. Kosack CS, Page A-L, Beelaert G, Benson T, Savane A, Ng'ang'a A, et al. Towards more accurate HIV testing in sub-Saharan Africa: a multi-site evaluation of HIV RDTs and risk factors for false positives. J Int AIDS Soc. 2017; 19 (1):21345. doi: 10.7448/IAS.20.1.21345.
19. Johnson CC, Sands A, Urassa W, Baggaley R. Alert, but not alarmed—a comment on "Towards more accurate HIV testing in sub-Saharan Africa: a multi-site evaluation of HIV RDTs and risk factors for false positives (Kosack et al. 2017)". J Int AIDS Soc. 2017; 20(1):22042. doi: 10.7448/IAS.20.1.22042
20. Kravitz Del Solar AS, Parekh B, Douglas MO, Edgil D, Kuritsky J, Nkengasong J. A Commitment to HIV Diagnostic Accuracy—a comment on "Towards more accurate HIV testing in sub-Saharan Africa: a multi-site evaluation of HIV RDTs and risk factors for false positives" and "HIV misdiagnosis in sub-Saharan Africa: a performance of diagnostic algorithms at six testing sites". J Int AIDS Soc. 2018;21:e25177.
21. Coleman SM, Gnatienko N, Lloyd-Travaglini CA, Winter MR, Bridden C, Blokhina E, et al. False-positive HIV diagnoses: lessons from Ugandan and Russian research cohorts. HIV Clin Trials. 2018;19:15–22.
22. Pant Pai N, Sharma J, Shivkumar S, Pillay S, Vadnais C, Joseph L, et al. Supervised and unsupervised self-testing for HIV in high- and low-risk populations: a systematic review. PLoS Med. 2013;10:e1001414.

# SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

**Data S1.** R code for reproducing analyses.

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RESEARCH ARTICLE

# Applying user preferences to optimize the contribution of HIV self-testing to reaching the "first 90" target of UNAIDS Fast-track strategy: results from discrete choice experiments in Zimbabwe

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## Abstract

**Introduction:** New HIV testing strategies are needed to reach the United Nations' 90-90-90 target. HIV self-testing (HIVST) can increase uptake, but users' perspectives on optimal models of distribution and post-test services are uncertain. We used discrete choice experiments (DCEs) to explore the impact of service characteristics on uptake along the testing cascade.

**Methods:** DCEs are a quantitative survey method that present respondents with repeated choices between packages of service characteristics, and estimate relative strengths of preferences for service characteristics. From June to October 2016, we embedded DCEs within a population-based survey following door-to-door HIVST distribution by community volunteers in two rural Zimbabwean districts: one DCE addressed HIVST distribution preferences; and the other preferences for linkage to confirmatory testing (LCT) following self-testing. Using preference coefficients/utilities, we identified key drivers of uptake for each service and simulated the effect of changes of outreach and static/public clinics' characteristics on LCT.

**Results:** Distribution and LCT DCEs surveyed 296/329 (90.0%) and 496/594 (83.5%) participants; 81.8% and 84.9% had ever-tested, respectively. The strongest distribution preferences were for: (1) free kits – a $1 increase in the kit price was associated with a disutility (U) of −2.017; (2) door-to-door kit delivery (U = +1.029) relative to collection from public/outreach clinic; (3) telephone helpline for pretest support relative to in-person or no support (U = +0.415); (4) distributors from own/local village (U = +0.145) versus those from external communities. Participants who had never HIV tested valued phone helplines more than those previously tested. The strongest LCT preferences were: (1) immediate antiretroviral therapy (ART) availability: U = +0.614 and U = +1.052 for public and outreach clinics, respectively; (2) free services: a $1 user fee increase decreased utility at public (U = −0.381) and outreach clinics (U = −0.761); (3) proximity of clinic (U = −0.38 per hour walking). Participants reported willingness to link to either location; but never-testers were more averse to LCT. Simulations showed the importance of availability of ART: ART unavailability at public clinics would reduce LCT by 24%.

**Conclusions:** Free HIVST distribution by local volunteers and immediately available ART were the strongest relative preferences identified. Accommodating LCT preferences, notably ensuring efficient provision of ART, could facilitate "resistant testers" to test while maximizing uptake of post-test services.

**Keywords:** discrete choice experiments; HIV self-testing; HIV testing; Zimbabwe; HIV; preferences

Additional Supporting Information may be found online in the Supporting information tab for this article.

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## 1 | INTRODUCTION

HIV testing is an important entry point for uptake of prevention, treatment and care services. The United Nations 90-90-90 targets are that by 2020, 90% of people living with HIV should be diagnosed, of whom 90% are on treatment and 90% of those on treatment are virally suppressed [1]. Although achievement of the "first 90" has already occurred in some countries, many countries have not yet attained these targets, with particularly suboptimal uptake of testing among men and young people [2,3]. HIV self-testing (HIVST), where an individual collects his/her own oral fluid or blood sample,

conducts the test and interprets results [4], is an additional testing modality that has increased the uptake and frequency of testing among individuals who would not otherwise test [5,6]. According to World Health Organization (WHO) guidelines [6], a reactive HIVST result should be followed by further confirmatory testing by a trained provider. There are several HIVST delivery models, including community-based, workplace, public and private sector facility-based, and secondary distribution strategies to sexual partners and peers [4].

Optimal models for distributing HIVST, which facilitate both uptake of testing and linkage to confirmatory testing (LCT), to reach those who are undiagnosed are unclear. Uncertainties around ideal service configurations include who should distribute kits, where and when they distribute them, how potential users should be engaged, and what strategies facilitate LCT. A limited number of papers have reported on preferences for service delivery characteristics that facilitate uptake of testing [7,8] and LCT [9]. Here, we report on two discrete choice experiments (DCEs) that were conducted to elicit the strength of users' preferences for both HIVST uptake and LCT to provide recommendations on how self-testing models can be optimized. DCEs are a quantitative survey method that elicit respondents' preferences for attributes of goods/services/programmes [10]. We also present the simulated impact of changing existing services to better support uptake of confirmatory testing.

## 2 | METHODS

### 2.1 | Setting, model of HIVST kit distribution and support for LCT

This study is part of the Unitaid-funded HIV Self-Testing AfRica (STAR) project that aimed to evaluate models of distributing HIVST kits in three countries, namely Malawi, Zambia and Zimbabwe [11]. In Zimbabwe, HIVST distribution was implemented by Population Services International (PSI), which conducts more than 20% of HIV tests in the country. PSI recruited and trained volunteers (community-based distribution agents: CBDA) to distribute HIVST kits door-to-door. Each CBDA was a resident of the same community – a defined geographical area (all or part of a village) in which he/she distributed kits for four to six weeks. According to Ministry of Health and Child Care guidelines [12], kits were offered to all residents ≥16 years old. CBDAs each received a one-off payment of US$50 at the end of the distribution period. To enable LCT, PSI conducted outreach visits at one and three weeks after commencement of distribution. During distribution, participants were told that they could access confirmatory testing either at PSI outreach, public clinics or any other HIV testing service. We evaluated the distribution strategy using a population-representative survey which was conducted in one in four randomly selected households approximately eight weeks after distribution ended. We nested the distribution and LCT DCEs within the survey in two rural districts, Mazowe and Mberengwa in Mashonaland Central and Midlands provinces respectively. Participants were eligible for the survey if they were aged ≥16 years and had lived in the community for at least three months. All eligible participants in a household were recruited.

### 2.2 | Defining DCE attributes and levels

To design the DCE, we used focus group discussions (FGDs) to identify key design attributes or service characteristics and levels (service options within a characteristic) that were most salient in driving decision-making on willingness to self-test for HIV and LCT [10]. FGDs were also used to inform pictorial illustrations of attributes and their levels.

FGDs were conducted by trained social scientists; eligible participants were aged ≥16 years and had lived in the community during HIVST distribution. We based our FGD sample sizes on standard practice that would enable theoretical saturation [13]. Discussions were held in the local language and were digitally recorded, transcribed and translated. Data analysis started soon after data collection began – field notes were written with view to emerging themes, followed by analytic summaries capturing both descriptive and analytic themes. These informed development of a coding framework. Coding was done using NVIVO 10.

We conducted sixteen FGDs to inform the distribution DCE (n = 150) and four FGDs for the LCT DCE (n = 33). The final attributes and levels are presented in Table 1. FGD guides and illustrations of attributes and attribute levels are presented in Appendices S1 and S2.

### 2.3 | Designing the DCE questionnaire

The DCE questionnaire, that is the specific set of repeated choices where participants choose between alternative service provision for HIVST distribution or for LCT, was generated using a d-efficient design created in NGENE 1.0 software [14]. A statistically generated experimental design ensures that the parameter or utility coefficient of each level can be retrieved with the least number of choice sets presented to the participant. DCEs assume that choices are made according to the utility maximization principle, where the best choice provides the highest utility/satisfaction to the decision maker.

For the HIVST distribution DCE, the questionnaire presented nine choice situations, each presenting two alternatives composed of seven attributes. Participants were asked to choose their preferred programme from each pair of alternatives, (Appendix S3a). For the LCT DCE, we used a design with three labelled alternatives, namely public clinic, PSI outreach testing facilities (New Start), and an opt-out presented as "I would not confirm my reactive HIV self-test result if these were the only two options available." Labels are generally used when the service has multiple dimensions, which cannot be fully described, often illustrated by brand names, while the attributes and levels are objective categories that can be fully described. We considered a labelled experiment suitable for the LCT DCE as the image and status of PSI outreach versus public clinics encompasses a vast range of attitudes and preferences and are not changeable. The LCT DCE questionnaire presented twelve choice situations with three alternatives (Appendix S3b).

### 2.4 | Sample size, data collection and analysis

There is no consensus on minimum sample size requirements for stated choice data [15]. We employed the commonly used rule of thumb by Johnson and Orme to ensure that we were able to estimate parameters for the full sample as well as

**Table 1. Attributes, levels and regression coding for the HIVST distribution and LCT DCEs**

| Distribution DCE | | LCT DCE – labelled design: Public clinic and PSI "New Start" outreach site | |
|---|---|---|---|
| **Attribute** | **Attribute level and regression coding** | **Attribute** | **Attribute level and regression coding** |
| Distribution method | Only directly to individuals willing to test (−1)<br>Deliver tests for whole household (1) | Proximity of clinic | Less than 30 minutes' walk from home (0)<br>About one hour's walk from home (1)<br>More than two hours' walk from home (2) |
| Kit price | Free (0)<br>US$0.50 (0.5)<br>US$1 (1) | Busyness of clinic | Few people (−1)<br>Many people (1) |
| Pretest support[a] | Information leaflet (−1)<br>Telephone helpline (1 or 0)<br>Face to face from distributor (1 or 0) | Time of operation | Open weekdays 8 am to 5 pm (−1)<br>Open weekdays and weekends 8 am to 5 pm (1) |
| Time of operation | Monday to Friday 8 am to 4 pm (−1)<br>All days, including evenings and weekends (1) | Antiretroviral treatment available immediately | Yes (−1)<br>No (1) |
| Distributor age | Below 30 years old (−1)<br>Above 30 years old (1) | User fee | None (0)<br>US $1 (1)<br>US $2 (2) |
| Distributor residence | From the same village as participant (−1)<br>From outside participant village (1) | Post-test support[a] | None (−1)<br>SMS reminder (1 or 0)<br>Call reminder (1 or 0)<br>In person follow-up (1 or 0) |
| Location of kit collection[a] | Collection from local clinic (−1)<br>Distributed door-to-door (1 or 0)<br>Collection from mobile testing outreach sites (1 or 0) | Time between kit distribution and PSI visit (applied only to PSI outreach) | Within one week (−1)<br>From two to three weeks (1) |

[a]Since this attribute has n levels and was not treated as a continuous variable, n–1 variables indicating the level were created for that attribute. For each of these variables, where the variable takes on the omitted reference category, included categories are coded −1, otherwise the non-reference categories take on conventional codes of 0 or 1. To retrieve the parameter for the reference category one must take: −1×sum (parameters of non-reference categories).

analyse preference heterogeneity between subgroups [16]. We aimed to recruit 300 and 500 consecutive household survey participants in Mazowe and Mberengwa, respectively.

Paper-based questionnaires were translated into local languages, colour-printed and administered by trained research assistants from June to October 2016.

We estimated the parameters (utility coefficients) using discrete choice models in NLOGIT 5 software [17]. All categorical attribute levels were effects coded, therefore, the parameter for the omitted level was retrieved using this formula: $-1*\sum$coefficient of non-omitted levels [18]. According to common practice, the multinomial logistic model (MNL) was first estimated, followed by iterations of more complex models including the nested logit (NL) and the random parameter logit (RPL) to capture more complex patterns of preference heterogeneity (i.e. variation in tastes across individuals). To estimate preferences for LCT, the NL model was first tested against the MNL model because of the three-alternative design: two LCT programmes and an opt-out, and its relative simplicity, while allowing for some scale heterogeneity. Model fit was assessed using the Akaike information criterion (AIC); the model with the lowest AIC indicates a better statistical fit [19].

We investigated interactions with age, sex, history of HIV testing and apostolic religion. We explored age and sex since both young people and men have suboptimal uptake of testing in Zimbabwe and elsewhere in Africa [3,20]. We explored religion because the largest religious group in Zimbabwe, the Apostolic sect [21], preaches faith cure and discourages the uptake of health services [22]. The above characteristics were interacted with selected attribute levels based on our literature review. All main effects (estimated on the full sample) and interaction effects (estimated by subgroups) were included simultaneously in all models.

A manual decision support system (DSS) using the nested logit model estimates was used to simulate LCT under varying service characteristics [19]. Simulation was not done for the HIVST distribution DCE because we did not have an opt-out alternative to capture a choice not to test. Simulated scenarios compared uptake of new service configurations to the base case scenario, as observed during implementation. Only attributes actionable by policy-makers were included in the simulation exercise: approaches for supporting LCT, clinic operating time, HIV treatment availability and user fees. LCT simulations were run on the full sample and by sex and HIV testing history subgroups. We tested for statistical differences using two-sample *t*-tests.

Additional information on the formative qualitative phase, the DCE design, data collection and analysis methods is presented in the Data S1.

### 2.5 | Ethical considerations

The study received ethical approval from Medical Research Council of Zimbabwe (MRCZ/A/2038) and London School of Hygiene & Tropical Medicine Ethics Committee (reference 11738). A written informed consent was obtained from all participants before study activities were conducted.

## 3 | RESULTS

Of 329 survey participants who were invited to participate in the distribution DCE, 296 (90%) were recruited. For the LCT DCE, an administrative challenge in the field caused a two-day break in DCE completion by survey participants. Out of 747 survey participants seen when DCE recruitment was open, 594 were offered participation. Of these, 496 (83.5%) participated in the DCE. There were no differences between those not offered DCE participation and those who were offered by sex and marital status: 39.9% and 38.7% ($p = 0.8$) were male, and 58.8% and 60.6% ($p = 0.7$) were married, respectively, (results not shown).

Participants' characteristics are presented in Table 2. More than half were women and a third were aged 16 to 25 years. Among distribution DCE participants, 54 (18.2%) had never tested for HIV, compared with 75 (15.1%) among LCT DCE participants. Across samples, we observed similar levels of education and marital status whereas the LCT DCE sample had higher employment rates than the distribution DCE sample (22.6% vs. 10.5%).

**Table 2. Sample Characteristics**

| Sample size | Distribution DCE 296, n (%) | Linkage DCE 496, n (%) |
|---|---|---|
| Sex | | |
| Male | 128 (43.2) | 189 (38.1) |
| Female | 168 (56.8) | 307 (61.9) |
| Mean age (standard deviation) | 37.10 (16.68) | 38.61 (18.08) |
| Age groups | | |
| 16 to 25 years old | 96 (32.4) | 148 (29.8) |
| 26 to 40 years old | 89 (30.1) | 136 (27.4) |
| >40 years old | 111 (37.5) | 211 (42.5) |
| Education level | | |
| O level incomplete | 192 (64.9) | 312 (62.9) |
| At least O level completed | 104 (35.1) | 184 (37.1) |
| Participants' religion | | |
| Apostolic | 134 (45.3) | 176 (35.5) |
| Non-apostolic | 162 (54.7) | 320 (64.5) |
| HIV testing experience | | |
| Never tested | 54 (18.2) | 75 (15.1) |
| Self-tested | 136 (45.9) | 260 (52.4) |
| Tested but never self-tested | 106 (35.8) | 161 (32.5) |
| Marital status | | |
| Married | 194 (65.5) | 297 (59.9) |
| Never married | 64 (21.6) | 113 (22.8) |
| Divorced/widowed/separated | 38 (12.8) | 86 (17.3) |
| Employment status-receive regular salary | | |
| No | 265 (89.5) | 384 (77.4) |
| Yes | 31 (10.5) | 112 (22.6) |

DCE, discrete choice experiment.

### 3.1 | Preference for distribution of kits

Table 3 reports findings from the MNL (Model 1) and RPL (Model 2), which both show similar results, providing some reassurance regarding the robustness of the analysis. Positive utilities show relative preference for the attribute level; a negative sign shows relative dislike. The AIC for the RPL model (AIC = 3260.9) is lower than the MNL model (AIC = 3488.3); therefore, we focus on the RPL model outputs.

The strongest relative preference was against paying for kits, where every $1 increase in price to users was associated with a disutility U = −2.017, $p < 0.01$. Participants strongly preferred door-to-door delivery of kits (U = 1.029, $p < 0.01$), over collection from public/mobile facilities (U = −0.970, $p < 0.01$). For pretest support, participants strongly preferred the availability of a telephone helpline (U = 0.415, $p < 0.01$) relative to face-to-face support from a distributor (U = −0.201, $p < 0.10$) or an information leaflet alone (U = −0.214, *p*: not available).

There were significant differences in preferences for the mode of distribution of HIVST kits. Batch distribution (distribution to whole households) was preferred among non-testers (U = 0.055 + 0.102 = 0.157, $p < 0.10$) and older participants (U = 0.055 + 0.004 = 0.059 per year increment, $p < 0.05$) while men (0.055 to 0.078 = −0.023, $p < 0.01$) and self-testers (U = 0.055 to 0.130 = −0.075, $p < 0.05$) valued individual kit distribution. Conventional testers slightly preferred the batch distribution method (U = 0.055 + (−1×(0.102−0.130)) = 0.083, $p < 0.10$).

The RPL model presents unobserved preference heterogeneity (variation in preferences not captured by the participants' characteristics included in the analysis) as shown by a significant standard deviation of utility coefficients (right two columns in Table 3). For example, there was significant unobserved heterogeneity across individuals in the effect of price on their choices.

### 3.2 | Preferences for LCT

The AIC shows that the NL has a better statistical fit (AIC = 8175.2) than the MNL (AIC = 8191.4 – not reported in this paper), but the RPL model (AIC = 7277.4) provided the best fit. The main and interaction effects estimated by the NL (Model 3) and RPL (Model 4) models are presented in Table 4.

There was no significant difference in preference between LCT at PSI outreach or the public clinic (i.e. the constant was not statistically significant between the two locations); what mattered were the specific service characteristics.

For both clinic types, lack of immediate antiretroviral treatment (ART) (public clinic: U = −0.614, $p < 0.01$; PSI outreach: U = −1.052, $p < 0.01$) was the biggest driver of choice. Consistent with the distribution DCE, participants were strongly averse to paying for services (public clinic: U = −0.380, $p < 0.05$; PSI outreach: U = −0.761, $p < 0.01$; per $ 1increase). The attribute of third relative importance for both locations

**Table 3. Models 1 and 2 estimation of preferences for HIVST distribution among the general population and by sex, age, HIV testing history and religion**

| | Model 1 (multinomial logit) | | Model 2 (random parameter logit) | | | |
|---|---|---|---|---|---|---|
| **Attribute (base case)[a]** | **β** | **SE** | **β** | **SE** | **SD** | **SE** |
| **Main effects** | | | **Random parameters** | | | |
| Distribution method (Only directly to individuals) | | | | | | |
| Deliver tests for whole household | 0.008 | 0.051 | 0.055 | 0.115 | 0.632*** | 0.054 |
| Kit price (per $1 increase) | −1.273*** | 0.272 | −2.017*** | 0.400 | 1.577*** | 0.214 |
| Pretest support (Information leaflet) | | | | | | |
| Telephone helpline | 0.290*** | 0.108 | 0.415*** | 0.152 | 0.048 | 0.158 |
| Face-to-face from distributor | −0.131 | 0.088 | −0.201* | 0.120 | 0.069 | 0.202 |
| Time of operation (Monday to Friday 8 am to 4 pm) | | | | | | |
| Monday to Friday 8 am to 4 pm + evenings and weekends | −0.008 | 0.040 | −0.032 | 0.059 | 0.036 | 0.130 |
| Distributor age (below 30 years old) | | | | | | |
| Above 30 years old | 0.008 | 0.020 | −0.016 | 0.036 | 0.258*** | 0.063 |
| Distributor residence (from the same village) | | | | | | |
| From another village | −0.116*** | 0.031 | −0.145*** | 0.052 | 0.462*** | 0.061 |
| Location kit collection (collection from local clinic) | | | | | | |
| Distributed door-to-door | 0.698*** | 0.219 | 1.029*** | 0.335 | 0.007 | 0.179 |
| Collection from mobile testing outreach sites | −0.648*** | 0.199 | −0.970*** | 0.309 | 0.404*** | 0.100 |
| **Interaction effects** | | | **Non-random parameters** | | | |
| Household distribution×Male | −0.057*** | 0.021 | −0.078*** | 0.047 | | |
| Household distribution×Age | 0.003** | 0.001 | 0.004** | 0.003 | | |
| Household distribution×Non-tester | 0.066* | 0.037 | 0.102* | 0.082 | | |
| Household distribution×Self-tester | −0.080*** | 0.028 | −0.130** | 0.064 | | |
| **Model fit statistics** | | | | | | |
| Number of participants | 296 | | 296 | | | |
| Number of observations | 2641 | | 2641 | | | |
| AIC | 3488.3 | | 3260.9 | | | |
| AIC/N | 1.321 | | 1.235 | | | |

AIC, Akaike information criterion; HIVST, HIV self-testing; SD, standard deviation; SE, standard error;.
[a]Since effects coding was applied, within each attribute, utility coefficients add up to zero, that is for two-level attributes, the coefficient of the omitted level is the same magnitude with opposite sign. *10%, **5%, ***1% level of significance with *p* value.

was proximity to the health facility. Regarding post-test support, call reminders were strongly preferred for PSI outreach. Although post-test support options were generally not significant for the public clinic, no support at all was disliked at both locations (local clinic: U = −0.337; PSI outreach: U = −0.826; *p*: not available).

While the preference above informs drivers of where people choose to go for LCT, the opt-out provides insights into loss-to-follow-up. While most people showed a strong preference to link following a positive HIVST, the opt-out was more often chosen among those who had never tested for HIV (U = −3.722 + 0.717 = −3.005, $p < 0.01$) or identified as apostolic (U = −3.722 + 0.144 = −3.628, $p < 0.05$). Those who had self-tested chose the opt-out option less often (U = −3.722 to 0.243 = −3.965, $p < 0.05$), that is, they were more likely to link for confirmatory testing at either location. This effect was stronger for those who had previously had a conventional HIV test (U = −3.722 + (−1× (0.717−0.243) = −4.196, $p < 0.05$). Non-testers had significantly different preferences in favour of receiving SMS reminders to support uptake of linkage at a public clinic (U = 0.065 + 0.295 = 0.360, $p < 0.01$) relative to those who have previously tested.

## 3.3 | Results of simulated linkage programmes compared to the base case scenario

Table 5 presents a summary of the simulation exercise; Appendices S5 and S6 show full model output and simulated uptake at public clinic and PSI outreach, and Figure 1 is a

**Table 4. Models 3 and 4 estimation of preferences for LCT among the general population and by sex, age, HIV testing history and religion**

| | Model 3 (nested logit) | | Model 4 (random parameter logit) | | | |
|---|---|---|---|---|---|---|
| **Attribute (base case)[a]** | **β** | **SE** | **β** | **SE** | **SD** | **SE** |
| **Main effects** | | | **Random parameters** | | | |
| **Public clinic** | | | | | | |
| Proximity of clinic (per hour walking from home) | −0.222*** | 0.043 | −0.348*** | 0.075 | 0.644*** | 0.077 |
| Busyness of clinic (few people) | | | | | | |
| Many people | −0.062 | 0.047 | −0.017 | 0.083 | 0.101 | 0.193 |
| Opening/operating hours (open weekdays 8 am to 5 pm) | | | | | | |
| Open weekdays and weekends 8 am to 5 pm | 0.065 | 0.046 | 0.091 | 0.082 | 0.285** | 0.122 |
| Treatment available immediately (yes) | | | | | | |
| No | −0.565*** | 0.060 | −0.614*** | 0.093 | 0.513*** | 0.162 |
| User fee (per $1 increase) | −0.361*** | 0.075 | −0.380** | 0.166 | 1.015*** | 0.078 |
| Post-test support (none) | | | | | | |
| SMS reminder | 0.037 | 0.058 | 0.065 | 0.094 | 0.213 | 0.252 |
| Call reminder | 0.110* | 0.060 | 0.129 | 0.097 | 0.415*** | 0.151 |
| In person follow-up | 0.112** | 0.055 | 0.143 | 0.090 | 0.336* | 0.178 |
| **PSI outreach** | | | | | | |
| Proximity of clinic (per hour walking from home) | −0.301*** | 0.071 | −0.328*** | 0.081 | 0.735*** | 0.077 |
| Busyness of clinic (few people) | | | | | | |
| Many people | −0.188*** | 0.069 | −0.347*** | 0.091 | 0.708*** | 0.097 |
| Opening/operating hours (open weekdays 8 am to 5 pm) | | | | | | |
| Open weekdays and weekends 8 am to 5 pm | 0.000 | 0.069 | −0.034 | 0.086 | 0.254 | 0.187 |
| Treatment available immediately (yes) | | | | | | |
| No | −0.614*** | 0.070 | −1.052*** | 0.120 | 1.664*** | 0.131 |
| User fee (per $1 increase) | −0.454*** | 0.114 | −0.761*** | 0.185 | 1.094*** | 0.081 |
| Post-test support (none) | | | | | | |
| SMS reminder | 0.054 | 0.084 | 0.054 | 0.097 | 0.413** | 0.189 |
| Call reminder | 0.561*** | 0.172 | 0.654*** | 0.185 | 0.209 | 0.177 |
| In person follow-up | −0.031 | 0.082 | 0.118 | 0.095 | 0.214 | 0.281 |
| Time between kit distribution and PSI visit (within one week) | | | | | | |
| From two to three weeks | −0.084 | 0.057 | −0.015 | 0.065 | 0.352*** | 0.098 |
| Constant (PSI outreach relative to public clinic) | −0.218 | 0.188 | 0.194 | 0.155 | | |
| | | | **Non-random parameters** | | | |
| Neither (not link to care, opt-out) | −3.479*** | 0.256 | −3.722*** | 0.237 | | |
| **Interaction effects** | | | | | | |
| Public clinic | | | | | | |
| SMS reminder×Non-tester | 0.152** | 0.063 | 0.295*** | 0.103 | | |
| Neither (not link to care, opt-out) | | | | | | |
| Neither×Non-tester | 0.655*** | 0.104 | 0.717*** | 0.134 | | |
| Neither×Self-tester | −0.239** | 0.100 | −0.243** | 0.114 | | |
| Neither×Apostolic | 0.145** | 0.070 | 0.144** | 0.090 | | |

**Table 4.** (*Continued*)

| **Model fit statistics** | | |
|---|---|---|
| Number of participants | 496 | 496 |
| Number of observations | 5940 | 5940 |
| AIC | 8175.2 | 7277.4 |
| AIC/N | 1.376 | 1.225 |
| IV parameter (nested logit) | 0.569*** | 0.071 |

AIC, Akaike information criterion; SD, standard deviation; SE, standard error.
[a]Since effects coding was applied, within each attribute, utility coefficients add up to zero, that is for two-level attributes, the coefficient of the omitted level is the same magnitude with opposite sign. *10%, **5%, ***1% level of significance with *p* value.

graphical illustration of results of the simulation. We found that the availability of ART had the most significant effect on LCT. Shortages of ART at public clinics (scenario 5) would lead to 24.3% of respondents no longer linking. Similarly, the availability of ART at outreach facilities (scenario 6) would result in improved LCT (+3.7%) with a notable shift from public sector clinic (−6.3%) to PSI outreach (+10.0%) (Appendix S6). Introducing user fees would decrease LCT, with user fees of $1 associated with a 15.8% reduction in LCT. Analysis by sex and HIV testing history did not reveal significant differences between these sub-groups.

## 4 | DISCUSSION

We found that individuals from two rural Zimbabwe districts prefer HIVST kits to be delivered door-to-door, free of charge and by locally based distributors. Males, young people and individuals who had already self-tested preferred individual kit distribution rather than have kits delivered to whole households. The availability of ART was important for linkage to confirmatory testing: immediate ART initiation was most preferred while simulations showed that unstable supplies at public clinics would reduce LCT by 24.3% and introducing ART at PSI outreach would decongest public clinics as 6.3% of testers would shift to PSI outreach. People also strongly disliked payment for LCT and preferred close proximity of facilities providing confirmatory testing. Importantly, participants would rather link to either public clinic or PSI outreach than not link. Groups that were resistant to testing were also resistant to LCT. To our knowledge, this is the first paper that presents preferences related to the full HIV self-testing cascade among participants previously exposed to community-based HIVST.

When comparing our results with findings from other DCEs, it is important to note that differences in context typically result in exploration of different attributes. The importance of user costs is apparent: they were universally reported in three papers: one by our group reporting preference for HIVST distribution among young people in Malawi, Zambia and Zimbabwe [8], one investigating preferences for HIV testing services in Zambia [7] and the last investigating preferences for LCT following HIVST in Zambia and Malawi [9]. All three reported a strong dispreference for paying for test kits or services. The DCE among young people had other similar findings

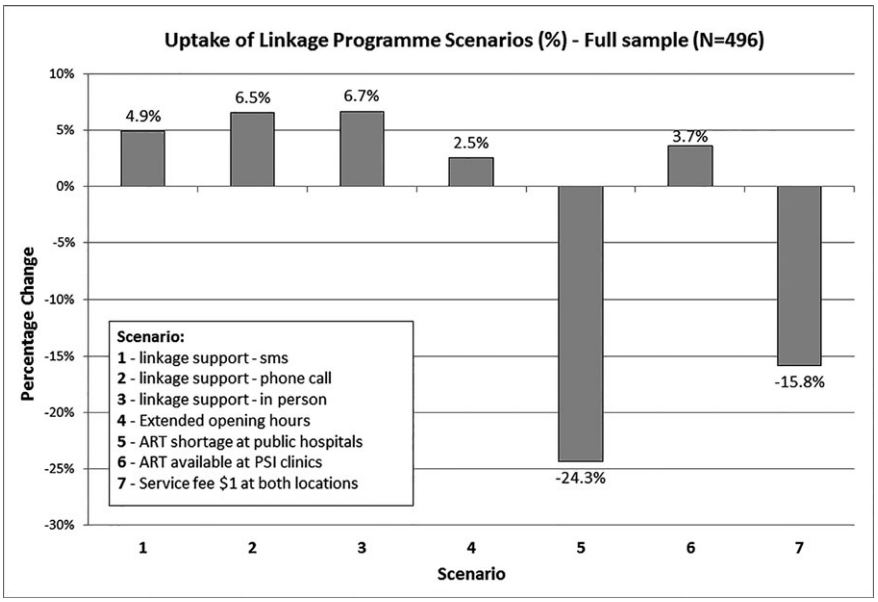


**Figure 1. Uptake of linkage programme scenarios (%) – full sample (N = 496)**

**Table 5. Change in uptake of simulated linkage programmes compared to base case for the full sample, by sex and HIV testing history (%)**

| Scenario | Scenario description | Full sample (n = 496), % | Female (n = 307), % | Male (n = 189), % | *t*-test by Sex | Testers (n = 421), % | Non-testers (n = 75), % | *t*-test by Testing history |
|---|---|---|---|---|---|---|---|---|
| 1 | Linkage support: SMS at public clinic and PSI outreach | 4.9 | 6.8 | 1.8 | - | 3.5 | 12.4 | - |
| 2 | Linkage support: call at public clinic and PSI outreach | 6.5 | 7.4 | 5.4 | - | 6.9 | 7.8 | - |
| 3 | Linkage support: in person at public clinic and PSI outreach | 6.7 | 7.9 | 4.6 | - | 6.3 | 10.0 | - |
| 4 | Extended hours at public clinic and PSI outreach | 2.5 | 1.6 | 4.0 | - | 2.9 | 0.4 | - |
| 5 | ART shortage at public clinic | −24.3[a] | −25.0[a] | −23.6[a] | NS | −25.2[a] | −22.0[a] | NS |
| 6 | ART available at PSI outreach | 3.7[a] | 3.9[a] | 3.1[a] | NS | 3.7[a] | 4.0[a] | NS |
| 7 | Service fee: $1 at public clinic and PSI outreach | −15.8[a] | −17.4[a] | −13.4[a] | NS | −16.0[a] | −15.7[a] | NS |

ART, antiretroviral therapy; NS, *t*-test not statistically significant. [a]Significant at $\alpha = 5\%$.

that we report here, including preference for home delivery of kits by lay distributors (of note, the young people aged 16 to 25 in the distribution DCE contributed to that analysis). In contrast to our findings on preference for door-to-door distribution, the study that was conducted in Zambia found no significant preferences for location of HIVST distribution, although they notably did not offer participants the option for door-to-door delivery of kits [7]. Important attributes that we report here that were not explored in other studies include immediate availability of ART and type of health facility for the LCT DCE.

Our findings show preference for the existing community-based HIVST distribution model, with one exception: some participants wanted kits distributed to whole households (i.e. family-based approaches). Our findings aligned with previous research; participants believed distribution to whole household would maximize testing uptake, including individuals who may not be at home during working hours [8]. Also, they felt it would encourage testing among reluctant testers such as men [8]. However, it was the men and young people who were opposed to household distribution of test kits, as it could potentially undermine their autonomy to decide whether they would self-test [8]. Coerced self-testing by partners has been reported by 3% of self-testers in Malawi, although none subsequently regretted testing [8]. Incorporating distribution of kits to whole households would require concerted efforts for mitigating the potential risk of coercive testing. Men and young people have the lowest uptake of HIV testing; hence, special consideration should be given to their needs, including alternative targeted models, such as provision at workplaces, Internet and VMMC programmes.

The LCT DCE showed the importance of both immediate ART initiation and continued reliable drug stocks. This has implications for national policies relating to outreach and home-based ART provision, which has been found to improve linkage to ART [23], and underscores the importance of ensuring reliable drug supplies. Individuals who had not previously tested preferred support through SMS reminders. This is a relatively low-cost intervention that can be implemented to support LCT in this group, and is likely to be feasible given that Zimbabweans have good access to mobile phones [24]. Notably, apostolic participants and those who had never tested for HIV were hesitant to link even if they did test, suggesting that "resistant testers" may also be "resistant linkers" for whom known status may not be enough to ensure engagement with the rest of the care cascade. In the overall survey in which the DCEs were nested, we found that 12% of participants had never tested for HIV. Interventions among this group may need to focus on shifting attitudes towards health seeking in general.

Before scale-up of both HIVST distribution and linkage models, it is important to consider their cost and sustainability. Although the community-based models have high impact in terms of testing groups that would not otherwise test, such as men and young people, we found that they cost more than standard provider-delivered testing [25]. Low-cost models of ensuring door-to-door HIVST distribution may be important: our group is presently evaluating the feasibility and cost of community-led HIVST distribution approaches.

The strengths of this study include use of simulations of how LCT could be affected by changes to programme attributes. We also present preferences for the full HIVST cascade. Although DCE preferences are hypothetical, our study was conducted in communities previously exposed to HIVST, so that participant preferences were shaped by their actual experiences. Using the simulation-based RPL to account for unobserved heterogeneity improves the model fit. However, its complex structure is not well-suited for use in simple excel-based decision support systems, where the utilities are manually entered to predict uptake. We rather used the output from the simpler NL model to simulate the impact of variations in LCT services. Table 3 shows that although the RPL has a better statistical fit, the NL is a good approximation. Nevertheless, there are some small

differences in relative utilities between the two estimators which lead to minor variations observed between the utility ranking and the simulation exercise. Another limitation is the possibility that people's preferences were shaped by current practice and experiences of self-testing and linkage to prevention and treatment services: we did not look at how preferences varied by linkage status. Also, LCT DCE participants included those who had tested HIV negative and those who had never tested; their views could be different from those with reactive HIVST results. For the LCT DCE, labels can sometimes take away attention from other service characteristics, nevertheless, many attributes had statistically significant findings while the location was not, suggesting that choices made by participants considered the full scenario. Notwithstanding this, we did not have information on people's familiarity or use of post-test services, which has potential to influence the choice of location of LCT services. Data were collected from only two districts, which may not be generalizable, although we do not expect that other Zimbabwe rural communities will be significantly different. Lastly, as is common with hypothetical choices, there may be a higher report of willingness to test and link.

## 5 | CONCLUSIONS

We found practical insights into how HIVST could be optimized, including the needs of specific population groups such as non-testers and those following the apostolic religion. Individuals who have resisted testing may also be resistant to linkage to confirmatory testing. Importantly, efficient provision of ART is central to engagement in post-test services. This study contributes clients' perspectives on how best to scale up HIVST services.

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### COMPETING INTERESTS

No competing interests are declared.

### AUTHORS' CONTRIBUTIONS

ELS, FMC, FTP, MDE, ELC, MT, MT and KH formulated the research study and design. NR, MT, CM and CW collected the data and informed the design of data collection methods. MDE, GM, FTP and PI analysed the data or contributed to the analysis. ELS and MDE wrote the first draft of the manuscript. ELC, FMC, CJ, JJO, KH, JRH and FTP substantially provided intellectual input to the manuscript.

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### REFERENCES

1. UNAIDS. 90-90-90: An ambitious treatment target to help end the AIDS epidemic. UNAIDS; 2014.
2. Joint United Nations Programme on HIV/AIDS (UNAIDS). Ending AIDS: progress towards the 90-90-90 targets. Geneva, Switzerland: UNAIDS; 2017.
3. Zimbabwe Ministry of Health and Child Care. Zimbabwe population-based HIV impact assessment (ZIMPHIA). Harare, Zimbabwe: MOHCC; 2016.
4. World Health Organization. Consolidated guidelines on HIV testing services 2015. Geneva, Switzerland: WHO; 2015.
5. Johnson CC, Kennedy C, Fonner V, Siegfried N, Figueroa C, Dalal S, et al. Examining the effects of HIV self-testing compared to standard HIV testing services: a systematic review and meta-analysis. J Int AIDS Soc. 2017;20 (1):21594. doi: 10.7448/IAS.20.1.21594
6. World health Organization. Guidelines on HIV self-testing and partner notification: supplement to consolidated guidelines on HIV testing services. Geneva: Switzerland; 2016.
7. Zanolini A, Chipungu J, Vinikoor M, Bosomprah S, Mafwenko M, Holmes C, et al. HIV self-testing in Lusaka Province, Zambia: acceptability, comprehension of testing instructions, and individual preferences for self-test kit distribution in a population-based sample of adolescents and adults. AIDS Res Hum Retroviruses. 2018;34:254–60.
8. Indravudh PP, Sibanda EL, d'Elbee M, Kumwenda MK, Ringwald B, Maringwa G, et al. 'I will choose when to test, where I want to test': investigating young people's preferences for HIV self-testing in Malawi and Zimbabwe. AIDS. 2017;31 Suppl 3:S203–12.
9. d'Elbee M, Indravudh PP, Mwenge L, Kumwenda MM, Simwinga M, Choko AT, et al. Preferences for linkage to HIV care services following a reactive self-test: discrete choice experiments in Malawi and Zambia. AIDS. 2018;32 (14):2043–9.
10. Mangham LJ, Hanson K, McPake B. How to do (or not to do)... Designing a discrete choice experiment for application in a low-income country. Health Policy Plan. 2009;24(2):151–8.
11. STAR Project. HIV Self-testing Africa Project. London, United Kingdom; 2017 [cited 2018 Mar 19]. Available from: http://hivstar.lshtm.ac.uk/
12. Zimbabwe Ministry of Health and Child Care. Zimbabwe National Guidelines on HIV Testing and Counselling. Harare, Zimbabwe: Ministry of Health and Child Care; 2014.
13. Green J, Browne J, editors. Principles of social research. London, United Kingdom: Oxford University Press; 2005.
14. ChoiceMetrics. NGENE software. 2016 [cited 2018 Apr 20]. Available from: http://www.choice-metrics.com/
15. de Bekker-Grob EW, Donkers B, Jonker MF, Stolk EA. Sample size requirements for discrete-choice experiments in healthcare: a practical guide. Patient. 2015;8(5):373–84.
16. Orme B. Getting started with conjoint analysis: strategies for product design and pricing research. Madison, WI, USA: Research Publishers LLC; 2010.
17. Econometric software Inc. NLOGIT software. 2016 [cited 2018 Apr 20] Available from: http://www.limdep.com/products/nlogit/
18. Bech M, Gyrd-Hansen D. Effects coding in discrete choice experiments. Health Econ. 2005;14(10):1079–83.
19. Hensher D, Rose J, Greene W. Applied choice analysis. 2nd ed. Cambridge, United Kingdom: Cambridge University Press; 2015.
20. UNAIDS. Global AIDS update 2017. Geneva, Switzerland: UNAIDS; 2017.
21. Zimbabwe National Statistics Agency (ZIMSTAT), ICF International. Zimbabwe Demographic and Health Survey 2015: Key Indicators. Rockville, Maryland: Zimbabwe National Statistics Agency (ZIMSTAT), ICF International; 2016.
22. Ha W, Salama P, Gwavuya S, Kanjala C. Is religion the forgotten variable in maternal and child health? Evidence from Zimbabwe. Soc Sci Med. 1982;2014 (118):80–8.
23. 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.
24. Ministry of Economic Planning and Investment Promotion, UNDP Resident Rrepresentative. Zimbabwe 2012 MDG Progress Report. Harare, Zimbabwe: MEPIP; 2012.
25. Cambiano V, Johnson C, Hatzold K, Terris-Prestholt F, Maheswaran H, et al. The impact and cost-effectiveness of community-based HIV self-testing in sub-Saharan Africa: a health economics and modelling analysis. J Int AIDS Soc. 2019;22(S1):e25243.

## SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

**Data S1.** Design of discrete choice experiments for preferences of HIVST distribution and linkage to confirmatory testing in Zimbabwe.

**Appendix S1.** Focus Group Discussion (FGD) guides – HIVST distribution and LCT DCE.

**Appendix S2.** Attributes, levels and pictorial illustrations for the HIVST distribution and LCT DCE.

**Appendix S3a.** Distribution DCE questionnaire – Sample of one choice situation (image file).

**Appendix S3b.** LCT DCE questionnaire – Sample of one choice situation (image file).

**Appendix S4.** Selected participants' characteristics – Spearman correlation matrices at significance level 5% (*).

**Appendix S5.** Nested logit models on the LCT DCE for the simulations among the full sample, men, women, testers and non-testers.

**Appendix S6.** Change in uptake of simulated linkage programmes compared to base case (%) differentiated by testing facility, sex and HIV testing history.

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RESEARCH ARTICLE

# HIV self-testing: breaking the barriers to uptake of testing among men and adolescents in sub-Saharan Africa, experiences from STAR demonstration projects in Malawi, Zambia and Zimbabwe

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## Abstract

**Introduction:** Social, structural and systems barriers inhibit uptake of HIV testing. HIV self-testing (HIVST) has shown promising uptake by otherwise underserved priority groups including men, young people and first-time testers. Here, we use characteristics of HIVST kit recipients to investigate delivery to these priority groups during HIVST scale-up in three African countries.

**Methods:** Kit distributors collected individual-level age, sex and testing history from all clients. These data were aggregated and analysed by country (Malawi, Zambia and Zimbabwe) for five distribution models: local community-based distributor (CBD: door-to-door, street and local venues), workplace distribution (WD), integration into HIV testing services (IHTS), or public health facilities (IPHF) and during demand creation for voluntary male medical circumcision (VMMC). Used kits were collected and re-read from CBD and IHTS recipients.

**Results:** Between May 2015 and July 2017, 628,705 HIVST kits were distributed in Malawi (172,830), Zambia (190,787) and Zimbabwe (265,091). Community-based models, the first to be established, accounted for 519,658 (82.7%) of kits distributed, with 275,419 (53.0%) used kits returned. Subsequent model diversification delivered 54,453 (8.7%) test-kits through IHTS, 23,561 (3.7%) through VMMC, 21,183 (3.4%) through IPHF and 9850 (1.7%) through WD. Men took 294,508 (48.2%) kits, and 263,073 (43.1%) went to young people (16 to 24 years). A higher proportion of male self-testers (65,577; 22.3%) were first-time testers than women (54,096; 17.1%) with this apparent in Zimbabwe (16.2% vs. 11.4%), Zambia (25.4% vs. 17.7%) and Malawi (27.9% vs. 25.9%). The highest proportions of first-time testers were in young (16 to 24 years) and older (>50 years) men (country-ranges: 18.7% to 35.9% and 13.8% to 26.8% respectively). Most IHTS clients opted for HIVST in preference to standard HTS in each of 12 delivery sites, with those selecting HIVST having lower HIV prevalence, potentially due to self-selection.

**Conclusions:** HIVST delivered at scale using several different models reached a high proportion of men, young people and first-time testers in Malawi, Zambia and Zimbabwe, some of whom may not have tested otherwise. As men and young people have limited uptake under standard facility-and community-based HIV testing, innovative male- and youth-sensitive approaches like HIVST may be essential to reaching UNAIDS fast-track targets for 2020.

**Keywords:** HIV self-testing; HIV testing; men; adolescents; stigma; Malawi; Zambia; Zimbabwe

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## 1 | INTRODUCTION

In 2016, 36.7 million people were living with HIV (PLHIV), with 1.8 million new HIV infections and one million HIV/AIDS-related deaths [1]. Despite substantial progress toward the 2020 "90/90/90 targets" current estimates suggest we are already off-track [2], with only an estimated 75% [55% to 92%] of PLHIV currently aware of their status [3]. This gap compromises the whole cascade, and also threatens global HIV prevention targets. By 2020, three million high-risk people should be accessing pre-exposure prophylaxis and 25 million men provided with

voluntary medical male circumcision (VMMC) in 14 African countries [4].

Low HIV testing, knowledge of status, and suboptimal treatment and prevention coverage among men and young people (15 to 24 years) in sub-Saharan Africa are key gaps in the HIV response. Recent population-based HIV impact assessments (PHIA) in Zimbabwe, Malawi and Zambia, showed that men with HIV were less likely to know their status than HIV-positive women [5-7]. Less than half of youth aged 15 to 24 years with HIV knew their status, which was substantially lower than coverage in older age groups [5-7]. Demographic and health surveys (DHS), conducted in 30 sub-Saharan African countries during 2011 to 2016, showed lower testing coverage among men compared to women for all age groups except 45- to 49-year olds [3].

Low coverage (defined as the proportion of population eligible for an intervention that has received it) of HIV testing and treatment among men in Africa is often due to poor utilization of public sector health facilities, reflecting both social and structural health systems barriers [8,9]. Prevailing social norms around masculinity that emphasize toughness, self-reliance and sexual success lead to an avoidance of health services, among other consequences [10-13]. For HIV, this is compounded by anticipated loss of social standing and sexual desirability if diagnosed HIV-positive, increasing fear of stigma and promoting a mindset whereby testing when "still healthy" is considered undesirable [10,13]. Greater formal and informal employment among men compared to women, can also hinder access due to job insecurity and high opportunity and indirect costs [13]. Likewise, young people have well-described age-specific barriers that make use of existing facility-based HIV testing services especially difficult [14]. Recognizing and responding with innovative male- and youth-sensitive approaches is likely to be an essential component to reaching UNAIDS fast-track targets for 2020.

HIV self-testing (HIVST) appeals to the very people left behind by existing HIV testing services (HTS), including young people (15 to 24 years), adult men, key populations (men who have sex with men, people who inject drugs, people in prisons and other closed settings, sex workers and transgender people) and partners of people living with HIV (PLHIV). HIVST provides an empowering opportunity for individuals to test when, where and with whom they want to [14]. The ability to test in private and having more control over the testing process have been cited as key motivators to self-test particularly among men and young people [13,14]. When followed by timely uptake of prevention and treatment services, HIVST can be a key element in the push towards ending AIDS [15,16]. While previous studies have reported on preferences and uptake of HIVST, there has yet to be a multi-country investigation into the impact of alternative distribution and linkage strategies to optimize testing, VMMC and treatment after HIVST among men. Here, we present quantitative programme data from different HIVST distribution models.

## 2 | METHODS

Distribution models are summarized in Table 1, with five main approaches described below. OraQuick HIV Self-Test (OraSure Technologies LLC, Bethlehem, PA, USA) kits were distributed in all countries. Data reported here relate to the first 15 months of distribution (May 2016 to July 2017).

Social harms monitoring systems were part of all distribution models. No suicides were identified and reports of other serious harms (potential life-threatening/life-changing) were rare (1 event per 10,000 HIVST kits distributed), as discussed in detail for Malawi in this JAIS Special Issue [17].

### 2.1 | Model 1: community-based HIVST distribution

Community-based distributors (CBDs) provided HIVST kits across 53 districts in Malawi, Zambia and Zimbabwe. Models are described in detail elsewhere [18-20]. In brief, CBDs needed to have completed secondary school education and be resident in the distribution community. CDB recruitment used participatory approaches with candidates nominated following community sensitization meetings. CBDs completed a two-day training provided by Population Services International (PSI) including basic facts about HIV transmission and treatment, antibody-based diagnosis, discordancy and the principles of consent and confidentiality, as well as familiarization with the kits and how to demonstrate use to recipients, and data capture tools. All trainees had to undergo competency testing at the end of the training course when training skills were assessed. CBDs promoted and offered free HIVST kits for use alone or with CBD support. The same methods were used by CBDs to offer HIVST kits in households and social venues such as market places, busy streets, bars and beer halls. Individuals could also collect kits from the CBDs home at any time, if preferred.

CBDs provided all clients with brief health information about HIV, information on the test, and an in-person or video-clip demonstration-of-use and instructional materials optimized for local use demonstration to supplement manufacturer's instructions-for-use that were available in local languages.

Clients could choose to self-test alone, or with the CBD, and were asked to return their used kit and results in a sealed envelope, together with a short, self-administered questionnaire (SAQ) in collection boxes at community locations. Illiterate and semi-literate participants were supported by the CBD who was reading out the questions and answers from the SAQ with participants then left to complete the check-box answers in private.

Additional post-test guidance was available from CBDs on demand. All self-testers received self-referral cards with several locally adapted options to facilitate results-based linkage into HIV care and prevention services. CBDs collected information on social harms related to HIVST and referred clients for additional management as needed. A toll-free hotline was available to answer questions about the testing process, results and referral options.

### 2.2 | Model 2: HIVST integration into PSI-led HTS facilities and mobile HTS outreach

Integrated HIVST was piloted from June 2016 and scaled-up from January 2017 as an alternative option to provider-delivered testing for clients attending existing PSI-led HTS clinics and 11 mobile outreach sites in Zimbabwe. Outreach sites included "hot spots" at bus and truck stops, mining areas and urban shopping malls, and other informal workplaces. The aim

**Table 1. Summary of models of distribution**

| Model | Target population | Distribution model description | Rationale |
|---|---|---|---|
| 1. Community based (mainly door-to-door) | Rural populations: esp. adult men, young people (16 to 24 years) unable to access conventional testing services | HIVST kits offered at household by CBD for clients to test on own or with assistance.<br>Referral facilitation by CBD for confirmatory testing, ART, and prevention services | Increases testing in populations who would otherwise not seek testing services, rapidly and drastically increases testing coverage |
| 2. HIVST integrated into Mobile Services or HIVST fixed sites | High risk adults, adult men (>25 years), adolescents 16 to 24, esp. girls & young women | Distribution at community hotspots e.g. shopping centres, taxi ranks, urban and rural hot-spots (bus or truck stops, growth points).<br>Confirmatory testing and in some cases ART on site | Test-for- triage:<br>fast track pre-screening, triaging out those who self-test HIV negative unless confirmatory testing desired.<br>Providers shift in attention:<br>to those who require more attention and increasing: – index testing and assisted partner notification, confirmative testing of HIV positives, initiation of ART |
| | | People can test themselves in a cubicle at the distribution point or HTS Clinic (with assistance available) or take kit home | Increase in demand for HTS, if mobile services or fixed HTS clinic services are promoted as outlets for HIVST kits |
| | Sexual partners of HIV+ index diagnosed at HTS (secondary distribution) | HIVST kit offered to HIV+ index to take to sexual partner(s). Follow up with index or partner for confirmative testing | Increases likelihood of sexual partner to take up HIV testing. Based on evidence high proportion of sexual partners of positive indexes are testing positive |
| 3. HIVST offered at male dominated workplaces | High risk adults, adult men (>20 years) | HIVST kits are offered to employees at male dominated workplaces after buy-in and agreement has been obtained from the employer. Employees can choose to perform HIVST in a private space provided at the workplace where assistance is available or take the HIVST kit home | Increases testing in populations who would otherwise not seek testing services, rapidly and drastically increases testing coverage |
| 4. Integrated with public sector facility | Patients accessing health care facilities in urban and rural areas | Facility-based counsellors and Health care workers are directly promoting HIVST at entry points of the health delivery system, e.g. outpatients, in-patients | Test-for-triage approach and HTS clinic shift in attention (as above) Increases numbers tested, and coverage of more targeted provider-initiated testing to maximize HIV diagnoses, ART initiation and prevention service uptake |
| | Sexual partners of HIV+ index diagnosed at HTS (secondary distribution) | HIVST kit offered to HIV+ index to take to sexual partner(s). Follow-up with index or partner for confirmative testing | Increases likelihood of sexual partner to take up HIV testing. Based on evidence high proportion of sexual partners of positive indexes are testing positive |
| | Male partners of pregnant women accessing public sector maternity services (secondary distribution) | HIVST kit is offered to all pregnant women regardless of HIV status to take to male partner | Increases the opportunity of male sexual partners of pregnant women to access HIV testing services, and to be linked to care, treatment and prevention, dependant of status |
| 5. Integration with VMMC Mobilization | Adult males, 20 and above, who are mobilized for VMMC services | HIVST is offered to adult males, who are mobilized for VMMC, to use at home before accessing VMMC services | Fear of a positive test result and fear of testing prevents adult males from taking up VMMC services<br>Offering HIVST can reduce this barrier and increase motivation to take up VMMC |

was to expand choice and support efficiency gains by integrating HIVST with conventional HTS. An additional four months of detailed distribution site data are included here (through November 2017).

After registration, HTS clients were offered a kit that they could use for HIVST on-site or at home. Clients opting for HIVST received a brief demonstration either by video or by a trained provider. Clients opting out of HIVST received conventional HTS. Private cubicles or tents, with offer of counsellor assistance, were provided to those self-testing on site. On-site confirmative testing was available for those reporting a reactive (positive) self-test result. If confirmed, PLHIV were referred for ART according to national guidelines, with immediate initiation if ART services were either available onsite, or through a referral form to ART services at public and private sector health care facilities.

All clients opting for HIVST received information about post-test support services and referral forms (confirmative testing and HIV treatment including ART for those with reactive results, information about prevention services for those with negative HIVST results) prior to HIVST. Men were encouraged to consider VMMC if they tested negative, and condom use was promoted. Clients who decided to self-test at home received information materials listing local prevention and treatment services, and a self-referral form suitable for either prevention or ART services, dependant on HIVST result.

HIV positive index clients diagnosed at the HTS site were offered self-test kits for secondary distribution to all their sexual partners for the purposes of index-testing [21]. Clients taking kits for secondary distribution were talked through the process of supporting their partner to use and interpret the kit correctly, how to access follow-on HIV services, and the need to maintain voluntariness [22].

Self-testers were asked to leave their used test kits with an SAQ in sealed envelopes at the site, while provider-delivered HTS clients had data captured by the counsellor. Used self-test kits were re-read by the providers on the same day, with this approach used to estimate the number and proportion of HIV-positive self-tests.

### 2.3 | Model 3: HIVST distribution at workplaces

At larger male dominated workplaces in the mining and farming industry, HIVST kits were distributed through peer-promotors or PSI HTS outreach workers, who provided pre-test information and in-person demonstrations of the self-testing process. Clients could self-test on site or at home and could take a test kit home for their partner to use, with support for secondary distribution as described above. Confirmatory testing was available on site, provided by the PSI HTS outreach team or by workplace HTS services, or through self-referral forms providing information on local private and public-sector health services. Confirmed PLHIV were referred for ART at public or private sector providers. A toll-free hotline number was provided to all clients.

### 2.4 | Model 4: HIVST distribution at public sector health facilities

Patients accessing public sector outpatient departments (OPD) or other clinical services were offered HIVST by healthcare providers, either nurses or counsellors working at OPD, before their consultation. Clients could self-test in a separate room following a brief demonstration, with the option of sharing their results during their consultation. Information on confirmatory testing, ART and HIV prevention services was provided to all patients. For those with positive self-tests, counselling, confirmatory testing and ART were available on-site through the routine facility services. HIVST-negative clients received HIV prevention messages by the nurse and healthcare provider in OPD and male clients were referred for VMMC.

### 2.5 | Model 5: HIVST integrated with VMMC promotion

VMMC was already being rolled-out in all three countries by PSI, and HIVST was integrated into mobilization strategies. VMMC mobilizers were trained to offer HIVST to all men who were interested in circumcision, but cited fear of HIV testing onsite. VMMC mobilizers, who had all received a two-day training course, as described for the CBDs, provided pre-test information and demonstration of kit use before offering a kit to each potential VMMC client. In Zambia, VMMC mobilizers also distributed HIVST kits to women.

### 2.6 | Data collection and analysis

HIVST kit distributors collected individual-level demographic and HIV testing history data from all clients, using either electronic or paper-based forms. Data from SAQs were entered into databases at country-level. Data were aggregated and presented by distribution model at PSI central level. STAR HIVST programme data from Malawi, Zambia and Zimbabwe was analysed according to age, sex, distribution model, testing history and compared between countries. We also compared characteristics of clients, including HIV result and number of HIV-positives identified, who took up the offer of HIVST with those of clients preferring provider-delivered HTS at PSI-led facilities and mobile outreach services. Given the high numbers of testing events (making standard p-values uninformative), and the intrinsic clustering nature of data from different sites, we present data descriptively without use of testing for statistical significance.

### 2.7 | Ethical considerations

All HIVST kits distributed before July 2017 were covered by country-level research protocols approved by the Ethics Committees of London School of Hygiene and Tropical Medicine, and the relevant ethics committees in Malawi, Zambia and Zimbabwe. As a public health intervention using a version of an HIVST product already approved for over-the-counter sale in USA and shown to have minimal potential for harm in Malawi, approved protocols included request for waiver of written or verbal informed consent for HIVST clients. Clients were instead informed about the investigational nature of the HIVST kit through community sensitization events, information leaflets and marking of kits as for research purposes only.

## 3 | RESULTS

A total of 628,705 HIVST kits were distributed in Malawi (172,830), Zambia (190,787) and Zimbabwe (265,091). The breakdown of distribution in each country under different models is shown in Table 2, together with the gender, age-group and numbers of first-time testers.

### 3.1 | HIVST distribution models and client characteristics

Community-based distribution by CBDs had already been established in Malawi as a model that was acceptable and could support accurate HIVST use and linkage to HIV care services with minimal social harms [23] and was the first model taken to scale in each country. The CBD model accounted for 94.5% of test kits distributed in Malawi, 82.2% in Zambia and 75.3% in Zimbabwe.

Other models were delayed by need for initial piloting, and some (notably HTS integration and VMMC demand creation) were also dependent on the scope and scale of suitable PSI programmes, which varied country-to-country. In this respect, Zimbabwe-PSI had a large HIV service provision platform from which to rapidly diversify and scale-up HIVST models based on integration into fixed and outreach teams already providing HTS, accounting for 52,254 of the 54,453 kits distributed using this model to July 2017. Similarly, in Zambia, the large pre-existing VMMC programmes supported rapid scale-up of HIV delivered through VMMC mobilizers (15,092), with Zambia also leading on integration of self-testing into public sector clinics.

Nearly half of HIVST kit recipients (294,502; 48.2%) were men (49.0% in Malawi, 50.7% in Zambia and 46.2% in Zimbabwe), and 263,973 (43.1%) were in the 16 to 24-year-old age-group (50.8% in Malawi, 48.9% in Zambia and 34.3% in Zimbabwe).

### 3.2 | Reach to first-time testers

The overall proportion of first-time testers (Tables 2 and 3) was 19.6% (119,673), varying from 26.8% in Malawi, to 21.6% in Zambia, to 13.6% in Zimbabwe (where self-testing was introduced to communities previously served by standard HTS delivered by mobile outreach teams). A higher proportion of men (overall 22.3%) than women (overall 17.1%) were first-time testers in each of the three countries.

A further breakdown of the proportion of all self-testers who were first-time testers is shown for men and women by age-group in Table 3. This shows higher proportions of first-time testers in the youngest age-group for both young men (29.4%) and women (24.4%), but with a substantial minority of clients in the older age-groups for both men (16.4% to 17.1%) and women (10.6% to 15.1%).

### 3.3 | Community-based distribution model

The CBD model was evaluated in detail for safety and population-level impact, with social harms monitoring and household surveys conducted to evaluate coverage and linkage, as reported elsewhere [17-20]. Use of distributed kits was confirmed for 275,419 (53.0%) by return of used kits, with country-level data for this variable being 53.2% (86,925) in Malawi, 58.8% in Zambia (92,247) and 48.2% in Zimbabwe (96,247).

CBD models varied substantially country-by-country [21-23], with the Zimbabwe model being based on delivery from mobile teams that supported training and brief (three to four weeks) but intensive HIVST distribution by temporarily employed distributors. CBDs in Malawi and Zambia were employed for 12 months to provide services less intensively. Recruitment and training are summarized under methods. The number and age of recruited distributors are shown in Table 4: 46.1% of CBDAs were men, with most (55.5%) being in the 30 to 49-year-old age-group. Costs per test distributed (US$7.23, US$14.58 and US$13.79 in Malawi, Zambia and Zimbabwe respectively) and evidence for likely economies of scale are detailed in an accompanying manuscript by Mangenah *et al*. in this issue [24].

### 3.4 | Integrated HTS model offering clients the choice between standard HTS and HIVST

In Malawi and Zimbabwe, HIVST was introduced at PSI HTS centres and mobile outreach, with 2199 (1.3%) of kits in Malawi, and 52,254 (19.7%) of kits in Zimbabwe to July 2018 distributed using this model (Table 2). Men made up half of HIVST clients (51.9% and 48.2% in Malawi and Zimbabwe).

Clients opting for HIVST and those preferring standard HTS clients are detailed together with the yield of positive HIV/HIVST results for 12 delivery sites in Table 5, which includes a further four months of delivery at scale (to November 2018 during which time HIVST distribution doubled under this model). Of the 119,991 individuals who accessed testing at 11 outreach and one fixed site, 101,624 (84.7%) opted for HIVST, with no difference in choice by sex. Very high proportions of individual testers: 92.4% (bus-terminus), 92.3% (HTS centre), 91.9% (workplace), 91.5% (truck stop) chose HIVST over provider-delivered standard testing (Table 5). When HTS and HIVST was offered at household level, 61.9% opted for HIVST.

Among those self-testing, 1908 (859 men and 1072 women) were newly diagnosed with HIV. Provider HTS clients had a substantially higher HIV prevalence (10.2% positive) than self-testers (1.9% positive).

### 3.5 | Other models of distribution

Other models (Table 2) included public sector facilities in Zambia (45.8% men) and Zimbabwe (29.0% men) and workplace distribution (9850 kits) in Malawi and Zimbabwe, with over 66.4% and 58.9% of HIVST kits taken by men.

A total of 23,561 tests were distributed to men reached with mobilization for VMMC in Malawi (1327), Zambia (15,092) and Zimbabwe (7142). Referral tracking data from Zimbabwe showed that 40.2% of males who had received HIVST kits prior to VMMC went on to be circumcised.

## 4 | DISCUSSION

STAR is the largest evaluation of HIVST implementation to date. With 628,705 kits distributed in Malawi, Zambia and

**Table 2. Number and percentage of HIVST kits distributed by country, distribution model, age, sex and previous testing history (first-time testing)**

| | Malawi | | Zambia | | Zimbabwe | | Total | |
|---|---|---|---|---|---|---|---|---|
| All distribution models | 172,830 | 100.0% | 190,784 | 100.0% | 265,091 | 100.0% | 628,705 | 100.0% |
| Community-based distributors | 163,300 | 94.5% | 156,806 | 82.2% | 199,552 | 75.3% | 519,658 | 82.7% |
| HTS integration (seven months) | 2,199 | 1.3% | | | 52,254 | 19.7% | 54,453 | 8.7% |
| Work place | 6,004 | 3.5% | 298 | 0.2% | 3,548 | 1.3% | 9,850 | 1.6% |
| Public sector | | | 18,588 | 9.7% | 2,595 | 1.0% | 21,183 | 3.4% |
| VMMC demand creation | 1,327 | 0.8% | 15,092 | 7.9% | 7,142 | 2.7% | 23,561 | 3.7% |
| Demographics available[a] | 172,830 | | 172,562 | | 265,091 | | 610,483 | |
| Male sex | 84,603 | 49.0% | 87,418 | 50.7% | 122,487 | 46.2% | 294,508 | 48.2% |
| Age group | | | | | | | | |
| 16 to 24 | 87,744 | 50.8% | 84,437 | 48.9% | 90,892 | 34.3% | 263,073 | 43.1% |
| 25 to 34 | 45,864 | 26.5% | 50,168 | 29.1% | 61,438 | 23.2% | 157,470 | 25.8% |
| 35 to 49 | 29,405 | 17.0% | 28,926 | 16.8% | 55,464 | 20.9% | 113,795 | 18.6% |
| 50+ | 9,817 | 5.7% | 9,031 | 5.2% | 57,298 | 21.6% | 76,146 | 12.5% |
| First time testers | 46,402 | 26.8% | 37,232 | 21.6% | 36,039 | 13.6% | 119,673 | 19.6% |
| Men | 23,585 | 27.9% | 22,180 | 25.4% | 19,812 | 16.2% | 65,577 | 22.3% |
| Women | 22,817 | 25.9% | 15,052 | 17.7% | 16,227 | 11.4% | 54,096 | 17.1% |

HIVST, HIV self-testing.
[a]Demographic data were available for all HIVST test users in Zimbabwe and Malawi. For Zambia, demographic data were available for 172,562/190,784 self-test users.

**Table 3. Number and percentage of HIVST kits distributed by sex and age for all tested and for all first-time testers**

| | All self-tested N | First-time testers N (%) |
|---|---|---|
| Men | 294,508 | 65,577 (22.3%) |
| Age group | | |
| 16 to 24 | 130,223 | 38,295 (29.4%) |
| 25 to 34 | 78,268 | 12,800 (16.4%) |
| 35 to 49 | 55,345 | 9,226 (16.7%) |
| 50+ | 30,672 | 5,256 (17.1%) |
| Women | 315,976 | 54,096 (17.1%) |
| Age group | | |
| 16 to 24 | 132,850 | 32,456 (24.4%) |
| 25 to 34 | 79,202 | 8,370 (10.6%) |
| 35 to 49 | 58,450 | 6,384 (10.9%) |
| 50-plus | 45,474 | 6,886 (15.1%) |

HIVST, HIV self-testing.

Zimbabwe within 15 months of introducing HIVST as a novel approach at community and facility-level, acceptability was high. We used five main distribution models, although community-based distribution accounted for 82.7% of kits distributed. Approximately half of all HIVST participants were men, with good male representation in all distribution models and age groups. A substantial minority of participants had never tested for HIV before, with this proportion higher for men (22.3%) than women (17.1%), and higher for young people (16 to 24 years: 26.9% first-time testers) than older age-groups. HIVST is a promising approach for reaching underserved sub-populations who have never tested before and contributing to the realization of the UNAIDS fast-track strategy.

Consistent with previous reports [15,16,22,23], all distribution models had high male participation in each country. Strategies that provide men with greater coverage of HIV testing and care are urgently needed both to address the disproportionately high testing gap and mortality from HIV in men, and also to reduce risk of onward transmission of HIV [3-7,25]. Peak HIV prevalence for men in southern Africa is now in the 40- to 49-year-old age-group [3-7], with older men among least likely to have accessed standard HIV testing services [5-7]. Older men appear relatively receptive to HIVST, however, as evidence by the data reported here as well as from implementation studies from Kenya, Lesotho and Zimbabwe [15,26-28]. For adolescent boys, HIVST can provide the first opportunity to test without fear of judgement from parents and healthcare workers [14], explaining the high uptake among this age group when HIVST was offered at community level. Thirty five percent of adolescent boys accepting self-testing were first-time testers in the STAR project in Malawi [14].

The STAR CBD distribution model was evaluated using household surveys, with uptake providing a measure of acceptability. Community-level coverage of HIVST was 42.5% of all surveyed adults in rural Malawi [29], and 50.3% in rural Zimbabwe [19]. This type of community-based HIVST distribution could then contribute to activities such as national HIV testing campaigns, targeted "catch-up" campaigns in districts with low testing coverage, and as a way of providing ongoing or periodical HIV testing access in remote communities. Costs (range US$7.23 per kit distributed in Malawi, to US$14.58 in

**Table 4. Demographic data (age, sex) of community-based distributors by country**

| | Malawi | | Zambia | | Zimbabwe[a] | | Total | |
|---|---|---|---|---|---|---|---|---|
| All | 189 | 100% | 165 | 100% | 1599 | 100% | 1953 | 100% |
| Men | 101 | 53.4% | 90 | 47.6% | 709 | 44.3% | 900 | 46.1% |
| Age group | | | | | | | | |
| 18 to 24 | 12 | 11.9% | 8 | 8.9% | 180 | 25.4% | 200 | 22.2% |
| 25 to 29 | 18 | 17.8% | 19 | 21.1% | 131 | 18.5% | 168 | 18.7% |
| 30 to 49 | 67 | 66.3% | 49 | 54.4% | 381 | 53.8% | 497 | 55.3% |
| 50-plus | 4 | 4.0% | 14 | 15.6% | 16 | 2.3% | 34 | 3.8% |
| Women | 88 | 46.6% | 75 | 45.5% | 890 | 55.7% | 1053 | 53.9% |
| Age group | | | | | | | | |
| 18 to 24 | 9 | 10.2% | 8 | 10.7% | 195 | 21.9% | 212 | 20.1% |
| 25 to 29 | 26 | 29.5% | 15 | 20.0% | 155 | 17.4% | 196 | 18.6% |
| 30 to 49 | 50 | 56.8% | 34 | 45.3% | 504 | 56.6% | 588 | 55.8% |
| 50-plus | 3 | 3.4% | 18 | 24.0% | 37 | 4.2% | 58 | 5.5% |

[a]Zimbabwe used a "campaign-style" distribution model with temporary distributors trained and employed for six weeks for distribution in their respective local community, while community-based distributors in Malawi and Zambia were employed for 12 months covering larger geographic areas of distribution.

Zambia) and affordability of the CBD model are discussed in the accompanying manuscript by Mangenah *et al.* [24], and the potential to devolve HIVST further through community-led approaches is currently under investigation within STAR. Community-led models can deliver better outcomes at or below the cost of less integrated approaches and are widely used in Africa for mass drug administration and distribution of insecticide-treated bed nets [30].

Integrating HIVST into routine HTS services and in clinical settings, where access barriers may preclude testing by everyone that requires it, also shows promise with over 80% of men and women accepting HIVST when offered as an alternative to provider-delivered HIV testing. Our data, alongside that from alternative models of integrated facility-based HIVST [31], suggest that HIVST can contribute substantially to comprehensive provider-initiated HTS in high volume and congested public sector clinics [31]. This model could be expanded to public sector healthcare facilities more widely, especially where the current testing capacity is limited or poorly implemented [31]. We also show marked preference for HIVST in all fixed and outreach HTS sites where HIVST was offered as alternative to standard HTS. Preference for HIVST was most pronounced when queuing was needed to access standard HTS, but was also apparent in home-based testing services where 61.9% of clients who tested opted for HIVST, supporting other suggestions that HIVST is generally preferred by many Africans [14,16].

Integrated HIVST offers potential efficiency gains, minimizing time commitments for clients and streamlining management for providers in part due to much lower HIV prevalence in those opting for HIVST over HTS. This suggest a pronounced "self-selection" as noted for sex workers – who mostly opted for standard HTS when entering dedicated sexual health services [32] before considering HIVST for subsequent tests, citing potential higher sensitivity of blood-based provider-delivered tests as being important to them given their high exposure. Although speculative, and needing further research to confirm this, if our data do indeed reflect self-selection with individuals at low risk for HIV more likely to opt for HIVST, then this has a number of advantages. From the perspective of service providers, this allows for task-sharing with low-risk clients, allowing counsellors to focus their time on the remaining clients with a high risk of being HIV positive, and to dedicate more time on more time-consuming testing options such as index testing and assisted partner notification.

Introducing the option of HIVST greatly increased the numbers of clients who could be served each day at rural and urban outreach services and consequently increased the number of positive cases identified per counsellor and per site at any given time [33]. A further low-cost facility-based model ("secondary distribution"), where HIVST kits can be delivered to partners by antenatal clinic attendees and newly diagnosed PLHIV [22,27] is being scaled-up under STAR in Malawi and Zimbabwe and is discussed further in the accompanying manuscript relating to social harms in this issue [17].

This study has a number of limitations. This analysis is based on programmatic data from three different countries and is based on self-reported client data, with some missing data. Data on HIVST with regards to first-time testers, motivators and barriers to HIVST may have been prone to social desirability bias. As reporting on first-time testing was based on a subset of self-test users who had returned their used tests together with the questionnaire, responses might not be representative for the entire HIVST population. For the difference in HIV prevalence in our integrated HTS model, we cannot exclude alternative explanations, including that some HTS clients were obtaining confirmation of an earlier positive test or self-test, as many clients coming in for HTS are reluctant to detail previous positive results for a variety of reasons. Finally, the results may not be generalizable to other programme contexts with less intensity of distribution or different starting attitudes and perceptions by potential HIVST users and HTS providers.

**Table 5. HIVST integration with HTS at 11 outreach and 1 fixed sites, Zimbabwe, HIVST was offered as alternative to provider delivered testing, 11 months of implementation to November 2018**

| | HIVST | | | | | Provider delivered testing | | | | | | | | | | Positivity rate | Positivity rate |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Targeting site type | Males screened negative by HIVST | Females screened negative by HIVST | Males screened positive by HIVST | Females screened positive by HIVST | Total males and females opting for HIVST | Males provider tested | Females provider tested | Total (males and females) opting for Provider testing | Proportion of total tested opting for HIVST, % | Males confirmed Positive after HIVST | Females confirmed Positive after HIVST | Males provider tested Positive Identified | Females provider Tested Positive Identified | Total positive identified | Total tested including HIVST | Including HIVST, % | Excluding HIVST testers, % |
| Bus terminus | 1243 | 633 | 40 | 47 | 1963 | 97 | 64 | 161 | 92.4 | 17 | 17 | 0 | 3 | 37 | 2124 | 1.70 | 23.00 |
| Commercial farms | 2089 | 1257 | 121 | 112 | 3579 | 578 | 548 | 1126 | 76.1 | 31 | 43 | 32 | 30 | 136 | 4705 | 2.90 | 12.10 |
| Formal mine | 689 | 173 | 34 | 15 | 911 | 168 | 53 | 221 | 80.5 | 4 | 2 | 8 | 0 | 14 | 1132 | 1.20 | 6.30 |
| Household testing | 4705 | 6608 | 572 | 1057 | 12,942 | 3678 | 4281 | 7959 | 61.9 | 218 | 326 | 535 | 669 | 1748 | 20,901 | 8.40 | 22.00 |
| Informal mines | 932 | 245 | 70 | 37 | 1284 | 325 | 95 | 420 | 75.4 | 16 | 6 | 9 | 11 | 42 | 1704 | 2.50 | 10.00 |
| Informal settlements | 277 | 314 | 27 | 27 | 645 | 31 | 40 | 71 | 90.1 | 7 | 10 | 2 | 3 | 22 | 716 | 3.10 | 31.00 |
| Workplace-market place | 1935 | 1852 | 88 | 106 | 3981 | 165 | 185 | 350 | 91.9 | 25 | 34 | 1 | 6 | 66 | 4331 | 1.50 | 18.90 |
| Resettled farms | 439 | 503 | 43 | 52 | 1037 | 131 | 240 | 371 | 73.7 | 7 | 14 | 6 | 9 | 36 | 1408 | 2.60 | 9.70 |
| Rural shopping centres | 5406 | 4237 | 298 | 286 | 10,227 | 977 | 888 | 1865 | 84.6 | 99 | 107 | 39 | 46 | 291 | 12,092 | 2.40 | 15.60 |
| HTS centres | 22,289 | 27,887 | 474 | 880 | 51,530 | 1821 | 2485 | 4306 | 92.3 | 241 | 486 | 194 | 261 | 1182 | 55,836 | 2.10 | 27.50 |
| Truck stops | 212 | 122 | 11 | 12 | 357 | 19 | 14 | 33 | 91.5 | 0 | 1 | 2 | 1 | 4 | 390 | 1.00 | 12.10 |
| Urban shopping centres | 6974 | 5476 | 317 | 401 | 13,168 | 818 | 666 | 1484 | 89.9 | 80 | 117 | 31 | 33 | 261 | 14,652 | 1.80 | 17.60 |
| Totals | 47,190 | 49,307 | 2095 | 3032 | 101,624 | 8808 | 9559 | 18,367 | 84.7 | 745 | 1163 | 859 | 1072 | 3839 | 119,991 | 3.20 | 20.90 |

HIVST, HIV self-testing.



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## 5 | CONCLUSIONS

Men and young people in sub-Saharan Africa contribute disproportionately to the number of PLHIV who are not aware of their status. Results from two years of large-scale implementation of HIVST through several distribution models demonstrate how targeted roll-out could increase coverage of HIV testing, contribute to case finding among difficult to reach priority populations, particularly among high-risk men and young people and increase efficiency and capacity of HTS in high volume and overcrowded clinics. HIVST offers clear advantages when provided in addition to existing services, and if scaled-up, can contribute to closing the gap towards the "first 90."

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### COMPETING INTERESTS

There are no competing interest.

### AUTHORS' CONTRIBUTIONS

K.H., E.L.C., C.J., P.S., S.G., M.M., R.C., V.M., G.S. M.N., N.M. and C.N. designed the project and its implementation. K.H., P.S. and H.A. designed the market research evaluation and M.A.M., P.M., T.K. and K.H. analysed the data with E.L.C. and C.J. providing technical guidance. K.H. completed the first draft with contributions by all co-authors. E.L.C and C.J. provided critical review of the article.

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### REFERENCES

1. UNAIDS. Global AIDS statistics 2017. December 1, 2017.
2. Stover J, Bollinger L, Izazola JA, Loures L, DeLay P, Ghys PD, et al. Correction: what is required to end the AIDS epidemic as a public health threat by 2030? The cost and impact of the fast-track approach. PLoS One. 2016;11(6): e0158253.
3. Joint United Nations Programme on HIV/AIDS. Knowledge is Power Knowledge is power: know your status, know your viral load. Geneva: Joint United Nations Programme on HIV/AIDS; 2018.
4. Joint United Nations Programme on HIV/AIDS. HIV Prevention 2020 Road Map Accelerating HIV prevention to reduce new infections by 75%. Geneva; 2017.
5. Ministry of Health Malawi. Malawi Population-based HIV Impact Assessment (MPHIA) 2015-16: first report. Lilongwe, Malawi: Ministry of Health; 2017.
6. Ministry of Health and Child Care (MOHCC), Zimbabwe. Zimbabwe Population-Based HIV Impact Assessment (ZIMPHIA) 2015-16: first report. Harare, MOHCC. July 2017.
7. Ministry of Health, Zambia. Zambia Population-based HIV Impact Assessment (ZAMPHIA) 2016: first report. Zambia, Ministry of Health. December 2017.
8. Cornell M, Cox V, Wilkinson L. Public health blindness towards men in HIV programmes in Africa. Trop Med Int Heal. 2015;20(12):1634–5.
9. Cornell M, McIntyre J, Myer L. Men and antiretroviral therapy in Africa: our blind spot. Trop Med Int Heal. 2011;16(7):828–9.
10. Dovel K, Yeatman S, Watkins S, Poulin M. Men's heightened risk of AIDS-related death: the legacy of gendered HIV testing and treatment strategies. AIDS. 2015;29(10):1123–5.
11. Musheke M, Ntalasha H, Gari S, McKenzie O, Bond V, Martin-Hilber A, et al. A systematic review of qualitative findings on factors enabling and deterring uptake of HIV testing in Sub-Saharan Africa. BMC Public Health. 2013;13(1):220.
12. Creighton G, Oliffe JL. Theorising masculinities and men's health: a brief history with a view to practice. Health Sociol Rev. 2010;19(4):409–18.
13. Siu GE, Seeley J, Wight D. Individuality, masculine respectability and reputation: how masculinity affects men's uptake of HIV treatment in rural eastern Uganda. Soc Sci Med. 2013;89:45–52.
14. Indravudh PP, Sibanda EL, d'Elbée M, Kumwenda MK, Ringwald B, Maringwa G, et al. I will choose when to test, where I want to test': investigating young people's preferences for HIV self-testing in Malawi and Zimbabwe. AIDS. 2017;31 Suppl 3:S203–12.
15. Johnson CC, Kennedy C, Fonner V, Siegfried N, Figueroa C, Dalal S, et al. Examining the effects of HIV self-testing compared to standard HIV testing services: a systematic review and meta-analysis. J Int AIDS Soc. 2017;20(1):21594. doi: 10.7448/IAS.20.1.21594
16. Indravudh PP, Choko AT, Corbett EL. Scaling up HIV self-testing in sub-Saharan Africa: a review of technology, policy and evidence. Curr Opin Infect Dis. 2018;31(1):14–24.
17. Kumwenda M, Johnson C, Choko A, Lora W, Sibande W, Sakala D, et al. Exploring social harms and HIV self-testing using mixed-methods in Malawi. J Int AIDS Soc. 2019;22(S1);e25251.
18. Neuman M, Indravudh P, Chilongosi R, d'Elbée M, Desmond N, Fielding F, et al. The effectiveness and cost-effectiveness of community-based lay distribution of HIV self-tests in increasing uptake of HIV testing among adults in rural Malawi and rural and peri-urban Zambia: protocol for STAR (Self-Testing for Africa) cluster randomized evaluations. BMC Public Health. 2018;18(1):1234.
19. Sibanda E, Neuman M, Tumushime M, Hatzold K, Watadzaushe C, Mutseta MN, et al. Linkage to care after HIV self-testing in Zimbabwe: a cluster-randomised trial (ID 3520). Late breaker Oral Presentation. 2018 Conference on Retroviruses and Opportunistic Infections (CROI), Boston, Massachusetts.
20. Neuman M, et al. Does Community Distribution of HIV Self-Test Kits Increase Uptake of HIV Testing at Population Level? Results of a Cluster-randomised Trial in Zambia. HIV Research for Prevention 2018: AIDS Vaccine, Microbicide and ARV-based Prevention Science (HIVR4P), 2018, Spain.
21. Dalal S, Johnson C, Fonner V, Kennedy CE, Siegfried N, Figueroa C, et al. Improving HIV test uptake and case finding with assisted partner notification services. AIDS. 2017;31(13):1867–76. https://doi.org/10.1097/QAD.0000000000001555.
22. Choko AT, Corbett EL, Stallard N, Maheswaran H, Lepine A, Johnson CC, Sakala D, Kalua T, Kumwenda M, Hayes R, Fielding K. Effect of HIV self-testing alone or with additional interventions including financial incentives on linkage to care or prevention among male partners of antenatal care attendees in Malawi: An adaptive multi-arm multi-stage cluster randomised trial. PLoS Med. 2019 Jan; 16(1): e1002719. Published online 2019 Jan 2. doi:10.1371/journal.pmed.100271.
23. Choko AT, MacPherson P, Webb EL, Willey BA, Feasy H, Sambakunsi R, et al. Uptake, accuracy, safety, and linkage into care over two years of promoting annual self-testing for HIV in Blantyre, Malawi: a community-based prospective study. PLoS Med. 2015;12(9):e1001873.
24. Mangenah C, Mwenge L, Sande L, Ahmed L, d'Elbée M, Chiwawa P, et al. Economic cost analysis of door-to-door community-based distribution of HIV self-test kits in Malawi, Zambia and Zimbabwe. J Int. AIDS Soc. 2019;22(S1):e25255.
25. Akullian A, Bershteyn A, Klein D, Vandormael A, Bärnighausen T, Tanser F. Sexual partnership age pairings and risk of HIV acquisition in rural South Africa. AIDS. 2017;31(12):1755–64.
26. Zerbe AV, DiCarlo AL, Mantell JE, Remien RH, Morris DD, Frederix K, et al. Acceptability and uptake of home-based HIV self-testing in Lesotho. Top Antivir Med. 2015;23:509–10.

27. Thirumurthy H, Masters S, Mavedzenge S, 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. Lancet HIV. 2016;3(6):e266–74.
28. Sibanda E, Mutseta M, Hatzold K, Gudukeya S, Dhliwayo A, Lopez C, et al. Community-based distribution of HIV self-test kits: results from a pilot of door-to-door distribution of HIV self-test kits in one rural Zimbabwean community. Presented at: 21st International AIDS Society; 2016. July 18–22; Durban, South Africa.
29. Indravudh P, Fielding K, Neuman M, Chilongosi R, Mkandawire P, Nyondo E, et al. Increasing knowledge of HIV status and demand for ART using community-based HIV self-testing in rural communities: a cluster randomised trial in Malawi. 22nd International AIDS Conference (AIDS 2018), Amsterdam, Netherlands THPDC0103.
30. CDI Study Group. Bull World Health Organ. Community-directed interventions for priority health problems in Africa: results of a multicountry study. Bull World Health Organ. 2010;88(7):509–18.
31. Nichols BE, Offorjebe OE, Cele R, Shaba F, Long LC, Rosen S, et al.; on behalf of EQUIP. Economic evaluation of HIV self-testing in outpatient departments in Malawi: Results from EQUIP. 22nd International AIDS Conference (AIDS 2018), Amsterdam, Netherlands THPDC0103.
32. Cowan FM, Davey C, Fearon E, Mushati P, Dirawo J, Chabata S, et al. Targeted combination prevention to support female sex workersin Zimbabwe accessing and adhering to antiretrovirals for treatment and prevention of HIV (SAPPH-IRe): a cluster-randomised trial. Lancet HIV. 2018;5:e417–26.
33. World Health Organisation. Knowing your status - then and now realizing the potential of HIV self-testing. Geneva 30th World AIDS Day Report STAR Initiative; Unitaid and World Health Organization December 2018.

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RESEARCH ARTICLE

# Exploring social harms during distribution of HIV self-testing kits using mixed-methods approaches in Malawi

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## Abstract

**Introduction:** HIV self-testing (HIVST) provides couples and individuals with a discreet, convenient and empowering testing option. As with all HIV testing, potential harms must be anticipated and mitigated to optimize individual and public health benefits. Here, we describe social harms (SHs) reported during HIVST implementation in Malawi, and propose a framework for grading and responding to harms, according to their severity.

**Methods:** We report findings from six HIVST implementation studies in Malawi (2011 to 2017) that included substudies investigating SH reports. Qualitative methods included focus group discussions, in-depth interviews and critical incident interviews. Earlier studies used intensive quantitative methods (post-test questionnaires for intimate partner violence, household surveys, investigation of all deaths in HIVST communities). Later studies used post-marketing reporting with/without community engagement. Pharmacovigilance methodology (whereby potentially life-threatening/changing events are defined as "serious") was used to grade SH severity, assuming more complete passive reporting for serious events.

**Results:** During distribution of 175,683 HIVST kits, predominantly under passive SH reporting, 25 serious SHs were reported from 19 (0.011%) self-testers, including 15 partners in eight couples with newly identified HIV discordancy, and one perinatally infected adolescent. There were no deaths or suicides. Marriage break-up was the most commonly reported serious SH (sixteen individuals; eight couples), particularly among serodiscordant couples. Among new concordant HIV-positive couples, blame and frustration was common but rarely (one episode) led to serious SHs. Among concordant HIV-negative couples, increased trust and stronger relationships were reported. Coercion to test or disclose was generally considered "well-intentioned" within established couples. Women felt empowered and were assertive when offering HIVST test kits to their partners. Some women who persuaded their partner to test, however, did report SHs, including verbal or physical abuse and economic hardship.

**Conclusions:** After more than six years of large-scale HIVST implementation and in-depth investigation of SHs in Malawi, we identified approximately one serious reported SH per 10,000 HIVST kits distributed, predominantly break-up of married serodiscordant couples. Both "active" and "passive" reporting systems identified serious SH events, although with more complete capture by "active" systems. As HIVST is scaled-up, efforts to support and further optimize community-led SH monitoring should be prioritized alongside HIVST distribution.

**Keywords:** HIV/AIDS; HIV self-test; HIV testing; social harms; Malawi

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## 1 | INTRODUCTION

Despite concerted efforts to scale-up HIV testing services, in 2017, approximately 25% of people with HIV remain undiagnosed [1]. Globally, men, young people and key populations are disproportionately contributing to this HIV "testing gap" [1]. In Malawi, men with HIV are 10% less likely to know their status than women, and only one third of adolescent (aged 15 to 19) boys and less than half of adolescent girls had ever tested [2]. HIV testing, prevention and treatment coverage for female sex workers (FSW) also remains suboptimal [3].

HIV self-testing (HIVST) can increase HIV testing coverage and frequency [4]. Several studies in Malawi have shown HIVST to be highly acceptable and able to reach first-time testers, young people (aged 16 to 25), men and couples and partners [5,6], with acceptable linkage into facility-based services when combined with facilitated linkage strategies [6-9]. As with any form of HIV testing, however, potential social harms (SHs) must be anticipated and mitigated [10-12].

SHs can be defined as any intended or unintended cause of physical, economic, emotional or psychosocial injury or hurt from one person to another, a person to themselves, or an institution to a person, occurring before, during or after testing for HIV [13]. SHs are well documented with all HIV testing approaches [14,15], but need to be balanced against the clear benefits of early treatment and the UNAIDS "90-90-90" targets – the first of which is to diagnose 90% of people with HIV by 2020 [16].

Couples and partner testing, including HIVST, is a highly effective way to reach those in need of testing, prevention and treatment services [10,11]. Despite the many benefits, coping with serodiscordant results (one partner HIV positive and one partner HIV negative) can be difficult [17,18]. Concerns raised by HIVST include potential misuse, and whether testing without in-person counselling may exacerbate negative behaviours and adverse consequences [19,20]. An estimated 37% of ever-partnered women in Africa report having experienced physical and/or sexual intimate partner violence (IPV) [21], and people with HIV, particularly women and adolescents, may have increased risk. Likewise, key populations continue to experience various forms of SHs and violence, including discrimination and criminalization [22].

Despite the concerns, reporting of serious SHs following HIVST appears to be rare [4]. Large-scale evaluations distributing more than one million HIVST kits in three African countries have not identified any suicides [4,23]. Psychological distress following HIVST for those who test positive also appears to be no more extreme than with other approaches to HIV testing, and often short-term in nature [4,6,11,24]. Furthermore, initial SHs can evolve into significant positive outcomes if reviewed in the longer term. Communities and self-testers also consistently report that access to HIVST is empowering, and that its private nature, in most instances, outweighs possible negative aspects [20,25].

Beyond clinical trials, efforts to identify and measure SH relating to HIV testing, including HIVST, are limited and not part of routine monitoring. Instead, efforts have focused on mitigation strategies to minimize harms [10,22]. Here, we describe SH events reported during HIVST implementation in Malawi over a six-year period, propose a community-led approach for SH monitoring and suggest a framework for grading SHs.

## 2 | METHODS

Six HIVST implementation studies carried out in Malawi between 2011 and 2017 distributed 175,683 HIVST kits and included 13 different SH substudies (Table 2). Five studies included both qualitative and quantitative components (mixed methods) from the design stage. The sixth study, Partnerships in Self-Testing in Malawi (PRISM), used a qualitative cohort design nested within a controlled cluster-randomized trial of HIVST kit distribution (HitTB). Health impacts, including testing coverage, linkage to HIV treatment and prevention, are reported elsewhere. Qualitative methods included focus group discussions (FGDs), in-depth interviews and critical incident narratives. Quantitative methods included post-test questionnaires, household surveys, active follow-up of all deaths and reports of IPV during HIVST implementation. For this analysis, we triangulate from different approaches used over the six studies [26,27].

The HitTB study (Table 2) was a cluster-randomized trial implemented in urban Blantyre, distributing 27,789 HIVST kits through trained distributors to 16,660 adult residents (≥16 years) over two years [6], with brief feedback requested from all HIVST participants using a self-administered questionnaire [6]. Outcomes captured at the cluster level included antiretroviral therapy (ART) initiations and deaths [28], with mortality captured through a community reporting system included from the start to capture and report community concerns on a weekly basis. One hundred and twelve "cluster representatives" were recruited with endorsement from community leaders. Cluster representatives reported SH events to a Community Liaison Officer. All deaths among cluster residents (irrespective of HIVST use) were captured through this system, and followed up with verbal autopsies [6]. PRISM and Self-test Impacts (ST-Impacts) were qualitative substudies recruiting cohorts of self-testers from HitTB to evaluate broader consequences of HIVST.

PRISM (Table 2) was a qualitative substudy of HitTB that recruited and followed up 67 individuals from 2012 to 2014 [25]. All participants were cohabitating and in established sexual relationships where either one or both partners had self-tested. Gender, HIV status, nature of self-testing (individual vs. couple testing) and test results (concordant HIV positive where both partners are HIV-positive, HIV-negative and discordant couples) were used for purposive selection. Self-tested individuals were interviewed using serial in-depth interview approach at baseline (within a week of HIVST) and followed up twice within 17 months post-interview. Five FGDs were also conducted with forty-three purposively selected community members (twenty women): two exclusively male, two exclusively female and one with male and female participants.

ST-Impacts (Table 2) recruited 300 HIVST participants from HitTB Study between 2012 and 2013 [29]. This mixed-methods substudy compared prospective reports of SHs identified through the community reporting system with those collected through serial biographical interviews, face-to-face questionnaires, FGDs, three-month-long longitudinal diaries and critical incident narratives.

Partner Assisted HIVST and Linkage (PASTAL) was a separate HIVST trial carried out from 2016 to 2017, recruiting 2349 pregnant women from three urban primary clinics for secondary distribution to male partners (two kits per woman) [9,30]. The primary outcome was linkage to HIV care and prevention services by the male partner. Secondary outcomes were reported by the woman at 28 days, and included safety: women were asked directly about IPV events resulting from delivery and use of HIVST kits using audio computer-assisted self interviews (ACASI) with all women 28 days after HIVST distribution. Incidents reported by participants through ACASI were followed up, documented onto standardized forms and classified by a qualitative researcher probing the nature and relatedness to HIVST of the incident.

For PASTAL, a framework was developed for adverse events reporting, focused on IPV and self-harm [9,13] and further adapted to Table 1. The approach used standard pharmacovigilance reporting [31] that defines potentially life-threatening/changing events as "serious," and events with no

or some effect on social- and work life as "mild" or "moderate" respectively. HIVST studies reporting data from earlier time periods did not systematically capture the data relating to life impact needed to classify severity, and so may have misclassified some serious events.

As part of the Self-Testing Africa Initiative (STAR), a community-based cluster-randomized trial in general populations (GP) (STAR-GP) [32] and a mixed-methods study among FSWs (STAR-FSW) [33], as described in Table 2. Across both, SHs were actively monitored (Figure 1) and graded using the adapted PASTAL framework that included stigma-related events (Table 1).

In STAR-GP [32], community-led SHs reporting was introduced into 22 villages (11 HIVST and 11 standard testing services). Pre-existing community structures (village heads, police, community health workers, religious leaders and marriage counsellors) were responsible for identifying and reporting harms relating to HIV testing. Community leaders documented, investigated, managed and reported SH episodes to the study's Community Liaison Officer. In HIVST clusters, distributors promoted HIVST kits and other health-related products. Reported SHs from distribution of 137,915 HIVST test kits in four rural districts are listed according to the nature of the reporting system under which they were captured in Table 2 (see Rows 7, 9 and 11). Qualitative process evaluation data were collected during and after HIVST distribution, including six FGDs with fifty healthcare workers, two with eighteen SH reporting-systems members from "evaluation villages" (see Row 9 of Table 2) and forty-six in-depth interviews with HIVST distributors and self-testers. Evaluation villages were selected to be representative of the wider STAR-GP distribution model, and had the same implementation strategy, but more intensive monitoring, but a more active community-led SH reporting system (Figure 1) and endline household surveys [32]. Determination of the severity of reported SHs was mostly based on researcher's opinion after a critical analysis of the event.

STAR-FSW (Rows 8, 12 and 13 of Table 2) assessed the distribution of 5281 HIVST kits in three districts (Blantyre = 2001, Chikwawa = 1237 and Mulanje = 2043). All kits were distributed to FSW by trained FSW who served as peer educators. Implementation, including SH, was monitored using a combination of peer-led community reporting system, ACASI

**Table 1. Proposed social harms grading matrix: adapted from Division of AIDS, and revised following use in three studies, including Self-Test Africa Research general population and female sex workers protocols**

| Grade 1 (mild)<br>No effect on social and work life. No doctor needed | Grade 2 (moderate)<br>Some effect on social or work life, and may need doctor or psychologist | Grade 3 (severe)<br>Unable to socialize or unable to work, and needs doctor or psychologist | Grade 4 (life-threatening)<br>Life-threatening/disability<br>Grade 5: fatal |
|---|---|---|---|
| Denying access to non-critical household resources<br>Being ignored<br>Being controlled (e.g. not allowed to leave house)<br>Being shouted at | Moderate verbal, emotional or psychological IPV<br>Coercion to self-test<br>Coercion to disclose a self-test result<br>IPV that includes, e.g. pushing or slapping with an open hand that does not result in pain or visible marks >24 hours<br>Psychologically coercive sex<br>Being shunned at home, work or school<br>Economic hardship resulting in skipping meals, missing school<br>Temporary separation lasting less than seven days | IPV that leads to pain, bruising or marks >24 hours.<br>Verbal threats of potentially lethal violence (e.g. statement of intent to kill, mock strangulation, threatened with a knife or gun)<br>Marriage break-up lasting greater than or equal to seven days (temporary or permanent)<br>Stigmatization sufficient to cause change of work, school or home<br>Suicidal ideation<br>Extreme economic stress: unable to meet basic needs of self/children | IPV leading to hospitalization<br>Attempted suicide leading to hospitalization<br>Attack using potentially lethal force (e.g. knife, gun, hammer, kicks to head, asphyxiation)<br>Rape or attempted rape<br>*[Any event leading to death is classified as a Grade 5 serious SH]* |
| Referred to community-based institutions for assistance, for example CBOs, Police. | Refer to community-based institutions for assistance<br>Reported to relevant authorities, for example Community Liaison Officer<br>Refer to community-based GBV support organizations | Report to marriage counsellors<br>Report to relevant authorities, for example Community Liaison Officer<br>Refer to community-based GBV support organizations | Discuss and refer to police/chief/other social support based on individual need and desire<br>Report mandatory events to police (suicide/homicide)<br>Report to relevant authorities, for example programme managers<br>Refer to community-based GBV support organizations<br>Ensure safe alternative abode before discharge |

IPV, intimate partner violence; CBOs: community-based organizations; GBV: gender-based violence.

**Table 2. Studies with nested qualitative data collection on SHs**

| Study | HIVST strategy | Methodology | Study year/ publication | Population: nature | HIVST clients | Adverse event N and % | | Serious SHs: N and % | | Comment |
|---|---|---|---|---|---|---|---|---|---|---|
| A: Active SHs identification systems (research) | | | | | | | | | | |
| 1. HitTB | Community-based | Representatives reporting deaths & community views on HIVST | 2011 to 2014 Choko 2015 [6] | All adults in HIVST area Years 1 and 2 | 27,789[a] | NA | NA | 0 | 0.0% | No deaths related to HIVST from 132 deaths with verbal autopsy. No serious events identified through Community liaison system, but not focused on IPV |
| 2. HitTB (subset of kits listed above) | Community-based | Self-completed post-HIVST questionnaire for coercions | 2012 to 2014 Choko 2015 [6] | Self-testers Year 1 data | 10,017[b] | 288 | 2.9% | NA | NA | Questionnaire asked only if "Forced to test": of coerced self-testers, 94.4% were still satisfied with and would recommend HIVST to others |
| 3. PRISM (substudy of HitTB) | Community-based | Cohort with serial interview | 2012 to 2013 Kumwenda 2014/ 2018 [25,49] | Self-testers | 67[b] | NA | NA | 5 | 7.5% | Purposive selection: all in stable relationship; over-representation of discordant couples |
| 4. ST-Impacts (substudy of HitTB) | Community-based | Cohort with serial interview | 2013 to 2015 | Self-testers | 300[b] | NA | NA | 4 | 1.3% | Purposive selection: 100 people in established couples, 100 single men and 100 single women |
| 5. ST-Impacts (substudy of HitTB) | Community-based | Critical incident narratives: all reported IPV) | 2013 to 2015 | Self-testers | 13,785[b] | 15 | 0.1% | 2 | 0.01% | All women reporting IPV to HIVST distributor, HitTB Community Representatives, police, support groups, marriage counsellors: from 150 interviewed, 15 reported links to HIVST |
| 6. PASTAL | Antenatal: Partner-delivered | Interviews using ACASI, 28 days post intervention | 2016 to 2017 Choko 2019 [9] | Pregnant women | 4698[a,d] | 3[3][d] | 0.1% | 0 | 0.0% | Woman given two HIVST kits. Systematic ACASI capture reflects primarily woman's experience |
| 7. STAR-GP | Community-based | Survey of rural villagers | 2016 to 2017 Indravudh 2019 [54] | Self-testers | 794[b] | 4 | 0.5% | NA | NA | Endline survey in randomly selected households of HIVST Evaluation Villages |



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**Table 2.** (*Continued*)

| Study | HIVST strategy | Methodology | Study year/ publication | Population: nature | HIVST clients | Adverse event N and % | | Serious SHs: N and % | | Comment |
|---|---|---|---|---|---|---|---|---|---|---|
| 8. STAR-FSW: Blantyre | Network-based | Cohort peer-reporting system | 2017 to 2018 | Self-testers | 2001[a] | 1 | 0.0% | 1 | 0.05% | Serial interviews and Longitudinal Diaries conducted but not yet analysed: provisional data |
| B: Community reporting systems | | | | | | | | | | Facilitated and formalized passive reporting |
| 9. STAR-GP: HIVST evaluation villages | Community-based | Community-led Reporting System established for HIVST | 2016 to 2017 Indravudh 2018 [54] | Self-testers | 9492[a] | ND | ND | 6 | 0.06% | Existing authorities and civil society groups engaged to establish a community-led system for harms reporting and management (Figure 1) |
| 10. STAR-GP: Control villages | No HIVST | Community-led reporting system for standard HTS | | Facility HIV testers | 3150[c] | NA | NA | [6][e] | 0.19% | Related to standard HIV testing, not HIVST. Same system as used for STAR HIVST evaluation villages |
| C: Other SHs identification systems | | | | | | | | | | |
| 11. STAR-GP: non-evaluation villages | Community-based | No community-led reporting system established | 2016 to 2017 | Self-testers | 128,423[a] | NA | NA | 1 | 0.00078% | Harms reporting relied on HIVST implementers, without establishing community-led system |
| 12. STAR-FSW: routine | Network-based | Routine reporting to implementer | 2017 to 2018 | Self-testers | 3280[a] | ND | ND | 0 | 0.00% | Not included in Serial interviews and ACASI |
| 13. STAR-FSW peer distributors | Not Applicable | FGDs | 2017 to 2018 | Distributors | 17[c] | 3 | 17.6% | 0 | 0.00% | Not anticipated or captured systematically: reported at FGDs to evaluate distributor experience |
| Total HIVST and serious SHs reported in Malawi | | | 2011 to 2018 | Self-testers | 175,683[a] | | | 19 | 0.011% | Affected individuals (total of 25 serious SHs) |

[a]A primary study contributing to the total number of 175,683 self-test kits distributed; [b]A subset/substudy of an already included primary study (not contributing to the total number of 175,683 self-test kits distributed); [c]Study component for which no HIVST kits were used (control or distributor data); [d]4698 HIVST kits provided to 2349 pregnant women, intended for use by the woman plus her main male partner. 3[3]: women were directly interviewed for SHs using ACASI of whom three reported an adverse event that also affected three male partners – none of whom reported the event spontaneously; [e][6] SHs related to standard HIV testing for residents of control villages where self-test kits were not distributed. Studies: HitTB: Cluster-randomized trial of health outcomes from introducing a community-based HIVST distribution strategy; PRISM: Partnerships in Self-Testing in Malawi; qualitative substudy of HitTB HIVST participants; ST Impact: Self-test Impact; qualitative substudy of HitTB HIVST participants; PASTAL: Partner Assisted HIVST and Linkage; cluster-randomized trial of six different approaches to providing HIV testing and encouraging linkage to post-test services for male partners of antenatal clinic attendees; STAR-GP: Self-Test Africa Research – general population protocol; STAR-FSW: STAR – female sex workers protocol. ACASI, audio computer-assisted self interviews; FGDs, focus group discussions; HIVST, HIV self-testing; HTS, HIV testing services; IPV, intimate partner violence; NA, not applicable; ND, not determined; SH, social harms.

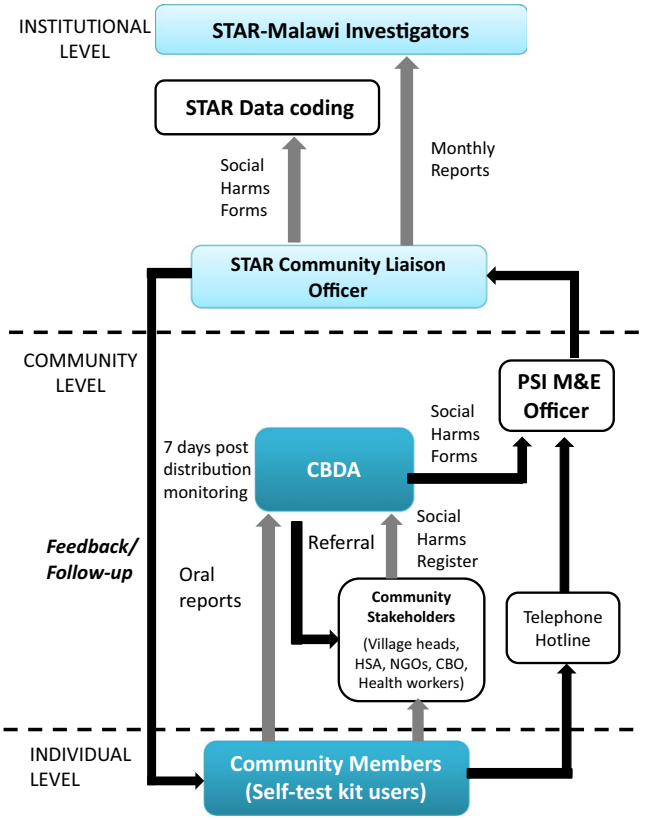


**Figure 1. Self-Test Africa Research (STAR) general population community-led social harm tracking system, based on engagement of existing authorities and civil society organizations to provide a community-led reporting system.**
PSI, Population Services International (implementing organization in STAR-Malawi); M&E, Monitoring and Evaluation; CBDA, community-based distribution agent; HSA, Community Health Worker cadre of Ministry of Health, Malawi; NGO, non-governmental organization; CBO, community-based organization.

(n = 268), longitudinal diaries, serial biographical interviews (n = 22), and four FGDs among FSWs (n = 3) and peer distributors (n = 1). Active SH monitoring was only implemented in Blantyre district. Only the peer-led community reporting system data, ACASI and FGDs are presented.

## 2.1 | Data analysis

Detailed descriptive scripts on episodes of SH were reviewed and compared across studies. MK-coded qualitative data according to the nature (category) of the incident (e.g. divorce/separation, physical violence, verbal abuse, etc.) and groups affected (i.e. men, women, couples, sex workers). Manual coding was used because the datasets on SH were small for any given study. Categories were defined purposively and deductively, to provide overarching guidance on both the nature of SHs within Malawi, and the groups of people who are likely to be susceptible.

While the majority of kit recipients across all studies reported positive experiences and benefits of HIVST [8], here we focus on SHs. Findings are presented as summary frequency tables, and using descriptive narrative supported by relevant quotes from those reporting and experiencing harms. As the focus of data collection and/or reporting was on serious SHs, we have not included estimates of the frequency or severity of all mild and moderate SHs here, with the exception of coercive testing and temporary separation of couples where data was systematically captured.

## 2.2 | Ethical considerations

All studies were approved by College of Medicine Research and Ethics Committee of the University of Malawi, and either London School of Hygiene and Tropical Medicine or Liverpool School of Tropical Medicine (ST-Impacts). All participants provided informed consent as per parent study requirements.

# 3 | RESULTS

Between 2011 and 2017, a total of 175,683 HIVST kits were distributed and 25 reported SH events were (0.011%) classified as serious SHs (Table 3). During this period, there were no reported deaths, suicides or incidents of self-harm, although one man had suicidal ideation (Table 3). Of the twenty-five serious SH events reported, most were marriage break-ups (sixteen individuals; in eight couples). In all studies, there was the disproportionate risk of separation when HIV serodiscordancy was newly identified by HIVST. Out of eight marriage break-ups reported, all but one was in a serodiscordant relationship. The other break-up was among a concordant HIV-positive couple.

Separating couples were more likely to report additional SHs related to physical IPV, or economic hardship, compared to individuals or other couples that stayed together. Except for serodiscordant couples, individuals with history of violence in their relationship were more likely to report experiencing SH than other groups. Pre-existing violence, prior to HIVST, such as verbal insults and physical violence were frequently experienced by FSWs, but with few instances directly related to HIVST. Economic hardship was rarely reported outside of the context of impending separation/marriage break-up.

Couples also reported HIVST had many benefits, suggesting it helped facilitate important discussions, built trust and enhanced partner fidelity and increased efforts to jointly reduce sexual risk behaviour. In particular, women reported HIVST was empowering, made them feel in control testing environment and provided new opportunities to discuss testing with their partners (Table 4, Q1 and Q2).

## 3.1 | "Coercion" to test and disclose

Men and FSW most commonly reported coercion to self-test. Some degree of coercion was reported by 288/10,017 (2.9%) self-testers in HitTB – 3.9% in men versus 2.2% in women [6], and by 29/268 (10.8%) FSWs in STAR-FSW ACASI. Overtly hostile coercion directly following HIVST was not identified. Although uncertain if related to HIVST, there was one case of coercion where a woman reported that her partner had forced her to repeat HIVST to confirm their results were discordant. No FSWs reported they were forced to self-test or disclose their results by clients or sex partners. However,

**Table 3. Summary of serious social harms (SHs), by nature of harms and whether related to HIV serodiscordancy or not**

| Nature of event | Individuals affected | Couples affected | Of couples: with HIV discordancy | Total serious SHs |
|---|---|---|---|---|
| Break-up of marriage/cohabiting couple | 16 | 8 | 7 | 20[a] |
| Resolved (after at least seven days separation) | 8 | 4 | | |
| Unresolved | 8 | 4 | | |
| IPV with temporary less than seven days separation | 1 | 1 | 0 | 1 |
| Suicidal ideation | 1 | 1 | 1 | 1 |
| Use of HIVST kit by 12-year-old girl with previously undisclosed and untreated perinatal-acquired HIV infection | 1 | 0 | NA | 3[b] |
| Total with at least one serious SH | 19 | 10 | 8 | 25 |

[a]One break-up with four individual serious SHs (two individuals affected by marriage break-up; woman subject to violent assault including a broken arm; woman left in extreme economic hardship). Two break-ups with three individual serious SHs (two individuals affected by each marriage break-up; both women subject to extreme economic hardship); [b]Girl tested in front of school friends and experienced severe stigmatization, psychological distress and economic upheaval with family moving to a new village. Additional family members are likely to have experienced serious SHs but these were undocumented.

FSWs reported frequent coercion by employers, facility owners and peer HIVST distributors. The two most commonly reported types of coercion were viewed by HIVST kit recipients as "well-intentioned" or "socially reasonable," and neither considered as harmful nor spontaneously reported as "harms."

The first type of coercion, involving women in long-term sexual relationships pressurising their male partner to test, was described as "well-intentioned" (Table 4, Q3 and Q4). Women, viewed as household "custodians of health" in Malawi, indicated that HIVST empowered them to actively promote testing to their male partner, since the discussion was immediate and located within the home (Table 4, Q5). This approach was largely seen during pregnancy where both men and women felt urgency to test. Thus, when pregnant women offered HIVST to their male partners, uptake was high [9,34]. Although uncommon, some incidents of arguments or brief separation were reported (Table 5) but no incidents of physical violence.

The second type of coercion where individuals showing signs of ill-health were persuaded to test to facilitate ART initiation was described as "compassionate coercion" (Table 4, Q4). Participants described these methods as often indirect. For instance, one man directed his household, including himself, to self-test, but subsequently stated having done so out of concern for his orphaned nephew's health. Again, these instances tended to be viewed by individuals and the community as benign, and so unlikely to be spontaneously reported.

## 3.2 | Verbal intimate partner violence

Arguments and verbal IPV, although infrequent, was more common following a reactive HIVST result, especially among couples and FSWs who disclosed their result. In these cases, ridicule, stigma, and blame tended to be directed towards the HIV-positive partner in discordant couples, or the partner with suspected infidelity – usually the man – in an HIV-positive concordant couples (Table 4, Q6 and Q7). These events were rarely reported, with participants tending to place blame on their partner, not the HIVST kit *per se*.

For FSWs, social stigma towards both users and peer distributors was reported. Some peer distributors reported they were insulted when distributing HIVST kits, particularly by FSWs who did not want to test (Table 4, Q8). Colleagues and neighbours also labelled some peer distributors as HIV positive, with others questioning their credentials and abilities to deliver HIVST (Table 4, Q9 and Q10).

## 3.3 | Physical violence

ST-Impacts followed up 150 women who reported physical violence to support organizations and identified 16 linked to HIVST. Of eleven women interviewed in-depth, eight reported pre-existing violence within their relationship, while three suffered violence for the first time after self-testing (Table 4, Q11 and Q12). In seven of these cases, men refused to self-test aggressively. Alcohol was a pre-existent problem in the households of nine women. All women reporting violence were dependent on income from their male partner. While most women experiencing violence were aware that it was inappropriate, they often reported being disempowered or unable to prevent it due to inequalities in access to resources and normalized inequalities of power (Table 4: Q13). The most serious case resulted in hospitalization: here, the woman self-tested negative prompting the man, who had been extremely violent in the past, to self-test himself and become enraged when his result was positive. A second case of IPV, reported following self-testing is detailed in Table 4 (Q13). No woman identified through critical incident interviews had been identified by the HIVST community representative system.

For FSWs, 92 of 268 women reported violent incidents but only two were confirmed to be HIVST-related. In both cases, the incident was with established sexual partners and was similar to those reported in GP (Table 4, Q14 and Q15). There was also one instance of maltreatment of a peer distributor by a FSW who had a reactive self-test result (Table 4, Q16).

### 3.4 | Separation and break-up

Four reconciled and four permanent marriage break-ups resulted from HIVST (Tables 2 and 3), including seven serodiscordant couples. Marriage break-ups tended to remain unreconciled in the early studies but were mostly reconciled in STAR-GP. HIVST distributor training and sensitization of community-led harms reporting system stakeholders (Figure 1.) included greater focus on serodiscordancy under STAR-GP, where community-led reporting systems identified the same number of marriage break-ups (three couples) for standard-of-care villages as for HIVST villages.

Serodiscordant partnerships were more likely to report SHs when the woman was HIV positive (Table 4, Q17, Q18, Q19). A variety of misconceptions led serodiscordant couples to view their relationship as one that could not last: first, the concept was perplexing, with couples failing to understand how HIV could fail to be transmitted during condomless sex. Second couples were not aware that treatment-as-prevention could enable them to resume condomless sex once the positive partner was established on (and remained adherent to) ART (Table 4, Q20). Without this knowledge, couples assumed HIV must have been introduced recently (implying infidelity), and that condoms would be required indefinitely, precluding a healthy sex-life or children (Table 4, Q21, for an HIV-positive concordant woman). Importantly, correcting these misconceptions led to some couples reconciling.

Events unrelated to serodiscordancy were rare but included reactions to the mere introduction of an HIVST kit into the house without the man's permission, and occasional break-up of concordant HIV-positive relationships (Table 4, Q18).

### 3.5 | Severe depression

One report of depression with suicidal ideation was documented within a recently formed serodiscordant relationship (Table 4, Q22). At 12 months, the HIV-positive man still experienced suicidal ideation; however, this was related to specific financial worries. Three other cases of mild depression following disclosure and discrimination were reported in STAR-GP.

### 3.6 | HIVST age <16 years outside the study area

All studies restricted HIVST to those aged 16 or older; however, tests did find their way into non-study areas. One case of self-testing under the age of consent was identified by implementers in a non-study area. In this case, a 12-year-old perinatally infected adolescent previously unaware of her status self-tested with friends and experienced multiple serious SHs including psychological distress, stigmatization and economic upheaval (Table 5), illustrating the importance of training HIVST distributers to prevent HIVST kits to those aged under 16.

## 4 | DISCUSSION

In the past six years, over 175,000 HIVST kits have been distributed in urban and rural Malawi, with services implemented in settings characterized by high HIV prevalence, economic vulnerability and high frequencies of IPV. We adapted the grading system used for therapeutic clinical trials and post-marketing pharmaceutical surveillance to classify both frequency and severity of SHs relating to HIVST. Despite the high levels of background SH, only 19 (0.011%) individuals involved in self-testing or offering kits reported a serious SH related to HIVST, with multiple events affecting some individuals (25 serious SH events). Rates tended to be higher when kit recipients were followed up with interview for serious SHs, consistent with likely under-reporting in less "active" surveillance systems [35-38], for example 4 of 300 (1.3%) self-tester from the general community, although no serious SHs were reported by 2349 pregnant women interviewed one month taking two HIVST kits home (Table 2). Our ability to comment on mild and moderate harms (defined as no/some effect on social and work life, respectively) was limited by the nature of data captured (Table 2), but the overall frequency of any reported SH from HIVST was within the range expected for standard HIV testing [36-38]. For instance, 0.5% of 794 self-testers included in post-intervention household survey reported any unwanted consequences in rural Malawi. Most serious events related to the broader issues and challenges of being diagnosed and living with HIV in Africa particularly for those in serodiscordant relationships, rather than testing modality.

As previously reported, many couples considered HIVST to be a helpful tool to start dialogues and discussions on sensitive topics, including HIV testing, and a way to build trust between partners [5,25]. In general, women found the ability to bring kits home increased their autonomy and left them feeling empowered by testing themselves and offering HIVST to their male partners. Empowerment for women did leave some men feeling "coerced" to self-test [6]; however, most described it as well-intentioned and socially acceptable within their established partnership [25], as also reported for men who have sex with men from China [19,39]. Nevertheless, several cases of coercion escalated into other forms of harm. It is important to reiterate that coercion and mandatory testing are never advised, including with HIVST [40]. Programmes need to develop strong and clear messages to self-testers and training for distributor to avoid overpressurising partners, especially when implementing index/partner-delivered or network-based distribution models, which encourage individuals to offer HIVST kits to sexual or social contacts with the endorsement of national health systems.

Because of high background rates of IPV among FSWs and previous reports of SH following HIVST [41-43], additional strategies to mitigate the risk of coercion and IPV among FSWs are needed. Approaches could include empowerment workshops and training for police and venue owners, which have been used more broadly in FSW programmes [44]. Messages that explain FSWs rights to choose when and how to self-test and disclosure, should be promoted. We found that high background IPV rates in FSWs made it difficult to directly relate events to HIVST, raising the need for additional methodologies or monitoring tools to better capture this information.

Couples with serodiscordant HIV results are an important target for HIV prevention in Africa, where serodiscordancy is common (e.g. 7% of Malawian couples jointly tested as part of the most recent Demographic and Health Survey [45] and transmission within serodiscordant couples accounts for a

**Table 4. Quotes on episodes of social harms from six studies from 2011 to 2017 in Malawi**

| Theme | Number | Quote |
|---|---|---|
| Social benefits | Q1 | "Our relationship has changed because we are having the same mind."<br>ST-Impacts: Woman who tested as a couple, concordant negative |
| | Q2 | "Because it's like you are now open to one another, everyone knows each other's status. But also, it helps that you should be open to one another."<br>ST-Impacts: Woman who tested individually, negative |
| Coercion to test and disclose | Q3 | "It is sometimes good . . . if one of you in the relationship is refusing to get tested you can doubt them. It is good at times to force someone to get tested so that you all know your HIV status. For someone like me who isn't married there is no reason to be forced to get tested."<br>ST-Impacts: individual man who self-tested |
| | Q4 | "It is necessary because they are wishing you well. People must know how they are (HIV status) before it is too late. It becomes very sad when people get really sick and yet all along their friends were telling them to get tested."<br>ST-Impacts: individual woman who self-tested negative |
| | Q5 | "When I got the kit, I took two days without testing, then my wife said that I won't eat that day If I don't test. She went to the bedroom and poured water on my clothes. There was force, I knew that if I don't test then there won't be sex for me."<br>ST-Impacts: Husband in a concordant negative couple |
| Verbal abuse | Q6 | "That is when he self-tested negative. From that moment, I did not understand that he did not have the HIV. That day, it was not a nice experience for me. He was shouting at me; 'you are a liar'. There is something that you have been doing behind my back."<br>PRISM: Female, 32 years, HIV-positive discordant |
| | Q7 | "My trust in you has now eroded and when I look at you now . . . I now see you as a monster because you have damaged my body [infected her with HIV]."<br>PRISM: Female, 24 years, HIV-positive concordant |
| | Q8 | "They face FSWs that don't want to test. Most FSWs say bad things to PDs for example swearing at them for approaching them with the kit."<br>STAR-FSW: Peer distributor, FGD |
| | Q9 | "They were insulting us, saying no FSW is negative. My neighbours were saying I am HIV positive that is why I was distributing the kits."<br>STAR-FSW: Peer distributor, FGD |
| | Q10 | "Neighbours were rude to us asking questions like are you a doctor? Did you go to school?"<br>STAR-KP: Female, Peer distributor, FSW, FGD |
| Physical violence | Q11 | "I couldn't have gone through this (the beating) if it weren't for self-testing. I know my husband is very angry right now because I put him through self-testing and he was found positive."<br>ST-Impacts: Wife (negative) in discordant relationship |
| | Q12 | "At first we were staying normally without any problem before this problem came into existence. I just saw a person start changing his ways and I questioned why he was doing this . . . All this was happening after getting tested. I didn't experience this before but when I got tested is when I started experiencing violence. When I just do something wrong what he will do is beat me."<br>ST-Impacts: Wife (negative) in discordant relationship |
| | Q13 | "Sometimes we women are attacked if we are not listening to what our husbands are telling us to do then they start attacking us. Violence also happen when a man wants to have sex with us and we are refusing. That's violence also, ' – it's not right that you should be beaten' because if he has loved you are supposed to love him back."<br>ST-Impacts: Married woman who tested with her partner and was discordant positive |
| | Q14 | "I once had a girl who tried to get her partner tested and he beat her up and left her house. But luckily they worked it out and he returned to the house after some time."<br>STAR-KP: Female, Peer distributor, FSW, FGD |

**Table 4.** (*Continued*)

| Theme | Number | Quote |
|---|---|---|
| | Q15 | "I got a report from a girl who was forced by her boyfriend to reveal her results. The guy did not believe her results and he wanted a kit too for himself."<br>STAR-KP: Female, Peer distributor, FSW, FGD |
| | Q16 | "A certain girl poured alcohol (Chibuku) on me after telling her that she was HIV positive. However, after everything she apologized and I helped her get medication and we've been friends since then."<br>STAR-KP: Female, Peer distributor, FSW, FGD |
| Separation and break-up | Q17 | "As of now there is nothing easy. As things are now, there is nothing that we can sit down and talk because we don't discuss things, because we cannot even sit down to eat nsima [Staple dish made from maize flour] together. When he comes he eats his nsima in the bedroom and the children and myself we eat here … But when my husband finds money, he keeps it for himself and when I have found mine I have to buy food in the house and everything in the house."<br>ST Impacts: Wife (positive) in concordant couple |
| | Q18 | "When I left my home to attend a funeral in my home village, he called me when I was planning to return to my house. He said 'please do not come back. I have married another woman who is now staying with me'. From that time, I have not gone back to my husband."<br>PRISM: Wife, aged 30, HIV positive from discordant couple |
| Reaction to Discordancy | Q19 | "When we tested, 'I did not drink water' [emotionally unsettled] that day. He said 'we have tested, you have HIV but I do not have it. Where did you get HIV? This marriage will end now and you will soon go to your village'. I sat there speechless. Now we always quarrel because he always speaks demeaning words to me because of my status."<br>PRISM: 32-year-old HIV-positive wife in a discordant relationship |
| Treatment-as-prevention (ART) | Q20 | "Some people when they know that someone has HIV and have started taking ARVs [Antiretroviral] drugs, they feel that they cannot have sex with that person fearing that they can also get infected."<br>PRISM: 29-year-old wife, HIV positive, concordant couple |
| | Q21 | "This medicine (ARVs) that I have started taking I feel it helps protect me since we do not use condoms because we are taking these drugs. These drugs help to protect our bodies from getting more viruses."<br>PRISM: 26-year-old wife, HIV positive in a concordant couple |
| Suicide threats | Q22 | "Even that day [of self-testing], he was so disappointed and did not even eat or bathe. He told me that while I was sleeping, he went away and planned to kill himself. But after thinking through it, he thought that it is shameful because people would be pointing their fingers at me that my husband has killed himself because of me."<br>PRISM: 19-year-old HIV-negative wife in discordant relationship |
| Economic violence | Q23 | Interviewer: Is there time that you stop him that he shouldn't buy this, and he accepts not to buy it?<br>PF: No isn't possible, he can't allow that, the way I know him I can't even talk about that.<br>Interviewer: What are you afraid of?<br>PF: I am afraid that we will exchange words.<br>ST Impacts: Married woman tested as couple, negative discordant |

FSWs, female sex workers; ST-Impact, Self-test Impact; STAR, Self-Test Africa Research; FGD, focus group discussion; ART, antiretroviral therapy; PRISM, Partnerships in Self-Testing in Malawi.

substantial fraction of all new HIV infections at the national level, and is readily preventable using ART-based strategies. However, coping with newly identified serodiscordancy is challenging with any mode of HIV testing [36-38,46]. For instance, 24% of 469 serodiscordant Kenyan couples separating during two years of follow-up in an HIV prevention trial [37], while in a multicountry East and Southern African trial [36], IPV was reported by 18% of HIV-positive women and 7% of HIV-positive men, respectively, in serodiscordant relationships.

Most serious and lasting SH identified across all HIVST studies reported here were also linked to newly identified serodiscordancy, making this a feature common to all HIV testing strategies [10,11,22]. What is unique to HIVST, however, is the ease with which couples can self-test together or soon after one another and share results. For this reason, HIVST appears to facilitate greater mutual knowledge of status between couples than other approaches [34,47]. There was anecdotal evidence in the PASTAL trial where 20 out of 46 male partners who self-tested HIV positive were confirmed to be in an HIV-discordant relationship. This presents an important opportunity for HIV prevention [48], but also responsibility to ensure that serodiscordancy is understood, with appropriate follow-up advice and management. We identified significant gaps in awareness and understanding of discordancy, both among couples and for health workers, as also reported from other African countries [49-51]. Providing clear messages and the need for

**Table 5. Listing of SHs, focused on serious SHs from self-testing studies in Malawi as reported through: A. active surveillance (serial interviews, ACASI, surveys), B. Integrated Community Reporting Systems (passive surveillance) and C. other mechanisms**

| Study | People with ≥1 SHs: n/N (%) | Type of SH | Description | Outcome | Severity grade and number |
|---|---|---|---|---|---|
| A: Data collected through active surveillance methods: serial interviews, ACASI, surveys | | | | | |
| PRISM<br>HIVST in GPs, but with discordant couples deliberately over-represented.<br>67 individuals<br>14 couples in seven discordant relationships | 4/67 (6.0%) self-testers with ≥1 SH<br>2/7 (29%) of discordant couples with ≥1 SH | Marriage break-up related to confirmed discordancy; plus, verbal and economic IPV | A 32-year-old woman tested together with her husband, a 32-year-old husband who was employed in the formal sector. The woman tested HIV positive, and the man tested HIV negative. The couple attended for couples-testing at a primary care clinic, where discordancy was confirmed. The man started to verbally insult his wife, and later abandoned her and their child. The wife was unable to economically fend for herself after being separated from the male partner. Both partners affected | Unresolved | Grade 3 SH × 2 (marriage breakdown)<br>Grade 3 SH × 1 (economic) |
| | | Marriage break-up related to confirmed discordancy | A 61-year-old man tested together with his 30-year-old wife and the result were discordant – the wife tested HIV positive. The HIV results were confirmed at clinic-based HTC. Soon after self-testing, the woman went to her home village to attend a funeral of her daughter. The male partner took advantage of her departure to marry another woman and in the process abandoning the other woman. Both partners affected | Unresolved | Grade 3 SH × 2 |
| | | Suicidal ideation related to confirmed discordancy | A new couple who had been married for five months, self-tested at home as a couple. The husband tested HIV positive while the wife tested HIV negative, with these discordant results confirmed on retesting at clinic.<br>Subsequently, the husband told the wife that he had been thinking about committing suicide. The wife gave this information to the research team during one of her serial in-depth interviews | Resolved | Grade 3 SH × 1 |

**Table 5.** (*Continued*)

| Study | People with ≥1 SHs: n/N (%) | Type of SH | Description | Outcome | Severity grade and number |
|---|---|---|---|---|---|
| ST-Impacts<br>Serial interview with 300 purposively selected HIVST participants in Blantyre (50 couples; 100 single men; 100 single women) | 4/300 (1.3%) self-testers with ≥1 SHs<br>2/4 (50%) separation of known discordant couples | Marriage break-up related to confirmed discordancy<br>Economic IPV | A woman was previously known HIV positive and on treatment, but her new husband refused to believe her, and she stopped taking ART. When self-testing was introduced the man self-tested HIV negative, and then brought two kits home for the couple to test together. When this showed discordancy (subsequently confirmed), the man stopped providing for his wife and had several periods of separation, with the marriage unlikely to survive. Both partners affected | Unresolved | Grade 3 SH × 2 (marriage breakdown)<br>Grade 3 SH × 1 Economic IPV |
| | | Temporary separation related to confirmed concordant HIV positive<br>Economic IPV | A man knew himself to be HIV positive and had not disclosed to his wife. She saw him taking medication, however, and so self-tested herself. Her HIVST result was HIV positive. Following this, the couple tested together and had confirmed concordant HIV-positive results.<br>The woman was unable to forgive the man for deceiving her about his status, and the couple had periods of separation. The man stopped providing for the woman's children from an earlier marriage | Resolved | Grade 3 SH × 2 (marriage breakdown)<br>Grade 2 SH Economic IPV |
| ST-Impacts: critical incident Interview of women reporting IPV to, for example police, women's support organizations) during Year 2 of HitTB in urban Blantyre | 2/13,785 (0.014%) self-testers with ≥1 SH | Physical IPV (woman) and marriage break-up separation (both) relating to unconfirmed discordant results | A woman self-tested negative, prompting her partner to self-test. The man reacted violently to his positive HIVST results, with a severe assault during which the woman sustained a broken arm and was hospitalized.<br>The male partner walked out from the relationship and has not returned | Resolved (admission)<br>Unresolved (marriage) | Grade 4 SH (life-threatening IPV requiring hospitalization)<br>Grade 3 SH × 2 (marriage breakdown)<br>Grade 3 SH × 1 (economic) |



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**Table 5.** (*Continued*)

| Study | People with ≥1 SHs: n/N (%) | Type of SH | Description | Outcome | Severity grade and number |
|---|---|---|---|---|---|
| PASTAL: pregnant women ACASI at 28 days, plus self-reporting to study team | 0/4698 (0%) self-testers with ≥1 SH<br>Six SHs (0.13%) reported by 2349 women distributing 4698 kits<br>Denominator # of discordant couples unknown | Temporary separation after bringing home HIVST kits<br>Verbal IPV | A pregnant woman took two HIVST kits and information leaflets home to her male partner, who reacted angrily and shouted at her for receiving these items without his authorization and knowledge. The man sent his wife to her village but later went to get her. Both partners affected | Resolved within two days | Grade 2 SH × 2 (marriage breakdown)<br>Grade 2 SH × 1 (verbal) |
| | | Temporary separation after bringing home HIVST kits<br>Verbal IPV | A pregnant woman took two HIVST kits and information leaflets home to her male partner, who reacted angrily, saying that this indicated lack of trust on her part. The woman left home for one night before the argument was resolved. Both partners affected | Resolved within one day | Grade 2 SH × 2 (marriage breakdown)<br>Grade 2 SH × 1 (verbal) |
| | | Coerced to test (man); Temporary separation | A pregnant woman took two HIVST kits and information leaflets home to her male partner, who refused to test. The couple argued, and the woman left home for one night. Both partners affected.<br>Woman withdrew from study before ACASI at 28 days | Resolved | Grade 2 SH × 2 (marriage breakdown)<br>Grade 2 SH × 1 (verbal) |
| STAR-GP Endline survey | SH in 4 (0.50%) of 794 self-testers | No severity grade/other details available | On interview of a random sample of 2581 adults living in clusters with CBDAs providing HIVST, 794 said that their last HIV test had been an HIV self-test. Of these, four agreed that "something bad happened" to them after self-testing | Not assessed | Not graded |

| Study | SHs: n/N (%) | Type of SH | Description | Outcome | Severity grade |
|---|---|---|---|---|---|
| B: Data collected through integrated social-harms community reporting systems (passive reporting) | | | | | |
| STAR-GP<br>Community reporting system during distribution of 9492 HIVST kits to 11 Evaluation Villages provided with community reporting system (CRS) | 6/9492 (0.063%) self-testers with ≥1 SH<br>Distributor training included module on discordancy | Temporary separation related to confirmed discordancy | A woman self-tested HIV positive, and took a kit for her husband, who self-tested negative. After confirmatory testing, the husband told the wife to leave their house. She reported this issue to the chief and religious leaders who were part of the SHs reporting system. The two were called to discuss the matter which was resolved within a month and the woman returned. Both partners affected | Resolved within a month | Grade 3 SH × 2 |
| | | Temporary separation related to confirmed discordancy | A woman who knew that she was HIV positive and was taking ART decided to use HIVST to disclose her status to her husband. She self-tested, showed her husband the used kit, and offered him a self-test kit to use himself. He initially refused, but then self-tested HIV negative. After confirmatory testing, the husband left the marriage, but the Community Health Worker talked to the husband and encouraged him to support his wife to resume ART. The couple came back together after one month. Both partners affected | Resolved after a month | Grade 3 SH × 2 |
| | | Temporary separation related to confirmed discordancy | A woman took two self-test kits for herself and her husband to test together. At first, the man was reluctant to test, but eventually agreed. He tested HIV positive and his wife was HIV negative. The woman threatened to end the marriage but agreed to seek help from their traditional marriage counsellor (*Nkhoswe*). The discordant HIV results have been confirmed. Both partners affected | Resolved after two months | Grade 3 SH × 2 |
| STAR-KP: FSWs<br>SHs reporting system included in peer distributor training | 1/2001 (0.050%) self-testers with ≥1 SH | Coerced to disclose | A FSW was forced to disclose her self-test result by her boyfriend. However, there were no long-term social or work-related consequences | Resolved | Grade 2 SH |
| | | Coerced to test (man), physical IPV (woman) and temporary separation (both) | A FSW had self-tested and wanted her regular partner to self-test. The partner felt pressurized and reacted violently, hitting the woman (details of severity unclear). The male partner walked out but returned to resume the relationship the following day. Both partners affected | Resolved | Grade 2 SH<br>Grade 3/2 SH (severity unclear)<br>Grade 2 SH × 2 |

**Table 5.** (*Continued*)

| Study | SHs: n/N (%) | Type of SH | Description | Outcome | Severity grade |
|---|---|---|---|---|---|
| C: SHs reported through other mechanisms (no integrated social-harms community reporting systems) | | | | | |
| STAR-GP<br>Reported to PSI during remainder of 137,915 HIVST kits delivered outside CRS | 1/120,000 (0.001%) self-testers with ≥1 SH episode from 120,000 HIVST kits distributed | Psychological distress; withdrawal from school; family relocation<br>Related to underage HIVST and non-disclose of perinatal HIV | A 12-year-old girl obtained a self-test kit, despite being under-age (minimum age of distribution under the STAR protocol is 16 years) and self-tested with friends. In this way, she found herself to be HIV positive.<br>Subsequent clinic counsellor interview showed that she had previously tested HIV positive (presumed mother-to-child transmission), but had never been made aware of this, and had never been treated.<br>The girl was shunned by her friends, left school, and the family relocated, leaving their property in their original village. She is now in a new school and has been started on ART with provision of additional post-test counselling provided by implementers and Ministry of Health personnel. Whole family affected | Partially resolved within a month (back in school)<br>Benefit: ART started | 3 SHs × 3 to girl:<br>Psychological distress<br>Stigmatization<br>Economic upheaval<br>Other family members:<br>likely multiple SHs, undocumented |
| STAR-KP: FSWs distributors<br>SHs reported during FGDs | No SHs.<br>3 SHs reported by 3 of 17 (17.6%) distributors | Physical assault of peer distributor | A FSW poured local beer (*Chibuku*) onto a peer distributor in reaction to a positive HIV self-test result | Resolved | Grade 2 SH |
| | | Verbal assault of peer distributor | A peer distributor was verbally assaulted by her neighbours for distributing self-test kits. The peer distributor felt sufficiently distressed to be unable to continue working | Unknown | Grade 2 SH |
| | | Verbal assault of peer distributor | A peer distributor was verbally insulted by her neighbours for distributing self-test kits, who said that she must be HIV positive to be doing this work. The peer distributor felt stressed and demoralized but continued working | Unknown | Grade 2 SH |

ACASI, Audio computer-assisted self interviews; SH, social harm; IPV, intimate partner violence; ART, antiretroviral therapy; HIVST, HIV self-testing; STAR-GP: Self-Test Africa Research – general population protocol; PASTAL, Partner Assisted HIVST and Linkage; CRS, community reporting systems; PSI, Population Services International; CRS, community reporting system; FSWs, female sex workers; FGD, focus group discussion; PRISM, Partnerships in Self-Testing in Malawi.



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further testing following a reactive self-test result is a key to ensure partners are properly supported. Updating and disseminating national guidance to appropriately address the needs for serodiscordant couples should be prioritized [11]. In this context, each of the three newly identified discordant couples who separated following HIVST and were provided with information and support under the community-led system of the STAR general population study recovered their relationship, whereas none of the three discordant couples who separated following standard HIV testing and counselling (HTC) in the control villages did so (Tables 2 and 5).

Although not captured in our matrix, SH reported by distributors also need to be anticipated, as many programmes will be reaching out to groups that experience stigma, discrimination and criminalization. We found that distributors delivering HIVST kits to FSWs experienced interpersonal violence, and stigmatizing and discriminatory attitudes. Programmes need to consider the context where they are implementing and identify ways to address these types of issues, and consider training distributors on techniques for avoiding and de-escalating conflict. Where feasible, community consultations should also be considered.

Monitoring SH is challenging, particularly for HIVST. Our findings suggest that community-led approaches are feasible, but subject to under-reporting. While intensive research methods identify more incidents, these approaches are not feasible for national programmes rolling-out HIVST. It will be important to share programmatic experiences to optimize and integrate SHs reporting into existing monitoring systems and to focus on methods that can be scaled-up. These approaches should also consider ways to identify and quantify social benefits, since this will help understand the broader social impact of HIVST at the individual and community levels.

Strengths of this study include the use of community-based reporting systems combined with in-depth qualitative and mixed methods to identify and understand SHs in the context of HIVST. Limitations include that our proposed harms grading system was developed iteratively, built on established pharmacovigilance methods to grade severity according to patient-centred criteria, and broadened from an initial focus on IPV and partnership dissolution. As such, data from earlier studies could not be completely mapped. Secondly, we do not have estimates of the numbers of newly identified serodiscordant couples who managed their relationship without separation, except for the smaller urban studies. To estimate the number of HIVST episodes, we used the total number of HIVST kits distributed as a proxy. Although we cannot define exact usage, participants receiving kits through community-based distributors were asked to return their used kits with a self-administered questionnaire. Use was confirmed by inspection of used kits for 75.7% of 27,789 distributed kits in HitTB (Study 1, Table 2) and 53.2% of 163,300 kits distributed under STAR-GP in Malawi [52] including 137,915 kits for which we report SHs (Studies 9 and 11, Table 2) [4,6,52]. Thus, while non-use of distributed kits will be contributing to underestimation of SHs, this has relatively little impact on our SH frequency-estimates reported here. For example, if true kit use was as low as 53%, then serious SH frequency would increase to 19/95,228 or 0.02%. Also, as return-and-reread of kits is not practical during routine implementation internationally recommendations are to report HIVST metrics based on kits distributed [53]. Finally, the studies presented here are from a single country, where background rates of IPV are high and the HIVST distribution models were primarily community-based and partner-delivered HIVST.

## 5 | CONCLUSIONS

Six years of large-scale HIVST implementation and in-depth investigation in Malawi identified no reported suicides and report of serious SHs to be rare. SH incidents reported mainly related to identification of serodiscordant HIV results within established relationships. Resolution tended to draw on existing structures, including community reporting. As access to HIVST increases, programmes need simple messages about both coercion and discordancy, urging restraint even when coercion is well-intentioned or "compassionate," and stressing the preventative benefits of treatment for serodiscordant couples.

Specific consideration must be given to HIVST programmes for FSW to make sure that distribution methods are safe and appropriate, and that clients or employers are not involved. It is also important that HIVST is available only to those who are of appropriate and legal age of consent to test. Continued efforts are needed to mitigate potential risks, optimize HIVST distribution and to monitor SHs and benefits following HIVST.

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### COMPETING INTERESTS

We have no competing interests to declare.

### AUTHORS' CONTRIBUTIONS

MK, CJ, ND and ELC drafted the manuscript with inputs from all authors. MT led the qualitative research network in STAR and contributed to the qualitative analysis. MK designed the PRISM study while ND and WL developed the ST-Impacts study. AC designed the PASTAL trial supported by MK and DS. ELC and PI led the research for STAR project in Malawi and were supported by WS and MK. KH and RC led the STAR implementation. All authors contributed to the final manuscript.

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## REFERENCES

1. UNAIDS. Global AIDS update 2018: miles to go: closing gaps, breaking barriers, righting injustices. Geneva: Joint United Nations Programme on HIV/AIDS; 2018.
2. Ministry of Health Malawi. Malawi Population-Based HIV Impact Assessment (MPHIA) 2015-2016: first report. Lilongwe, Malawi: Ministry of Health; 2017.
3. Baral S, Beyrer C, Muessig K, Poteat T, Wirtz AL, Decker MR, et al. Burden of HIV among female sex workers in low-income and middle-income countries: a systematic review and meta-analysis. Lancet Infect Dis. 2012;12(7):538–49.
4. Johnson CC, Kennedy C, Fonner V, Siegfried N, Figueroa C, Dalal S, et al. Examining the effects of HIV self-testing compared to standard HIV testing services: a systematic review and meta-analysis. J Int AIDS Soc. 2017;20(1):21594.
5. Choko A, Kumwenda M, Johnson C, Sakala D, Chikalipo M, Fielding K, et al. Acceptability of woman-delivered HIV self-testing to the male partner: a qualitative study of antenatal clinic-linked participants in Blantyre, Malawi. J Int AIDS Soc. 2017;20(1):21610.
6. Choko AT, MacPherson P, Webb EL, Willey BA, Feasy H, Sambakunsi R, et al. Uptake, accuracy, safety, and linkage into care over two years of promoting annual self-testing for HIV in Blantyre, Malawi: a community-based prospective study. PLoS Med. 2015;12(9):e1001873.
7. Sibanda E, Neuman M, Tumushime M, Hatzold K, Watadzaushe C, Mutseta M, et al. Linkage to care after HIV self-testing in Zimbabwe: a cluster-randomised trial. Conference on Opportunistic Infections and Retroviruses; 2018 March 3-8; Boston.
8. Indravudh P, Choko A, Corbett E. Scaling up HIV self-testing in sub-Saharan Africa: a review of technology, policy and evidence. Curr Opin HIV Res. 2018;31(1):4.
9. Choko AT, Corbett EL, Stallard N, Maheswaran H, Lepine A, Johnson CC, et al. HIV self-testing alone or with additional interventions, including financial incentives, and linkage to care or prevention among male partners of antenatal care clinic attendees in Malawi: an adaptive multi-arm, multi-stage cluster randomised trial. PLoS Med. 2019;1:e1002719.
10. WHO. Guidance on couples HIV testing and counselling – including antiretroviral therapy for treatment and prevention in serodiscordant couples: recommendations for a public health approach. Geneva: World Health Organization; 2012.
11. WHO. Guidelines on HIV self-testing and partner notification: a supplement to the consolidated guidelines on HIV testing services. Geneva: World Health Organization; 2016.
12. Obermeyer C, Neuman M, Desclaux A, Waynenze R, Ky-Zerbo O, Cherutich P, et al. Associations between mode of HIV testing and consent, confidentiality, and referral: a comparative analysis in four African countries. PLoS Med. 2012;9(10):e1001329.
13. WHO. Responding to intimate partner violence and sexual violence against women. Geneva: World Health Organization; 2013.
14. WHO. Guidance on couples HIV testing and counselling – including antiretroviral therapy for treatment and prevention in serodiscordant couples. Annex 11: concerns about intimate partner violence (IPV) following CHTC. Geneva: World Health Organization; 2012.
15. Kamya M, Wanyenze R, Namale A. Routine HIV testing: the right not to know versus the rights to care, treatment and prevention. Bull World Health Organ. 2007;85(5):B.
16. Baggaley R, Hensen B, Ajose O, Grabbe K, Wong V, Schilsky A, et al. From caution to urgency: the evolution of HIV testing and counselling in Africa. Bull World Health Organ. 2012;90(9):652-8B.
17. Van Der Straten A, Vernon KA, Knight KR, Gómez CA, Padian NS. Managing HIV among serodiscordant heterosexual couples: serostatus, stigma and sex. AIDS Care. 1998;10(5):533–48.
18. Beckerman NL, Letteney S, Lorber K. Key emotional issues for couples of mixed HIV status. Soc Work Health Care. 2000;31(4):25–41.
19. Ong JJ, Li H, Dan W, Fu H, Liu E, Ma W, et al. Coercion and HIV self-testing in men who have sex with men: implementation data from a cross-sectional survey in China. J Acquir Immune Defic Syndr. 2018;77(2):e22–5.
20. Indravudh PP, Sibanda EL, d'Elbee M, Kumwenda MK, Ringwald B, Maringwa G, et al. "I will choose when to test, where I want to test": investigating young people's preferences for HIV self-testing in Malawi and Zimbabwe. AIDS. 2017;31 Suppl 3:S203–12.
21. WHO. Global and regional estimates of violence against women: prevalence and health effects of intimate partner violence and non-partner sexual violence. Geneva: World Health Organization; 2013.
22. WHO. Consolidated guidelines on HIV prevention, diagnosis, treatment and care for key populations. Geneva: World Health Organization; 2014.
23. Mutseta M. Impact of HIVST on uptake of HIV testing among unreached populations and those living with undiagnosed HIV: experiences from the STAR project in Malawi, Zambia and Zimbabwe. 9th International AIDS Conference; 2017 July 23-26; Paris, France.
24. Brown A, Djimeu E, Cameron D. A review of the evidence of harm from self-tests. AIDS Behav. 2014;18 Suppl 4:S445–9.
25. Kumwenda M, Munthali A, Phiri M, Mwale D, Gutteberg T, MacPherson E, et al. Factors shaping initial decision-making to self-test amongst cohabiting couples in urban Blantyre, Malawi. AIDS Behav. 2014;18 Suppl 4:S396–404.
26. Moran-Ellis J, Alexander VD, Cronin A, Dickinson M, Fielding J, Sleney J, et al. Triangulation and integration: processes, claims and implications. Qual Res. 2006;6(1):45–59.
27. O'Cathain A, Murphy E, Nicholl J. Three techniques for integrating data in mixed methods studies. BMJ. 2010;341:c4587.
28. 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.
29. Desmond N, Nagelkerke N, Lora W, Chipeta E, Sambo M, Kumwenda M, et al. Measuring sexual behaviour in Malawi: a triangulation of three data collection instruments. BMC Pub Heal. 2018;18(1):807.
30. Choko AT, Fielding K, Stallard N, Maheswaran H, Lepine A, Desmond N, et al. Investigating interventions to increase uptake of HIV testing and linkage into care or prevention for male partners of pregnant women in antenatal clinics in Blantyre, Malawi: study protocol for a cluster randomised trial. Trials. 2017;18(1):349.
31. DAIDS, NIAID, NIH, HSS. Division of AIDS (DAIDS) table for grading the severity of adult and pediatric adverse events, version 2.0. Rockville, Maryland: Division of AIDS (DAIDS); 2017.
32. Neuman M, Indravudh P, Chilongosi R, d'Elbée M, Desmond N, Fielding K, et al. The effectiveness and cost-effectiveness of community-based lay distribution of HIV self-tests in increasing uptake of HIV testing among adults in rural Malawi and rural and peri-urban Zambia: protocol for STAR (self-testing for Africa) cluster randomized evaluations. BMC Pub Heal. 2018;18(1):1234.
33. STAR Initiative. Monitoring social harms following peer-led delivery of HIV self-testing to key populations in Malawi. 2016 [cited 2019 Jan 23]. Available from: http://hivstar.lshtm.ac.uk/files/2016/11/STAR-Malawi-Key-Population-LSHTM-V2.0-1.pdf
34. Masters SH, Agot K, Obonyo B, Napierala Mavedzenge S, Maman S, Thirumurthy H. Promoting partner testing and couples testing through secondary distribution of HIV self-tests: a randomized clinical trial. PLoS Med. 2016;13(11):e1002166.
35. Hazell L, Shakir SA. Under-reporting of adverse drug reactions: a systematic review. Drug Saf. 2006;29(5):385–96.
36. Were E, Curran K, Delany-Moretlwe S, Nakku-Joloba E, Mugo NR, Kiarie J, et al. A prospective study of frequency and correlates of intimate partner violence among African heterosexual HIV serodiscordant couples. AIDS. 2011;25(16):2009–18.
37. Mackelprang RD, Bosire R, Guthrie BL, Choi RY, Liu A, Gatuguta A, et al. High rates of relationship dissolution among heterosexual HIV-serodiscordant couples in Kenya. AIDS Behav. 2014;18(1):189–93.
38. Medley A, Garcia-Moreno C, McGill S, Maman S. Rates, barriers and outcomes of HIV serostatus disclosure among women in developing countries: implications for prevention of mother-to-child transmission programmes. Bull World Health Organ. 2004;82(4):299–307.
39. Ong JJ, Wu D, Huang W, Fu H, Desmond N, Ma W, et al. Pressured HIV testing "in the name of love": a mixed methods analysis of pressured HIV testing among men who have sex with men in China. J Int AIDS Soc. 2018;21(3):e25098.
40. WHO, UNAIDS. Statement on HIV testing and counseling: WHO, UNAIDS re-affirm opposition to mandatory HIV testing. Geneva: World Health Organization; 2012.
41. Chanda MM, Ortblad KF, Mwale M, Chongo S, Kanchele C, Kamungoma N, et al. HIV self-testing among female sex workers in Zambia: a cluster randomized controlled trial. PLoS Med. 2017;14(11):e1002442.
42. Ortblad K, Kibuuka M, Ngabirano T, Nakitende A, Magoola J, Kayiira P, et al. Direct provision versus facility collection of HIV self-tests among female sex workers in Uganda: a cluster-randomized controlled health systems trial. PLoS Med. 2017;11:e1002458.
43. 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. Lancet HIV. 2016;3(6):e266–74.

44. WHO, UNFPA, UNAIDS, NSWP, World Bank. Implementing comprehensive HIV/STI programmes with sex workers: practical approaches from collaborative interventions. Geneva: World Health Organization; 2013.
45. Bellan SE, Fiorella KJ, Melesse DY, Getz WM, Williams BG, Dushoff J. Extra-couple HIV transmission in sub-Saharan Africa: a mathematical modelling study of survey data. Lancet. 2013;381(9877):1561–9.
46. Kennedy CE, Haberlen S, Amin A, Baggaley R, Narasimhan M. Safer disclosure of HIV serostatus for women living with HIV who experience or fear violence: a systematic review. J Int AIDS Soc. 2015;18 Suppl 5:20292.
47. Gichangi A, Wambua J, Gohole A, Mutwiwa S, Njogu R, Bazant E, et al. Impact of HIV self-test distribution to male partners of ANC clients: results of a randomized controlled trial in Kenya. J Acquir Immune Defic Syndr. 2018;79 (4):467–73.
48. Celum C, Baeten JM. Serodiscordancy and HIV prevention in sub-Saharan Africa. Lancet. 2013;381(9877):1519–21.
49. Kumwenda MK, Corbett EL, Chikovore J, Phiri M, Mwale D, Choko AT, et al. Discordance, disclosure and normative gender roles: barriers to couple testing within a community-level HIV self-testing intervention in urban Blantyre, Malawi. AIDS Behav. 2018;22(8):2491–9.
50. Maeri I, El Ayadi A, Getahun M, Charlebois E, Akatukwasa C, Tumwebaze D, et al. "How can I tell?" Consequences of HIV status disclosure among couples in eastern African communities in the context of an ongoing HIV "test-and-treat" trial. AIDS Care. 2016;28 Suppl 3:59–66.
51. Colombini M, James C, Ndwiga C, Mayhew SH. The risks of partner violence following HIV status disclosure, and health service responses: narratives of women attending reproductive health services in Kenya. J Int AIDS Soc. 2016;19(1):20766.
52. Hatzold K, Gudukeya S, Mutseta M, Chilongosi R, Nalubamba M, Nkhoma C, et al. HIV self-testing: breaking the barriers to uptake of testing among men and adolescents in sub-Saharan Africa, experiences from STAR demonstration projects in Malawi, Zambia and Zimbabwe. J Int AIDS Soc. 2019;22(S1):e25244.
53. WHO. HIV self-testing framework: a guide for planning, introducing and scaling up. Geneva: World Health Organization; 2018.
54. Indravudh P, Fielding K, Neuman M, Chilongosi R, Mkandawire P, Nyondo E, et al. Increasing knowledge of HIV status and demand for ART using community-based HIV self-testing in rural communities: a cluster randomised trial in Malawi. 22nd International AIDS Conference; 2018 July 23-27; Amsterdam, The Netherlands.

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VIEWPOINT

# Challenges in measurement of linkage following HIV self-testing: examples from the STAR Project

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Knowledge of HIV status through HIV testing constitutes the first step towards HIV treatment and prevention services. HIV self-testing (HIVST), whereby individuals collect their own specimen, conduct their own test and interpret the results, allows individuals to learn their HIV status conveniently and privately, as well as to decide when and where to attend post-test services. Accurate estimation of the proportion of those tested who link to additional HIV care, treatment and prevention services is critical in quantifying the health impact of HIV testing. As HIVST becomes integrated into testing programmes worldwide, implementers in diverse settings will need to measure the effectiveness of their programmes to ensure self-testers link to onward care and services. This can be challenging, and community health programmes in many contexts find it difficult to track referral uptake and equity [1].

We draw upon experience from the Self-Testing in AfRica (STAR) Initiative in 2015 to 2017 to identify three lessons for measurement of linkage following HIVST. In STAR, two pragmatic cluster-randomized trials evaluated the effectiveness of continuous HIVST distribution over 12 months in increasing testing coverage and linkage to care in Malawi and Zambia. A third trial, in Zimbabwe, evaluated the effectiveness of an incentive to promote linkage following a short, campaign-style HIVST distribution programme, and included a non-randomized component assessing the association between HIVST distribution and antiretroviral therapy (ART) initiations in nearby clinics. Details are provided elsewhere [2,3]. Each trial incorporated a household survey and data collection from health facilities to evaluate changes in HIV testing coverage and linkage to confirmatory testing, care and prevention (Table 1).

## LESSON 1. COLLECT USAGE INFORMATION FROM USERS, NOT JUST FROM DISTRIBUTORS AND CLINICS

User household surveys and qualitative research are typically more time-consuming to collect than routine data from distributors and clinics. However, this type of data is vital for understanding how self-tests are being used. For example, in Zimbabwe, 289 survey respondents reported a reactive HIVST, of whom 216 (75%) were already on ART [2]. Formative qualitative work indicated that individuals already known to be positive self-tested in trial communities to avoid inadvertent disclosure, to confirm their status or check for cure. Without accounting for unintended use of HIVST by persons already diagnosed and linked into HIV care, the number of HIVSTs used by undiagnosed individuals will be overestimated, and both linkage and cost-effectiveness measures are likely to be overestimated.

## LESSON 2. THE QUALITY OF LINKAGE MEASURES USING CLINIC DATA DEPEND NOT ONLY ON THE QUALITY OF CLINIC DATA, BUT ALSO ON THE SELF-TESTING DISTRIBUTION MODEL AND LOCAL CONTEXT

In two STAR trials, we had contrasting findings about the effectiveness of self-test distribution on increasing ART initiations at local clinics, measured by routine clinic data. In Malawi, clinics in areas with self-test distribution had a 14% increase in ART initiations compared with clinics in areas without HIVST distribution (adjusted risk ratio (aRR) = 1.14; 95% CI: 0.75 to 1.75) [4], but the wide confidence intervals suggest limited statistical evidence for effectiveness. In contrast, the study in Zimbabwe showed a somewhat larger increase in local ART initiations in areas with HIVST distribution with stronger evidence for effectiveness (aRR=1.27; 95% CI: 1.14 to 1.43) [5].

These studies used different designs, and the trial in Zimbabwe had more clusters receiving HIVST distribution and more power to detect differences. However, we believe these estimates may also have been driven by the context and the duration of distribution. Universal test-and-treat interventions,

**Table 1. STAR initiative trials and confirmatory testing and linkage to care and prevention measurements**

| Trial location | Trial research questions | Primary and secondary trial outcomes | Household survey linkage questions | Clinic data linkage measures |
|---|---|---|---|---|
| Malawi [10] | What is the impact of community-based HIVST distribution over 12 months on HIV testing and ART initiation? | **Primary:** HIV testing within 12 months of start of HIVST distribution<br>**Secondary:** Lifetime HIV testing, ART initiation | **Confirmatory testing and HIV care:**<br>After each of last three HIV tests, if test was reactive:<br>• After this HIV test, did you receive a test confirming your HIV diagnosis or additional care related to your HIV status?<br>• If yes, what care did you receive?<br>o Follow-up test to confirm results of this test<br>o Start ART for the first time<br>o Restarted on ART<br>o Other care (not including either confirmatory test or ART)<br>**VMMC:** After each of last three HIV tests, if test was non-reactive or no result reported, and respondent was male: Did you go for VMMC after this test? | During 12 months of HIVST distribution:<br>• ART initiations and HTS by month for 12 months using clinic data<br>• ART initiations among clients reporting HIVST use<br>• Zambia study also collected data on HTS by month. |
| Zambia [11] | What is the impact of the community-based distribution of HIVST over 12 months on recent HIV testing? | **Primary**: HIV testing within 12 months prior to endline survey<br>**Secondary**: Lifetime HIV testing, ART initiation, ART retention, uptake of VMMC services among men | | |
| Zimbabwe [12] | Do financial incentives for distributors in two-month HIVST campaigns improve timely linkage among clients?<br>Do community-based HIVST campaigns increased facility-based ART initiation? | **Primary**: Attendance at any care service<br>**Secondary**: Self-test uptake, uptake of PSI outreach services, uptake of VMMC among men, uptake of confirmatory testing among respondents with reactive HIVST, uptake of ART among respondents with reactive HIVST, uptake of self-tests among people on ART | **Confirmatory testing:** Did you have an HIV test in order to confirm the results you obtained during self-testing?<br>**HIV care and VMMC**: Since about six weeks ago (when community-based distributors came to your area to distribute self-test kits), have you been to a clinic or HIV testing facility for any service that you wanted for yourself? If yes, what services did you seek?<br>• HIV counselling and testing<br>• Treatment for an ailment I was suffering from<br>• Filling of my regular prescription/completing my regular medical check-up<br>• HIV counselling only<br>• CD4 testing<br>• Family planning services<br>• TB screening<br>• Blood pressure checks<br>• Cervical cancer screening<br>• Voluntary medical male circumcision<br>Biomarkers for measuring HIV status, viral load, recency of infection and ART use collected | Count of ART initiations per clinic data at government clinics in districts where HIVST occurred, including data from six months prior to distribution campaign and three months after distribution campaign |

ART, antiretroviral therapy; HIVST, HIV self-testing; HTS, HIV testing services; PSI, Population Services International; VMMC, voluntary medical male circumcision.

including the HPTN 071 (PopART) and ANRS 12249 trials, have found that linkage to care remains low even after substantial efforts supporting testing and linkage. This suggests that it is necessary to consider how contextual factors apart from the availability of HIV testing services impact linkage to care [6,7]. The Zimbabwe study used a shorter, campaign approach to distributing HIVST and the implementing organization (Population Services International) had initiatives facilitating linkage-to-care across the study area. In contrast, distribution in Malawi was continuous over 12 months, with linkage more diffuse across an extended period. It is likely easier to detect increased linkage at facilities if HIVST kits are distributed in short concentrated periods and in contexts where linkage after testing is relatively easy for users. For programmes working in areas or in populations where linkage is difficult, or for those distributing HIVST over an extended period, alternative methods of measuring linkage may provide more power to detect effects.

## LESSON 3. MEASURE BOTH LINKAGE TO TREATMENT AND TO PREVENTION

Increasing the availability and uptake of HIV prevention services is increasingly recognized as necessary for reducing HIV incidence rates [8]. As testing and treatment expand, the number of new diagnoses identified by testing programmes is likely to decrease, and consequently, the denominators of linkage-to-care measures will shrink. Expanding to include linkage-to-prevention of persons not infected with HIV will increase power to detect impacts of HIVST on population health.

In the STAR trials described above, linkage to prevention was a consideration, but not the focus. For example, in Zambia, voluntary medical male circumcision (VMMC) mobilizers affiliated with HIVST intervention clinics received HIVST kits to distribute to clients. However, only four of the six intervention clinics had affiliated VMMC mobilizers and the proportion of test kits distributed within each area by VMMC mobilizers was low overall (<1% to 11% across areas). There was a positive association between the intervention and self-reported VMMC uptake, but this was not statistically significant (aRR: 1.36; 95% CI: 0.49 to 3.78) [5]. With collaborators, STAR is now undertaking trials to assess whether HIVST can be used to generate demand for prevention services, including pre-exposure prophylaxis (PrEP) among adolescent girls and young women in KwaZulu-Natal, South Africa [9] and VMMC among men in urban Zimbabwe.

To summarize, defining and estimating linkage following HIVST is complex, and there is no single measurement strategy that will fit the needs of all HIVST implementers. Researchers and implementers must account for contextual factors that may affect users' likelihood of linking and the amount of time required to link when developing strategies to measure linkage following HIVST. In STAR studies, it was difficult to anticipate who would use HIVST, and where and when self-testers would link to care. Where possible, collecting data on users' self-testing and linkage experiences can provide valuable insight.

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### COMPETING INTERESTS

The authors have no competing interests.

### AUTHORS' CONTRIBUTIONS

MN, HAW and KF conceptualized the paper. MN wrote the first draft. All authors provided comments on the paper.

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### REFERENCES

1. McCollum R, Gomez W, Theobald S, Taegtmeyer M. How equitable are community health worker programmes and which programme features influence equity of community health worker services? A systematic review. BMC Public Health. 2016;16:419.
2. Sibanda E, Neuman M, Tumushime M, Hatzold K, Watadzaushe C, Mutseta M, et al. Linkage to care after HIV self-testing in Zimbabwe: a cluster-randomized trial. Conference on Retroviruses and Opportunistic Infections. Boston, MA; 2018.
3. Neuman M, Indravudh P, Chilongosi R, d'Elbee M, Desmond N, Fielding K, et al. The effectiveness and cost-effectiveness of community-based lay distribution of HIV self-tests in increasing uptake of HIV testing among adults in rural Malawi and rural and peri-urban Zambia: protocol for STAR (Self-Testing for AfRica) cluster randomized evaluations. BMC Public Health. 2018;18:1234.
4. Indravudh P, Fielding K, Neuman M, Chilongosi R, Mkandawire P, Nyondo E, et al. Increasing knowledge of HIV status and demand for ART using community-based HIV self-testing: a cluster randomised trial in rural Malawi. Paper presented at AIDS 2018, Amsterdam, Netherlands, 23-27 July 2018. http://programme.aids2018.org/Abstract/Abstract/7310.
5. Tsamwa D, Handima N, Sigande L, Nalubamba M, Simwinga M, Mwinga A, et al. Does community-based distribution of HIV self-test kits increase uptake of HIV testing at population level? Results of a cluster-randomised trial in Zambia. HIVR4P; 2018.
6. Hayes R, Floyd S, Schaap A, Shanaube K, Bock P, Sabapathy K, et al. A universal testing and treatment intervention to improve HIV control: one-year results from intervention communities in Zambia in the HPTN 071 (PopART) cluster-randomised trial. PLoS Med. 2017;14(5):e1002292.
7. Iwuji CC, Orne-Gliemann J, Larmarange J, Balestre E, Thiebaut R, Tanser F, et al. Universal test and treat and the HIV epidemic in rural South Africa: a phase 4, open-label, community cluster randomised trial. Lancet HIV. 2018;5(3):e116–25.
8. Isbell MT, Kilonzo N, Mugurungi O, Bekker L-G. We neglect primary HIV prevention at our peril. Lancet HIV. 2016;3(7):e284–5.
9. Corbett EL, Shahmanesh M, Seeley J, Baisley K, Pillay D, Koole O. Peer delivery of HIV self-screening to support linkage to HIV prevention in rural KwaZulu-Natal, South Africa: a Cluster Randomised Control Trial (cRCT) (study protocol). 2018.
10. Desmond N, Corbett EL, Gibson S, Indravudh P, Lora W, Mkandawire P, et al. A cluster randomised trial of providing HIV self-testing kits through community-based distribution agents (study protocol). 2017.
11. Ayles H, Bond V, Chintu N, Handima N, Kapaku K, Maluzi K, et al. Self-testing for HIV (HIVST) amongst urban, peri-urban and rural communities in Zambia, including a cluster-randomised trial of community-based HIVST distribution (study protocol). 2017.
12. Corbett EL, Cowan F. A cluster randomised trial of interventions to improve linkage to care following community-based distribution of HIV self-test kits in rural Zimbabwean communities (study protocol). 2017.

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RESEARCH ARTICLE

# Economic cost analysis of door-to-door community-based distribution of HIV self-test kits in Malawi, Zambia and Zimbabwe

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## Abstract

**Introduction:** HIV self-testing (HIVST) is recommended by the World Health Organization in addition to other testing modalities to increase uptake of HIV testing, particularly among harder-to-reach populations. This study provides the first empirical evidence of the costs of door-to-door community-based HIVST distribution in Malawi, Zambia and Zimbabwe.

**Methods:** HIVST kits were distributed door-to-door in 71 sites across Malawi, Zambia and Zimbabwe from June 2016 to May 2017. Programme expenditures, supplemented by on-site observation and monitoring and evaluation data were used to estimate total economic and unit costs of HIVST distribution, by input and site. Inputs were categorized into start-up, capital and recurrent costs. Sensitivity and scenario analyses were performed to assess the impact of key parameters on unit costs.

**Results:** In total, 152,671, 103,589 and 93,459 HIVST kits were distributed in Malawi, Zambia and Zimbabwe over 12, 11 and 10 months respectively. Across these countries, 43% to 51% of HIVST kits were distributed to men. The average cost per HIVST kit distributed was US$8.15, US$16.42 and US$13.84 in Malawi, Zambia and Zimbabwe, respectively, with pronounced intersite variation within countries driven largely by site-level fixed costs. Site-level recurrent costs were 70% to 92% of full costs and 20% to 62% higher than routine HIV testing services (HTS) costs. Personnel costs contributed from 26% to 52% of total costs across countries reflecting differences in remuneration approaches and country GDP.

**Conclusions:** These early door-to-door community HIVST distribution programmes show large potential, both for reaching untested populations and for substantial economies of scale as HIVST programmes scale-up and mature. From a societal perspective, the costs of HIVST appear similar to conventional HTS, with the higher providers' costs substantially offsetting user costs. Future approaches to minimizing cost and/or maximize testing coverage could include unpaid door-to-door community-led distribution to reach end-users and integrating HIVST into routine clinical services via direct or secondary distribution strategies with lower fixed costs.

**Keywords:** HIV self-testing; costs and cost analysis; community; Malawi; Zambia; Zimbabwe

Additional Supporting Information may be found online in the Supporting information tab for this article.

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## 1 | INTRODUCTION

In East and Southern Africa, freely available HIV services have led to a 42% reduction in AIDS-related deaths between 2010 and 2016. Despite such gains, 24% of people living with HIV (PLWH) remain undiagnosed [1]. UNAIDS has set global targets for 90% of PLWH to know their status, 90% of known HIV-positive individuals, to be on ART and 90% of those on antiretroviral therapy (ART) to have their viral load suppressed by 2020 [2]. To surpass and sustain high levels of awareness of HIV status, greater efforts are needed to ensure that HIV testing reaches those individuals who have not yet been tested for HIV. This, however, is likely to require more significant financial investments, innovative approaches and new technologies, including HIV self-testing (HIVST).

HIVST is defined as a process where a person collects his/her own specimen (oral fluid or blood) and then performs an HIV test and interprets the result, often in a private setting,

**Table 1. Key setting characteristics**

| | Malawi | Zambia | Zimbabwe | Source |
|---|---|---|---|---|
| National HIV prevalence among adults 15 to 59 years (%) | 10.0 | 12.0 | 14.6 | [8–10] |
| Number of districts | 4 | 4 | 8 | [11] |
| Number of sites | 11 | 16 | 44 | [11] |
| Catchment population of sites: mean (range) | 27,439 (5500 to 82,581) | 18,266 (7673 to 50,094) | 3196 (549 to 6699) | [11] |
| Location: rural (urban or peri-urban) | 11 (0) | 16 (8) | 44 (0) | [11] |
| Scale of current HTS – based on facility HTS in same communities and period | 16,921 | 27,888 | 44,727 | [16] |
| Men attendance at HTS – based on facility HTS – % men | 34 | 37 | 26 | [8–10] |
| Health facility HTS cost per person tested in US$: mean (range) | $5.03 ($2.96 to $9.24) | $4.24 ($2.49 to $6.24) | $8.79 ($3.38 to $21.51) | [16] |

HTS, HIV testing services.

either alone or with someone they trust. The World Health Organization recommends HIVST to reach the "at risk" and "untested" populations including men as a complement to current conventional testing approaches, including facility-based and targeted community outreach-based testing [1,3-5]. The cost of HIVST kits has declined in some settings, with the OraQuick® HIV self-test now costing US$2 per kit in 50 low- and middle-income countries [6]. However, at US$2, it is around twice the price of standard HIV rapid diagnostic tests currently used for HIV testing in Africa [7]. Although HIVST kit price may be higher, impact analyses show that it can have an important public health benefit and offer value for money if implemented as a complement to current testing approaches [4,5].

The HIV Self-Testing AfRica (STAR) project has delivered over one million HIVST kits in Malawi, Zambia and Zimbabwe between 2016 and 2017 through a combination of distribution approaches, including facility-based distribution at outpatient departments, within voluntary medical male circumcision (VMMC) services and in the community. This study presents the costs of the model that uses community-based distribution agents (CBDAs) to deliver HIVST either at people's homes or within the community setting, hereafter "the CBDA model," to generate evidence to inform the scale-up of cost-effective HIV testing services (HTS).

## 2 | METHODS

### 2.1 | Setting, intervention and evaluation

Table 1 presents key setting characteristics across countries. In short, the adult HIV prevalence rates in Malawi, Zambia and Zimbabwe were approximately 10.0%, 12.0% and 14.6% respectively [8-10]. While Malawi and Zimbabwe CBDA model sites were exclusively rural, a third of Zambia sites were peri-urban or urban. Malawian and Zambian distribution sites were fewer and each served large populations, while Zimbabwe delivered kits to a larger number of smaller communities. This difference in site size is also reflected in the unit costs of conventional facility-based testing, with higher costs in the smaller facilities in Zimbabwe. It is also notable that men contribute only 26% to 37% of HTS clients in these facilities.

In the CBDA model, all individuals aged ≥16 years who were present in the homestead at the time of CBDAs' home visit were eligible for self-testing. Testing was done by the self-tester themselves after kit use demonstration and information on test result interpretation and linkage to follow-on care by the CBDAs. CBDAs provided a self-referral card to all testers to facilitate linkage to the local health facility for confirmatory testing and care for individuals with reactive HIVST results. In some cases, CBDAs were present during the self-test to provide reassurance and support if testers requested their presence or assistance. Table 2 presents the characteristics of the CBDA model implemented across countries. Narrative descriptions of the models can be found in Data S1. The impact of the CBDA model on uptake of HIV testing and ART is being evaluated in three cluster-randomized trials (CRTs). Detailed methodology of these CRTs is published elsewhere [11].

### 2.2 | Costing methods

We estimated the full economic cost of delivering HIVST within the CBDA model from the providers perspective, following international costing guidelines [12]. This included start-up and training costs, prior to the first HIVST kit distributed. Annual costs were estimated, with implementation costs collected between June 2016 and May 2017, depending on country implementation timelines. Start-up, training and all other capital costs were annualized using a 3% discount rate. All costs were converted to 2017 US dollars using average annual exchange rates and the dollar inflation rate [13-15].

This top-down costing collated all financial expenditures and categorized each line item by input type and distribution model. Inputs were allocated to distribution sites following predefined allocation factors, based on project monitoring and evaluation (M&E) data, including the percentage of kits distributed, percentage of distributors based in each site, distance from central office and percentage of direct expenditures, which is a weighted average of the preceding

**Table 2. Overview of door-to-door community-based HIVST delivery models**

| | Malawi | Zambia | Zimbabwe |
|---|---|---|---|
| Type of cadre used for distribution of HIVST kits | • Trained CBDAs<br>• Some with prior experience distributing other reproductive health products for PSI | • Trained facility and CBDAs<br>• Recruited from communities with prior links to respective health facilities | • Trained CBDAs<br>• Information on HIVST and linkage to post-test services |
| Mode of distribution | • Door-to-door community-based distribution<br>• PSI field teams-maintained stocks | • Door-to-door distribution by CBDA's within communities and households<br>• Facility-based distributors-maintained stocks for CBDAs | • Campaign-style door-to-door community distribution to households for four to six weeks<br>• PSI field teams-maintained stocks |
| Services offered to HIV self-test clients | • Introduction and demonstration of HIVST kit use (including interpretation of results)<br>• CBDAs typically revisited clients a few days after dropping off the kit to:<br>o enquire whether it had been used,<br>o pick up the used kit<br>o disclosed non-reactive HIVST: referral to VMMC<br>o disclosed reactive HIVST: referral to linkage to HIV care | • Introduction and demonstration of HIVST kit use (including interpretation of results)<br>• CBDAs typically revisited clients a few days after dropping off the kit to:<br>o enquire whether it had been used<br>o pick up the used kit<br>o disclosed non-reactive HIVST: referral to VMMC<br>o disclosed reactive HIVST: referral to linkage to HIV care | • Introduction and demonstration of HIVST kit use (including interpretation of results)<br>• Follow-on services by PSI-Zimbabwe mobile outreach teams at one to two weeks post HIVST kit distribution<br>o confirmatory HTS plus<br>o family planning<br>o blood pressure checks and CD4 count when available<br>o clients alerted to linkages to government health facilities |
| Used HIVST kit returns | • Specially designed and locked drop-boxes to return used self-test kits located:<br>o at all intervention sites | • Specially designed and locked drop-boxes were used to return used self-test kits, located:<br>o at each facility and<br>o local community public areas | • Specially designed and locked drop-boxes, located:<br>o at CBDA's homestead<br>o each health facility<br>o local community public areas |
| CBDA reimbursement | • Per HIVST kit distributed US$0.15 (MWK 100) | • Monthly US$78 (ZMW 750) independent of performance.Later changed to:<br>• Per HIVST distributed US$0.52 (ZMW 5) and per used HIVST kit returned US$0.21 (ZMW 2) | • Per ward campaign (four to six weeks) US$50 with a maximum of 100 kits per distributor<br>• Per HIVST client linking to any PSI outreach service: $0.20 in half of the evaluation clusters |

HIVST, HIV self-testing; CBDA, community-based distribution agent; PSI, Population Services International; MWK, Malawi Kwacha; ZMW, Zambian Kwacha.

allocation factors. Table S1 presents how each allocation factor was applied to input type. Further detail of the definitions of project phase and inputs can be found in Data S2.

To estimate economic costs, the expenditure analysis was complemented by a valuation of all other resources used in the CBDA model. Observations of distribution in each site strengthened the economists' understanding of the intervention and allowed for collection of data on donated goods and services. As a vertical model, these were relatively limited, and include a value for district or health facility storage contributed by the public health system. During the life of the project, the price of HIVST kits dropped from nearly $4 per kit to $2 per kit. The latter was imputed in place of the higher observed prices as it was considered the relevant kit price for any decision-making building upon this analysis. Total costs, total kits distributed and average cost per kit distributed were estimated at the country level, and for each country, at the site level. The latter provides a range of average costs by site and allows for identification of economies of scale.

## 2.3 | Sensitivity analysis

We undertook a series of one-way sensitivity analyses to assess the impact of key cost assumptions on the unit cost

per HIVST kit distributed. We varied the discount rate used to annualize costs from the base case of 3% to 0% and 15% to capture the impact of not discounting or using a higher local central bank discount rate. Prevailing discount rates during the study period were 15% in Malawi, 12.5% in Zambia and 7% in Zimbabwe [13-15]. We further evaluated the impact of applying alternative allocation factors that is swapping % of kits distributed and % of CBDAs per site. We varied annualization (economic life years) time frames: training & sensitization was varied between one and three years (base case is two years) and project start-up life between 2.5 and 7.5 years (base case is five years) to assess impact if the project goes on for shorter or longer than assumed.

### 2.4 | Scenario analysis

In anticipation of planned programme scale-up by respective country ministries of health, we conducted scenario analysis varying salaries ±10% to assess the impact of integration into public health services, and variation in kit distribution by ±10%. We also modelled the impact of HIVST kit price between the observed average kit price (US$3.40), a recent Bill and Melinda Gates Foundation subsidized price (US$2) and a hypothetical price approximately equal to current rapid finger prick test price (US $1) [16]. Finally, we estimated a best- and worst-case scenario, the point where all the parameters yield the lowest/highest unit cost per kit distributed. To generate estimates that are comparable with the costs of ongoing facility HTS in the same communities in Malawi, Zambia and Zimbabwe [16], we also present costs without above site-level costs and start-up.

### 2.5 | Ethics

The study did not involve patient-level data collection; we did, however, obtain permission from ministries of health in the three countries to collate data from administrative, M&E records at facility level for cost allocation. Ethical approvals for the parent study were obtained from the Medical Research Council of Zimbabwe, Malawi College of Medicine Research Ethics Committee, University of Zambia Biomedical Research Ethics Committee, London School of Hygiene and Tropical Medicine Ethics Committee and University College London Ethics Committee. The trials are registered under the Clinical Trials Network (ClinicalTrials.gov) under registration numbers NCT02793804; NCT02718274; Pan African clinical trials registry PACTR201607001701788 for Malawi, Zambia and Zimbabwe.

## 3 | RESULTS

### 3.1 | Community-based distribution model programme outcomes

During the costing period, 152,671, 103,589 and 93,459 HIVST kits were distributed in Malawi, Zambia and Zimbabwe against the approximate targets of 62,500, 416,294 and 224,116 through a total of 138, 139 and 1009 CBDAs respectively. The average number of HIVST kits distributed was 12,538 (range: 4556 to 42,134) across 11 sites in Malawi, 7206 (range: 1758 to 20,450) across 16 sites in Zambia and 2124 (range: 319 to 4201) across 44 sites in Zimbabwe, where distribution was intentionally restricted by campaign duration (Table S2). Nearly half (49%, 51% and 43%, respectively) of the HIVST kits were distributed to men.

### 3.2 | Total HIVST costs and cost composition

Table 3 summarizes the findings of the cost analysis. The total distribution costs were calculated as US$1,243,940.66, US $1,700,730.45 and US$1,293,135.00 in Malawi, Zambia and Zimbabwe respectively. Capital costs accounted for 3%, 4% and 2% of the total costs with start-up costs accounting for 15%, 10% and 6% in Malawi, Zambia and Zimbabwe respectively. Within recurrent costs, personnel costs accounted for a significant portion of total costs, at 26%, 52% and 42% of costs in Malawi, Zambia and Zimbabwe respectively. Although the price of kits was centrally negotiated and thus the same across countries, kits contributed to the largest portion of total costs in Malawi (34%) and the second largest proportion in both Zambia and Zimbabwe (14% and 17% respectively).

### 3.3 | Unit costs

The country-level costs per HIVST kit distributed were US$8.15 for Malawi, US$16.42 for Zambia and US$13.84 in Zimbabwe. The cost per HIVST kit distributed across the sites ranged from US$7.20 to US$17.04 in Malawi, US$7.90 to U$50.00 in Zambia and from US$10.19 to US$54.44 in Zimbabwe. Figure 1 shows the unit cost per HIVST kit distributed plotted against the scale of HIVST kits across the three countries. Unit costs were generally lower at sites that were distributing a larger number of self-test kits, suggesting a spreading of fixed costs across variable numbers of kits. When above site-level and start-up costs are removed our estimates were comparable to the facility HTS unit costs estimated in the same communities [16]: US$6.67, US $10.42 and US$10.18 for the CBDA model, compared with facility HTS unit costs of $5.03 ($2.96 to $9.24), $4.24 ($2.49 to $6.24) and $8.79 ($3.38 to $21.51) in Malawi, Zambia and Zimbabwe respectively.

### 3.4 | Sensitivity and scenario analysis

Figures 2a,b,c show results from the univariate sensitivity and scenario analyses by country. Our unit costs per HIVST kit distributed remained robust when key cost parameters were varied. Varying life of start-up training and sensitization between one and three years resulted in costs of US$7.85 and US $16.42 versus US$9.07 and US$15.05 in Malawi and Zambia respectively. For Zimbabwe, however, there was no change to the base case cost of US$13.84 as training and sensitization costs were classified as recurrent due to the sequential and short-term nature of distribution across the eight districts, requiring training of CBDA who distribute for just four to six weeks. Varying life of start-up life or development phase between 2.5 and 7.5 years resulted in costs of US$8.23, US $15.40 and US$14.42 compared to US$8.13, US$14.28 and US $13.63 in Malawi, Zambia and Zimbabwe respectively.

Varying HIVST kit price between US$1 and US$3.40 yielded costs of US$6.44, US$15.15 and US$12.25 versus US $8.87, US$17.60 and US$14.99 in Malawi, Zambia and Zimbabwe respectively. Varying salaries by ±10% yielded costs of US$7.94, US$15.57 and US$13.24 versus US$8.37, US$17.27 and US$14.43 respectively. Varying kit quantity by ±10%

**Table 3. HIV self-test kit distribution cost breakdown and key cost contributors (in 2017 US$)**

| | Malawi Kits distributed: 152,671 12 months: June 2016 to May 2017 | | Zambia Kits distributed: 103,589 11 months: July 2016 to May 2017 | | Zimbabwe kits distributed: 93,459 10 months: August 2016 to May 2017 | |
|---|---|---|---|---|---|---|
| **Input type** | **Intervention cost** | **%** | **Intervention cost** | **%** | **Intervention cost** | **%** |
| Start-up | | | | | | |
| Training | $11,313.34 | 1% | $31,000.73 | 2% | $3,149.10 | 0% |
| Sensitization | $58,485.72 | 5% | $58,306.80 | 3% | $2,694.30 | 0% |
| Start-up other | $108,409.87 | 9% | $84,745.15 | 5% | $75,942.83 | 6% |
| Capital costs | | | | | | |
| Building and storage | | | | | | |
| Central | $16,755.33 | 1% | $54,077.43 | 3% | $3,266.62 | 0% |
| Warehouse | $– | – | $– | – | $– | – |
| Site level | $– | – | $– | – | $– | – |
| Equipment | | | | | | |
| Central equipment | $28,026.91 | 2% | $13,597.20 | 1% | $14,759.28 | 1% |
| Site level | $– | – | $– | – | $7,621.29 | 1% |
| Vehicles and bicycles | $3,162.38 | 0% | $– | – | $– | – |
| Other capital | $– | – | $– | – | $35.14 | 0% |
| Total costs (capital and start-up) | $226,153 | 18% | $241,727 | 14% | $107,468 | 8% |
| Recurrent costs | | | | | | |
| Personnel | $318,129.23 | 26% | $880,688.56 | 52% | $555,187.86 | 42% |
| HIV self-test kits | $418,584.61 | 34% | $237,303.53 | 14% | $219,627.52 | 17% |
| Supplies | | | | | | |
| T-shirts, bags, flipcharts | $35,611.73 | 3% | $78,569.63 | 5% | $67,757.98 | 5% |
| Other supplies | $– | – | $– | – | $142,543.96 | 11% |
| Vehicle operation, maintenance and transport | $109,240.41 | 9% | $148,117.37 | 9% | $57,396.14 | 4% |
| Building operation/maintenance | | | | | | |
| Central | $2,204.87 | 0% | $19,416.76 | 1% | $18,602.17 | 1% |
| Warehouse | $– | – | $– | – | $13,141.39 | 1% |
| Site level | $– | – | $– | – | $– | – |
| Recurrent training | $13,409.18 | 1% | $19,235.49 | 1% | $90,440.92 | 7% |
| Waste management | $– | – | $– | – | $554.89 | 0% |
| Other recurrent | $120,607.08 | 10% | $75,671.83 | 4% | $20,414.02 | 2% |
| Total costs (recurrent) | $1,017,787 | 82% | $1,459,003 | 86% | $1,185,667 | 92% |
| Total CBDA HIVST costs | $1,243,940 | 100% | $1,700,730 | 100% | $1,293,135 | 100% |
| Cost per kit distributed | $8.15 | | $16.42 | | $13.84 | |

Note that totals have been rounded to the nearest US$.
HIVST, HIV self-testing; CBDA, community-based distribution agent.

yielded costs of US$7.41, US$15.63 and US$12.83 versus US $9.06, US$17.60 and US$15.07 respectively. The best-case scenario was US$6.14, US$13.99 and US$12.32 per kit distributed, whereas the worst-case scenario was US$10.27, US $20.12 and US$21.85 per kit distributed.

## 4 | DISCUSSION

This is the first published study to present costs of door-to-door CBDA delivery of HIVST kits in Malawi, Zambia and Zimbabwe. Costs ranged from as low as US$7.20 at a very large distribution site where CBDA distribution of HIVST kits was integrated with the delivery of other health products, to US$54.55 with campaign-style delivery in a very small community in Zimbabwe that would otherwise not have access to testing. Staff costs contributed a substantial portion of the costs highlighting potential opportunities for lower cost models from reconfiguring distribution to rely on unpaid volunteers within door-to-door community-led distribution models. Additionally, economies of scale can clearly be optimized. In this analysis, we showed how unit costs fall as the number of

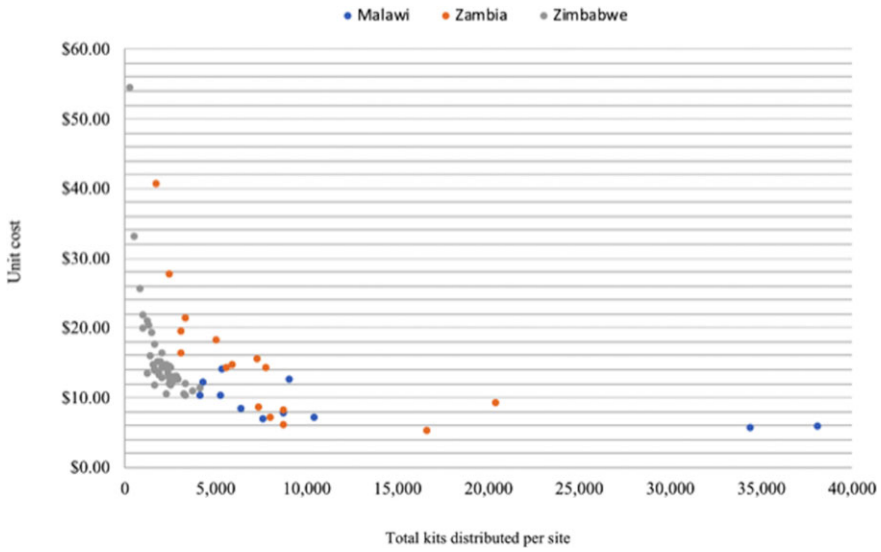


**Figure 1. HIV self-testing (HIVST) costs per HIVST kit distributed by site and quantity in 2017 US$.**

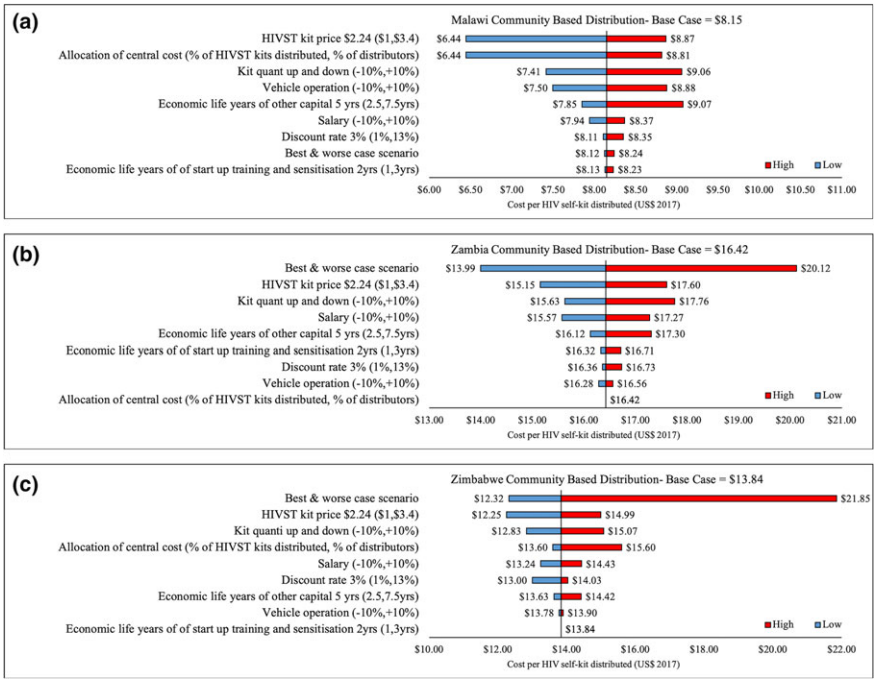


**Figure 2. (a, b, c) Tornado diagrams of findings from deterministic sensitivity analysis (univariate and scenario analyses) in Malawi, Zambia and Zimbabwe.**

kits distributed increases. As all modes of testing are scaled up and testing coverage increases, it will be critical to target populations efficiently, with special focus on communities underserved by facility-based HTS.

Although costs are presented from a provider's perspective, door-to-door community HIVST distribution relieves users from substantial direct and indirect costs of attending health facilities. A study in these same communities in Malawi showed the mean costs of accessing HIV testing among women and men as US$1.83 and US$3.81, respectively, with men reporting significantly higher opportunity costs (i.e. lost income) [17]. Community HIVST distribution reduces these costs to nearly zero, as kits are delivered in the home with no waiting times. We can, therefore, estimate the societal costs of facility-based HIV testing in Malawi as US$6.86 for women and US$8.84 for men (the user costs reported above and the provider costs as reported by Mwenge et al. [16]). This is comparable with our observed HIVST societal costs (excluding start-up and above service level costs: US$6.67) in Malawi. Thus, HIVST may provide for unmet testing needs among

remotely or never-tested individuals, or others with high user costs of accessing facility-based testing.

HIVST costs reflected across all three countries are not dissimilar to those reported previously in Malawi ($8.78 in 2016 US$) [18]. We also found the cost of door-to-door community HIVST distribution to be comparable to standard community-based HIV testing in sub-Saharan Africa (range: US$7.37 to US $36.93) [19,20]. While we did find that CBDA delivered HIVST under this early demonstration and research programmes were more costly than facility-based HIV testing [16,18], we also found HIVST reached many more individuals. During the period of this costing study, health facilities serving the study communities provided HIV testing to approximately 17,000, 28,000 and 45,000 people, while the HIVST service distributed approximately 152,671, 104,000 and 94,000 kits in Malawi, Zambia and Zimbabwe respectively. Importantly, half of the HIVST kits were distributed to men, while only 26% to 37% of facility HIV testing clients were men [8-10], the population group primarily contributing to the HIV testing gap.

We anticipate potential for substantial economies of scale as HIVST programmes scale-up and mature. The door-to-door community HIVST distribution model costed for this current study was implemented by a non-governmental organization, under a research protocol, using paid and incentivized CBDAs and delivered to predominantly rural communities with no previous knowledge of, or experience with, HIVST. Interventions delivered in a research context tend to be associated with higher costs, as the primary objective is achieving effectiveness. Large-scale implementation through door-to-door community-led HIVST distribution with ordinarily paid government providers or community residents is likely to be significantly less costly. There are additional potential costs savings. First, we found costs were lower in high kit distribution sites suggesting economies of scale and ability to deliver at lower costs in more densely populated communities. Second, 10% to 20% of the costs were start-up and initial capital costs, which would decrease as services mature. Third, as general populations and providers gain a better understanding of HIVST as a screening technology, we would expect less intense need for CBDAs (and therefore, less intense need for training workshops) and community sensitization activities.

Additionally, CBDAs could incorporate HIVST delivery into other health service activities thereby delivering cost savings to providers through economies of scope in services delivered by the CBDAs. Finally, as the HIVST market grows, technology advances and newer manufacturers enter, the price of HIVST kits will likely fall to prices comparable to blood-based kits currently used in health facilities and in-person support requirements could, in theory, could become cheaper than provider-supervised testing. In this case, HIVST could save costs and allow providers to focus on confirmatory testing and strengthening linkage to ART [21,22]. To identify this, it will be important to take a full system costing approach. Such data have been collated and will be analysed jointly to inform cost-effectiveness modelling.

From a research perspective, the wide cost variations highlight the importance of evaluating costs across a variety of settings in order to generate means and confidence intervals. Future analyses of these data may generate useful insights into efficiency and provide key inputs into modelled cost-effectiveness analyses. It would also be important to expand conventional sensitivity analyses to assess unit costs when these observed ranges are included or when unit costs are incorporated as a function of scale. Furthermore, considering that our analysis only shows the costs of implementing CBDA model for a non-governmental perspective and that these costs can vary if the kits were distributed differently, an important next research question will be to explore the costs of possible HIVST distribution modalities such as secondary distribution and social marketing models among others.

## 4.1 | Limitations

The findings of our cost analyses are limited to unit costs per kit distributed as the private nature of the HIVST did not allow us to estimate the costs of identifying new HIV-positive individuals or those HIV-positive individuals linked to treatment through HIVST. In addition, our results are borne out of a research trial setting and may not truly reflect a real-world situation: for example, site fixed transport costs are likely higher due to the distances between the trial communities, while in routine scale-up, all communities would receive HIVST kits and transport would be shared across far higher scale.

Additionally, as HIVST was a new product, distribution was conservative, restricting the numbers of kits that each CBDA could distribute in Zimbabwe, and so constraining opportunities to operate at larger scale. Consequently, costs were likely higher than future routine implementation. The benefits of HIVST distribution may also be restricted by test performance characteristics such as sensitivity, specificity and ability of the user to read the test as well as rates of linkage to care. An important consideration would be the optimal, setting-specific incentive structure for door-to-door community-based distribution of the kits. It is important to highlight that for purposes of this analyses authors had not collated and analysed data on self-test kit utilization. However, previous work has not only shown high uptake of HIVST but also high levels of kit utilization by recipients [4]. Key strengths of this cost analysis are the estimation of costs across seventy-one sites in three Southern African countries. The costing teams used standardized costing guidelines and collaboratively analysed data ensuring consistency of methods across countries and application of a range of sensitivity and scenario analyses exploring the impact of our assumptions.

## 4.2 | Implications

Countries keen to achieve impact and meet the global testing and treatment targets will likely need to invest in a mixture of HIV testing approaches, including door-to-door community delivered HIVST targeted at populations with financial or other barriers to obtaining HIV testing in health services, that is people living in settings with high undiagnosed HIV or remote communities, and groups such as men and adolescents. Reducing costs during short-term scale-up and implementation of this model should focus on economies of scope and scale and ensure efficiencies in personnel and transportation costs. Alternative cost-minimization approaches also need to be explored for acceptability, impact and affordability, aiming to provide affordable access to HIVST nationally, for example integrating HIVST within the existing facility and community health services, secondary distribution from facilities including partner delivered and peer-network approaches.

## 5 | CONCLUSIONS

Staff costs were a substantial cost contributor highlighting the potential for lower cost models if distribution relied on unpaid volunteers within door-to-door community-led distribution models.

Economies of scale can also be optimized with our costs showing reductions when kits are distributed in higher numbers. Across all three countries, our HIVST cost estimates were not dissimilar to previous door-to-door community-based HIVST and standard community-based HIV testing models costed in sub-Saharan Africa. Although the costs of CBDA delivered HIVST were higher than facility-based HIV testing the evidence shows HIVST reaches many more individuals. A significant portion (almost half) of HIVST kits were distributed to men (key contributors to the HIV testing gap) compared to only 26% to 37% for facility HIV testing.

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### COMPETING INTERESTS

The authors have no conflicts of interest to declare.

### AUTHORS' CONTRIBUTIONS

CM, LM, LS, NA, MD, HM and FTP conceptualized and designed the study. CM, LM, LS, NA, PC, TC and SK collected and facilitated the collection of data. CM, LM, LS, NA, PC, TC, SK, MD, JJO, HM and FTP analysed and interpreted the data. CM, LM, LS, NA, MD, PC, TC, SK, JJO, MM, MN, RC, PI, ELS, MNE, GN, OM, KH, CJ, HA, ELC, FC, HM and FTP drafted the manuscript and revised it critically. MM, MN, RC, PI, ELS, MNE, GN, OM, KH, CJ, HA, ELC, FC, HM and FTP supervised the study and facilitated the acquisition of the cost data. All co-authors approved the final version to be published.

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### REFERENCES

1. UNAIDS. UNAIDS data 2017. [cited 2018 Apr 13.] Available from: http://www.unaids.org/sites/default/files/media_asset/20170720_Data_book_2017_en.pdf
2. UNAIDS. 90-90-90: an ambitious treatment target to help end the AIDS epidemic. Geneva: UNAIDS; 2015.
3. Cambiano V, Johnson C, Hatzold K, Terris-Prestholt F, Maheswaran H, Thirumurthy H, et al. The impact and cost-effectiveness of community-based HIV self-testing in sub-Saharan Africa: a health economic and modelling analysis. J Int AIDS Soc. 2019;22(S1):e25243.
4. Choko AT, MacPherson P, Webb EL, Willey BA, Feasy H, Sambakunsi R, et al. Uptake, accuracy, safety, and linkage into care over two years of promoting annual self-testing for HIV in Blantyre, Malawi: a community-based prospective study. PLoS Med. 2015;12(9):e1001873.
5. WHO. Consolidated guidelines on HIV testing services. 2015 [Cited 2018, April 5.] Available from: http://www.who.int/hiv/pub/guidelines/hiv-testing-services/en/
6. OraSure Technologies Inc. OraQuick – HIV self-test – What is the Bill and Melinda Gates Foundation agreement with OraSure Technologies? 2017 [cited 2018 Apr 27.] Available from: http://www.orasure.com/products-infectious/products-infectious-oraquick-self-test.asp
7. Unitaid, World Health Organization. Market and technology landscape: HIV rapid diagnostic tests for self-testing, 3rd edn. Geneva: Unitaid; 2017.
8. Ministry of Health, Malawi. Malawi Population-based HIV Impact Assessment (MPHIA) 2015-16: First Report. Lilongwe, Ministry of Health. November 2017.
9. Ministry of Health, Zambia. Zambia Population-based HIV Impact Assessment (ZAMPHIA) 2016: First Report. Zambia, Ministry of Health. December 2017.
10. Ministry of Health and Child Care (MOHCC), Zimbabwe. Zimbabwe Population-Based HIV Impact Assessment (ZIMPHIA) 2015-16: First Report. Harare, MOHCC. July 2017.
11. London School of Hygiene and Tropical Medicine. PSI/UNITAID STAR – HIV self-testing AfRica – protocols and tools. 2018 [cited 2018 Apr 24.] Available from: http://hivstar.lshtm.ac.uk/protocols/
12. Vassall A, Sweeney S, Kahn JG, Gomez G, Bollinger L, Marseille E, et al. Reference case for estimating the costs of global health services and interventions. 2017 [cited 2017 Nov 12.] Available from: https://ghcosting.org/pages/standards/reference_case
13. Bank of Malawi. Statistics/Exchange rates. [cited 2018 Apr 24.] Available from: https://www.rbm.mw/Statistics/MajorRates/
14. Bank of Zambia. Monetary policy committee statement. 2018 [cited 2018 Apr 24.] Available from: http://www.boz.zm/MPCStatementFeb2018.pdf
15. Bank of Zimbabwe. Press statement on the introduction of bond notes. 2016 [cited 2018 Apr 24.] Available from: http://www.rbz.co.zw/assets/press-statement-on-the-introduction-of-bond-notes.pdf
16. Mwenge L, Sande L, Mangenah C, Ahmed N, Kanema S, d'Elbée M, et al. Costs of facility-based HIV testing in Malawi, Zambia and Zimbabwe. PLoS ONE. 2017;12(10):e0185740.
17. Sande L, Maheswaran H, Mangenah C, Mwenge L, Mkandawireg P, Indravudh P, et al. Costs of accessing HIV testing services among rural Malawi communities. AIDS Care. 2018;30 Suppl 3:27–36.
18. 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(1):34.
19. Tabana H, Nkonki L, Hongoro C, Doherty T, Ekstrom AM, Naik R, et al. A cost-effectiveness analysis of a home-based HIV counselling and testing intervention versus the standard (facility based) HIV testing strategy in rural South Africa. PLoS ONE. 2015;10(8):e0135048.
20. Sharma M, Ying R, Tarr G, Barnabas R. Systematic review and meta-analysis of community and facility-based HIV testing to address linkage to care gaps in sub-Saharan Africa. Nature. 2015;528(7580):S77–85.
21. 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.
22. Hatzold K, Gudukeya S, Mutseta M, Chilongosi R, Nalubamba M, Nkhoma C, et al. HIV self-testing: breaking the barriers to uptake of testing among men and adolescents in sub-Saharan Africa, experiences from STAR demonstration projects in Malawi, Zambia and Zimbabwe. J Int AIDS Soc. 2019;22(S1):e25244.

## SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

**Table S1:** Cost allocation factors across the interventions by cost input type.

**Table S2:** Site-level total and unit costs of HIVST and facility-based testing.

**Data S1:** Narrative description of the CBDA models across countries.

**Data S2:** Definitions of cost category and cost inputs and allocation factors.

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RESEARCH ARTICLE

# The impact and cost-effectiveness of community-based HIV self-testing in sub-Saharan Africa: a health economic and modelling analysis

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## Abstract

**Introduction:** The prevalence of undiagnosed HIV is declining in Africa, and various HIV testing approaches are finding lower positivity rates. In this context, the epidemiological impact and cost-effectiveness of community-based HIV self-testing (CB-HIVST) is unclear. We aimed to assess this in different sub-populations and across scenarios characterized by different adult HIV prevalence and antiretroviral treatment programmes in sub-Saharan Africa.

**Methods:** The synthesis model was used to address this aim. Three sub-populations were considered for CB-HIVST: (i) women having transactional sex (WTS); (ii) young people (15 to 24 years); and (iii) adult men (25 to 49 years). We assumed uptake of CB-HIVST similar to that reported in epidemiological studies (base case), or assumed people use CB-HIVST only if exposed to risk (condomless sex) since last HIV test. We also considered a five-year time-limited CB-HIVST programme. Cost-effectiveness was defined by an incremental cost-effectiveness ratio (ICER; cost-per-disability-adjusted life-year (DALY) averted) below US$500 over a time horizon of 50 years. The efficiency of targeted CB-HIVST was evaluated using the number of additional tests per infection or death averted.

**Results:** In the base case, targeting adult men with CB-HIVST offered the greatest impact, averting 1500 HIV infections and 520 deaths per year in the context of a simulated country with nine million adults, and impact could be enhanced by linkage to voluntary medical male circumcision (VMMC). However, the approach was only cost-effective if the programme was limited to five years or the undiagnosed prevalence was above 3%. CB-HIVST to WTS was the most cost-effective. The main drivers of cost-effectiveness were the cost of CB-HIVST and the prevalence of undiagnosed HIV. All other CB-HIVST scenarios had an ICER above US$500 per DALY averted.

**Conclusions:** CB-HIVST showed an important epidemiological impact. To maximize population health within a fixed budget, CB-HIVST needs to be targeted on the basis of the prevalence of undiagnosed HIV, sub-population and the overall costs of delivering this testing modality. Linkage to VMMC enhances its cost-effectiveness.

**Keywords:** HIV testing, community-based HIV self-testing; cost-effectiveness; mathematical modelling; HIV; benefits and cost

Additional Supporting Information may be found online in the Supporting information tab for this article.

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## 1 | INTRODUCTION

The ambitious UNAIDS targets, set in 2014, of diagnosing 90% of people living with HIV, having 90% of those diagnosed on antiretroviral treatment (ART) and having virological suppression in 90% of those on treatment by 2020 has prompted concerted programmatic efforts and review of progress around these three indicators [1]. The annual volume of HIV tests performed in sub-Saharan Africa (SSA) has more than doubled over ten years.

Based on UNAIDS estimates, awareness of HIV status among people living with HIV (PLHIV) continues to increase rapidly, from 45% in 2014 [1] to 75% in 2017 [2]. Recent population-based surveys (2015 to 2017) in Eastern and Southern African countries found that between 52% and 85% of PLHIV were aware of their status [3–7]. These may, indeed,

be underestimates, as people tend to under-report HIV diagnosis [8]. Of concern though, despite increases in HIV testing, challenges remain, as men, adolescents (10 to 19 years) and key populations remain underserved by current testing strategies [9,10] with lower proportions diagnosed than in the general population [2]. To reach the first 90 target, and possibly the even more ambitious future goals, it will be necessary to implement approaches that reach those in need of HIV testing and who are being missed.

Community-based HIV self-testing (CB-HIVST), defined as the distribution of HIVST by approaches such as home distribution, mobile outreach campaigns, distribution of HIVST at workplaces, bars or educational establishments, is highly acceptable, even to populations otherwise resistant to testing [11]. It provides complementary coverage to other approaches, including reaching people who have never tested before, and is reasonably accurate [12]. CB-HIVST in urban Malawi reached 68% of men aged ≥16 years and 89% of young people (16 to 29 years) within the first year of implementation [13]. Similar levels of uptake were seen among men and young people through CB-HIVST in rural Zimbabwe [14] and slightly lower in a subsequent cluster randomized controlled trial: 46.5% of men and 46.2% of people aged less than 25 [15]. In both Malawi and Zimbabwe, approximately a third of those who accessed CB-HIVST reported never testing before [13,15].

A measure of relevance for all HIV testing models is the proportion of people tested in whom the test result is positive (referred here as the test positivity rate). CB-HIVST models report test positivity rates of approximately 8% [15] (excluding retesting while taking ART and studies that used late-read, given the issues with the stability of the test results when reread after 72 hours), while facility-based HIVST distribution (excluding studies that used late-read) have found test positivity rates as high as 11% [16] and even higher rates with distribution of HIVST among female sex workers (FSW): 27% in Malawi [16] and 30% in Zimbabwe [17]. However, the positivity rate may not correspond to the proportion of tests that actually result in a first diagnosis because retesting among those previously diagnosed is common in all these studies, albeit that this occurs also with standard HIV testing services (HTS) [18]. The proportion of tests resulting in a first diagnosis has been shown to be an important driver of whether HIVST distribution is cost-effective [19]. As countries get closer to reaching the first "90," the prevalence of undiagnosed HIV will decline further and test positivity rates of HIV testing models will fall, potentially impacting on whether different HIV testing approaches remain cost-effective.

The HIV Self-Test AfRica (STAR) project recently estimated the unit cost per individual tested across health facilities testing services [20] and CB-HIVST sites in Zimbabwe, Malawi and Zambia [21]. Using a mathematical model previously used to evaluate the potential cost-effectiveness of HIVST [19], we aimed to identify which HIV epidemic and programmatic attributes and in which populations in SSA CB-HIVST would have the greatest epidemiological impact, and whether CB-HIVST could be cost-effective, using the costs per individual tested estimated in STAR. This builds on another piece of work using the same mathematical model aimed at estimating the cost of HIV testing per diagnosis at which HIV testing programmes are cost-effective [22].

# 2 | METHODS

## 2.1 | Synthesis model

We used an individual-based stochastic model of HIV transmission, progression and the effect of ART in adult populations in SSA. More detailed description of the model can be found in previous papers [19,22,23] and in the S1. Each time the model program is run, it samples values of variables including the number of short-term condomless sex partners, whether they have a long-term condomless sex partner, HIV testing, HIV acquisition, and additionally, for people with HIV, viral load, CD4 count, use of specific ART drugs, adherence to ART, resistance to specific drugs and risk of HIV-related death, each updated in three-month time steps from 1989.

The model provides means by which we can quantify the health effects of testing which occur via increases in the proportion of PLHIV on ART, with the consequent beneficial effects on both individual health and onward transmission. This allows estimation of the overall number of disability-adjusted life years (DALYs) averted in the whole adult population as a result of these effects. Possible linkage to pre-exposure prophylaxis for people tested negative is not included.

Parameters intrinsic to biological properties of HIV transmission and progression and effects of ART have been informed by data from European cohorts and confirmed by data from Africa, where available, and are kept fixed. We sampled parameter (see distributions in the Table S1) values relating to sexual behaviour, HIV transmission, HIV testing (including proportion of the population who is willing to test only if symptomatic or if HIVST is available), linkage to care and retention in care and on ART in order to generate a range of scenarios applicable to different settings in SSA (hereafter referred to as setting-scenarios) in terms of HIV epidemic, HIV testing and ART programme characteristics.

We track a population of approximately 20,000 living adults (15 to 64 years old; increasing over time) which is then scaled up to obtain estimates relevant for a population of around nine million (in 2018, Zimbabwe 7.8 million [24], Malawi 9.8 million [25], Zambia 8.2 million [26]). We excluded simulations where in 2004 there was an HIV prevalence among women below 5% or above 30% and in 2016 a number of women having condomless transactional sex (defined as having had more than three condomless sex partners in a three-month period in the last year) below 1460 or above 146,000. These were deemed implausible given the estimates from sentinel antenatal clinics [27] and on the percentage of women who are women having transactional sex (WTS) in SSA [28]. In total, 150 setting-scenarios were obtained. Table 1 shows the characteristics of the 150 setting-scenarios in 2017, along with examples of observed data (see S1 for more information).

## 2.2 | Implementation options under consideration

For each setting-scenario, we projected forward for 50 years from 2018 to 2068 under seven possible CB-HIVST implementation options (see Table 2). The reference option assumed that the current pattern and level of testing continues, including in WTS, in pregnant women (twice per pregnancy), in people presenting with potential HIV symptoms and in men presenting for voluntary medical male circumcision

(VMMC), but that no CB-HIVST is available. In the other six implementation options, HIVST is introduced through community-based distributors in addition to the current testing in one of the following sub-populations: young people (15 to 24 years), WTS and adult men (25 to 49 years). In these implementation options, HIVST is assumed to partially replace standard HTS

**Table 1. Characteristics of the HIV epidemic/ART programme setting-scenarios in 2017 in SSA countries with an adult population age 15 to 64 years approximately nine million**

| Indicator | Median (90% range) across Setting-scenarios (n = 150) | Examples of observed data |
|---|---|---|
| Population size (in million) | | |
| Overall (15 to 64 years) | 9.1 (8.2 to 9.9) | Zimbabwe 15 to 64 (2018): 7.8 million [24] |
| Women (15 to 49 years) | 4.1 (3.8 to 4.3) | Malawi 15 to 64 (2018): 9.8 million [25] |
| Men (15 to 49 years) | 3.9 (3.6 to 4.1) | Zambia 15 to 64 (2018): 8.2 million [26] |
| Young (15 to 24 years) | 3.2 (3.1 to 3.2) | Lesotho 15 to 64 (2018): 1.2 million [45] |
| Adult men (25 to 49 years) | 2.3 (2.0 to 2.6) | |
| WTS (15 to 64 years) | 0.16 (0.07 to 0.25) | |
| HIV prevalence | | |
| Overall (15 to 49 years) | 12.8% (4.7% to 27.5%) | Zimbabwe DHS 2015 [10]:14% |
| Women (15 to 49 years) | 13.0% (4.5% to 29.4%) | Tanzania DHS 2011 [46]: 5% |
| Men (15 to 49 years) | 12.6% (5.0% to 23.3%) | Uganda DHS 2011 [47]: 9% |
| | | Lesotho DHS 2014 [48]: 25% |
| Prevalence of undiagnosed HIV | | |
| Overall (15 to 64 years) | 2.1% (0.7% to 4.8%) | Malawi PHIA 2016 [4]: 2.9% |
| Women (15 to 49 years) | 1.2% (0.4% to 3.5%) | Zimbabwe PHIA 2016 [6]: 3.8% |
| Men (15 to 49 years) | 3.3% (1.0% to 7.0%) | Zambia PHIA 2016 [5]: 4.0% |
| | | Rwanda [38]: approximately 0.3% |
| | | (Survey estimates could be overestimates due to undisclosed diagnosed HIV [8]) |
| HIV incidence (age 15 to 49 years) per 100 person years | 0.91 (0.23 to 2.19) | Malawi PHIA 2016 [4]: 0.37% |
| | | Zimbabwe PHIA 2016 [6]: 0.45% |
| | | Zambia PHIA 2016 [5]: 0.66% |
| | | Swaziland [7]: 2.4% |
| | | Lesotho [3]: 1.5% |
| | | Mbongolwane and Eshowe published in 2014 (KZN) [49]: 1.2% |
| Number of HIV tests in year | | |
| Overall (15 to 64 years) | 2,300,000 (1,293,000 to 3,327,000) | Zimbabwe 2.2 million (2015) [50], |
| Women (15 to 49 years) | 1,485,000 (708,000 to 2,271,000) | Malawi 1.9 million (2014) [51] |
| Men (15 to 49 years) | 796,000 (461,000 to 1,072,000) | |
| ANC services | 721,000 (96,000 to 1,595,000) | |
| WTS (15 to 64 years) | 78,000 (30,000 to 142,000) | |
| Symptomatic (PLHIV)[a] | 22,000 (8,000 to 47,000) | |
| Symptomatic (HIV–) | 181,000 (160,000 to 200,000) | |
| VMMC services | 150,000 (114,000 to 189,000) | |
| Percentage of tests resulting in new HIV diagnosis[b] | | |
| Overall (15 to 64 years) | 3.2% (1.1% to 8.3%) | Observed data estimates are susceptible to bias due to rediagnosis of people who do not report previous diagnosis. 6% to 55% depending on group [52] |
| Women (15 to 49 years) | 2.4% (0.7% to 6.3%) | |
| Men (15 to 49 years) | 5.1% (1.6% to 11.3%) | |
| Young (15 to 24 years) | 2.2% (0.4% to 5.7%) | |
| ANC services | 2.9% (0.6% to 17.5%) | Malawi first quarter 2016 [53]: 5% |
| WTS (15 to 64 years) | 18.0% (3.3% to 35.1%) | |
| Symptomatic | 9.4% (3.5% to 18.2%) | |
| VMMC services | 3.2% (0.6% to 6.9%) | |

**Table 1.** (*Continued*)

| Indicator | Median (90% range) across Setting-scenarios (n = 150) | Examples of observed data |
|---|---|---|
| Proportion tested in past year | | |
| Women (15 to 49 years) | 29% (15% to 41%) | Zimbabwe DHS 2015 [10]: 49% women, 36% men (age 15 to 49 years) |
| Men (15 to 49 years) | 19% (12% to 27%) | |
| Women (15 to 24 years) | 25% (11% to 38%) | Namibia DHS 2013 [54]: 49% women, 38% men (age 15 to 49 years) |
| Men (15 to 24 years) | 17% (11% to 23%) | |
| When symptomatic (PLHIV)[a,c] | 16% (9% to 24%) | Nigeria DHS 2013 [55]: 10% women, 10% men |
| In pregnancy (15 to 49 years) | 93% (30% to 98%) | |
| WTS (15 to 64 years) | 39% (22% to 52%) | |
| Proportion of HIV-positive people diagnosed | | |
| Overall (15 to 64 years) | 83% (73% to 90%) | Malawi PHIA 2016 [4]: 73%; 76% in women, 67% in men |
| Women (15 to 49 years) | 90% (79% to 95%) | Zimbabwe PHIA 2016 [6]: 74% |
| Men (15 to 49 years) | 74% (61% to 85%) | Zambia PHIA 2016 [5]: 67% |
| Women (15 to 24 years) | 79% (56% to 88%) | Mbongolwane and Eshowe (KZN) published in 2014 [49]: 75% |
| Men (15 to 24 years) | 43% (26% to 57%) | |
| WTS (15 to 64 years) | 75% (58% to 87%) | District of Chiradzulu (rural Malawi) 2013 [56]: 77% |
| | | Botswana 2013 to 2015 [57]: 78%, higher in women than men |
| | | Survey estimates likely to be over-estimates due to undisclosed diagnosed HIV [8] |
| Proportion of diagnosed people on ART | | |
| Overall (15 to 64 years) | 88% (59% to 92%) | Malawi PHIA 2016 [4]: 89% |
| Women (15 to 49 years) | 89% (59% to 92%) | Zimbabwe PHIA 2016 [6]: 87% |
| Men (15 to 49 years) | 87% (56% to 91%) | Zambia PHIA 2016 [5]: 85% |
| Women (15 to 24 years) | 89% (42% to 93%) | Botswana 2013 to 15 [57]: 85% |
| Men (15 to 24 years) | 79% (33% to 91%) | |
| WTS (15 to 64 years) | 90% (50% to 94%) | |
| Proportion of people on ART with VL < 1000 copies/mL | | |
| Overall (15 to 64 years) | 85% (81% to 89%) | World Bank South Africa [58]: 60% to 88% over districts |
| | | Malawi PHIA 2016 [4]: 91% |
| | | Zimbabwe PHIA 2016 [6]: 87% |
| | | Zambia PHIA 2016 [5]: 89% |
| | | District of Chiradzulu (rural Malawi) 2013 [56]: 91% |
| | | Mbongolwane and Eshowe (KZN) published in 2014 [49]: 90% |
| | | Rural Uganda and Kenya [59]: 90% |
| | | Botswana 2013 to 2015 [57]: 94% (among citizens of Botswana) |

ANC, antenatal care; ART, antiretroviral therapy; DHS, Demographic and Health Surveys; KZN, KwaZulu-Natal; PHIA, Population-based HIV Impact Assessment; PLHIV, people living with HIV; VMMC, voluntary male medical circumcision; WTS, women having transactional sex.
[a]Symptoms of a WHO Stage 3 or 4 condition; [b]This is also referred to as yield. In our model, this is the same as test positivity rate as within the Synthesis model people who received a diagnosis of HIV cannot test again, so this is the ratio between the number of new diagnoses and the number of tests performed; [c]in this case is not in the past year but of those symptomatic/pregnant in a specific time period.

(see Table 2). In our base case, CB-HIVST implementation options involved continuous CB-HIVST availability for the entire timeframe (50 years). We based assumptions on accuracy of CB-HIVST on the overall results for oral fluid HIVST in a systematic review and meta-analysis of HIV self-test performance in field settings, including low- and middle-income countries (sensitivity of 93.9% and specificity of 99.2%) [12]. However, we made the conservative assumption that neither the standard HTS nor the CB-HIVST in SSA can detect HIV within three months of infection (the time step in the model). In addition, we assumed that a positive result using a CB-HIVST is not sufficient to make an HIV diagnosis but that a confirmatory test performed by a trained healthcare worker is required for the person to be diagnosed with HIV and be able to be linked to care and treatment. The main assumptions related to HIVST are summarized in Table 3 (and Table S2).

**Table 2. Description of implementation options**

| | Core testing | Population in which CB-HIVST is available | Possibility of using CB-HIVST if no CLS since last test | Replacement of HTS with CB-HIVST |
|---|---|---|---|---|
| Ref | Current level of testing continues, | None | Not applicable | Not applicable |
| 1 | in particular testing in: | Young people (15 to 24 years) | Yes[a] | 30%[b] |
| 2 | • General population (including WTS) | Adult men (25 to 49 years) | | 30%[b] |
| 3 | • In pregnant women (twice per pregnancy) | WTS (15 to 64 years) | | 50%[d] |
| 4 | • In people presenting with potential | Young people (15 to 24 years) | No[c] | 30%[b] |
| 5 | HIV symptoms | Adult men (25 to 49 years) | | 30%[b] |
| 6 | • In men presenting for VMMC | WTS (15 to 64 years) | | 50%[d] |

CB-HIVST, community-based HIV self-testing; CLS, condomless sex; HTS, HIV testing services; PLHIV, people living with HIV; VMMC, voluntary medical male circumcision; WTS, women reporting transactional sex.
[a]They can HIVST only once per year, but they can HIVST even if they had HTS in the last year (% self-tested per year indicated in Table 4). [b]Study offered standard HTS or HIVST and 30.9% men opted for HIVST [60]. [c]They can use HIVST only if they had condomless sex since last test (HTS or CB-HIVST) but they can test more than once per year if having CLS. [d]54% of women who attended a FSW clinic where provider initiated testing and counselling was available (n = 604) and were offered HIVST opted for it [17]. Higher rate of substitution has been reported as well [61,62].

**Table 3. Assumptions on CB-HIVST**

| Parameter | Value assumed for base case | Source |
|---|---|---|
| Sensitivity of CB-HIVST | 93.9% | [12] |
| Specificity of CB-HIVST | 99.2% | [12] |
| Sensitivity of HTS[a] | 98% | [63] |
| Specificity of HTS[a] | 99.2% | [64] |
| Confirmatory HTS following positive CB-HIVST | 50% by three months, 78% by one year from positive CB-HIVST[b] | At six weeks: 50% in the arm without incentive after excluding those retesting on ART [15] Evidence on disclosure from [13] and % self-reported linking to care in STAR |
| Proportion initiated on ART of those who had a positive (not previously diagnosed) CB-HIVST | 36% by three months[c] | At six weeks: 30% in the arm without incentive after excluding those retesting on ART [15] |
| Change in condomless sex in those who are tested HIV positive by HTS | With long-term partner: none, with short-term partner: −17% in the first six months, −9% after | [65,66] |
| Change in condomless sex in those tested HIV negative by HTS | No change | [67] Among FSW no difference in condom use, but reduction in number of partners following HIVST at four months [68] |
| Change in condomless sex after CB-HIVST (and before any confirmation with HTS) | No change | Among FSW no difference in condom use, but reduction in number of partners following HIVST at four months [68] |

ART, antiretroviral therapy; CB-HIVST, community-based HIV self-testing; HTS, HIV testing services.
[a]Assumed as facility-based rapid diagnostic test. [b]It is assumed that people can have a confirmatory test as a consequence of a positive CB-HIVST only within one year of the positive CB-HIVST. [c]This is the median proportion initiated on ART at three months; the probability of initiating ART in people engaged to care is 0.8 per three months; for people diagnosed with HIV not linked to care by three months since diagnosis, there is a probability of linkage to care (or re-engaging into care if lost) per three months which is sampled from a distribution 0.1 (90% range: 0.03 to 0.32).

In addition, we considered several sensitivity analyses around the implementation option of CB-HIVST being available for adult men aged 25 to 49 years: (1) five-year time-limited CB-HIVST programme; (2) assuming that the increase in the number of tests obtained by introducing CB-HIVST is instead introduced with standard HTS (to understand, in case CB-HIVST was not cost-effective, whether this was due to characteristics intrinsic to CB-HIVST or whether any increase in testing is not cost-effective regardless of mode of testing); (3) assuming that 10% of men with negative CB-

HIVST and aged 25 to 50 link to VMMC; and (4) assuming a discount rate of 10% for both costs and health benefits. In the base case, we considered the conventional discounting rate of 3.0% per annum [29].

To reduce stochastic variability, we performed two repetitions of the projections of the population from 2018 for each implementation option in each simulation, except for the options involving WTS, where four repetitions were performed due to the small sample size of this subgroup, or in the 5-year CB-HIVST distribution implementation option, and we calculated the mean across these repetitions.

We assumed that all people are eligible for ART at diagnosis from 2017 and that viral load monitoring was used from mid-2016 (at six and twelve months, and then annually).

Disability weights to calculate DALYs were derived from a comprehensive study (conditions included are: TB, WHO Stages 4 and 3) [30].

### 2.3 | Costs and cost-effectiveness approach

We used the fully loaded average recurrent cost per CB-HIVST estimated in STAR in Zimbabwe and Malawi, respectively, US $10.18 and US$5.61 [21] (see further details in the S2), and a cost per person tested for HIV testing performed by a healthcare worker (except for community-based), derived from [31], of, respectively, US$8.66 for Zimbabwe (US$9.37 if positive) and US$4.82 for Malawi (US$5.82 if positive). Other unit costs are provided in the Table S3 but, in brief, the annual cost (including 20% of supply chain costs) of the first-line regimen of efavirenz, lamivudine, tenofovir is US$98 per person [32], programme costs for clinic visits (not including drug or viral load or CD4 count tests) are US$20 per three months [33,34] with an assumed reduction to US$10 per three months when viral load is measured to be <1000 copies/mL [20].

The cost-effectiveness analysis was undertaken from the health provider perspective. Costs were estimated in 2016 US dollars. Health outcomes were quantified in DALYs averted and, as mentioned above, a discount rate of 3% was applied to both costs and health outcomes [29]. We calculated incremental costs and DALYs averted for the CB-HIVST implementation options compared with the reference over a 50-year time horizon, in order to capture all costs and effects relevant to this decision problem. The CB-HIVST implementation option was deemed cost-effective if the incremental cost-effectiveness ratio (ICER) was below US$500 per DALY averted, or if it resulted in both cost savings and DALYs averted. This use of the cost-effectiveness threshold reflects the health foregone (opportunity costs) due to resources committed to HIV testing consequentially being unavailable to provide other interventions (i.e. so that US$500 reflects the cost-per-DALY-averted of these foregone activities [35,36]). Severe constraints on overall healthcare spending in low-income countries in the region, notably for Malawi [37] mean that this cost-effectiveness threshold is only likely to be relevant for resource allocation within the HIV programme, which is overwhelmingly reliant on donor funds.

## 3 | RESULTS

Overall, the median (90% range) HIV prevalence across setting-scenarios in 2017 was estimated to be 12.8% (4.7% to 27.5%), the prevalence of undiagnosed HIV (ratio between the number of PLHIV who are undiagnosed and the entire population) was 2.1% (0.7% to 4.8%) and the test positivity rate (which in our model corresponds to the proportion of tests resulting in a first diagnosis) was 3.2% (1.1% to 8.3%) (see Table 1). As expected, the test positivity was higher for women having condomless transactional sex (18.0%), adult men 15 to 49 (5.1%) and symptomatic individuals (9.4%). We modelled CB-HIVST introduction in three independent subpopulations: young people (aged 15 to 24 years) amounting to 3.2 million people in 2017 (35% of people aged 15 to 64 years), adult men (aged 25 to 49 years) amounting to 2.3 million men (2.0 to 2.6; 25% of people aged 15 to 64 years) and WTS (160,000 women; 70,000 to 250,000; 1.8% of people aged 15 to 64 years).

Table 4 illustrates the scope of implementation and the epidemiological impact of the considered implementation options; the highest average number of tests was required when CB-HIVST was available continuously in the future; people self-tested even if not exposed to risk of HIV acquisition (no sex without condom) since last test; and CB-HIVST was available for young people (3,744,000 additional test/year compared to the reference option, +97%). Targeting adult men entailed 2,631,300 additional tests/year (+68%) and targeting WTS resulted in 222,400 additional test/year (+6%). Of note, we assumed that similar uptake of CB-HIVST could be achieved nationally as reported for the STAR subnational demonstration projects and cluster randomized trials: respectively, 87% in young people, 73% in WTS and 71% in adult men.

In terms of epidemiological impact, in the base case for the implementation options offering CB-HIVST to adult men had the highest impact, with an average (across setting-scenarios) of 1500 HIV infections averted per year, followed by targeting of young people (1490 HIV infections averted per year) and WTS (1430 HIV infections averted per year). Similarly, deaths averted (in PLHIV and without HIV) were highest when CB-HIVST was targeted at adult men (520 death averted/year), followed by young people (360 death averted/year) and WTS (330 death averted/year). Health benefits from CB-HIVST for adult men were enhanced if 10% of men with negative HIVST in the 25- to 50-year age group link to VMMC (1720 HIV infections averted per year vs. 1500; 580 deaths averted/year vs. 520). However, in terms of numbers-needed-to-test to avert one new HIV infection, targeting WTS was by far the most efficient strategy requiring 160 additional tests per HIV infection averted, compared to 2500 for young people and 1750 for adult men. For deaths, the equivalent numbers of additional tests was 670 per death averted for strategies targeting WTS, compared to 10,460 for young people and 5060 for adult men. Numbers of additional tests needed were almost halved for young people if CB-HIVST was taken up only if they had condomless sex since their last test. Similarly, the five-year time-limited CB-HIVST programme reduced the number of additional tests per HIV infection averted and per death averted to 180 and 710 respectively.

Figure 1 shows the cost per DALY averted (compared to the reference option) using a 50-year timeframe and two sets of costs for CB-HIVST and HTS for the base case scenarios (assuming a maximum of one standards HTS annually, but regardless of sexual risk-taking) and for several sensitivity analyses. The cost per DALY averted using a 20-year timeframe is

**Table 4. Mean over 50 years (2018 to 2068) of intermediate measures describing the implementation and the epidemiological impact of the options considered (across 150 setting-scenarios)**

| Implementation option | Sub-population receiving HIVST | Number of HIV tests (HTS or HIVST)/year – age 15 to 64 years (additional test compared to no intervention, relative increase) | Number of new diagnoses per year (age 15 to 49 years) | Number of new diagnoses per year in the sub-population of interest | % tested in the past year (HTS or HIVST; age 15 to 49 years) | % tested in the past year in the sub-population of interest | % self-tested in the past year (age 15 to 49 years) | % self-tested in the past year in the sub-population of interest | % ever tested (HTS or HIVST; age 15 to 49 years) | % ever tested (HTS or HIVST) in the sub-population of interest |
|---|---|---|---|---|---|---|---|---|---|---|
| No Intervention | NA | 3,860,300 (-) | 58,500 | Young: 16,500<br>WTS: 15,400<br>Adult men: 22,900 | 25% | Young: 21%<br>WTS: 39%<br>Adult men: 21% | 0% | Young: 0%<br>WTS: 0%<br>Adult men: 0% | 74% | Young: 50%<br>WTS: 85%<br>Adult men: 82% |
| HIVST is available – no requirement for CLS – base case | Young people | 7,604,300 (3,744,000, +97%) | 55,500 | 18,900 | 51% | 91% | 35% | 87% | 98% | 99% |
| | WTS | 4,082,800 (222,400, +6%) | 55,000 | 16,300 | 26% | 86% | 2% | 73% | 79% | 99% |
| | Adult men | 6,481,600 (2,621,300, +68%) | 57,800 | 24,700 | 42% | 76% | 24% | 71% | 81% | 99.6% |
| HIVST is available – requirement for CLS | Young people | 5,947,900 (2,087,600, +54%) | 55,300 | 17,900 | 30% | 35% | 10% | 24% | 78% | 54% |
| | WTS | 4,088,400 (228,100, +6%) | 54,700 | 15,900 | 26% | 58% | 1% | 39% | 78% | 86% |
| | Adult men | 6,150,400 (2,290,000, +59%) | 57,100 | 23,800 | 33% | 47% | 12% | 35% | 78% | 90% |
| HIVST is available, next five years | Adult men | 4,082,800 (222,400, +6%) | 55,700 | 21,800 | 27% | 27% | 3% | 7% | 79% | 93% |
| HIVST is available – as good as HTS | Adult men | 6,457,200 (2,596,900, +67%) | 58,200 | 25,200 | 42% | 75% | 24% | 70% | 81% | 99.6% |
| HIVST is available – linkage to VMMC | Adult men | 6,485,800 (2,625,500, +68%) | 57,100 | 24,200 | 42% | 76% | 24% | 71% | 81% | 99.6% |

CB-HIVST, community-based HIV self-test; CLS, condomless sex; HTS, HIV testing services; NA, not applicable; VL, viral load; VMMC, voluntary medical male circumcision; WTS, women having transactional sex.

illustrated in Figure S1. In addition, variation in CB-HIVST cost-effectiveness in different settings was considered by stratifying simulations by prevalence of undiagnosed HIV (quartiles). The timeframe considered has a crucial impact on cost-effectiveness: under the 50-year timeframe, introduction of CB-HIVST is cost-effective if introduced among WTS (whether the use is limited to when having condomless sex or not), for a five-year programme among adult men (unless the prevalence of undiagnosed HIV is below approximately 1% and cost per CB-HIVST is US$10.18) and among adult men provided that the prevalence of undiagnosed HIV is relatively high (>3% if cost per CB-HIVST is US$5.61, >5.5% if US$10.18). However, when considering a 20-year time horizon, it was cost-effective only when offered to WTS in setting with a

| % who never tested before, out of those who use HIVST for the first time | % of HIVST resulting in a diagnosis (referred to as positivity rate; age 15 to 49 years) | % of HIV-positive people diagnosed (age 15 to 49 years) | % of HIV-positive people diagnosed in the sub-population of interest | % of people with HIV and VL > 1000 (out of the entire population; age 15 to 64 years) | Number of condomless (short term and long term) infectious partnership | Number of people living with HIV with VL > 1000 copies/mL | Number of deaths per year (averted compared to the no intervention) | Number of HIV infections per year (averted compared to the no intervention) | Number of additional tests per HIV infection averted (per death averted) |
|---|---|---|---|---|---|---|---|---|---|
| NA | NA | 86% | Young: 67%<br>WTS: 74%<br>Adult men: 80% | 3.2% | 944,500 | 416,900 | 43,300 (-) | 17,560 (-) | - (-) |
| 97% | 0.28% | 89% | 84% | 2.8% | 871,800 | 367,900 | 43,000 (360) | 16,060 (1490) | 2500 (10,460) |
| 34% | 2.92% | 88% | 81% | 2.9% | 875,900 | 380,700 | 43,000 (330) | 16,130 (1430) | 160 (670) |
| 21% | 0.80% | 91% | 94% | 2.7% | 876,800 | 351,700 | 42,800 (520) | 16,060 (1500) | 1750 (5060) |
| 20% | 0.61% | 88% | 77% | 2.9% | 882,700 | 376,800 | 43,000 (340) | 16,160 (1400) | 1490 (6070) |
| 6% | 3.42% | 88% | 81% | 2.9% | 866,700 | 380,500 | 43,000 (340) | 16,040 (1520) | 150 (660) |
| 3% | 1.03% | 90% | 91% | 2.8% | 884,200 | 361,000 | 42,900 (460) | 16,100 (1460) | 1570 (4960) |
| 25% | 1.31% | 88% | 84% | 2.9% | 907,700 | 384,000 | 43,000 (310) | 16,340 (1220) | 180 (710) |
| 21% | 0.92% | 93% | 96% | 2.7% | 874,400 | 346,900 | 42,800 (550) | 15,970 (1590) | 1640 (4760) |
| 21% | 0.78% | 92% | 94% | 2.7% | 879,300 | 348,700 | 42,800 (580) | 15,830 (1720) | 1520 (4530) |

prevalence of undiagnosed HIV above 5.5% and if the cost of CB-HIVST was relatively low ($5.61). The cost of delivering CB-HIVST, not surprisingly, plays a crucial role in determining the ICER. Applying higher discounting rates of 10% to additional costs and health benefits renders CB-HIVST among adult men not cost-effective regardless of the prevalence of undiagnosed HIV.

## 4 | DISCUSSION

CB-HIVST offers the opportunity to reduce the "testing gap" in men, young people and WTS: subgroups that are hard to reach with standard HIV testing services. Here, we show that, when health benefits and costs are considered over a relatively long time horizon, targeted CB-HIVST can be cost-

| | | ICER, Mean Cost per DALY averted (Additional cost in US$ million /DALYs averted in 1,000s) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | High cost of CB-HIVST (US$10.18) and HTS (US$8.66 if negative; US$9.37 if positive) | | | | | Low Cost of CB-HIVST (US$5.61) and HTS† (US$4.82 if negative; US$5.82 if positive) | | | | |
| | | Overall | Prevalence of undiagnosed HIV | | | | Overall | Prevalence of undiagnosed HIV | | | |
| | | | 0.3 - 1.6% | 1.6 – 2.4% | 2.4 – 3.7% | 3.7 – 7.4% | | 0.3 - 1.6% | 1.6 – 2.4% | 2.4 – 3.7% | 3.7 – 7.4% |
| **HIVST is available – no requirement for CLS (base case)** | **Young** | 2,000 (943/483) | 5,400 (965/177) | 2,800 (947/339) | 1,700 (950/574) | 1,100 (913/837) | 1,100 (528) | 3,100 (545) | 1,600 (529) | 930 (535) | 600 (504) |
| | **WTS** | 120 (51/412) | 380 (75/201) | 220 (64/290) | 100 (53/517) | 20 (12/638) | 60 (27) | 260 (53) | 140 (40) | 50 (28) | -20 (-13) |
| | **Adult men** | 880 (693/786) | 2,700 (732/267) | 1,200 (700/605) | 770 (700/908) | 470 (642/1,352) | 520 (410) | 1,600 (421) | 670 (405) | 470 (426) | 290 (388) |
| **Sensitivity analyses** | | | | | | | | | | | |
| **HIVST is available – requirement for CLS** | **Young** | 1,200 (515/419) | 3,000 (488/161) | 1,700 (492/282) | 980 (487/498) | 810 (590/730) | 680 (286) | 1,700 (282) | 970 (274) | 560 (277) | 430 (311) |
| | **WTS** | 110 (45/410) | 370 (72/196) | 210 (62/293) | 70 (36/525) | 20 (10/622) | 50 (20) | 260 (51) | 130 (38) | 20 (13) | -30 (-20) |
| | **Adult men** | 930 (591/636) | 2,500 (568/226) | 1,100 (580/540) | 750 (549/729) | 640 (665/1,039) | 550 (347) | 1,500 (330) | 620 (336) | 450 (331) | 370 (389) |
| **HIVST is available for the next 5 years** | **Adult men** | 230 (115/502) | 690 (142/205) | 310 (121/388) | 220 (122/559) | 90 (77/851) | 150 (74) | 470 (95) | 200 (78) | 150 (83) | 50 (40) |
| **HIVST is available - as good as HTS** | | 680 (594/869) | 1,800 (612/335) | 970 (602/621) | 560 (605/1,091) | 390 (560/1,420) | 410 (359) | 1,100 (354) | 580 (358) | 350 (379) | 240 (346) |
| **HIVST is available – linkage to VMMC‡** | | 780 (693/887) | 2,000 (739/367) | 1,100 (705/665) | 660 (693/1,052) | 440 (634/1,455) | 460 (410) | 1,200 (427) | 620 (411) | 400 (419) | 260 (379) |
| **Base case – 10% discounting rate** | | 1,600 (250/154) | 4,400 (257/59) | 2,200 (250/116) | 1,400 (251/181) | 940 (243/259) | 1,000 (159) | 2,600 (155) | 1,300 (154) | 900 (163) | 630 (162) |

**Figure 1. Cost per DALY averted of community-based HIVST by implementation option, prevalence of undiagnosed HIV (quartile) and cost of testing in the sub-population indicated – 2018 to 2068.**

Cost-saving; ICER $0-$249 per DALY; ICER $250-$499 per DALY; ICER $500-$999 per DALY; ICER $1,000-$2,499 per DALY; ICER ≥$2,500 per DALY; †DALYs averted not reported when showing the ICERs using the cost of CB-HIVST of $5.61 and HTS of $4.82, as the same regardless of the costs assumed; ‡10% of men with negative HIVST and aged 25-50 link to circumcision; CB-HIVST: community-based HIVST; DALY: disability-adjusted life years; HIVST: HIV self-test; HTS: HIV testing services; ICER: incremental cost-effectiveness ratio; VMMC: voluntary medical male circumcision; WTS: women having transactional sex;

effective using strategies that vary by the prevalence of undiagnosed HIV. The most efficient approaches are targeted to WTS, which remain cost-effective at all levels of prevalence of undiagnosed HIV in our setting-scenarios (approximately 1% to 5.6%). A five-year time-limited CB-HIVST programme can also be cost-effective for adult men, at all levels when using cost for the CB-HIVST of US$5.61 and at levels of prevalence of undiagnosed HIV above 1% when using CB-HIVST cost of US$10.18. This is due to the fact that by considering an intervention that lasts for only five years, the cost is reduced substantially and the HIV testing earlier in time is more beneficial as the undiagnosed prevalence is declining over time. Indefinite introduction of CB-HIVST for adult men is cost-effective only at relatively high initial prevalence of undiagnosed HIV, depending on the cost of CB-HIVST. When considering CB-HIVST in WTS, it is important to note that we have assumed the same cost per person tested as in the other populations. Data on these costs have been collected as part of the STAR project but final estimates are not available yet.

Current estimates of the prevalence of undiagnosed HIV from national surveys range from 0.3% in Rwanda [38] to 4% in Zimbabwe [6] and Zambia [5] with considerable variation also within countries. For example, in Zimbabwe estimates range from 2.9% in Manicaland to 5.8% in Matabeleland South [6] and in Zambia from 1.9% in Muchinga to 5.3% in Lusaka [5]. Thus, health benefits from investments at the national level can be maximized through implementation of different HIVST strategies in different geographical regions [39,40]. The corollary of this argument is that implementers may need to limit CB-HIVST efforts, potentially through periodic campaign style implementation, in settings with very low HIV awareness, as the benefits of testing people with very low probability of being infected will be limited. Community-based distribution of HIVST kits can take place in different ways and this partly drives the differences in costs seen in Zimbabwe compared to Malawi. The costs of government implementation CB-HIVST may be lower than estimated in the STAR project [21] and we anticipate that delivery costs will continue to fall due to economies of scale and efficiencies from increasing familiarity with this concept. This would increase the likelihood of HIVST programmes being cost-effective. However, the issue of "diminishing returns" will reduce the cost-effectiveness of all HIV testing strategies as the prevalence of undiagnosed HIV falls. In the context of declining undiagnosed prevalence, programme metrics such as the cost of testing per new HIV diagnosis have potential use for monitoring programme cost-effectiveness and in other work we have described approaches to link this metric to programme cost-effectiveness [22].

Secondary distribution models, where HIVST kits are distributed to sexual partners of WTS or pregnant women, which have high positivity rates and similar delivery costs [41,42], are likely to offer cost-effective approaches to distributing HIVST [43]. Additionally, improving linkage of those who test HIV negative to HIV prevention services may improve cost-effectiveness. In our sensitivity analysis, we explored the possibility that 10% of men with a negative CB-HIVST result are linked into VMMC and show that this would improve the benefits and cost-effectiveness of CB-HIVST targeted to men (considering the additional cost of VMMC). While not included in the scenarios modelled, the

addition of linkage to pre-exposure prophylaxis could also enhance impact of HIVST.

Previous cost-effectiveness analysis of adding CB-HIVST to existing testing services are available from urban Blantyre, Malawi [44] and for secondary distribution models, delivering self-testing kits to sexual partners of antenatal clinic attendees in South Africa [43]. The Blantyre study was in a setting of high HIV prevalence and high levels of undiagnosed and untreated PLHIV and assumed constant HIV incidence. That analysis concluded that over a 20-year time horizon adding CB-HIVST to facility-based testing was cost-effective and was suited to early ART initiation strategies. In the South African study, secondary distribution of self-testing kits to partners of pregnant women became cost-saving when considering the total cost of the HIV programme, although expenditure by the testing programme was increased. These findings concur with our current analysis, that community-based strategies targeting a large group of the population, such as young people and adult men, achieve the greatest population level-impact in terms of proportion diagnosed, but are not very cost-effective, unless the prevalence of undiagnosed HIV is relatively high.

This work has limitations. As for any economic evaluation which takes an appropriately long-time horizon, we rely on a mathematical model to give predictions of the long-term impact of the alternative implementation options. We consider the implementation in three specific groups, which are either underserved by current testing approaches or characterized by a high incidence, but we could have considered slightly different groups.

## 5 | CONCLUSIONS

CB-HIVST provides a new option for reaching relatively underserved sub-populations and can provide health benefits cost-effectively if targeted to WTS,as well as adult men for a limited time. The prevalence of undiagnosed HIV, assumptions relating to linkage to prevention post-HIVST and the cost of CB-HIVST are then critical in determining whether or not wider intervention strategies, which have not only higher potential benefits but also much higher costs, should be introduced.

## RECOMMENDATIONS

- Targeting adult men with community-based HIV self-testing (CB-HIVST) tends to allow aversion of a large number of infections as this is a large group which is currently under tested.
- Linkage to voluntary medical male circumcision (VMMC) following a negative HIVST should be considered as this can enhance the impact.
- Providing CB-HIVST to women having transactional sex (WTS) offers the best value for money and should be implemented.
- The introduction of CB-HIVST among adult men is cost-effective, provided that the undiagnosed HIV prevalence is above 3% or the distribution programme is limited to 5 years duration. Shortening the intervention period improves the cost-effectiveness because as we continue testing at the same rate the test positivity rate declines while the cost (except for discounting) remains the same.
- At its current cost, introduction of CB-HIVST among young people does not offer value for money.
- When deciding whether to implement CB-HIVST the overall cost of CB-HIVST (not only the kit cost) should be considered as well as the current prevalence of undiagnosed HIV.

### COMPETING INTEREST

The authors declare that they have no competing interests.

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VC, CJ, KH, FTP, FC, PR, LC and AP substantially contributed to the formulation of research question and conceptualized the study. VC and AP worked on development and programming of the HIV synthesis model. VC performed the modelling analysis. VC and AP analysed the simulations. VC, CJ, KH, FTP, HM, TH, CF, FC, ES, GN, PR, RCB, LC and AP drafted the manuscript or critically revising it for important intellectual content. All authors gave final approval of the version to be published.

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### REFERENCES

1. The Joint United Nations Programme on HIV/AIDS. 90-90-90 An ambitious treatment target to help end the AIDS epidemic. Geneva; 2014.
2. The Joint United Nations Programme on HIV/AIDS. Miles to go: closing gaps, breaking barriers, righting injustices. Geneva; 2018.
3. ICAP at Columbia University. Lesotho population-based HIV impact assessment LePhia 2016–2017. 2017.
4. ICAP at Columbia University. Malawi population-based HIV impact assessment MPHIA 2015–2016. 2016.
5. ICAP at Columbia University. Zambia population-based HIV impact assessment ZAMPHIA 2015–2016. 2016.
6. ICAP at Columbia University. Zimbabwe population-based HIV impact assessment ZIMPHIA 2015–2016. 2016.
7. Justman J, Reed JB, Bicego G, Donnell D, Li K, Bock N, et al. Swaziland HIV Incidence Measurement Survey (SHIMS): a prospective national cohort study. Lancet HIV. 2017;4(2):e83–92.
8. Kim AA, Mukui I, Young PW, Mirjahangir J, Mwanyumba S, Wamicwe J, et al. Undisclosed HIV infection and antiretroviral therapy use in the Kenya AIDS

indicator survey 2012: relevance to national targets for HIV diagnosis and treatment. AIDS. 2016;30(17):2685–95.
9. National Statistical Office (NSO) [Malawi] and ICF. Malawi Demographic and Health Survey 2015–2016. Zomba, Malawi, and Rockville, Maryland, USA; 2017.
10. Zimbabwe National Statistics Agency and ICF International. Zimbabwe Demographic and Health Survey 2015: Final Report. Rockville, Maryland, USA: Zimbabwe National Statistics Agency (ZIMSTAT) and ICF International; 2016.
11. 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.
12. Figueroa C, Johnson C, Ford N, Sands A, Dalal S, Meurant R, et al. Reliability of HIV rapid diagnostic tests for self-testing compared with testing by health-care workers: a systematic review and meta-analysis. Lancet HIV. 2018;5(6):e277–90.
13. Choko AT, MacPherson P, Webb EL, Willey BA, Feasy H, Sambakunsi R, et al. Uptake, accuracy, safety, and linkage into care over two years of promoting annual self-testing for HIV in Blantyre, Malawi: a community-based prospective study. PLoS Med. 2015;12(9):e1001873.
14. Sibanda EL, Mutseta M, Hatzold K, Gudukeya S, Dhliwayo A, Lopez C, et al. Community-based distribution of HIV self-test kits: results from a pilot of door-to-door distribution of HIV self-test kits in one rural Zimbabwean community. 21st International AIDS Conference; 2016 Jul 18–22; Durban, South Africa.
15. Sibanda E, Neuman M, Tumushime M, Hatzold K, Watadzaushe C, Mutseta MN, et al. Linkage to care after HIV self-testing in Zimbabwe: a cluster-randomized trial. 25th Conference on Retroviruses and Opportunistic Infections; 2018 Mar 4-7; Boston, USA.
16. Mutseta M. Impact of HIVST on uptake of HIV testing, Experiences from the STAR Project in Malawi, Zambia and Zimbabwe. 9th International AIDS Society Conference on HIV Pathogenesis and Treatment; 2017 July 23-26; Paris, France.
17. Mavedzenge S, Sibanda E, Dirawo J, Hatzold K, Mugurungi O, Cowan F. Feasibility of HIV self-test programming among female sex workers in Zimbabwe. 9th International AIDS Society Conference on HIV Science; 2017 Jul 23-26; Paris, France.
18. Johnson CC, Fonner V, Sands A, Ford N, Obermeyer CM, Tsui S, 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:pp. 7-18. ISSN 1758-2652. https://doi.org/10.7448/ias.20.7.21755.
19. 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.
20. Working Group on Modelling of Antiretroviral Therapy Monitoring Strategies in Sub-Saharan A. Sustainable HIV treatment in Africa through viral-load-informed differentiated care. Nature. 2015;528(7580):S68–76.
21. Mangenah C, Mwenge L, Sande L, Ahmed N, d'Elbée M, Chiwawa P, et al. Economic cost analysis of door-to-door community-based distribution of HIV self-test kits in Malawi, Zambia and Zimbabwe. J Int AIDS Soc. 2019;22(S1):e25255.
22. Phillips A, Cambiano V, Bansi-Matharu L, Nakagawa F, Wilson D, Jani I, et al. Cost-of-testing-per-new-HIV-diagnosis as a metric for monitoring cost-effectiveness of testing programmes in low income settings in Southern Africa: health economic modelling analysis. 22nd International AIDS Conference; 2018 Jul 23-27; Amsterdam, The Netherlands.
23. Phillips AN, Cambiano V, Nakagawa F, Revill P, Jordan MR, Hallett TB, et al. Cost-effectiveness of public-health policy options in the presence of pretreatment NNRTI drug resistance in sub-Saharan Africa: a modelling study. Lancet HIV. 2018;5(3):e146–54.
24. Central Intelligence Agency. The World Factbook – Zimbabwe. 2018 [cited 19/04/2018]. Available from: https://www.cia.gov/library/publications/the-world-factbook/geos/zi.html
25. Central Intelligence Agency. The World Factobok – Malawi. 2018 [cited 19/04/2018]. Available from: https://www.cia.gov/library/publications/the-world-factbook/geos/mi.html
26. Central Intelligence Agency. The World Factobok – Zambia. 2018 [cited 19/04/2018]. Available from: https://www.cia.gov/library/publications/the-world-factbook/geos/za.html
27. UNAIDS. Evidence for HIV decline in Zimbabwe : a comprehensive review of the epidemiological data. 2005.
28. Vandepitte J, Lyerla R, Dallabetta G, Crabbe F, Alary M, Buve A. Estimates of the number of female sex workers in different regions of the world. Sex Transm Infect. 2006;82 Suppl 3:iii18–25.
29. Wilkinson T, Sculpher MJ, Claxton K, Revill P, Briggs A, Cairns JA, et al. The international decision support initiative reference case for economic evaluation: an aid to thought. Value Health. 2016;19(8):7.
30. Salomon JA, Vos T, Hogan DR, Gagnon M, Naghavi M, Mokdad A, et al. Common values in assessing health outcomes from disease and injury: disability weights measurement study for the Global Burden of Disease Study 2010. Lancet. 2012;380(9859):2129–43.
31. Mwenge L, Sande L, Mangenah C, Ahmed N, Kanema S, d'Elbée M, et al. Costs of facility-based HIV testing in Zambia, Malawi and Zimbabwe. PLoS One. 2017;10(12):e0185740.
32. Clinton Health Access Initiative. ARV Market report; The state of the antiretroviral drug market in low- and middle-income countries, 2016-2021. 2017.
33. Tagar E, Sundaram M, Condliffe K, Matatiyo B, Chimbwandira F, Chilima B, et al. Multi-country analysis of treatment costs for HIV/AIDS (MATCH): facility-level ART unit cost analysis in Ethiopia, Malawi, Rwanda, South Africa and Zambia. PLoS One. 2014;9(11):e108304.
34. Siapka M, Remme M, Obure CD, Maier CB, Dehne KL, Vassall A. Is there scope for cost savings and efficiency gains in HIV services? A systematic review of the evidence from low- and middle-income countries. Bull World Health Organ. 2014;92(7):499–511.
35. Woods E, Revill P, Sculpher M, Claxton K. Country-level cost-effectiveness thresholds: initial estimates and the need for further research. University of York; 2010. Contract No.: 109.
36. Claxton K, Walker S, Palmer S, Sculpher M. Appropriate perspectives for health care decisions. 2010.
37. Ochalek JM, Claxton KP, Revill P, Sculpher M, Rollinger A. Supporting the development of an essential health package: principles and initial assessment for Malawi. York, UK: University of York; 2016. Contract No.: 136.
38. Nsanzimana S, Remera E, Kanters S, Mulindabigwi A, Suthar AB, Uwizihiwe JP, et al. Household survey of HIV incidence in Rwanda: a national observational cohort study. Lancet HIV. 2017;4(10):e457–64.
39. Anderson SJ, Cherutich P, Kilonzo N, Cremin I, Fecht D, Kimanga D, et al. Maximising the effect of combination HIV prevention through prioritisation of the people and places in greatest need: a modelling study. Lancet. 2014;384(9939):249–56.
40. McGillen JB, Anderson SJ, Dybul MR, Hallett TB. Optimum resource allocation to reduce HIV incidence across sub-Saharan Africa: a mathematical modelling study. Lancet HIV. 2016;3(9):e441–8.
41. 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. Lancet HIV. 2016;3(6):e266–74.
42. Masters SH, Agot K, Obonyo B, Napierala Mavedzenge S, Maman S, Thirumurthy H. Promoting partner testing and couples testing through secondary distribution of HIV self-tests: a randomized clinical trial. PLoS Med. 2016;13(11):e1002166.
43. Johnson L. Optimal HIV testing strategies to increase HIV diagnosis in South Africa. 25th Conference on Retroviruses and Opportunistic Infections; 2018 Mar 4-7; Boston, USA.
44. Maheswaran H, Clarke A, MacPherson P, Kumwenda F, Lalloo DG, Corbett EL, et al. Cost-effectiveness of community-based human immunodeficiency virus self-testing in Blantyre, Malawi. Clin Infect Dis. 2018;66(8):1211–21.
45. Central Intelligence Agency. The World Factobok – Lesotho. 2018 [cited 19/04/2018]. Available from: https://www.cia.gov/library/publications/the-world-factbook/geos/lt.html
46. Ministry of Health, Community Development, Gender EaCMTM, Ministry of Health (MoH) [Zanzibar], National Bureau of Statistics (NBS), Office of the Chief Government Statistician (OCGS), et al. Tanzania HIV/AIDS and Malaria Indicator Survey 2011-12. Dar es Salaam, Tanzania, and Rockville, Maryland, USA: TACAIDS, ZAC, NBS, OCGS and ICF International; 2013.
47. Uganda Bureau of Statistics (UBOS), Inc. II. Uganda Demographic and Health Survey 2011. Kampala, Uganda, and Rockville, Maryland, USA: UBOS and ICF International Inc.; 2012.
48. Ministry of Health [Lesotho], International. I. Lesotho Demographic and Health Survey 2014. Maseru, Lesotho and Rockville, Maryland, USA: Ministry of Health [Lesotho] and ICF International.; 2016.
49. Huerga HM. Mbongolwane and Eshowe HIV Impact in Population Survey. 2014.
50. Republic of Zimbabwe. Global AIDS Response progress report 2016. Zimbabwe Country Report - Reporting Period: January 2015 -December 2015. Harare, Zimbabwe; 2016.
51. Government of Malawi. Malawi AIDS Response Progress Report 2015. 2015.
52. Sharma M, Ying R, Tarr G, Barnabas R. Systematic review and meta-analysis of community and facility-based HIV testing to address linkage to care gaps in sub-Saharan Africa. Nature. 2015;528(7580):S77–85.

53. Government of Malawi. Health Mo. Integrated HIV Program Report – January-March. 2016.
54. The Namibia Ministry of Health and Social Services (MoHSS), ICF International. The Namibia Demographic and Health Survey 2013. Windhoek, Namibia and Rockville, Maryland, USA: MoHSS and ICF International; 2014.
55. National Population Commission (NPC) [Nigeria], International I. Demographic and Health Survey 2013. Nigeria Abuja, Nigeria and Rockville, Maryland, USA: NPC and ICF International; 2014.
56. Maman D, Chilima B, Masiku C, Ayouba A, Masson S, Szumilin E, et al. Closer to 90-90-90. The cascade of care after 10 years of ART scale-up in rural Malawi: a population study. J Int AIDS Soc. 2016;19(1):20673.
57. Gaolathe T, Wirth KE, Holme MP, Makhema J, Moyo S, Chakalisa U, et al. Botswana's progress toward achieving the 2020 UNAIDS 90-90-90 antiretroviral therapy and virological suppression goals: a population-based survey. Lancet HIV. 2016;3(5):E221–30.
58. MacLeod WB, Crawford K, Carmona S. Analysis of Big Data for better targeting of ART Adherence Strategies. Spatial clustering analysis of viral load suppression by South African province, district, sub-district and facility (April 2014–March 2015). 2015.
59. Brown LB, Havlir DV, Ayieko J, Mwangwa F, Owaraganise A, Kwarisiima D, et al. High levels of retention in care with streamlined care and universal test and treat in East Africa. AIDS. 2016;30(18):2855–64.
60. Hatzold K, Mutseta M, Sibanda E, Gudukeya S, Tumushime M, Lopez C, et al. Closing the HIV testing gap: facility-based integration of HIV self-testing, a way to improve testing coverage, yield and efficiency of client-initiated HIV testing services in Zimbabwe. 9th International AIDS Society Conference on HIV Pathogenesis and Treatment; 2017 Jul 23-26; Paris, France.
61. Chanda MM, Ortblad KF, Mwale M, Chongo S, Kanchele C, Kamungoma N, et al. HIV self-testing among female sex workers in Zambia: a cluster randomized controlled trial. PLoS Med. 2017;14(11):e1002442.
62. Ortblad K, Kibuuka Musoke D, Ngabirano T, Nakitende A, Magoola J, Kayiira P, et al. Direct provision versus facility collection of HIV self-tests among female sex workers in Uganda: a cluster-randomized controlled health systems trial. PLoS Med. 2017;14(11):e1002458.
63. Pant Pai N, Balram B, Shivkumar S, Martinez-Cajas JL, Claessens C, Lambert G, et al. Head-to-head comparison of accuracy of a rapid point-of-care HIV test with oral versus whole-blood specimens: a systematic review and meta-analysis. Lancet Infect Dis. 2012;12(5):373–80.
64. World Health Organization. HIV assays: laboratory performance and other operational characteristics. Rapid Diagnostic tests (Combined detection of HIV-1/2 antibodies and discriminatory detection of HIV-1 and HIV-2 antibodies). Report 18. 2015.
65. Fonner VA, Denison J, Kennedy CE, O'Reilly K, Sweat M. Voluntary counseling and testing (VCT) for changing HIV-related risk behavior in developing countries. Cochrane Database Syst Rev. 2012;9:CD001224.
66. Kennedy CE, Fonner VA, Sweat MD, Okero FA, Baggaley R, O'Reilly KR. Provider-initiated HIV testing and counseling in low- and middle-income countries: a systematic review. AIDS Behav. 2013;17(5):1571–90.
67. Cremin I, Nyamukapa C, Sherr L, Hallett TB, Chawira G, Cauchemez S, et al. Patterns of self-reported behaviour change associated with receiving voluntary counselling and testing in a longitudinal study from Manicaland, Zimbabwe. AIDS Behav. 2010;14(3):708–15.
68. Oldenburg C, Chanda MM, Ortblad KF, Mwale M, Chongo S, Kamungoma N, et al. Effect of HIV self-testing on the number of sexual partners among female sex workers in Zambia: a randomized controlled trial. AIDS. 2018;32:645–52.

## SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

**Table S1.** Parameter distributions sampled for each model run
**Table S2.** Assumptions on HIVST (extended version of Table 3)
**Table S3.** Costs included in the cost-effectiveness evaluation
**Table S4.** Disability weights
**Figure S1.** Cost per DALY averted by implementation option, prevalence of undiagnosed HIV (quartile) and cost of testing (20 years timeframe)
**Figure S2.** HIV prevalence 15 to 49 in each setting-scenario
**Figure S3.** HIV incidence 15 to 49 in each setting-scenario
**Figure S4.** Mean percentage of HIVST resulting in a diagnosis (referred to as positivity rate; age 15 to 49 years)
**S1.** Synthesis model description.

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COMMENTARY

# The Self-Testing AfRica (STAR) Initiative: accelerating global access and scale-up of HIV self-testing

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## Abstract

**Introduction:** HIV self-testing (HIVST) was first proposed as an additional option to standard HIV testing services in the 1980s. By 2015, two years after the first HIVST kit was approved for the American market and the year in which Unitaid invested in the "HIV Self-Testing AfRica (STAR) Initiative," HIVST remained unexplored with negligible access in low- and middle-income countries (LMIC). However, rapid progress had been made. This commentary outlines the interlinked market, regulatory and policy barriers that had inhibited product development and kept HIVST out of LMIC policy. We detail the components of STAR that enabled rapid HIVST scale-up, including critical investments in implementation, research, market forecasting, and engagement with manufacturers and regulators.

**Discussion:** The STAR Initiative has generated crucial information about how to distribute HIVST products effectively, ethically and efficiently. Service delivery models range from clinic-based distribution to workplace and partner-delivered approaches to reach first-time male testers, to community outreach to sex workers and general population "hotspots." These data directly informed supportive policy, notably the 2016 WHO guidelines strongly recommending HIVST as an additional testing approach, and regulatory change through support for WHO prequalification of the first HIVST kit in 2017. In July 2015, only two countries had national HIVST policies and were implementing HIVST. Three years later, 59 countries have policies, actively implemented in 28, with an additional 53 countries reporting policies under development. By end-November 2018 several quality-assured HIVST products had been registered, including two WHO prequalified tests. STAR Initiative countries have drafted regulations governing *in vitro* diagnostics, including HIVST products. With enabling policies, pre-qualification and regulations in place, donor procurement of kits has increased rapidly, to a forecasted estimate of 16 million HIVST kits procured by 2020.

**Conclusions:** The STAR Initiative provided a strong foundation to introduce HIVST in LMICs and allow for rapid scale-up based on the wealth of multi-country evidence gathered. Together with sustained coordination and acceleration of market development work, HIVST can help address the testing gap and provide a focused and cost-effective means to expand access to treatment and prevention services.

**Keywords:** HIV testing; HIV self-testing; market shaping; scale-up; prevention; linkage to care; cost effectiveness

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## 1 | INTRODUCTION

HIV testing is the gateway to treatment and care and expanded prevention coverage. The first of the United Nations' 90-90-90 Fast Track targets to end the HIV epidemic calls for 90% of people living with HIV (PLHIV) to know their HIV status by 2020 [1]. Access to and uptake of HIV testing services (HTS) in low- and middle-income countries (LMICs) has increased substantially over the last three decades due to advances in treatment, rapid testing and greater availability of HIV testing in facility and community. Despite these advances, an estimated 25% of PLHIV globally still do not know their status [2]. In eastern and southern Africa where the HIV burden is greatest, it is estimated that 2.7 million PLHIV still do not know their status [3,4].

To address these gaps, innovative and strategic approaches to HIV testing are needed [5]. HIV self-testing (HIVST), has been highlighted as an additional tool to increase access and uptake of HIV testing in higher risk populations with low coverage and particularly in environments with high rates of stigma [6]. In addition, HIVST has the potential to improve efficiency of the health system by triaging those without HIV straight to prevention services and freeing up health workers' time and could consequently reduce costs of HTS [6].

HIVST was first proposed as an additional option to standard HTS in the 1980s [7]. By 2015, three years after the first HIVST kit was approved for the American market [8], HIVST remained unexplored with negligible access in LMIC. By the end 2015, only two high-income countries were actively implementing HIVST services as part of their public health HIV response primarily in the private sector, and WHO had yet to state an official position.

In 2013, WHO convened the first global consultation on HIVST identified that development of the necessary normative guidance for HIVST was largely hampered by lack of evidence on safety, acceptability, feasibility and scalability; uncertain distribution methods for HIVST kits; unclear processes for linking self-testers to care and treatment; and lack of clarity on methods for creating demand among target populations [9,10].

As with any new health technology, the introduction of HIVST kits in LMICs faced several immediate policy, regulatory and market challenges [11].

First, because of the lack of WHO prequalified products for self-test use, opportunities to generate evidence for the public health benefit and to create demand were limited. Although the first discussion of HIVST introduction dates back to 1986, the first HIVST product only became available in 2012 when OraQuick® In-Home HIV Test (OraSure Technologies, Bethlehem, Pennsylvania USA) was approved by the US Food and Drug Administration [8,12]. It was not until mid to late-2015 that Conformité Européenne-marked products autotest VIH® (AAZ Labs, Boulogne-Billancourt France) and BioSURE HIV Self Test (BioSURE UK Ltd., Essex, England UK) became available for sale and use in the private sector in the United Kingdom and France.

Before 2015, there were no HIVST products registered by national regulatory authorities in Africa [11,13,14]. At that time, while HIVST was being assessed through controlled research studies in the region, the market for, and awareness of, official HIVST in Africa, and LMICs more broadly, was extremely limited. Without evidence, WHO normative guidelines could not be made to support HIVST introduction – nor guidance on how it should be implemented, limiting countries' ability to take on or prioritize HIVST as part of a national strategy. Furthermore, because of global and national level policy barriers, there were no regulatory pathways nor clear data collection systems to assure the quality of the HIVST products or to monitor the most ethical, acceptable and effective ways to implement self-testing.

Second, a healthy HIVST market also requires solidified demand from end-users and buyers including both national governments and donors. Before 2015, investment from governments and large-scale donors was constrained by a lack of evidence that HIVST could be a safe and effective way to increase testing rates. Because of this, the President's Emergency Plan for AIDS Relief (PEPFAR) and the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund), two of the biggest procures of HIV test kits globally, had yet to procure HIVST outside of small quantities for research. At the same time, little was understood about potential levels of consumer demand for HIVST, including how consumers would want to access HIVST and the HIVST product attributes likely to drive uptake or impact outcomes.

Third, in the absence of HIVST guidelines and clearly defined quality assurance pathways, governments and donors had little ability to understand the degree by which various products met minimum quality standards. Without evidence to support paying a higher cost for self-tests as opposed to professional use products, governments and donors signalled a very low willingness to pay. As a result, public sector procurement was largely frozen. A competitive market with several manufacturers has driven down the cost of professional-use HIV rapid diagnostic tests. While these issues apply to HIVST kits, they also face further challenges as they must be designed and packaged for self-test use, which incurs additional costs, and requires additional approvals and regulations. Faced with the prospect of low margins, unclear approval pathways, and limited concrete volumes, manufacturers responded by minimizing investment and adapting professional use products for self-testing. In addition, several suppliers with promising products lacked deep experience operating in LMIC markets [15].

Addressing the interlinked market, regulatory and policy barriers that had inhibited HIVST product development through a comprehensive approach was the goal of the Unitaid investment through the HIV Self-Testing AfRica (STAR) Initiative.

This commentary provides a broad overview of the strategies and achievements of the STAR Initiative in the introduction of HIVST in LMICs and the development of the HIVST market and considers the remaining challenges for bringing HIVST to scale.

## 2 | DISCUSSION

In 2015 Unitaid invested in a comprehensive effort to develop the market for HIVST by:

1 Establishing the evidence for its safety, acceptability, feasibility and scalability;
2 Creating an enabling environment with regards to normative guidelines, national policies, and regulatory frameworks based on the foundation of research evidence;
3 Generating diverse demand through multiple distribution channels adapted to the needs of priority populations and create advocacy for additional financing; and
4 Accelerating market entry for suppliers at affordable and sustainable prices.

This commitment resulted in the support of the five-year "HIV Self-Testing in AfRica (STAR) Initiative" with Population Services International (PSI) and a consortium of partners, including London School of Hygiene and Tropical Medicine, Liverpool School of Tropical Medicine, University College London, and Society for Family Health (SFH) and the University of Witwatersrand Reproductive Health and HIV Institute (Wits RHI) in South Africa, initially in three Southern African countries (Malawi, Zambia and Zimbabwe), expanding to include South Africa, Lesotho and Swaziland in 2017 (Figure 1).

### 2.1 | Evidence framework for safety, acceptability, feasibility and scalability

An increasingly strong set of evidence from a range of different populations and settings, demonstrates that the

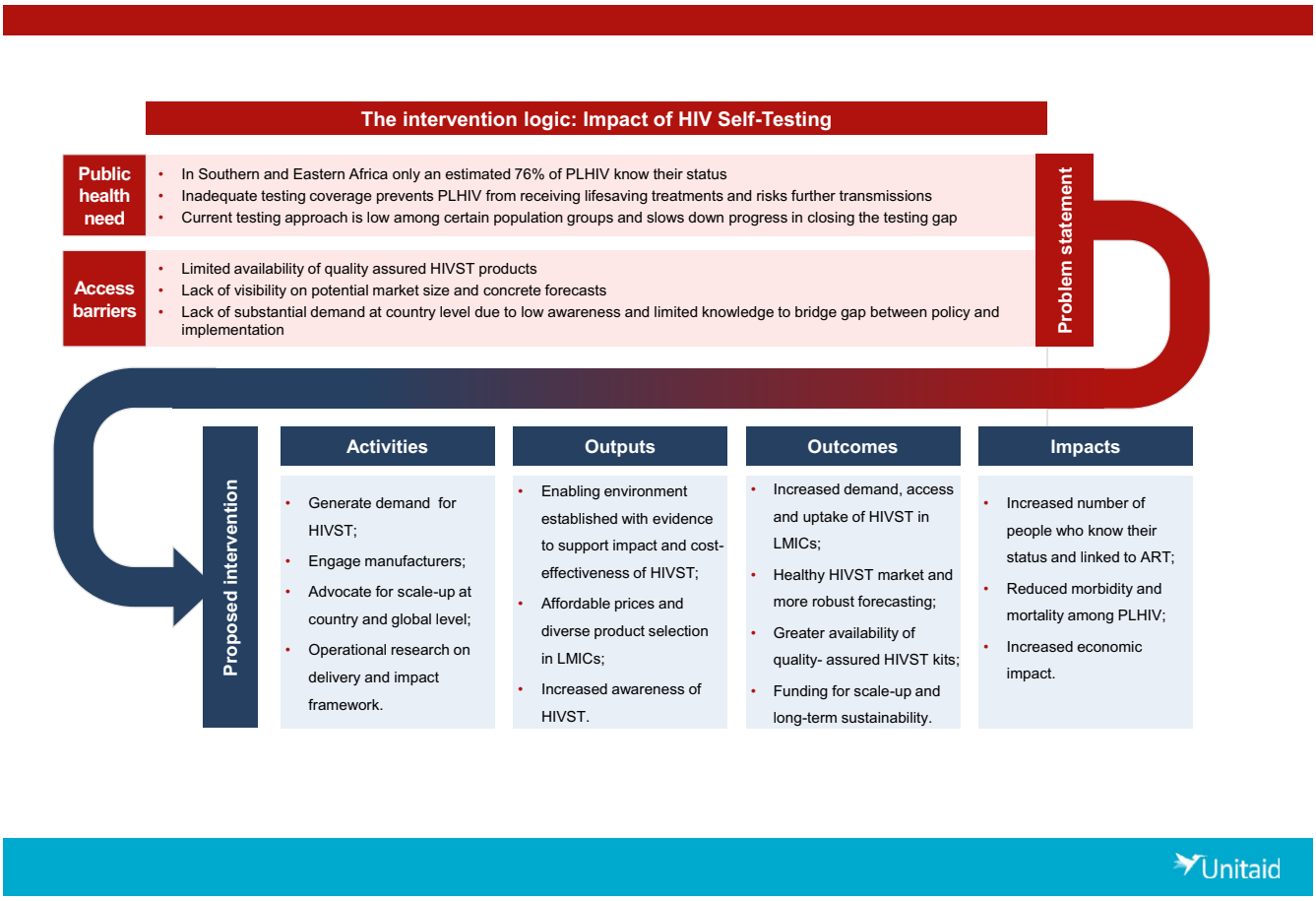


**Figure 1. Unitaid-PSI HIV STAR Project: implementation for impact.**
PSI, Population Services International; STAR, Self-Testing AfRica; PLHIV, people living with HIV; HIVST, HIV self-testing; LMIC, low- and middle-income countries.

implementation of HIVST is safe, acceptable and effective when kits are used correctly, and can contribute to increased HIV testing coverage [6,16,17].

The STAR Initiative partners worked collaboratively to identify, design and implement a research agenda to inform normative guidelines, the foundation upon which many national health policies are based. This was a major turning point for the creation of an enabling environment since most countries would not adopt policies for HIVST and donors would not invest in the product without these guidelines.

The agenda, which was in part funded by other partners, included formative research and accuracy studies to establish that HIVST was acceptable, safe, and could be correctly performed by priority populations [18,19]. Further studies tested user preferences and established simple distribution models aimed at using HIVST for maximum public health impact [18,20,21]. Data from these early distribution models informed costing and cost-effectiveness studies to establish the evidence for HIVST scalability and sustainability [20,22,23]. This collaboration helped generate important aspects of the evidence needed to inform WHO Guidelines on HIVST and Partner Notification (i.e., HIVST normative guidelines) published in December 2016, and the operational guidance at country level that followed.

## 2.2 | Creating an enabling environment for national policies, and regulatory frameworks

The STAR Initiative supported efforts to widely disseminate the guidelines and contribute to national policy and strategy development, informing HIVST roll-out across LMICs. As policy was being established, the STAR Initiative worked with country governments in Southern Africa through technical working groups (TWGs) to ensure that research was continuously informing implementation. The TWGs were chaired by MoHs and included representatives from the national regulatory bodies, WHO, in-country donors supporting national HIV programmes, civil society and PLHIV advocacy and support groups, as well as PSI and local research partners. To increase knowledge-sharing across countries and stakeholders, and to drive development of an enabling environment beyond STAR countries, the STAR Initiative developed toolkits to guide research design and HIVST implementation and met on a regular basis to share experiences. This included direct country exchanges between STAR Initiative countries and other African countries.

The STAR Initiative hosted a pivotal workshop in Nairobi in April 2017, linked to a WHO regional guidelines workshop, to share their HIVST implementation experience with MoH

representatives. This workshop provided the information necessary to transform normative guidance into implementation and led to a series of country implementation visits, catalysing action across Africa such as MoH tours of STAR implementation projects to learn directly about challenges and successes (e.g. eSwatini, Lesotho, Malawi, Uganda, and Zimbabwe). Botswana and Mozambique HIVST policy adoption and/or pilots were initiated as a result of this meeting. A number of West African countries (e.g. Côte d'Ivoire, Mali, and Senegal) were approved for funding by Unitaid through the ATLAS project to pilot HIVST shortly after the workshop. Another workshop was organised in Bangkok in collaboration with Unitaid, WHO and UNAIDS in October 2018, to share evidence and experience with HIVST with governments and implementers from 13 countries in Asia and the Pacific including the launch of the WHO strategic framework on HIVST [24] to accelerate the introduction and scale-up of HIVST in this region [Meeting report forthcoming].

To support the operationalization of policy, the STAR Initiative provided technical assistance and held regional workshops to clarify diagnostic regulatory frameworks and identify the steps necessary to establish external quality assurance and post-market surveillance systems for HIVST [25]. As a result, targeted solutions were developed in each country and included activities such as establishing medical device committees, defining responsibilities of regulatory bodies, introducing laws to parliament for product oversight, and evaluating and registering products. Harmonization of these regulatory processes has been desired since the first diagnostic products were introduced in Africa.

As a result of these efforts and advocacy, momentum around HIVST is increasing and many additional countries have indicated their interest in introducing HIVST. As of July 2018, 59 countries now have policies explicitly allowing HIVST, of which 28 are now fully implementing [26]. In addition, 32 countries are actively piloting HIVST [26].

## 2.3 | Generating diverse demand through multiple distribution channels and advocacy for additional financing

For a developed and sustainable market, demand for HIVST products must be generated from end-consumers, MoHs and donors. The STAR Initiative conducted in-depth research to understand consumer preferences and provider perceptions of HIVST and used this evidence to inform and refine the design of eight facility- and community-based distribution models in Malawi, Zambia and Zimbabwe [18,20]. In its first two years, the STAR project showed that community-based and partner-delivered HIVST can be an effective testing approach with several advantages that complement conventional options [26,27]. HIVST also demonstrated the ability to reach those who are not currently accessing services, such as first-time testers, and facilitated frequent re-testing, particularly among those with high ongoing risk [28]. HIVST may also improve efficiency and effectiveness of overburdened health systems, by refocusing testing services and resources on those with a reactive self-test result in need of confirmatory testing, thereby increasing the efficiency of conventional testing systems [29].

A concern about HIVST is the need to maximize rapid links to confirmatory testing and antiretroviral therapy (ART) for people with reactive tests, in addition to linking those with a non-reactive test to appropriate and effective prevention services, such as pre-exposure prophylaxis (PrEP) and voluntary medical male circumcision (VMMC). Research and programmatic data from STAR has demonstrated that HIVST offered by community mobilizers can increase demand, motivation for and uptake of VMMC [27]. In a community-based HIVST project in Zimbabwe, demand for ART was significantly increased, with survey data also showing that linkage to confirmatory testing and ART initiation among those who tested positive and were not previously on ART ranged between 30% and 46% six weeks after an HIVST campaign [30]. Assuming the same level of ART initiation among those newly diagnosed, HIVST is likely to result in additional 60,000 to 230,000 PLHIV receiving life-saving treatment annually from 2020 or combined total of 110,000 to 460,000 (2019 to 2020), in addition to significant linkage to appropriate prevention options, including PrEP [28].

A review of evidence in sub-Saharan Africa, including evidence from the STAR Initiative, indicates that delivery models have had varying acceptability across different targets [29]. Additional evidence shows that the use of HIVST can be cost-effective [31]. However, to maximize population health impact within the budget available, HIVST needs to be targeted based on the prevalence of undiagnosed HIV, likely HIV incidence, and the overall costs of delivering this testing modality. For example, with community-based HIVST likely to be cost-effective if introduced for women having transactional sex and adult men, provided that the undiagnosed HIV prevalence is above 3% and when delivered through campaign distribution, such as every five years [31].

Consistent engagement with MoH, Global Fund and PEPFAR through the routine dissemination of the STAR Initiative's findings allowed these key partners to integrate HIVST into longer-term scale-up plans and funding, including within Global Fund concept notes and PEPFAR country operational plans. In 2018, HIVST was included as a dedicated testing strategy in PEPFAR country guidance and received a substantial funding increase. Efforts are also underway to embed HIVST into domestic health budgets and determine the most cost-effective way of delivering testing services, including HIVST. For example, to enable the transition to domestic financing in South Africa, the potential cost-savings of HIVST will be quantified and incorporated into the HIVST investment case being developed for the South African National Department of Health.

## 2.4 | Accelerating market entry for suppliers at affordable and sustainable prices

Without normative guidance, demand for HIVST kits was weak, with uncertain forecasts ranging from 4 to 80 million tests until 2016. To provide greater clarity on potential demand, with funding from the Bill and Melinda Gates Foundation (BMGF), PSI developed estimates of the size of the HIVST market. PSI estimated that by 2020, the market would reach either 3.3 to 5.7 million or 11 to 15 million tests per year in nine African countries depending upon whether conservative or moderate assumptions were applied [15].

Based on the "moderate scenario" of the Expanding Access to HIVST report, which assumes that donors will invest to support development of both public and private sector markets, the HIVST market size could be between 13 and 15 million kits annually by 2020 [26]. Currently 99 countries had included HIVST in procurement planning, representing more than 85% of the global HIV burden. Preliminary estimates based on these findings suggest HIVST is likely to result in at least 200,000 to 500,000 additional PLHIV who will know their status annually.

In order to ensure a high-quality supply of HIVST kits, regulators and manufacturers needed to understand how HIVST fits into the current regulatory structures. Under the STAR Initiative, WHO worked to clarify the pre-qualification (PQ) requirements with manufacturers. By leveraging the accuracy and usability studies conducted in-country, PSI was able to identify product and instruction changes needed to achieve PQ or Global Fund/Unitaid Expert Review Panel for Diagnostics (ERPD) approval and national registration for OraQuick®, the only product with the evidence required to submit a dossier at the time. Wits RHI simultaneously conducted studies in South Africa to inform the WHO PQ submissions for several HIVST products, including blood-based products. However, as of 2016, significant gaps remained between the available evidence for blood-based HIVST versus oral-fluid HIVST. This gap had the potential to hinder diverse market supply. With the support of BMGF, the STAR Initiative conducted consumer usability studies on four blood-based HIVST products, optimizing instructions for use, and piloting the use of the most suitable blood-based HIVST products [32].

To improve the availability of information about the HIVST market, Unitaid and WHO developed a series of HIVST landscape reports to inform demand, assist with product selection and application, and incentivize supplier participation [26,33]. The landscape reports included a summary of the key evidence to support the use of HIVST, the current state of HIVST policy and regulation, and detailed information about available and pipeline HIVST products. The landscape reports also included information on HIVST demand.

Despite this progress towards international approvals, manufacturers remain concerned that in some countries the regulatory process remains opaque, the responsible authorities for the registration of HIVST products are still unclear, and even with WHO PQ, in-country validation and registration are still required. These complications add to the cost of doing business for manufacturers and threaten the sustainability of affordable prices for HIVST.

## 3 | REMAINING MARKET CHALLENGES

Despite this growing interest, however, the HIVST market is still nascent and the current volumes are unlikely to be sufficient to make the LMIC market healthy and attractive to multiple suppliers. Market conditions are further compounded by continued ambiguity surrounding forecasting and regulatory environments. High volumes of demand for HIVST kits, and HIV testing in general, will be needed to establish the viable market necessary for long term sustainability of HIVST. Approximately 2.5 million HIVST kits were sold worldwide between 2012 and 2017 [33]. In July 2018, the first global HIVST forecast showed at least 5 million HIVST kits would be procured by the end of 2018 and that with current donor and private sector investments the market would reach nearly 20 million kits by 2020 [26].

Currently there are only two WHO prequalified HIVST products, the INSTI HIV Self Test (bioLytical, Richmond, British Columbia Canada) and the OraQuick HIV Self-Test (OraSure Technologies), with others under review [34]. Through the Global Fund/Unitaid ERPD four other HIVST products, all of which are blood-based, have also become available for use in the context of operational research and demonstration projects [35].

While HIVST has been shown to be effective, the investment in additional testing is being scrutinized. In countries where the first 90-90-90 target has been reached or nearly attained, diagnosing the few people with HIV who do not know their status may be challenging and costly. In countries with slower progress towards achieving the first 90 target, a major shift will be needed in the approach to testing to improve effectiveness and efficiency in finding those with an undiagnosed HIV infection. There is currently still lacking clarity on how HIVST can fit and contribute to reaching the remaining PLHIV in need of diagnosis and contributing to uptake of prevention. Creating an investment case that is country context specific is critical to the sustainability and accelerated scale up of HIVST.

Notwithstanding these challenges, the prospects for the HIVST market in LMICs have improved notably over the last few years. This is due in no small measure to significant investments committed by Unitaid and other partners, including the BMGF and the Children's Investment Fund Foundation's Charitable Support Agreement with OraSure (2017) which reduced the price of the only WHO Prequalified product to US$2 for 50 countries [36]. This agreement is only valid for four years, and the price may increase if the requisite volumes are not established and maintained by the end of the term. An increase in demand and adoption as well as the presence of other affordable products will reduce this threat and offer countries a choice in product selection based on the preferences of different user populations.

Despite having a better understanding of how to deliver HIVST and an increasing number of countries introducing it, coverage remains low in comparison to the current need, and this is due to limited awareness of users and providers. Both the demand and supply for HIVST remain limited, hindering the establishment of a healthy market with affordable products.

While the findings from the STAR Initiative have been successful in motivating country governments and funding agencies, the need for additional evidence of cost-effectiveness of the different HIVST delivery models is critical to securing increased scale-up funding. Likewise, there is the need to demonstrate the impact of HIVST in enabling countries to meet their HIV coverage targets as part of the UN 90-90-90 to make a compelling investment case. Increased effectiveness of HIVST will require a balance between targeting delivery for high testing coverage for new testers versus benefits from re-testers. Such a balance is important to achieve efficiencies in the health system because health services and resources will be focused on confirmatory testing and linkage to treatment while those with a negative test can be triaged to prevention services [6].

## 4 | CONCLUSIONS

The STAR Initiative has provided a strong foundation to introduce HIVST, in LMICs, and allow for rapid scale-up based on collection of multi-country evidence and rapid dissemination to inform policy and practice through national TWGs, international workshops, and regulators and manufacturers fora. The increasingly strong evidence base has shown that HIVST is preferred by many Africans to all other testing modalities and can reach those who do not test and are at high risk of HIV in LMICs. The market for HIVST is expanding and national HIV programmes, with support from external donors, are beginning to move beyond the policy and pilot stage to scale up HIVST through multiple distribution models. Ensuring an enabling environment with systems and structures in place that are supportive of HIVST, having safeguards in place to keep inferior products out of LMIC markets, to prevent social harms, and effective targeting of low cost models for HIVST distribution and linkage into prevention and care services in high prevalence populations will maximize the important potential for public health impact. Together with sustained coordination and acceleration of market development work outside of the Africa region, HIVST can help address the testing gap and provide a focused and cost-effective means to expand access to treatment and prevention services.

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### COMPETING INTERESTS

The authors declare that they have no competing interests.

### AUTHORS' CONTRIBUTIONS

H.I., O.M. and A.L.R. made substantial contributions to formalize the concept of the commentary and development of the draft. R.L. contributed to the concept and evolution of the commentary. R.B., E.C., K.H. and C.J. have been involved in reviewing the commentary and providing valuable input. All authors have given final approval of the version to be published.

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### REFERENCES

1. UNAIDS. 90-90-90: an ambitious treatment target to help end the AIDS epidemic. Geneva: UNAIDS; 2014.
2. UNAIDS. Miles to go – closing gaps, breaking barriers, righting injustices. Geneva: UNAIDS; 2018.
3. WHO, UNAIDS, UNICEF. TOWARDS UNIVERSAL ACCESS: scaling up priority HIV/AIDS interventions in the health sector. Geneva: WHO, UNAIDS, UNICEF; 2007.
4. UNAIDS. Global AIDS update. Geneva: UNAIDS; 2017.
5. Stover J, Bollinger L, Izazola JA, Loures L, DeLay P, Ghys PD, et al. What is required to end the AIDS epidemic as a public health threat by 2030? The cost and impact of the fast-track approach. PLoS ONE. 2016;11(5):e0154893.
6. WHO. Guidelines on HIV self-testing and partner notification: supplement to consolidated guidelines on HIV testing services. Geneva: World Health Organization; 2016.
7. Alexander TS. Human immunodeficiency virus diagnostic testing: 30 years of evolution. Clin Vaccine Immunol. 2016;23(4):249–53.
8. United States Food and Drug Administration. OraQuick in-home HIV test: premarket approval 2012. [cited 2018 May 20]. Available from: https://www.fda.gov/biologicsbloodvaccines/bloodbloodproducts/approvedproducts/premarketapprovalspmas/ucm310436.htm
9. WHO. Report on the first international symposium on self-testing for HIV: the legal, ethical, gender, human rights and public health implications of HIV self-testing scale-up. WHO, UNAIDS, Brocher Foundation, Liverpool School of Tropical Mediciine, editor. Geneva: WHO; 2013.
10. Napierala Mavedzenge S, Baggaley R, Corbett EL. A review of self-testing for HIV: research and policy priorities in a new era of HIV prevention. Clin Infect Dis. 2013;57(1):126–38.
11. Wong V, Johnson C, Cowan E, Rosenthal M, Peeling R, Miralles M, et al. HIV self-testing in resource-limited settings: regulatory and policy considerations. AIDS Behav. 2014;18(4):415–21.
12. Mavedzenge S, Baggaley R, Lo Y, Corbett L. HIV self-testing among health workers: a review of the literature and discussion of current practices, issues and options for increasing access to HIV testing in Sub-Saharan Africa. Geneva: World Health Organization; 2011.
13. Corbett E. Health worker access to HIV/TB prevention, treatment and care services in Africa: situational analysis and mapping of routine and current best practices. London and Geneva: London School of Hygiene and Tropical Medicine. Global Health Workforce Alliance; 2007.
14. United States Agency for International Development (USAID). Assessment of over-the-counter HIV rapid test kits in Namibia. Arlington: USAID; 2012.
15. Population Services International. Expanding access to HIV self-testing: a market development approach; 2016 [cited 2018 May 20]. Available from: https://www.psi.org/wp-content/uploads/2016/10/HIVSTReport_Oct2016.pdf
16. Ortblad K, Musoke DK, Ngabirano T, Nakitende A, Magoola J, Kayiira P, et al. Direct provision versus facility collection of HIV self-tests among female sex workers in Uganda: a cluster-randomized controlled health systems trial. PLoS Med. 2017;14(11):e1002458.
17. Lippman SA, Lane T, Rabede O, Gilmore H, Chen Y-H, Mlotshwa N, et al. High Acceptability and Increased HIV-Testing Frequency After Introduction of HIV Self-Testing and Network Distribution Among South African MSM. J Acquir Immune Defic Syndr. 2018;77(3):279–87.
18. Indravudh PP, Sibanda EL, d'Elbee M, Kumwenda MK, Ringwald B, Maringwa G, et al. "I will choose when to test, where I want to test": investigating young people's preferences for HIV self-testing in Malawi and Zimbabwe. AIDS. 2017;31 Suppl 3:S203–12.
19. Neuman M, Indravudh P, Chilongosi R, d'Elbee M, Desmond N, Fielding K, et al. The effectiveness and cost-effectiveness of community-based lay distribution of HIV self-tests in increasing uptake of HIV testing among adults in rural Malawi and rural and peri-urban Zambia: protocol for STAR (self-testing for Africa) cluster randomized evaluations. BMC Public Health. 2018;18(1):1234.
20. d'Elbée M, Indravudh PP, Mwenge L, Kumwenda MM, Simwinga M, Choko AT, et al. Preferences for linkage to HIV care services following a reactive self-test: discrete choice experiments in Malawi and Zambia. AIDS. 2018;32(14):2043–9.
21. Choko AT, Kumwenda MK, Johnson CC, Sakala DW, Chikalipo MC, Fielding K, et al. Acceptability of woman-delivered HIV self-testing to the male partner, and additional interventions: a qualitative study of antenatal care participants in Malawi. J Int AIDS Soc. 2017;20(1):21610.

22. Maheswaran H, Clarke A, MacPherson P, Kumwenda F, Lalloo DG, Corbett EL, et al. Cost-effectiveness of community-based human immunodeficiency virus self-testing in Blantyre, Malawi. Clin Infect Dis. 2017;66(8):1211–21.
23. Sande L, Maheswaran H, Mangenah C, Mwenge L, Indravudh P, Mkandawire P, et al. Costs of accessing HIV testing services among rural Malawi communities. AIDS Care. 2018;30 Suppl 3:27–36.
24. WHO. HIV self-testing strategic framework: a guide for planning, introducing and scaling up. Geneva: WHO; 2018.
25. Dacombe R, Watson V, Nyirenda L, Madanhire C, Simwinga M, Chepuka L, et al. Regulation of HIV self-testing in Malawi, Zambia and Zimbabwe: a qualitative study with key stakeholders. J Int AIDS Soc. 2019;22(S1):e25229.
26. Unitaid, WHO. Market and technology landscape: HIV rapid diagnostic tests for self-testing. 4th ed. Geneva: Unitaid, WHO; 2018.
27. Mavhu W, Hatzold K. Program data presented at AIDS 2018. 10th International AIDS Conference. Amsterdam, The Netherlands; 2018.
28. Ortblad KF, Chanda MM, Musoke DK, Ngabirano T, Mwale M, Nakitende A, et al. Acceptability of HIV self-testing to support pre-exposure prophylaxis among female sex workers in Uganda and Zambia: results from two randomized controlled trials. BMC Infect Dis. 2018;18(1):503.
29. Indravudh PP, Choko AT, Corbett EL. Scaling up HIV self-testing in sub-Saharan Africa: a review of technology, policy and evidence. Curr Opin Infect Dis. 2018;31(1):14.
30. Sibanda E, Neuman M, Tumushime M, Hatzold K, Watadzaushe C, Mutseta M. Linkage to care after HIV self-testing in Zimbabwe: a cluster-randomised trial. 25th CROI Conference. Boston (MA); 2018.
31. Cambiano V, et al. The impact and cost-effectiveness of community-based HIV self-testing in sub-Saharan Africa: a health economic and modelling analysis. J Int AIDS Soc. 2019;22(S1):e25243.
32. Cowan F. Exploring potential social harms of self testing. Learning from cognitive interviews with HIVST users using blood-based self tests in Zimbabwe and Malawi. 22nd International AIDS Conference. Amsterdam, The Netherlands; 2018.
33. Unitaid, WHO. Market and technology landscape: HIV rapid diagnostic tests for self-testing. 3rd ed. Geneva: Unitaid, WHO; 2017.
34. WHO. WHO prequalification of in vitro diagnostics public report. Geneva, Switzerland: World Health Organization; 2017.
35. Global Fund to Fight AIDS TaM. List of HIV diagnostic test kits and equipments classified according to the Global Fund Quality Assurance Policy Geneva 2018. [cited 2018 May 20]. Available from: https://www.theglobalfund.org/media/5878/psm_productshiv-who_list_en.pdf
36. OraSure Technologies. What is the Bill and Melinda Gates Foundation agreement with OraSure Technologies? Bethlahem, Pennsylvania United States 2017 [cited 2018 May 20]. Available from: http://www.orasure.com/products-infectious/products-infectious-oraquick-self-test.asp.

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