Preparing for Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Self-Testing Implementation: Lessons Learned From HIV Self-Testing

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INTRODUCTION

The number of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) cases and associated death continue to rise globally. Widespread testing for SARS-CoV-2 infection is crucial in order to identify individuals who need to need to be isolated, thereby reducing their chances to infect others and allowing them to seek treatment earlier which can prevent further negative health outcomes and mortality (1). Currently, the most common testing method for SARS-CoV-2 diagnosis is Real-Time Polymerase Chain Reaction (RT-PCR) from nasopharyngeal, throat or saliva specimens (2). However, SARS-CoV-2 testing has been hampered in many countries due to inadequate test kits, uncomfortable testing procedures, shortages of personal protective equipment (PPE) for health care workers, and low demand among people to seek testing for SARS-CoV-2 at health facilities (3–7).

In response, the United States Food and Drug Administration (FDA) provided Emergency Authorization Use for several SARS-CoV-2 self-sampling kits (SARS-CoV-2SS) that allow individuals to self-collect nasal swabs and saliva specimens and send to a lab for testing (8). Other efforts to increase testing include drive-through methods that include both self-sampling and health care-collected samples (9, 10). The National Institute of Health has also launched the Rapid Acceleration of Diagnostics (RADx) program to accelerate the development of, scale up, and deploy innovative point-of-care of technologies, support the scale-up of more advanced technologies, and nontraditional approaches for testing as well as establish community-engaged implementation projects to improve access to testing in underserved and vulnerable populations (11). Similar research and programmatic activities to increase testing capacity SARS-CoV-2 are also being implemented in other regions (12–16).

The efforts to increase testing capacity for SARS-CoV-2 diagnosis testing will be enhanced with the availability and widespread promotion of self-sampling and eventually SARS-CoV-2 self-testing (SARS-CoV-2ST) (17–19). The benefits of self-sampling and self-testing include their abilities to help decentralize care, promote social distancing, conserve PPEs, address transportation and privacy barriers for individuals who do not want to test at a clinic or a drive-through setting, and...
reach more individuals who are not reached with current testing modalities (12, 17, 20). Unlike self-sampling, SARS-CoV-2ST will allow individuals to receive their results at home without the need to ship their specimens to a laboratory for testing (21, 22). To our knowledge, there is only one FDA-approved SARS-CoV-2ST diagnostic kit for individuals to use and receive their results at home as of November 17, 2020 (23). However, a number of other different at-home SARS-CoV-2ST kits are being developed and evaluated to either detect antibodies or active viral infections (24). Antibody SARS-CoV-2ST kits reveal markers of immune response that show up in blood more than a week after a person has been infected whereas active infections will be detected with nucleic acid SARS-CoV-2ST kits through the virus’ genetic materials (24, 25).

As researchers, federal health agencies, and public health practitioners prepare to implement SARS-CoV-2ST, lessons learned from the global implementation and scaling up efforts for HIV self-testing (HIVST) can prove useful. We describe research related to questions that emerged regarding HIVST and how they are similar or different to the questions that will need to be addressed for SARS-CoV-2ST before this crucial strategy can be implemented and scaled up successfully. We also discuss the findings of the first antibody SARS-CoV-2ST acceptability and usability study (22) and the public health implications of and recommendations people who obtain a positive SARS-CoV-2ST result for antibodies or active viral infections. Lastly, we identify key structural inequities in communities that are most affected by COVID-19 that need to be addressed during future SARS-CoV-2ST implementation efforts.

IN-HOME HIV SELF-TESTING HISTORY

In 2012, the US FDA approved the first over-the-counter rapid HIVST kit, the OraQuick In-Home HIV Test which allows users to test for antibodies using saliva sample, similar to the new saliva-based SARS-CoV-2ST kit (26), and receive a preliminary result at home in 20 min (27). The benefits of HIVST include privacy, an increase of access to HIV testing, earlier diagnosis of HIV, confidentiality of results, and reducing queues for facility-based HIV testing (28). HIVST can also help bypass social barriers such as stigma and discrimination that deter people from accessing facility-based HIV testing (28). Since the approval of HIVST, several questions emerged about its accuracy, acceptability, feasibility, the lack of pre-and-post-test counseling, whether users would seek a confirmatory test, and link to care (29). There is now overwhelming evidence that HIVST is accurate, acceptable, feasible, and effective with minimal social harms (29). As a result from these studies, the World Health Organization (WHO) now recommends HIVST as one of the testing strategies for HIV prevention efforts (30). These studies, including our own (31–39), have provided evidence on different distribution strategies from online platforms, peers to sexual partners, community health workers (40–42). Similarly, these studies have assessed different approaches to verify HIVST results either through direct supervision by health provider, requesting participants to return used HIVST kits, electronic transmission of photographs, or using Bluetooth sensors (43).

ANTIBODY SARS-CoV-2 SELF-TESTING ACCEPTABILITY AND USABILITY

In the first published SARS-CoV-2ST study, researchers in England examined the acceptability and feasibility of two types (i.e., Guangzhou Wondfo Biotech Co Ltd and Fortress Orient Gene Biotech Co Ltd) of SARS-CoV-2ST lateral flow immunoassays (LFIAs) or rapid point-of-care tests that use a blood sample from a finger-prick and produce a self-read result after 10 or 15 min for detection of SARS-CoV-2 antibodies (Immunoglobin M and Immunoglobin G) (22). Participants received LFIAs by mail and recorded their interpretation of their results in an online survey with the option to upload a photograph of the results (22). To assess participants’ ability to correctly interpret the test results, a clinician reviewed all the samples of the uploaded photographs that were reported as positive and unable to read as well as a random sample of 200 participant-reported negative or invalid results. Acceptability in the national study was high with 99.3% (8,693/8,754) and 98.4% (2,911/2,957) of participants reporting that they attempted to use the two LFA types (22). Feasibility was also high in the pilot and national studies with 86.5% (225/260) of pilot participants and 97.5 and 97.8% of participants in the national study reporting they completed all the steps for the tests successfully, respectively (22). The majority of participants 85.8% (7,272/8,475) and 84.8% (2,416/2,848) uploaded the photographs of their results with substantial agreement between participant and clinician interpreted results for both test types (22). However, there were differences between some of the self-reported results and those reported by the clinician and some participants reported some difficulties with using the lancet and pipette of the test kits (22).

DISCUSSION

The scientific and clinical fields involved in HIV prevention have provided extensive experience, amassed over decades, regarding the value of testing and the added benefits of in-home self-testing (30). This experience can be brought to bear for SARS-CoV-2ST, including strategies that can help avoid repeating the pitfalls encountered during the path toward implementing and scaling up HIVST. For example, limited evidence on the public health impact and cost-effectiveness of HIVST, uncertain levels of consumer demand and concerns about potential social harms amongst others delayed the roll out of HIVST (44). Global efforts and collaborations between WHO, researchers, local health agencies, donors, and policy makers have addressed some of these limitations. Initiatives such as but not limited to the Self-Testing AfRica (STAR), the largest HIVST implementation science project to date (44), 4 Youth by Youth crowdsourced HIVST interventions (45, 46), and Self-Testing Education and Promotion (STEP) project (28, 33), have created a market for HIVST in sub-Saharan Africa. These initiatives combined with other studies around the globe have accelerated access to
HIVST by gathering the necessary acceptability, feasibility, and fidelity data, creating an enabling environment with regards to HIVST policies, generating diverse demand through multiple distribution channels, and creating advocacy for additional financing, as well as accelerate market entry for suppliers at affordable and sustainable prices (44, 45, 47–49). Similar initiatives are needed swiftly to gather additional accuracy, acceptability, feasibility, and programmatic data to encourage policy makers, donors, and local health agencies to support for SARS-CoV-2ST implementation and scale up.

While the findings from the first antibody SARS-CoV-2ST acceptability and usability study in England were promising, some participants reported difficulties using the pipette and applying the blood drop to the cassette (22). Thus, more studies are needed to assess ease of use of SARS-CoV-2ST and how to provide the support that potential users may need. One potential strategy to support SARS-CoV-2ST users is online real-time instructions, which has been evaluated with HIVST and found to be acceptable and successful in increasing HIV testing (50). A recent SARS-CoV-2SS study has shown that participants are willing to self-collect specimens [saliva, oropharyngeal swab (OPS), and dried blood spot (DBS) card] at home while being observed by a clinician through a telehealth session (51). A total of 159 participants were mailed kits and 153 scheduled a video appointment with the majority of the (n = 143) completing all three self-collected samples (52). A similar approach can be assessed for SARS-CoV-2ST to move beyond simply observing potential users to providing additional instructions and post-test supports in the self-testers receive a positive result.

The public health implications of potential positive antibody SARS-CoV-2ST results extend beyond treatment since individuals with antibodies for SARS-CoV-2 are considered to have recovered from COVID-19 and should less symptomatic. However, a positive antibody SARS-CoV-2ST result will allow individuals, including skeptics, to learn indeed whether they had a COVID-19 infection—increasing their perception of risk and potentially positively influencing future behaviors to prevent COVID-19 re-infection. Alternatively, a positive antibody SARS-CoV-2ST result has the potential to help individuals make informed decisions about their risk levels as they consider returning to work or interact with infected individuals (19). In addition, antibody SARS-CoV-2ST results can help identify qualified individuals who may be interested in donating blood for convalescent plasmaexternal icon as a treatment for COVID-19. The Centers for Disease Control and Prevention (CDC) describe general recommendations for positive antibody test results that people who receive a positive antibody SARS-CoV-2ST result can follow such as continuing with normal activities, washing hands often, avoiding close contact, wearing a mask when around others, and continued use of PPE if the person is a health care worker or first responder (53, 54). On the other hand, a nucleic acid SARS-CoV-2VST kit will provide individuals with active infections an instant preliminary positive result that can allow them to follow recommendations for people who are sick such as self-isolate in order to prevent potential transmission and seek confirmatory diagnostic testing and early treatment (19).

We must also be mindful that the SARS-CoV-2 transmission profile is not the same as HIV and it presents immense new challenges that will require us to envision and test new ways for its easy and reliable detection and its equitable access among marginalized racial groups, sexual minority ages, incomes and the multitude of intersections between them. As is the case with HIV, Black communities are disproportionately affected by COVID-19 (55). This population has experienced extensive barriers to facility-based HIV testing and HIVST (35) and the pattern seems to be repeating for COVID-19. We need novel ways to ensure the most vulnerable populations, who are also the most likely to be infected with and die from COVID-19, have access to affordable SARS-CoV-2ST. It is important for investigators who are validating SARS-CoV-2ST kits in community settings to design the studies in a way that ensures adequate representation from the populations most vulnerable to COVID-19 infection and mortality. To promote adequate representation of special populations (elderly aged 65 years and older, youth aged 17 years and younger, Black, Latinx, Tribal communities indigenous to North America, and Spanish-speaking and francophone populations) in SARS-CoV-2ST research and programs, there are several lessons learned from HIV research and HIVST that can be applied to COVID-19.

**AUTHOR CONTRIBUTIONS**

DFC conceived the idea for the manuscript and drafted it before all authors reviewed and edited the manuscript into this final form. All authors contributed to the article and approved the submitted version.

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**REFERENCES**

1. Why COVID-19 Testing Is the Key to Getting Back to Normal. National Institutes of Health Announcements (2020). Available online at: https://www.nia.nih.gov/news/why-covid-19-testing-key-getting-back-normal (accessed October 25, 2020).
2. Sethuraman N, Jeremiah SS. Ryo interpreting diagnostic tests for SARS-CoV-2. JAMA. (2020). doi: 10.1001/jama.2020.8259
3. Seidu AA, Hagan JE, Ameyaw EK, Ahinkorah BO, Schack T. The role of testing in the fight against COVID-19: current happenings in Africa and the way forward. Int J Infect Dis. (2020) 98: 237–40. doi: 10.1016/j.ijid.2020.06.089

4. Siegel JM, Hall E, Luisi N, Zlotorzynska M, Wilde G, Sanchez T, et al. Willingness to seek laboratory testing for SARS-CoV-2 with home, through, and clinic-based specimen collection locations. medRxiv. (2020). doi: 10.1093/ofid/ofaa269

5. Ranney ML, Grifith V, Jha AK. Critical supply shortages—the need for ventilators and personal protective equipment during the Covid-19 pandemic. N Engl J Med. (2020) 382:e41. doi: 10.1056/NEJMp2006141

6. Tu YP, Jennings R, Hart B, Cangelosi GA, Wood RC, Wehber K, et al. Swabs collected by patients or health care workers for SARS-CoV-2 testing. N Engl J Med. (2020). doi: 10.1056/NEJMsc2016321

7. Rowan NJ, Laffey JG. Challenges and solutions for addressing critical shortage of supply chain for personal and protective equipment (PPE) arising from Coronavirus disease (COVID19) pandemic—Case study from the Republic of Ireland. Sci Total Environ. (2020) 725:138532. doi: 10.1016/j.scitotenv.2019.138532

8. Thomas K, Singer N. FDA Authorizes First In-Home Test for Coronavirus. New York Times (2020). Available online at: https://www.nytimes.com/2020/04/21/health/fda-in-home-test-coronavirus.html (accessed September 25, 2020).

9. Ton AN, Jethwa T, Waters K, Speicher LL, Francis D. COVID-19 drive through testing: an effective strategy for conserving personal protective equipment. Am J Infect Control. (2020) 48:731–2. doi: 10.1016/j.ajic.2020.04.010

10. Kojima N, Turner F, Slepnev V, Bascelar A, Deming L, Kodeboyina S, et al. Self-collected oral fluid and nasal swabs demonstrate comparable sensitivity to clinician collected nasopharyngeal swabs for Covid-19 detection. medRxiv. (2020). doi: 10.1101/2020.04.11.20062372

11. Tromberg BJ, Schwert TA, Pérez-Stable EJ, Schwetz TA, Bright RA, Converse et al. Preparing for SARS-CoV-2 Self-Testing. York Times (2020). Available online at: https://www.nytimes.com/2020/05/08/health/fda-coronavirus-spit-test.html (accessed September 25, 2020).

12. Technologies O. Final Advisory Committee Briefing Materials: Available for Public Release. Washington, DC: Food and Drug Administration (2012).

13. Converse DF, Muessig KE, Mahoko LL, Shirima S, Kilonzo MN, Maman S, et al. Mate Yako Afya Yako: formative research to develop the Tanzania HIV self-testing education and promotion (TANZSTEP) project for men. PLoS ONE. (2018) 13:e0202521. doi: 10.1371/journal.pone.0202521

14. World Health Organization. Guidelines on HIV Self-Testing and Partner Notification: Supplement to Consolidated Guidelines on HIV Testing Services. Geneva: World Health Organization (2016).

15. Choko AT, Nanfuka M, Birungi J, Taaai G, Kiseombo P, Hellingr S. A pilot trial of the peer-based distribution of HIV self-test kits among fishermen in Bulisa, Uganda. PLoS ONE. (2018) 13:e0208911. doi: 10.1371/journal.pone.0208911

16. Mathews A, Converse D, Mason H, Alston LM, Rennie S, Tucker J. ‘Informed disease 2019 (COVID-19) and the SARS-CoV-2 virus in Latin America and the Caribbean: morbidity, mortality and molecular testing trends in the region. medRxiv. (2020). doi: 10.1101/2020.04.25.20079863

17. Choko AT, Corbett EL, Stallard N, Maheshwaran 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: a qualitative multi-arm, multi-stage cluster randomised trial. PLoS Med. (2019) 16:e1002719

18. Converse DF, Mbita G, Alema D, Njau B, Liia J, Komba A. Developing a peer-led HIV self-testing education and promotion intervention for networks of men in Tanzania. In: APHA 2019 Annual Meeting and Expo (Nov. 2-Nov. 6). American Public Health Association (2019).

19. Converse DF, Alemu D, Yanamis T, Maman S, Kajula L. “He told me to check my health”: a qualitative exploration of social network influence on Men’s HIV testing behavior and HIV self-testing willingness in Tanzania. Am J Mens Health. (2018) 12:1185–96. doi: 10.1177/1557859X18777674

20. Mathews A, Farley S, Converse DF, Knight K, LeMarais A, Blumberg M, et al. “Meet people where they are”: a qualitative study of community barriers and facilitators to HIV testing and HIV self-testing among African Americans in urban and rural areas in North Carolina. BMC Public Health. (2020) 20:1–10. doi: 10.1186/s12889-020-08582-z

21. 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:e1001873. doi: 10.1371/journal.pmed.1001873

22. Mathews A, Converse D, Mason H, Alston LM, Rennie S, Tucker J. ‘Informed and empowered’: a mixed-methods study of crowdsourcing contests to promote uptake of HIV self-testing kits among African Americans. J Virus Erad. (2020) 6:74–80. doi: 10.1052/virus-2019054600(20)30020-0

23. Converse DF, Michel J, Adrien Demes JE, Chéry JM, Balan JG, Choko AT, et al. Local and national stakeholders’ perceptions towards implementing and scaling up HIV self-testing and secondary distribution of HIV self-testing by Option B+ patients as an assisted partner service strategy to reach men in Haiti. PLoS ONE. (2020) 15:e0233606. doi: 10.1371/journal.pone.0233606

24. Jawaunmor J, Ezechi O, Obiezu-Umed C, Gbaja-biamila T, Nwaozuru U, Oladele D, et al. The 4 youth by youth crowdsourcing contest: using participatory design to reach and increase uptake of HIV self-testing among young people in Nigeria. In: 12 th Annual Conference on the Science of Dissemination and Implementation. AcademyHealth (2019).
40. MacGowan RJ, Chavez PR, Borkowf CB, Owen SM, Purcell DW, Mermin JH, et al. Effect of internet-distributed HIV self-tests on HIV diagnosis and behavioral outcomes in men who have sex with men: a randomized clinical trial. JAMA Intern Med. (2020) 180:117–25. doi: 10.1001/jamainternmed.2019.5222
41. Mulubwa C, Hensen B, Phiri MM, Shanaube K, Schaap AJ, Floyd S, et al. Community based distribution of oral HIV self-testing kits in Zambia: a cluster-randomised trial nested in four HPTN 071 (PopART) intervention communities. Lancet HIV. (2019) 6:e81–92. doi: 10.1016/S2352-3018(18)30258-3
42. 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 care and post-partum care in Kenya: a cohort study. Lancet HIV. (2016) 3:e266–74. doi: 10.1016/S2352-3018(16)00041-2
43. Tahli KM, Ong JJ, Rosenberg NE, Tang W, Conserve DF, Nkengasong S, et al. Verification of HIV self-testing use and results: a global systematic review. AIDS Patient Care STDS. (2020) 34:147–56. doi: 10.1089/apc.2019.0283
44. Ingold H, Mwerinde O, Ross AL, Leach R, Corbett EL, 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:e25249. doi: 10.1002/jia2.25249
45. Iwelunmor J, Ezechi O, Obieu-Umeh C, Gbaja-Biamila T, Nwaozuru U, Oladele D, et al. The 4 youth by youth HIV self-testing crowdsourcing contest: a qualitative evaluation. PLoS ONE. (2020) 15:e0235698. doi: 10.1371/journal.pone.0235698
46. Nwaozuru U, Gbajabiamila T, Obieu-Umeh C, Mason S, Tahli K, Oladele D, et al. An innovation bootcamp model to develop HIV self-testing social enterprise among young people in Nigeria: a youth participatory design approach. Lancet Global Health. (2020) 8:S12. doi: 10.1016/S2214-109X(20)30153-4
47. 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-testing in Malawi and Zimbabwe. AIDS. (2017) 31:S203. doi: 10.1097/QAD.0000000000001516
48. Catania JA, Haun C, Dolcini MM, Urban AJ, Fleury N, Ndyetabula C, et al. Overcoming cultural barriers to implementing oral HIV self-testing with high fidelity among Tanzanian youth. Transl Behav Med. (2019). doi: 10.1093/tb/thz157
49. Korte JE, Kisa R, Vrana-Diaz CJ, Malek AM, Bureguye E, Matovu JK, et al. HIV oral self-testing for male partners of women attending antenatal care in central Uganda: uptake and linkage to care post-test in a randomized trial. JAIDS J Acquir Immune Defic Syndr. (2020). doi: 10.1097/QAI.0000000000002341
50. Wang Z, Lau JT, Ip M, Ho SP, Mo PK, Latkin C, et al. A randomized controlled trial evaluating efficacy of promoting a home-based HIV self-testing with online counseling on increasing HIV testing among men who have sex with men. AIDS Behav. (2018) 22:190–201. doi: 10.1007/s10461-017-1887-2
51. Valentine-Graves M, Hall E, Guest J, Adam E, Valencia R, Hardee I, et al. At-home self-collection of saliva, oropharyngeal swabs and dried blood spots for SARS-CoV-2 diagnosis and serology: post-collection acceptability of specimen collection process and patient confidence in specimens. medRxiv. (2020). doi: 10.1101/2020.06.10.20127845
52. Guest JL, Sullivan PS, Valentine-Graves M, Valencia R, Adam E, Luisi N, et al. Suitability and sufficiency of telehealth clinician-observed, participant-collected samples for SARS-CoV-2 testing: The iCollect Cohort Pilot Study. JMIR Public Health Surveill. (2020) 6:e19731. doi: 10.2196/19731
53. CDCP. Interim Guidelines for COVID-19 Antibody Testing (2020). Available online at: https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antibody-tests-guidelines.html (accessed September 25, 2020).
54. CDCP. How to Protect Your Health (2020). Available online at: https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/prevention.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fprepare%2FPrevention.html (accessed September 25, 2020).
55. Yancy CW. COVID-19 and African Americans. JAMA. (2020). doi: 10.1001/jama.2020.6548

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