STUDY PROTOCOL

Title: Exploring Use of a Real-time, Remote Monitoring and Follow-up System for Home-based, HIV Self-testing Among High-risk Men Who Have Sex With Men (MSM)

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Project Title: **Real-time, remote monitoring system for home-based HIV testing among high-risk men who have sex with men**

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A. Lay Person Summary

Rates of new HIV infections continue to increase among men who have sex with men (MSM), despite stability or decline among other risk groups. While a large proportion of these new HIV transmissions originate from among MSM who are aware of their infection but not engaged in care, up to 50% of infections may be transmitted by individuals who are unaware of their status. Home-based self-HIV testing (HBST) offers considerable promise for increasing the number of MSM who are aware of their status by overcoming many prominent obstacles to clinic-based testing, such as concerns about confidentiality and inconvenience. Studies suggest that many MSM who have never tested would prefer to do so at home and feel they would test more often with HBST. HBST may also be uniquely well-suited for connecting particularly high-risk, "hard to reach" segments of MSM with testing. MSM who meet partners online and via mobile apps are among these, and an extensive body of research has shown clear relationships between meeting partners online and higher HIV-risk behavior. Despite the promise of HBST for expanding access to testing among these high-risk and "difficult to reach" MSM, prominent concerns prevent their widespread integration into prevention programs. Among the most vital of these are concerns that HBST users may not be adequately linked with post-testing resources, such as counseling, confirmatory HIV testing, testing for other sexually-transmitted diseases (STIs), and other prevention resources (e.g., pre-exposure prophylaxis). As a result, HBST users may delay seeking care. OraSure's® OraQuick, the only FDA-approved HBST available, offers a free, 24-hour helpline that provides these services to users who seek it, but few users do and this "passive" approach may miss critical opportunities to engage with "hard to reach" populations. Coupling existing and ubiquitous technologies with the delivery of HBSTs can enable a more "active" system for engaging with HBST users after testing to offer timely follow-up and post-test counseling remotely. Monitoring HBST use in real-time and providing prompt follow-up could be an intervention-in-itself that increases the likelihood of future testing and the number of users who are successfully linked with care and other prevention services. Given these gaps in HBST service delivery, the goals of this exploratory research are to: (1) refine technology that enables real-time, remote monitoring of HBST kits, allowing timely delivery of post-test counseling and referrals to HBST users over the phone ("Enhanced HBST"), and (2) test whether this "enhanced HBST" increases the likelihood of any testing, repeat testing, and successful linkage to other prevention services compared to standard HBST in a sample of high-risk MSM who meet partners online. Findings can inform whether proactively following-up with HBST users is feasible, acceptable, and useful, and can encourage future research exploring optimal methods for providing follow-up.

B. Proposal for Funding

See attached.

C. Study Protocol

(C.1) Significance and Specific Aims of Project

(C.2) Participant Population
(C.3) Recruitment Procedures
(C.4) Design and Methods

C.1 Significance and Specific Aims of Project

Overall estimates of new HIV infections in the United States have remained steady in the last decade[1], reflecting considerable advances made in treatment and prevention using combination biomedical, behavioral, and social approaches[2]. However, annual HIV incidence continues to rise among men who have sex with men (MSM). MSM accounted for 63% of all new infections in 2010[3,4] and this rate is expected to climb 3% each year[5]. Despite these increases, modeling studies suggest that nearly 90% of new infections can be prevented using tools that already exist[6]. However, for this goal to be realized, innovative strategies are needed to speed the proliferation of these tools and increase their uptake among at-risk and "hard to reach" groups.

While studies suggest that many new HIV transmissions originate from those who are aware of their infection but not engaged in care, up to 50% of new infections may originate from those who are unaware of their infection[7,8]. As such, exploring ways to expand access to HIV testing and encourage frequent and regular testing among at-risk groups is key to reducing the spread of HIV and could have a profound impact on the epidemic. In 2012, the first home-based, rapid self-administered HIV test (HBST; OraSure® Technologies, Bethlehem, PA) was approved by the FDA and made publicly available for sale. HBST offers many advantages over clinic-based testing, including the potential to reach more individuals who are at-risk for HIV infection and encourage them to test more often. Past studies suggest that the majority of MSM, including MSM who have never tested[15,16], would prefer to test at home, and many felt they would do so more often with HBST[11,13,14]. Among the most prominent obstacles to traditional testing include difficulty seeking testing during work hours and the inconvenience of attending clinics (e.g., travel, wait times) [11,12]. HBST may also be well-suited for connecting particularly high-risk, "hard to reach" segments of MSM with testing. MSM who meet partners on mobile apps are among these. An extensive body of research has shown clear relationships between meeting partners online and higher HIV-risk behavior[9]. Although few studies are available, some evidence suggests that these individuals are less likely to have ever had an HIV test and may be more likely to use HBST versus clinic-based testing[10]. Together, these studies suggest that HBST could overcome many of the most common barriers to testing, and that it may be useful for engaging high-risk MSM who meet partners online.

Despite HBST's promise for expanding testing in this high-priority population, many salient concerns remain about its use in real-world settings. Among the more critical of these is that HBST users may not be adequately linked with vital resources after testing, which may result in critical delays in seeking care and additional resources, such as confirmatory testing, testing for other sexually-transmitted infections (STIs), and other prevention resources (e.g., pre-exposure prophylaxis [PrEP], risk reduction counseling)[11].Others have also expressed concern about the lack of post-test counseling in HBST[12,13]. Currently, OraSure® offers a 24-hour helpline that provides test counseling and referrals to local HIV prevention/care services[13], but this approach is passive and relies on users to "reach out" for these services. Coupling existing and ubiquitous technologies with the delivery of HBSTs can enable a more "active" system for engaging with HBST users after testing to offer prompt follow-up and post-test counseling over the phone. In this "enhanced HBST" system, a mobile monitoring sensor detects when HBST kits are opened, triggering an alarm on dedicated mobile phones carried by qualified HIV test counselors

(QHTC), prompting them to follow up with users over the phone within 24 hours. Conducting active follow-up through "enhanced HBST" may increase the number of HBST users who receive follow-up counseling and are referred/linked with care, confirmatory testing, and additional services. Providing timely follow-up counseling via enhanced HBST could also be an intervention-in-itself that increases the likelihood of future testing. To address this gap in service deliver, this proposal aims to:

Specific Aim 1: Refine technology that enables real-time, remote monitoring of HBST kits, allowing delivery of post-test counseling and service referrals to HBST users over the phone ("Enhanced HBST"). This will be accomplished using an iterative developmental process informed by qualitative methods with target group members to produce a feasible and acceptable system for conducting "active" follow-up after HBST.

Specific Aim 2: Explore whether "enhanced HBST" results in higher rates of (2a) any and repeat testing, (2b) receipt of post-test counseling, and (2c) follow up for additional services (e.g., STI testing, PrEP) versus standard HBST.

Secondary Aims: We will also explore potential within- and between-subject effects of Enhanced HBST versus standard HBST on positive/negative affect, social support, sex risk behavior, and health empowerment.

Overview of the research: During a "start-up" period of 6 months, we will use qualitative methods (focus group [*N*=8], individual interviews [*N*=10]) to inform ongoing consultation with Devicix (an electrical and software engineering firm) on refining a mobile technology for monitoring HBST use, ultimately preparing it for deployment. Then, during the "study phase," 40 high-risk MSM in the Providence, RI area will be randomly assigned to one of two conditions: An "enhanced" HBST condition (*N*=20) or standard HBST (*N*=20). In both conditions, 3 HBST kits will be sent by mail at 3-month intervals over the course of 6 months (baseline, 3-months, 6-months). We chose to deliver HBSTs by mail given recent evidence that a majority of MSM prefer this method of receiving kits (as opposed to pharmacy pickup or vending machines)[50,51]. In the "enhanced" HBST condition, mailed test enclosures will be equipped with a mobile monitoring sensor (see Section 3C.3.1.) that triggers an alarm on dedicated mobile phones carried by qualified HIV test counselors (QHTC). QHTCs will then conduct a follow-up call to the user within 24 hours. In the HBST alone condition, test kits will simply be mailed to participants with contact information for local HIV care, confirmatory testing, STI testing, and PrEP. All participants will be oriented to the study during a baseline, in-person appointment at Brown University. Then, participants will complete monthly assessments online over the course of 7 months while on the study (see Fig. 1 for a timeline). To complete the project within the 2-year period, 4 participants per month will be recruited on a rolling basis (beginning in month 6 of year 1), allowing all participants to finish the study by month 10 in Year 2.

C.2 Participant Population

The research has three phases: (1) Focus group phase [*N* = 8], (2) individual interview phase [*N* = 10], and (3) pilot study phase [*N* = 40]. *All* participants (regardless of which phase they are participating in) will meet the same criteria.

Inclusion criteria are as follows:

1. Biologically male
2. Aged 18 or older

3. Have not been tested for HIV in the last year
4. Report unprotected anal sex (or anal sex without a condom or having taken PrEP that day) with a casual male partner at least once in the past 6 months
5. Sex with a partner met online in the past year
6. Stable residence
7. Use of an Android smartphone with service contract and data plan
8. Fluent in English

Exclusion criteria:

1. Individuals who are HIV-positive
2. Individuals who participated in other phases of the research
3. Individuals who report being coerced to participate

C.3 Recruitment Procedures

We will recruit participants using ads in social networking mobile apps and websites that gay men often use to meet partners (e.g., Grindr, Jack'd, Adam4Adam). App users who click on an ad will be directed to a webpage that provides more information on the study. If they are interested in participating, a link an online screening survey will be made available at the bottom of the page. Participants will provide their informed consent prior to answering questions on the screen. The screening questionnaire will be collected using Qualtrics® survey software. Screening items will only address eligibility criteria (see Appendix B, Section I.). Participants determined to be eligible based on this brief screening will be contacted by email and phone to provide more information about the study. Participants who are interested in participating in the full study will then schedule an appointment to come to the research offices at Brown.

C.4 Design and Methods

Phase I: Start-Up and Qualitative Research

Focus groups. At the start of the project period, we will conduct a focus group with 8 participants from the target group in which we will present the proposed monitoring and follow-up system, and solicit participant feedback. Key questions to be addressed include the desirability of "active" follow-up after HBST, when and how participants would like to receive follow-up, and what users would like follow-up calls to address. $50 will be paid to focus group participants.

Individual interviews. After test versions of the technologies are available, we will recruit 10 high-risk MSM to use the system and provide their feedback. We will recruit participants who are "willing to take a home HIV test" online and meet similar eligibility criteria to that of the full study (see 3C.4.2). Those eligible will be asked to come to the research offices, where the study will be explained. Consenting participants will then download study software onto their smartphones, and research assistants (RAs) will provide them with an HBST kit equipped with a BLE sensor, asking them to use the test within 1 week. They will be informed that a QHTC will contact them by phone within 24 hours of opening the test. During calls, QHTCs will conduct the normal follow-up procedures (e.g., post-test counseling, referral for services, see Section 3C.4.4), and a brief, 20-minute qualitative interview about their experience using the system. Interviews will also inquire about participants' preferences for receiving follow-up (e.g., when and how follow-ups are conducted) and other aspects they would like QHTCs to address during calls. Participants will be paid $30.

Analysis and study set-up. Recordings of focus groups and individual phone interviews will be collected and transcribed. Themes about important considerations for conducting follow-up, (e.g., how long after testing to do so, issues to address during contacts) and issues with the monitoring system will be extracted and used to inform iterative changes in the monitoring hardware/software prior to the study phase. This data will also inform the process of providing monitoring and follow-up during the study phase. This 6-month start-up phase will also be used to refine manual data entry systems needed to conduct the proposed research, such as a front-end that can be used by study staff to enter data into the study database (e.g., RAs pairing beacons with participants, QHTCs entering data about whether post-test counseling and specific referrals provided during follow-up calls). Devicix has provided assurance that the prototype can be refined for implementation in the proposed project within the allotted timeframe (see Letter of Support).

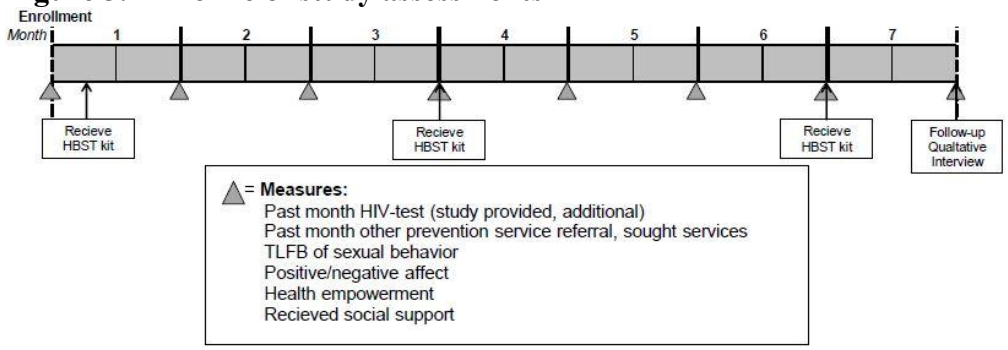
Phase II: Pilot Study Phase

Experimental conditions. In this 7-month longitudinal study, 40 participants will be randomized to receive either "enhanced" HBST (*N*=20) or standard HBST (*N*=20). All will have 3 OraSure® test kits shipped to their homes 1-week after baseline, 3-months, and 6-months. Those in the "enhanced" HBST condition will receive follow-up calls within 24 hours after opening their tests. Those in standard HBST will be provided contact information for local services in their test kits, in addition to the information provided by OraSure®.

Measures. Demographics, past HIV testing history, sexual behavior, and other relevant variables will be collected at baseline. Throughout the 7-month study period, participants will complete online assessments each month inquiring about whether they used a study-provided HBST kits in the last month and what the result was. Items will also assess whether they were provided referral to a local agency for additional prevention services (e.g., additional HIV testing, STI testing, PrEP consultation, HIV risk reduction counseling) by a professional in the last month, and whether they sought each service over the last month. Participants will also complete Timeline Follow Back (TLFB[55,56]) assessments of their sexual behavior over the past month. The TLFB has proven to be one of the more reliable and valid assessments available for sexual behaviors[57-64], and recent evidence suggests that optimal accuracy in reporting may be achieved with short follow-up periods (e.g., 30 days)[52]. Monthly online assessments will also measure general positive/negative affect over that time using the positive and negative affect scales of the PANAS-X[65], a 20-item scale that asks participants to rate various emotion words according to the extent they have "felt this way over the past month," on a 1 (*very slightly*) to 5 (*extremely*) scale. These subscales have excellent psychometric properties when used to measure trait affect[65]. Health empowerment will be measured each month using the Patient Activation Measure (PAM-13[66]), and social support will be assessed with 3 subscales of the Received Support Scale (Emotional, Informational, Satisfaction). Both measures have excellent psychometric properties[66-69].

Procedure. See Figure 3 for study timeline. Interested participants will be screened online, and those eligible will be contacted by a research assistant (RA), who will schedule an in-person appointment to begin the study. At this appointment, participants will complete baseline measures and be oriented to the study. In the "enhanced" HBST condition, participants will be informed that sensors will accompany their HBST kits and to expect a call from study QHTCs within 24 hours after opening them, should they choose to test. Study software will then be downloaded onto the participant's phone, and they will be instructed to keep their Bluetooth feature enabled at all times and to keep their phone near them as much as possible over the 7-month study. They will also be instructed to inform study staff as soon as possible should they lose their phones, change phones, or their current service contract lapses. One week after the initial appointment, an HBST kit will be sent to participants' verified addresses. Shipment tracking will be used to record data about when HBST participants receive their tests. In "enhanced" HBST, participants, opening their mailed test enclosure will trigger an alert on the study database, which is monitored regularly by staff QHTCs. These alerts will instruct QHTCs to conduct a follow-up call with participants. QHTCs will be CAAS postdoctoral trainees with Ph.D.'s in clinical psychology who have completed additional training in HIV testing counseling (offered by Dr. Chan), suicide prevention intervention (offered by nearby Lifespan Hospital), and study-specific follow-up procedures. QHTCs will take turns placing follow-up calls. QHTCs will conduct calls while in private offices on Brown University's campus. As such, they will be able to access the study database while conducting the calls, so as to allow check-ins about previous referrals and data entry during calls. QHTCs will follow up with participants within 24 hours after the test is opened. During follow-up calls, QHTCs will verify whether the participant has completed the test, what the result was, and ask whether the participant would like to receive counseling, entering this data into the study database. For reactive results, QHTCs will facilitate appointments for confirmatory testing. For non-reactive results, QHTCs will inquire about participants' interest in other prevention services (e.g., STI testing, counseling). QHTCs will also screen for suicidality and record this information using the data entry forms, providing intervention/referral if needed. If participants indicate they have not taken the test yet but plan to do so, QHTCs will ask when they plan to take the test and whether there is a better time to contact them again. If a participant cannot be reached during the 24-hour post-test window, the 3 additional follow-up attempts will be made over the following 72 hours. This process will repeat for tests sent at 3 and 6 months. To facilitate monthly study assessments, participants will receive an email with a link to an each assessment specific to that participant and time period. Participants will be asked to complete these on a desktop computer within 2 days of receipt, and failing to do so within that time will prompt the RA to follow up via phone and email to encourage adherence. Once the study is complete, the RA will follow-up with participants over the phone to conduct a 30-minute qualitative interview. This interview will assess participants'

Figure 3. Timeline of study assessments



perceptions of "enhanced" HBST or HBST alone, additional procedures/services they might have preferred. Those in the "enhanced" condition will be asked about their impressions of counseling over the phone and the usability of the monitoring method. Participants will be paid $20 for completing the baseline in-person appointment and $15 per monthly assessment ($105 total), with a $55 bonus for completing all assessments on time (within +/- 5 days of being assigned).

Planned Analyses/Power Considerations. As this is a preliminary study, the primary goal is to explore evidence for the feasibility, acceptability, and utility of "active" monitoring and follow-up with HBST, as well as its effects on testing likelihood and frequency compared with usual HBST. As such, data analysis will be primarily descriptive. To address Aim 1, we will explore the number of successful phone contacts with those in the "enhanced" HBST condition, whether contacts involved counseling and/or referral, and qualitative data/ratings of acceptability, feasibility, and preferences. To address Aim 2a, we will compare the overall number of participants reporting any HBST use and the mean number of tests used across the conditions over the study period. To address Aim 2b/c, we will also compare the number of participants receiving HIV test counseling, referral for additional prevention services, and the number who successfully followed-up with these services. Finally, to address the secondary aims, we will compare mean frequencies of unprotected anal sex (condomless or without having taken PrEP that day) and mean levels of positive/negative affect, health empowerment, and social support by condition and testing status. We are aware of the limitations of relying on small scale studies for generating broad conclusions about the efficacy and/or effect sizes of interventions[96]. As such, we are primarily interested in examining the pattern of results, rather than definitively testing hypotheses. We believe a sample size of 40 should allow some exploration of the direction of effects, while remaining within the scope of an exploratory project.

C.5. Human Subjects Involvement, Characteristics, and Design

Participants will be 40 males who are 18 years of age or older, who report having sex with a partner met online in the past year, and who have not received an HIV test in the last year. Focusing recruitment toward these individuals will allow us to examine whether remote monitoring and follow-up after HBST are helpful specifically among those who rarely test and may be "hard to reach" with more traditional HIV prevention services. Eligible participants will also report having had unprotected anal sex (anal sex without a condom or having taken PrEP that day) with a casual male partner at least once in the last 6 months. This criterion will ensure that the research is conducted among MSM who are at high risk for HIV. Since the research involves receiving HBST kits by mail, eligible participants will also be required to have a secure and stable residence to minimize the potential that tests may be stolen or diverted. This criteria was informed by past qualitative studies suggesting that most high-risk MSM prefer to receive tests by mail[50; 51], as opposed to other delivery avenues (e.g., vending machine, pharmacy pickup). However, future research should address methods for providing "active" follow-up after HBSTs that are delivered via these routes, since many at highest risk may not have stable residences. Next, to be eligible, participants must currently have an Android smartphone with a data plan. If successful, we hope to extend this technology to iPhone users, since they constitute a large share of the overall smartphone market. However, acquiring approval for iPhone-compatible software is an extensive process that often takes months. The Android platform is open source, allowing flexibility in deployment, so the current study will focus on Android users.

Finally, eligible participants will also be required to be fluent in English. While many of the study's materials could be easily translated into Spanish (or other languages), hiring bilingual or Spanish-speaking QHTCs that are able to conduct follow-ups would be prohibitive for a study of this scope. No special or vulnerable populations, as defined by 45 CFR Part 46 (e.g., prisoners, pregnant women, fetuses) are involved.

Participants will be recruited from the community using ads in popular gay social networking mobile apps (e.g., Grindr, Jackd, Scruff). Participants expressing interest in the study will be screened online. Those meeting eligibility criteria will be contacted by phone and email to schedule an in-person appointment to begin the study. Next, participants will complete baseline measures online. Then, participants will be randomized to a condition. For those in the "enhanced" condition, RAs will inform participants about the study's purpose and guide them in downloading study software onto their smartphones. Although participants will not need to actively provide any input through the app, RAs will instruct participants to keep the app installed, their Bluetooth sensor enabled, and their phones near them throughout the 7-month study. RAs will also ask participants to notify them as soon as possible if they lose their phone or get a new one, their data is erased, or if their service plan changes. Next, RAs will inform all participants that they should expect to receive an email each month with a unique link, and that clicking this link will allow them to complete their monthly assessments. They will also be informed that HBST kits will be mailed to them 1 week after their appointment, and then again in 3 months and 6 months, which they can choose to take or not. However, should they choose to do so, those in the "enhanced" condition will be told that they should expect a call from a QHTC associated with the study within 24 hours after opening their test, and that these calls are intended to provide counseling and referrals after taking the test (which participants can refuse). Finally, participants will be asked to complete a 30-minute follow-up interview about the study via phone after completing the study. They will be informed that they can pick up payments for completing study assessments at the research offices anytime during or after the study.

Those in the "enhanced" HBST condition will receive follow-up calls within 24 hours after opening their tests. These calls will be made by CAAS Postdocs who have Ph.D.'s in clinical psychology and who will receive training in HIV test counseling (provided by Dr. Chan) and suicide prevention intervention (provided by behavioral health staff at The Miriam Hospital). Training by Dr. Chan will involve modeling counseling interactions, role playing with QHTCs, and direct observation during clinic-based testing conducted at the Miriam Immunology Clinic. Dr. Chan will also provide ongoing supervision to these QHTCs throughout the study. Follow-up calls will follow the CDC's guidelines for HIV counseling, testing, and referral[80], and as such, will involve the same post-test counseling procedures offered by paraprofessionals and service providers in clinic- and community-based settings worldwide. Participants will be screened for suicidality during these calls, and if necessary, intervention will be provided according to National Suicide Prevention Lifeline procedures[81,82]. Referrals will be offered to local, LGBT-friendly agencies for additional HIV/STI testing, additional HIV prevention services (PrEP, risk reduction counseling), substance abuse treatment, mental health treatment, and primary care. During 3- and 6-month follow-up calls, QHTCs will also assess whether referral for these specific services was provided during the previous call, and if so, whether the participant sought these services (questions also assessed via monthly online assessments). For participants testing positive, participants will be assured that an initially reactive result is not a confirmed positive result, and will be scheduled for an appointment to conduct confirmatory testing at The Miriam

Immunology Clinic (MIC) as soon as possible. The MIC has standard procedures for providing newly diagnosed patients ongoing HIV care.

All study procedures, including data collection, will be conducted by research staff, the PI (Dr. Wray) or Co-Investigators (Dr. Chan and Dr. Operario). Research staff will receive intensive training in all study procedures from Dr. Wray, Dr. Chan, and Dr. Operario.

C.5.1 Sources of Materials

Self-report data collected from participants throughout the course of the study will be obtained using the following methods:

1. Focus groups will be conducted in-person during the study's start-up phase to solicit feedback about the mobile monitoring system. It will also solicit feedback about use and follow-up issues that will be used to refine the technology use (during the start up phase) and follow-up procedures (during the study phase).
2. Individual interviews will be collected over the phone during the start-up phase to collect feedback from individual high-risk MSM about their experiences using the mobile monitoring system that inform further refinement of the system and procedures used during the study phase. Phone interviews will also be conducted at the conclusion of the study among all participants to address general usability of HBSTs, preferences for follow-up, and experiences using the "enhanced HBST" system (for those in this condition). Phone interview data will also be collected during follow-up calls placed during the study phase to those in the "enhanced HBST" condition, and will assess whether participants used their test, what the result was, whether they would like to receive post-test counseling, whether they would like to receive referrals, and whether they followed up on any referrals offered during the previous follow-up calls.
3. Online questionnaires, will be used to collect screening, baseline, and monthly assessment data.
4. Online web application, used to specifically collect TLFB data in monthly assessments

Focus group data will be collected during in-person focus group meetings with members of the target population. These methods will produce qualitative data in the form of handwritten notes, digital recordings (collected using a digital voice recorder) and transcripts for analysis. Focus groups will be moderated by Dr. Operario, and will generate data in the form of written notes, voice recordings, and transcripts, none of which will contain participant identifiers. Contact data will be collected via online screening to facilitate scheduling focus groups, but will be deleted after focus groups are completed. We will use this data to inform both the refinement of the "enhanced HBST" system and how we conduct follow-ups after testing during the study phase.

Individual interviews will be collected over the phone from a 10 participants from the target population during the start-up phase, and from all participants in the study phase after completing the study. These interviews will also be recorded, and will generate data in the form of written notes, digital recordings, and typed transcripts, all of which will contain no participant identifiers. Interviews will be conducted by a trained RA, with Dr. Operario providing comprehensive training and supervision. Interviews collected during the start up phase will inform both refinement of the "enhanced HBST" system and how we conduct follow-ups after

testing during the study phase. Interviews conducted after "study phase" participants complete the study will focus on the unique experiences participants have using the "enhanced HBST" system over multiple tests delivered by mail and will inform further refinement of the system for use in future research and prevention.

Online questionnaire data will be collected using Qualtrics© web survey software, which uses Transport Layer Security encryption for any data transmitted, protects surveys with passwords, and uses HTTP referrer checking. Data collected via Qualtrics© will only contain participants' unique study ID codes and will be briefly stored via Qualtrics, but downloaded weekly to Brown University's secure internal servers and password protected so that they are accessible only to essential research staff. TLFB data collected via online web application will be stored directly on Brown University's servers and will be similarly encrypted and password-protected.

Finally, interview data collected during telephone contacts will be entered into a custom database that can be accessed by QHTCs while on the Brown University campus. This database will be hosted on Brown's internal servers and will be password-protected. Post-study interview data will be stored separately from other study data, in secure, password-protected files.

To facilitate remote monitoring and follow-up, the following data will be obtained, relayed, and stored without input from users:

1. Bluetooth low energy (BLE) beacons, will transmit a unique code (UUID) and native sensor data about the state of the HBST kit enclosures when the sensor changes to "open."
2. Participant-side mobile application, will use the Bluetooth sensor on the participant's smartphone to relay the unique code of the BLE and its state (open, closed) to a database hosted on Brown servers.
3. Centrally-hosted database, which will store minimally-identifying data about participants that is needed to facilitate follow-up, links this information with BLE UUID's via participants' unique study ID numbers, and listens for changes in the state of these BLE UUIDs to "push" relevant information to the research-side mobile application.

The BLE will only transmit its unique code (UUID) and the state of its sensor (open, closed) to the participant-side mobile app, and is not identifiable. The participant-side mobile app only "listens" for a change in the BLE's state, and transmits this data and the beacon's UUID to the centrally-hosted database. Given this, this data is also not identifiable, and will be stored only briefly via the device's internal memory until it is relayed, and then erased. **The app itself will only consist of a splash screen with the School of Public Health logo on it, and will be named "Test Helper."** The centrally-hosted database will use Filemaker, and will be used to store minimally-identifying data (e.g., unique study ID, first name, phone number) about participants for the purposes of conducting monitoring and follow-up. The database will also be used to link incoming data (UUIDs, sensor state) with participant data (via unique study ID numbers), and to provide notifications/scheduling to QHTCs who need to conduct follow up calls to participants. The database will also provide a front-end that facilitates data entry by QHTCs as they are conducting follow-up. This database will be hosted on Brown University's secure servers and password protected, so that only essential research staff will have access.

Finally, a separate database containing participants' full contact information (including address) and a unique linking ID number will be stored in a separate location on Brown's internal servers. This database will be used by RAs to ship HBSTs to the addresses participants have provided. It will be password-protected and only accessible to essential research staff via computers physically located in the research offices. This database will contain no other study data, and can only be linked with other study data via a linking ID.

D. Risks to Participants and Procedures to Protect Against Risk

Participation in this study involves no physical risk above those ordinarily encountered in daily life. However, there may be several non-physical risks:

1. There is a small risk of loss of privacy and confidentiality of data, including data that is sensitive (sexual risk-taking, psychological characteristics). We take this risk very seriously, and will take steps to protect participants' confidential data and anonymity, as detailed in Section B2. We will ensure that personal identifiers are removed from any stored data after the study is completed, as well as any reports/publications arising from the study. Informed consent documents will bring confidentiality risks to participants' attention.

2. Participants may also experience psychological discomfort while in the study, as a result of completing HIV testing at home, receiving "reactive" results from these tests, or while completing study questionnaires, since these inquire about sensitive behaviors (e.g., sexual behavior, affect).

D1. Adequacy of Protections against Risk

We will make every attempt to minimize risks to participants throughout the study protocol, including loss of privacy or confidentiality and psychological discomfort.

D.1.1. Recruitment and Informed Consent Procedures

Recruitment. All participants will be recruited via advertisements placed on gay-oriented social networking mobile applications (e.g., Grindr, Scruff). Interested participants will be instructed to contact research staff via phone or email, and upon doing so, will be directed to an online screen that assesses the study eligibility criteria. A separate online survey will be used to collect contact information, and will be linked to participants' screening responses using a unique ID code. Datasets containing screening data and contact information will be stored in separate locations on Brown University's secure servers and password-protected. A single dummy variable will be used to identify eligible participants, who will be contacted by research staff to provide further details about the study and inquire about participants' interest in enrolling. If interested, participants will be scheduled for an appointment to come to the research offices to complete baseline measures and be oriented to the study. Those recruited for focus groups will be asked to attend the group meeting, and will be shown the "enhanced HBST" system and asked for their feedback. During the individual interview phase of start-up, participants "interested in providing feedback after taking a home HIV test" will be recruited. They will be scheduled for an in-person appointment at the research offices, and provided with a beacon-monitored HBST kit, and told to expect a follow-up call 24 hours after opening their test. After conducting the normal follow-up call procedures (i.e., providing post-test counseling and referral, if desired), QHTCs will conduct a brief follow-up qualitative interview about

participants' experiences using the test. Those randomized to a study condition during the study phase will be mailed HBST test kits to their home addresses, which will be stored in a database hosted on Brown University's secure internal servers, password-protected, and can only be accessed from computers physically located at the research offices. A unique link will also be emailed to participants each month over the course of the study to facilitate completion of monthly assessments. Screening, baseline, and monthly assessment data will be stored according to protocols for handling sensitive information, and we will destroy all identifying information after the study is completed. Participants will be compensated based on completion of study appointments, monthly assessments, and follow-up interviews. Focus group participants (N=8) will be paid $50. Individual interview participants (N=10) will be paid $30. Participants will be paid $20 for completing the baseline in-person appointment and $15 per monthly assessment ($105 total), with a $55 bonus for completing all assessments on time (within +/- 5 days of being assigned). This compensation schedule is consistent with standard reimbursement amounts for research involvement at the Center for Alcohol and Addiction Studies at Brown University, thus posing little risk of coercion. Payments will be issued in cash. Recruitment and compensation procedures have been approved by the Brown University Research Protections Office IRB.

Informed Consent. The informed consent process will be conducted by trained staff members that possess research experience working with the target populations and who are also trained in the ethical treatment of human subjects. Staff members will also be trained in more advanced research topics, such as protocol adherence, quality assurance, data management, and so on. The process of informed consent involves presenting a detailed verbal description of the study as it is described on the printed, IRB-approved consent form. Staff will emphasize that participation is voluntary, and that participants can refuse to answer any question and/or can discontinue participation at any time without penalty. Interviewers will ask whether participants have experienced any coercion to take part in the study; those that describe any pressure or coercion to participate will be excluded. Potential subjects receive an item-by-item reading of the consent form by the study staff. Participants will be informed of the procedures for ensuring their confidentiality, including: the use of unique non-personally identifying ID numbers instead of names on research materials, and maintenance of data on secure computers, devices, and servers. Compensation for participation will be explained. All participants will be given the contact numbers of the Principal Investigators and Research Protections Office to answer questions about the study or one's rights as a human subject as well as a research site contact number. All consenting participants will be offered a copy of the informed consent form.

D.2 Procedures to Protect Against Risk

Several measures will be implemented to protect against the loss of privacy and/or confidentiality. First, digital audio recordings from focus groups and phone interviews will be stored in a locked cabinet in a locked office until they are transcribed, which will take place no longer than a week after they are collected. No participant identifiers will be associated with these recordings, and prior to conducting the interviews/focus groups, participants will be asked to refrain from providing any information that could identify them. Once transcribed, original voice recordings will be destroyed, and any identifying information provided during the interview will be edited out of transcripts by RAs. Transcript files will be stored in secure, password-protected files on Brown University's servers. Handwritten notes collected by staff during focus groups/individual interviews will also contain no identifying information, and will

be stored briefly in a locked file cabinet in the Investigators' offices until they can also be transcribed (no longer than a week after they are generated), and then destroyed.

Screening, baseline, and monthly assessment data collected online will be stored briefly via Qualtrics© web survey software in de-identified format, before being downloaded weekly and stored in de-identified, password-protected files on Brown University's secure servers. Participant identifying information will be kept in a separate database from study data, in a password-protected file that contains only their unique study ID. Data facilitating monitoring (e.g., participant first names, contact phone number) will be stored in a database that is centrally hosted on Brown University's secure internal servers, and password-protected so that only essential study staff have access. Sensor and BLE ID numbers are not identifiable, and the participant-side mobile app will only be used to relay this information to the centrally-stored database on Brown's servers. As such, the participant-side mobile application will not store any participant data. After being linked with participant IDs in the secure centrally-hosted database a notification and calendar event will be created to let QHTCs who regularly monitor the database know that they need to conduct a follow-up call with participants. These follow-up calls will be conducted in private offices available at Brown University. HBST test kits will be mailed to participants in discreet packaging and participants will be trained to look for these at 1-week, 3-months, and 6-month intervals. They will also be provided with tips for allowing maximum privacy when opening and taking the test. Participants will also be instructed about how to properly dispose of any tests they take, and OraSure's® test kit provides packaging for discreet and safe disposal. When conducting follow-up calls, QHTCs will first ensure that participants have adequate privacy to discuss the test over the phone, and if not, follow-up calls will be re-scheduled. Finally, while monthly email notifications providing the link for monthly assessments will contain no identifying information or other data, participants will be instructed to delete these emails after they have completed their assessment.

Several measures will also be employed to minimize psychological discomfort or distress as a result of the research. First, while participants may experience some discomfort while taking an HIV test at home, past research suggests that this risk is low [42-44], and OraSure's clinical trial data suggests that HBST can be completed safely, resulting in minimal distress. The FDA has also deemed that this product can be used safely by the general public. Nevertheless, participants in either condition will be encouraged to report any distress they experience as a result of testing to study staff, who will provide referral to LGBT-friendly treatment providers in the local area. Second, while some participants may receive "reactive" results during the study, staff will prepare them for this during their orientation visit and encourage participants to interpret this merely as "reactive" (rather that "positive"), since further testing is needed to confirm "positive" results. Participants in either condition will also be encouraged to report receiving "reactive" results to study staff as soon as possible, and will be provided with contact information for doing so. These participants will then be scheduled for confirmatory testing appointments at MIC, which has established procedures for conducting follow-up testing and engaging these patients in care. Finally, the risk of distress or discomfort from study assessments is low, but participants will again be encouraged to report this to study staff as soon as possible. Staff will then provide referrals to local MSM-friendly treatment resources and emergency services. In addition, research staff will be trained in responding to adverse events, including participant distress. These events will be reported promptly to the Brown University IRB.

Finally, to ensure that *all* participants are encouraged to seek follow-up testing and care after testing, participants indicating that they have taken a test on the monthly assessment (either

provided by us or from another clinic) will be asked what the results of this test were. If it was reactive or positive, we will ask whether confirmatory testing has been completed or is pending and whether participants are currently under the care of a physician who is attending to these issues. For those noting having received a “reactive” result from a study test, who is not pursuing confirmatory testing and/or is not under the care of a physician who is aware of this issue, we will follow-up with these participants as soon as possible over the phone. The monthly assessment data will only contain participants’ unique study ID numbers, and will not be identifiable until it is downloaded and imported into the study databases. We will download and monitor the study monthly survey data every 48 hours, and for every participant with this constellation of responses, we will follow up with them over the phone to offer to make appointments with them for confirmatory testing and follow-up care.