Title: Evaluation of rapid HIV self-testing among MSM in high prevalence cities, Randomized Controlled Trial

Investigators: Patrick Sullivan, DVM, PhD
Laura Gravens, MS, MPH
Akshay Sharma, MBBS, MPH
Kate Winskell, PhD, MA

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PROTOCOL FOR ESTAMP PART 4: RANDOMIZED CONTROLLED TRIAL, KIT DISTRIBUTION EVALUATION AND QUALITATIVE COMPONENT

Table of Contents

1. BACKGROUND

To evaluate the acceptability, use and effectiveness of HIV home-test kits among men who have sex with men (MSM), the study "Evaluation of Rapid HIV Self-Testing among MSM in High Prevalence Cities", known as eSTAMP, is being conducted in the US and Puerto Rico. The study will be conducted in four parts; each part will provide information to develop and implement the next part of the study. Part 1 will assess willingness to participate in the study and the acceptability of home testing, and will evaluate the materials, packaging and instructions for conducting home-test activities through focus groups and individual in-depth interviews to obtain feedback and reactions from participants about materials proposed for Parts 2, 3 and 4. Part 2 will evaluate the use of the home-test materials and dried blood spot (DBS) collection by participants under controlled conditions, assessing the extent to which untrained users can proficiently conduct testing procedures with the use of provided printed and video instructions. Participant testing procedures will be observed by trained HIV counselors who will also verify participants' results. Part 3 will be an evaluation of the performance of the home-test kits by the proposed study population in real world settings by sending participants a package containing test kits and a DBS specimen collection kit with packaging for specimen transport, then comparing the user-administered and interpreted rapid HIV home-test results to a standard of a laboratory-administered immunoassay (IA). Part 3 will provide sensitivity estimates of both tests compared to the laboratory-administered IA, and assess participants' preference of home test kit types (oral fluid vs. finger-stick blood tests). Part 4 will evaluate the use and effectiveness of home-test kits as a public health strategy for increasing testing among MSM by determining whether the distribution of user-administered and user-interpreted HIV home-tests to HIV-negative or HIV status unknown MSM results in a higher frequency of MSM HIV testing (of at least 3 times in a 12 month period) compared to a standard of care, referring MSM to testing locations. A secondary aim of Part 4 is to evaluate the extent to which MSM (both HIV-negative and HIV-positive) distribute study HIV home-test kits to their social and sexual networks.

This protocol outlines the procedures for Part 4, which aims to evaluate the use and effectiveness of home-test kits as a public health strategy for increasing HIV testing among MSM. The study will enroll men who report their HIV status as negative or report being unaware of their HIV status into a randomized controlled trial. They will be assigned to either the intervention group or the comparison group (standard of care). We expect to consent/screen about 16,000 potential participants (maximum 24,000) to fully enroll 3,200 participants, defined as people who consented and screened eligible, register for the study, complete the baseline survey, and are randomly allocated to the intervention or comparison group. All participants will take a baseline survey, and the intervention group will receive 4 rapid HIV test kits (i.e., 2 oral fluid tests [OraQuick] and 2 finger-stick blood tests [Sure Check]) upon randomization to that group. All men in the randomized controlled trial will complete short follow-up surveys at 3-month intervals during the 12-month follow-up period, and men in the intervention arm will be allowed to order additional test kits online to replenish the ones they use or give away at those intervals. At month 12, all participants who were HIV-negative and unaware of their HIV status at the time of random allocation to intervention arm or comparison arm and who did not seroconvert during the study will be sent 1 oral fluid test (OraQuick), 1 finger-stick blood test (Sure Check), and a DBS specimen collection kit to be mailed back after collecting a blood sample for laboratory testing. Participants who report seroconversion during study follow-up will be sent the 3-test kit after reporting seroconversion.

The study will assign 150 additional participants who report being HIV-positive to a one-arm descriptive cohort to assess test kit distribution by HIV-infected persons. We expect to consent 750 potential participants to achieve 150 study participants, defined as people who consent, take the eligibility screener and are eligible, register, and complete the baseline survey, which triggers automated kit shipment.

Therefore, we will consent up to a total of 24,750 participants in order to reach 3,350 total enrolled participants. Participants in the HIV-positive group will take a baseline survey and will receive 2 rapid HIV test kits (2 oral fluid tests [OraQuick]) to distribute to persons in their social and sexual networks. Men in the HIV-positive group will complete a short follow-up survey at 3 months.

After completing the randomized trial and test kit distribution evaluation (described above), we will conduct a qualitative component. A sample of participants from the other portions of Part 4 study will be recruited to participate in focus group discussions or individual in-depth interviews, to obtain a greater understanding of their experiences in the study.

2. RESEARCH TEAM

The research team is composed of 6 researchers from the Rollins School of Public Health, Emory University, Atlanta (Sullivan, McNaghten, Winskell, Gravens, Sharma, and Sineath) researchers from Northwestern University (Mustanski, Newcomb, and Greene), and from Public Health Solutions (Chiasson and Hirshfield). Sullivan (PhD, DVM), McNaghten (PhD), and Winskell (PhD) are faculty with the Rollins School of Public Health, Emory University, and have considerable experience in HIV research and quantitative methodologies. Mustanski (PhD), Newcomb (PhD), and Greene are faculty at Northwestern University. Mustanski and Newcomb are trained clinical psychologists, and Greene is a community psychologist. Chiasson (DrPH) and Hirshfield (PhD) are research scientists with experience conducting studies among populations at high risk for HIV infection. All members of the research team will provide input on the study procedures and contribute to the development of the data collection instruments.

The CDC Project Officers (Robin MacGowan and Pollyanna Chavez) will provide technical assistance, as needed, including consultation about study design, monitoring study progress, data management, and supervising data transfer via an encrypted flash drive or CD. The CDC Project Officers and other CDC staff including Jonathan Mermin, Andrew Margolis, Lisa Belcher, Michele Owen, Craig Borkowf, and Laura Wesolowski, will conduct data analyses, prepare manuscripts, and present at scientific meetings. The CDC Project Coordinator (Arin Freeman) will assist the CDC Project Officers to coordinate project-related activities.

The CDC Project Officers or other CDC staff will not collect data, interact with research participants, or have access to personally identifiable data and therefore are not engaged in the research activities. MANILA will transfer all study data to CDC via an encrypted flash drive or CD during the conduct of the study. While individual identifiers (numbers) will link to the data in the local database, no individually identifiable private information will be shared with CDC.

3. PRELIMINARY STUDIES IN THE AREA THAT SUPPORT THIS RESEARCH

Dr. Sullivan (lead principal investigator from Emory University) has considerable experience recruiting MSM online, and recruiting MSM into online research studies with an emphasis on HIV prevention. In the past 2 years, Sullivan's research team has collected over 15,000 internet-based surveys of MSM in the United States and Africa. In Sullivan's Barriers to Online HIV Prevention (BOPR) Study (funded by Emory Center for AIDS Research), a 29-day period of advertising on MySpace.com in March and April 2009 resulted in 30,559 click-throughs. Of the men who clicked on the advertisement, 9,005 MSM were eligible

and consented to participate in a non-incentivized 40-minute online survey, which queried participants on sexual risk behavior and HIV testing history. In May 2010, a five-day period of advertising on Facebook resulted in the recruitment of 1,923 MSM (who self-reported being in a relationship for a minimum of three months) for an online survey of couples HIV counseling and testing. Additionally, a national online HIV prevention survey of MSM, for which banner advertisements were displayed on both Facebook and Black Gay Chat, enrolled 3,428 MSM in November 2010 in a period of 14 days. Both of the aforementioned studies were not incentivized.

Sullivan's research team has also had success in recruiting MSM into longitudinal research over the past 4 years. For the *Checking In.* study (RC1MD004370), 3,524 MSM consented to participate in a 12-month prospective study of HIV behavioral risks, for which the eligibility criteria was restrictive on race/ethnicity, mobile phone ownership, and willingness to receive an at-home specimen collection kit for HIV testing. The number of consenting participants, who represent a geographically diverse sample of MSM, is the result of 14 weeks of banner advertisements displayed on MySpace.com, Facebook.com, and Black Gay Chat. The *Checking In*. study includes at-home specimen collection for HIV testing at baseline and month 12, through a partnership with Home Access Health Corporation. In the eligibility/screening survey, men were asked: "Are you willing to receive a free at-home HIV test kit and provide a blood sample to be tested for HIV?" The survey question included a link to a PDF which explained how the blood sample would be tested and who would receive the results from the HIV test. Fifty-four percent of participants indicated that they were willing to receive an at-home HIV test kit; those responding that they were not willing to receive a test kit were not offered enrollment in the 12-month study. In total, 896 C*hecking In.* participants were sent a test kit to an address that they provided (it was not a requirement to be a home address). Of those, 735 (82%) returned their blood specimen to the Home Access laboratory. Among white participants, 85% (481 of 564) returned their kit, compared with 73% (115 of 157) of black participants and 79% (139 of 175) of Hispanic participants. Twenty-five (3.4%) of the 735 participants who returned their kit had had a positive HIV test result.

Similar to the retention strategies utilized for follow-up surveys, there were retention guidelines used by research staff to encourage completion of the at-home HIV test. Research staff delivered two types of reminders to *Checking In.* participants in regards to their test kit sample. First, if the Home Access laboratory had not received a participant's blood sample within 21 days of the test kit being shipped to the participant, the participant was reminded to return their test kit to the laboratory. Second, if the participant had not called to receive their HIV test results within 14 days of the receipt of the blood specimen by the laboratory, the participant was reminded to call into Home Access to receive their result via telephone. For both reminders, the participant was able to choose the method in which they wanted to be contacted (i.e., email, text message, or phone call). Research staff manually reminded participants who were outside of their 'window' for either returning the kit or calling for their results, using the contact method chosen by the participant. Each participant received up to three reminders if they had not sent back their kit or called for their results.

Checking In. participants were required to mail their blood specimen to a laboratory for HIV testing (which required drop-off in a postal mail box as well as the participant's comfort with sending a sample in the mail for testing in a centralized laboratory). Since over 80% of participants returned their blood specimen in *Checking In.*, we expect a similar proportion of participants in this study to complete rapid HIV home-tests and return a DBS specimen via mail for laboratory testing using IA.

4. TRAINING

All research personnel employed by MANILA and subcontractors under this contract will have completed Collaborative Institutional Training Initiative (CITI) training before they are permitted to participate in research or view personally identifying information. In addition, all study personnel employed by MANILA and subcontractors under this contract who will have access to study data will sign a confidentiality agreement.

5. SPECIFIC AIMS OF PART 4

1. To assess the acceptability and use of rapid HIV home-tests among MSM residing in the US and Puerto Rico
2. To understand if the provision of free HIV home-test kits to MSM results in participants being tested at least 3 times in a 12 month period
3. To understand if the provision of free HIV home-test kits to HIV-negative or HIV status unknown and HIV-positive MSM results in the distribution to and use of test kits among persons in their social and sexual networks
4. To explore the likelihood of persons with a preliminary positive test result of requesting, being referred to, and accessing follow-up supplemental HIV testing and care services
5. To examine if the provision of free HIV home-test kits results in sexual behavior change among study participants, including number of sex partners, unprotected anal intercourse, and serosorting
6. To assess perceptions of possible uses, benefits and disadvantages of HIV home-testing and participants' home-testing preferences regarding types of kits, and how to access kits, HIV information and support services through surveys, focus groups, and in-depth interviews.

6. SIGNIFICANCE/JUSTIFICATION

Part 4 is a randomized trial of HIV home-test kit use and distribution intended to evaluate the use and effectiveness of home-test kits as a public health strategy for increasing testing among MSM, compared to standard of care, defined in this study as Web-based local clinic identification.

7. STUDY DESIGN: RANDOMIZED CONTROL TRIAL

Sample

Population: The population for the randomized trial will be men age 18 and over who self-report that they are HIV-negative or unaware of their HIV status, and have had anal sex with at least one man in the past year. A database of linkage resources is available for the participants. Trained HIV counselors will be available by telephone to link participants to care services. By monitoring participant demographics using data collected in the eligibility screener, we will ensure that at least 20% of participants are black and at least 15% are Hispanic by temporarily or permanently making other races or ethnicities ineligible.

Vulnerable populations: No vulnerable populations will be included in Part 4.

Inclusion criteria: The inclusion criteria for the Part 4 randomized controlled trial are: (1) male sex at birth; (2) currently identify themselves as male; (3) able to provide informed consent; (4) at least 18 years of age; (5) self-report being HIV-negative or unaware of their HIV status; (6) resident of United States or Puerto Rico; (7) able to read instructions and complete study survey instruments in English; (8) self-

reported anal sex with at least one man in the past 12 months; (9) have a valid email address, a cell phone capable of sending and receiving text messages, and a physical shipping address to receive kits; (10) never diagnosed with a bleeding disorder; (11) not part of an HIV vaccine trial; (12) not taking antiretroviral medication for HIV; and (13) not a participant in Parts 1, 2 or 3.

Exclusion criteria: The exclusion criteria for the Part 4 randomized controlled trial are: (1) not male sex at birth; (2) do not currently identify themselves as male; (3) not able to provide informed consent; (4) under 18 years of age; (5) self-report being HIV-positive; (6) not a resident of the United States or Puerto Rico.; (7) not able to read instructions and complete study survey instruments in English; (8) do not report anal sex with at least one man in the past 12 months; (9) do not have a valid email address, a cell phone capable of sending and receiving text messages, or a physical shipping address to receive kits; (10) ever diagnosed with a bleeding disorder; (11) part of an HIV vaccine trial; (12) taking antiretroviral medication for HIV; and (13) participated in Parts 1, 2 or 3.

Setting and Recruitment

Online recruitment: Our goal is to recruit participants online who to participate in a web-based study of HIV home-testing. We will solicit potential participants by placing English-language banner Ads on Facebook, and additional banner Ads on Web sites that may include music sites, dating sites, and sites selected by Ad placement networks. We will target men at least 18 years old who live in the United States or Puerto Rico.

When men click on a banner advertisement (Appendix A), they will be taken to a page containing basic study information that includes a short description of study activities (Appendix B). If they click on a button to advance, they will be taken to the study consent form (Appendix C), and if they consent they will be directed to a short eligibility screener (Appendix D) to determine whether they meet the eligibility criteria for Part 4. Men who do not consent or do not meet the eligibility criteria will be taken to a screen thanking them for their interest and directing them to AIDSVu, an online tool with graphical interfaces that allows users to explore the HIV epidemic, and access critical resources such as HIV testing center locations and NIH-Funded HIV Prevention and Vaccine Trials Sites (Appendix E). Men who are eligible to participate will be prompted to complete the registration process (Appendix F). During registration they will be asked to provide their contact information, including an email address, a cell phone number that can receive text messages, a shipping address, and a nickname or name. A text message with a 4-digit code will be immediately sent to the cell phone number provided by the participant. The participant must enter this code to verify his phone number and complete registration. An email with a verification link will be immediately sent to each participant's email address. The participant must click on this link to indicate his email is valid before he can complete registration and take any surveys. Successful registrants will be logged into the study Web site upon e-mail verification and prompted to complete the baseline survey.

Procedures

Two rapid HIV tests will be used in this study. The OraQuick® In-Home HIV Test was approved for home use by the FDA within a year after this contract was awarded. Despite its approval there are specific concerns related to oral fluid rapid tests that were considered and that prompted the inclusion in the study design of a blood-based rapid test. The Sure Check® HIV 1/2 Assay is FDA approved for

professional use, and the manufacturer had indicated intentions to pursue an over-the-counter indication for their product.

Study design: The Part 4 randomized controlled trial aims to determine the frequency and success of use of HIV home-test kits among MSM, and their willingness to distribute test kits to people in their social and sexual networks. Men will be randomly allocated to the intervention or comparison group after registration. All men in the randomized trial will complete the baseline survey (Appendix G) and will receive follow-up surveys (Appendix H) at 3, 6, 9 and 12 months. At 12 months or upon seroconversion, all men will be sent 1 oral fluid HIV test kit (OraQuick) and 1 finger-stick blood HIV test kit (Sure Check) and a DBS specimen collection kit. They will be asked to test themselves and report their results, and to collect the DBS specimen and send it to Emory (who will transport the cards to the CDC for laboratory testing).

Intervention arm: After completing the baseline survey (Appendix G), men randomly allocated to the intervention arm will view a welcome greeting orienting them to the study and will receive a welcome kit with 4 rapid tests (2 oral fluid test kits [OraQuick] and 2 finger-stick blood test kits [Sure Check]) to use and/or give away. The message they view will include the same resources links provided to the comparison arm. The online information will cover the importance of testing, links to AIDSVu and resources to locate HIV testing services and prevention information in their area. No information recommending frequency of testing will be given in the welcome greeting. Intervention arm participants will receive a web link to complete follow-up surveys (Appendix H) at 3, 6, 9 and 12 months, and will have the option to order additional test kits to replace the ones that they have used or given away at 3, 6 and 9 months. If at any time the kits that participants have received have not been reported used and are coming close to their expiration date, participants will be notified by email to be aware of the expiration date of their tests and to throw away and not use tests that have expired. Participants will be notified by email and will receive a text reminder to check their email for important information from the KnowAtHome study. If emails bounce back to the KnowAtHome system, then participants will be contacted via phone to notify them. Study staff will use the email text as a guide for phone notification.

Comparison arm: After completing the baseline survey (Appendix G), comparison arm participants will view a welcome greeting and the same resource links provided to the intervention arm. The online information will cover the importance of testing, links to AIDSVu and resources to locate HIV testing services and prevention information in their area. No information recommending frequency of testing will be given in the welcome greeting. Comparison arm participants will receive a web link to complete follow-up surveys (Appendix H) at 3, 6, 9 and 12 months.

8. Study Design: Evaluation of Home Test Kit Distribution by HIV-positive MSM

Sample

Population: The population for the test kit distribution evaluation will be 150 men at least 18 years of age who self-report that they are HIV-positive and have had anal sex with at least one man in the past year. We expect to consent 750 potential participants to achieve 150 study participants, defined as people who consent, take the eligibility screener and are eligible, register, and complete the baseline survey, which triggers automated kit shipment. By monitoring participant demographics using data collected in the eligibility screener, we will ensure that at least 20% of participants are black and at least 15% are Hispanic by temporarily or permanently making other races or ethnicities ineligible.

Vulnerable populations: No vulnerable populations will be included in Part 4.

Inclusion criteria: The inclusion criteria for the Part 4 kit distribution by HIV-positive MSM are: (1) male sex at birth; (2) currently identify themselves as male; (3) able to provide informed consent; (4) at least 18 years of age; (5) self-report being HIV-positive; (6) resident of the United States of Puerto Rico.; (7) able to read instructions and complete study survey instruments in English; (8) self-reported anal sex with at least one man in the past 12 months; (9) have a valid email address, a cell phone capable of sending and receiving text messages, and a physical shipping address to receive kits; and (10) not a participant in Parts 1, 2 or 3.

Exclusion criteria: The exclusion criteria for the Part 4 kit distribution by HIV-positive MSM are: (1) not male sex at birth; (2) do not currently identify themselves as male; (3) not able to provide informed consent; (4) under 18 years of age; (5) self-report being HIV-negative or unaware of HIV status; (6) resident of the United States of Puerto Rico.; (7) not able to read instructions and complete study survey instruments in English; (8) do not report anal sex with at least one man in the past 12 months; (9) do not have a valid email address, a cell phone capable of sending and receiving text messages, or a physical shipping address to receive kits; and (10) participated in Parts 1, 2 or 3.

Setting and Recruitment

Online recruitment: Our goal is to recruit participants online to participate in a web-based study of distribution of rapid HIV test kits for home use. We will solicit potential participants online, through banner Ads. We would place English-language banner Ads on Web sites that may include Facebook, music sites, dating sites, and sites selected by Ad placement networks. Potential participants may also be recruited by email blast if they previously provided their contact information to study staff and indicated that they would like to be contacted for future research. We will only use this option if other recruitment efforts are lagging, or if we are lagging in recruiting a certain demographic. We will target men at least 18 years who live in the United States or Puerto Rico.

When men click on a banner advertisement or email link, they will be taken to a page containing basic study information that includes a short description of study activities (Appendix B). If they click on a button to advance, they will be taken to the study consent form (Appendix C), and if they consent they will be directed to a short eligibility screener (Appendix D) to determine whether they meet the eligibility criteria for Part 4. Men who do not consent or do not meet the eligibility criteria will be taken to a screen thanking them for their interest and directing them to AIDSVu, an online tool with graphical interfaces that allows users to explore the HIV epidemic, and access critical resources such as HIV testing center locations and NIH-Funded HIV Prevention and Vaccine Trials Sites (Appendix E). Men who are eligible to participate will be prompted to complete the registration process (Appendix F). During registration they will be asked to provide their contact information, including an email address, a cell phone number that can receive text messages, a shipping address, and a nickname or name. A text message with a 4-digit code will be immediately sent to the cell phone number provided by the participant. The participant must enter this code to verify his phone number and complete registration. An email with a verification link will be immediately sent to each participant's email address. The participant must click on this link to indicate his email is valid before he can complete registration and take any surveys. Upon completion of the baseline survey, a package with two OraQuick tests will be shipped so that participants in this cohort can distribute them.

Procedures

All men in the HIV-positive group will complete the baseline survey (Appendix G) online. Upon completion of the survey they, will be informed that a package containing a welcome kit including 2 rapid oral fluid tests (OraQuick) is being sent to their shipping address. They will be informed that these tests are to give to other people, such as sexual partners or friends, and reminded to tell test recipients that the tests are being distributed as part of a study. HIV-positive group men will receive a link to a follow-up survey (Appendix H) at 2 months.

9. STUDY DESIGN: QUALITATIVE DATA COLLECTION

The qualitative research component aims to examine the experiences of participants in the study. Participants for the qualitative data collection will be drawn from the intervention arm of the randomized controlled trial and the HIV-positive men participating in the test kit distribution evaluation. Two data collection techniques will be used: on-line focus group discussions (FGDs) and individual in-depth interviews (IDIs) conducted by phone. A separate consent process will be used for participants enrolled in the qualitative data collection. Approximately 216 participants will take part in the FGDs and 30 participants in the IDIs, for a total of 246 participants for the qualitative data collection.

Sample

Population: The population for the FGDs and IDIs will be subsamples of men who participated in the randomized trial and test kit distribution evaluation. Three sets of FGDs will be conducted with subsets of men randomized to the intervention arm who remain HIV-negative at the end of the study: a) men who never ordered additional tests; b) men who tested themselves and ordered additional kits but did not distribute test kits to others; and c) men who tested themselves and ordered additional test kits and distributed test kits to others. FGDs will be conducted online. IDIs will be conducted with two groups of HIV-positive men: men who participated in the cohort of men with known HIV (i.e., prevalent positives) and men who enrolled in the randomized trial and subsequently seroconverted (i.e., incident positives). For both FGDs and IDIs, we will ensure that at least 20% of participants are black and at least 15% are Hispanic by random recruitment and enrollment. All participants will be recruited for IDIs and FGDs by phone calls from study staff placed in random order until saturation and target enrollment is achieved (see further details below).

Vulnerable populations: No vulnerable populations will be included.

Focus Group Discussions:

Inclusion criteria: We will include only HIV negative individuals who were recruited and enrolled in the intervention arm of the randomized trial. Inclusion criteria for the FGDs are: (1) male sex at birth; (2) currently identify themselves male; (3) able to provide informed consent; (4) at least 18 years of age; (5) resident of the United States of Puerto Rico; (6) able to read instructions and participate in the FGD in English; (7) was a participant in Part 4; (8) was randomized to the intervention arm; and (9) HIV-negative at the end of the randomized trial.

Exclusion criteria: The exclusion criteria for the FGDs are: (1) not male sex at birth; (2) do not currently identify themselves male; (3) not able to provide informed consent; (4) under 18 years of age; (5) not a resident of the US or Puerto Rico; (6) not able to read instructions and participate in the FGD in English;

(7) not a participant in Part 4; (8) was not randomized to the intervention arm; and (9) HIV-positive or unaware at the end of the randomized trial.

In-depth Interviews:
Inclusion criteria: We will include only HIV positive individuals who were recruited and enrolled in the intervention arm of the randomized trial or the test kit distribution evaluation. Inclusion criteria for the IDIs are: (1) male sex at birth; (2) currently identify themselves male; (3) able to provide informed consent; (4) at least 18 years of age; (5) a resident of the US or Puerto Rico; (6) able to read instructions and participate in the IDI in English; (7) was a participant in Part 4; and (8) was assigned to the HIV-positive group or was assigned to the intervention arm and identified as HIV positive during the study.

Exclusion criteria: The exclusion criteria for the IDIs are: (1) not male sex at birth; (2) do not currently identify themselves male; (3) not able to provide informed consent; (4) under 18 years of age; (5) not a resident of the US or Puerto Rico; (6) not able to read instructions and participate in the IDI in English; (7) not a participant in Part 4; (8) not assigned to the HIV-positive group or intervention arm; and HIV-negative or unaware at the end of the study.

Setting and Recruitment
All qualitative data collection will take place after the randomized trial and test kit distribution evaluation activities are completed Participants for the FGDs will be recruited from the randomized trial participants, and participants for the IDIs will be recruited from the randomized trial and test kit distribution evaluation participants. Contact details for each participant will come from the randomized trial and test kit distribution evaluation. Approximately one month before the scheduled start of the qualitative data collection, all participants will be contacted (via their preferred mode of contact) and asked if they would be willing to take part in either a FGD (for HIV negative individuals) or an IDI (for HIV positive individuals). Calls will be made in random order to eligible participants. Interested participants will inform the study staff, who will then match them to an available time slot. The aim is to employ the rule of saturation: that is, we will stop collecting data once we stop hearing new information from participants. This is standard practice in qualitative research. We estimate that it will take 16-18 FGDs and 24-30 IDIs to achieve saturation.

Procedures
Eligible randomized trial and test kit distribution evaluation participants will be sent a message approximately one month prior to the qualitative data collection asking for their interest in participation. Participants who contact the study staff will be invited to participate in either a FGD or IDI, depending on their serostatus.

10. HIV TESTING

The rapid home HIV tests used in this project are the OraQuick® In-Home HIV Test (Orasure Technologies) that is already approved for home-testing and the SURE CHECK® HIV 1/2 Assay (Chembio Diagnostic Systems, Inc.) that has not been approved by the FDA for over-the-counter use. An investigational device exemption (IDE) for the off-label research use of Sure Check is secured.

All test kits will have a label on the box indicating that it is a test kit being distributed as part of the study, and by opening the test kit package the person agrees to use this product as part of a research study. The label will also request that the user report their results and will provide the study web site

address and study support number to call if assistance is needed with the testing process or for assistance with linkage to services if the tester receives a positive rapid HIV test result. The labeling on the Sure Check box will also contain the FDA's caution message, informing the user that the test is an investigational device.

A. Randomized Controlled Trial

Intervention arm participants: The welcome kit will include 4 HIV rapid home-tests (2 oral fluid tests and 2 finger-stick blood tests). Each test kit will contain an educational brochure with study information (i.e., study website URL, referral support system phone number), and will inform users that rapid test results for persons who are HIV-infected may not be accurate if the person is taking antiretroviral medications. Participants will also have access to online written test instructions in both English and Spanish and instructional videos for each test. Intervention arm participants will receive instructions to log in to the study web site using their username and password to indicate whether they used any study tests, to report the serial number of the test used, and to report their results both by selecting text (i.e., positive, negative, invalid, not working) and visually (by clicking on the picture that looks most like his test). They will then receive a message based on their result (positive, negative, invalid or not working) that will direct them to the study referral support system for access to care and supplemental HIV testing (Appendix J).

After completing each follow-up survey at months 3, 6 and 9 and reporting their test results and/or providing details of who they gave test kit(s) to, participants in the intervention arm will have the opportunity to order up to 4 additional rapid tests (2 oral fluid tests and 2 finger-stick blood tests) to use themselves and/or to distribute to others. Ordering forms will be presented to participants after they complete their 3, 6, and 9 months follow-up survey. The number of kits an intervention arm participant can order at the time of each follow-up survey will depend on the number of kits used and/or distributed. For example, if they report the results of one test online, or in a follow-up survey, and report in a follow-up survey that they distributed one test, after providing the details of who they gave the test kit to, they will be eligible to order up to 2 additional tests (either 1 OraQuick and 1 Sure Check, or 2 OraQuick or 2 Sure Check). As with the tests provided in the welcome kit, additional test kits will also contain the test-specific instructional booklets and test users will be able to access written and video instructions online. Participants will be instructed to report the results online after every test (Appendix I). Intervention arm participants can report results as often as they test themselves; i.e., they may take more than one results reporting survey during a three-month follow-up interval.

At any time during the study, study participants who report a positive, test is not working, or invalid test result (and have not already contacted the study referral support system using the toll-free number) will be contacted by trained Emory study staff the next business day. A list of participants who should be contacted based on their reported result or image or result selected will be automatically generated daily for counseling staff. For persons reporting a preliminary positive test result, Emory study staff will arrange referral to supplemental testing and care at a facility in the city where the participant lives. For persons reporting an invalid test result, Emory study staff will discuss with the participant how the test was conducted to try to understand the reason for the invalid result, and provide counseling to the participant regarding what this test result means and next steps for determining the participant's serostatus. In addition, Emory will ask participants with preliminary positive results whether they would like to participate in the Performance Assessment right away or delay until one year from when they enrolled in KnowAtHome.

Participants who have not completed their surveys within one week of the initial email asking to complete surveys will be reminded by phone, text message or email by Emory study staff. Emory study staff will send up to 6 reminders to participants who have not completed their surveys per time point of survey collection (3 month follow up, 6 month follow up, 9 month follow up and 12 month follow up). The system will issue automated reminders to complete active or incomplete study tasks by email and text. The participant can choose to receive automated reminders less frequently, not at all, or by either email or text only.

After completing the month 12 survey, or immediately after reporting any positive HIV test result during the study period, participants in either arm of the randomized trial will be provided with materials to conduct the performance activity (See Section B. Performance Assessment of Rapid Home HIV Tests, below).

Guests of Trial Participants: Men in the intervention arm may give tests to other people, including sexual partners or friends, whom we call "guests." Each test and related packaging and instructions is identical to those described above, and accordingly comes with the same instruction booklets and educational brochure with study information (i.e., study website, referral support system phone number), and will inform users that rapid test results for persons who are HIV-infected may not be accurate if the person is taking antiretroviral medications. Guests will also have access to online written test instructions in both English and Spanish and instructional videos for each test. Guests will have access to the study web site where they can log on as a "guest" (i.e., not as a study participant, and no registration is required) and sign a consent form indicating they are at least 18 years old, agree to use the test kits as part of a study, agree to use an investigational device (Sure Check), and agree to participate in the study (Appendix I). Consenting guests will be prompted to complete a survey that includes background information and rapid results reporting. They will receive messages based on their results (positive, negative, not working, or invalid) that will direct them to the study referral support system for access to care and supplemental HIV testing (if one or more tests is positive) or additional resources (if test result is negative) (Appendix I).

***Comparison arm participants*:** The welcome greeting will be accompanied by HIV prevention information about the importance of testing, a link to AIDSVu, and resources to locate HIV testing services and prevention information in their area.

At month 12, or immediately after reporting any positive HIV test result during the study period, participants in either arm of the randomized trial will be provided with materials to conduct the performance activity (See Section B. Performance Assessment of Rapid Home HIV Tests, below).

Participants who have not completed their surveys within one week of the initial email asking to complete surveys will be reminded by phone, text message or email by Emory study staff. Emory study staff will send up to 6 reminders to participants who have not completed their surveys per time point of survey collection (3 month follow up, 6 month follow up, 9 month follow up and 12 month follow up). In addition, the system will issue automated reminders to complete active or incomplete study tasks by email and text, unless the participant changes his automated reminder preferences. He can choose to receive automated reminders less frequently, not at all, or by either email or text only.

B. Performance Assessment of Rapid Home HIV Tests

***Performance assessment participants*:** At month 12, or immediately after reporting any positive HIV test result during the study period, participants in either arm of the randomized trial will be provided with materials to conduct the performance assessment activity. Participants in the performance assessment will be mailed a performance assessment kit containing 1 oral fluid test (OraQuick), 1 finger-stick blood test (Sure Check) and a DBS specimen collection kit. Each test kit will contain an educational brochure with study information (i.e., study website URL, referral support system phone number). They will be instructed to follow the package instructions to begin the process of first conducting the oral fluid test, second collecting a DBS specimen, and third conducting the finger-stick blood test. They will be instructed to dry the DBS card, package it in a storage bag, and return it to Emory in a pre-paid shipping envelope provided in the kit for transport to the CDC for laboratory testing with IA. Written instructions for conducting the tests and collecting the DBS specimen will be provided in English and Spanish, and online instructional videos will also be available. They will be asked to complete all three testing activities within 48 hours of each other. Participants who within 1 week of receiving the package have not entered their results for the rapid tests or have not indicated they have mailed the DBS specimen card or their DBS card has not been received by Emory, will be contacted by Emory study staff via email, text or phone call. Emory study staff will send up to 6 reminders to participants who have not sent their DBS specimen. In addition, the system will issue automated reminders to complete active or incomplete study tasks by email and text, unless the participant changes his automated reminder preferences. He can choose to receive automated reminders less frequently, not at all, or by either email or text only. The participant will receive a token of appreciation worth $30 for reporting their rapid test results and sending in the DBS specimen.

Emory study staff will contact participants with any of the following results: positive rapid or IA test; discordant rapid and IA results (the participant reported their home-test results as negative but the result of the CDC laboratory DBS specimen testing was positive, or the participant reported their home-test results as positive but the result of the DBS specimen testing was negative), invalid or “test not working result. Emory study staff will make up to 10 attempts to reach the participant by phone, email or text message. The text or email message will not contain any information about HIV or the participant’s test results. Emory study staff will arrange referral for the participant based upon his preferences and needs to receive supplemental HIV testing and care at a facility in the city where the participant lives.

C. HIV Positive Group

***HIV-positive group participants*:** HIV-positive group participants will receive instructions to log in to the study web site using their username and password to complete the baseline survey. Three months after they take the baseline survey, participants with known HIV will be prompted to log in to knowathome.org and take a follow-up survey. Although we ask HIV-positive group members distribute the 2 oral fluid kits in the welcome kit to people with negative or unknown HIV status, some may use one or both kits to test themselves. The follow-up survey for men with HIV asks whether they used the kits themselves and, if so, why. We want to know if participants test themselves, and also if the participant receives negative result, we want the opportunity to explain to the participant why these tests may come back as negative if they are on antiretroviral therapy. The kits themselves are identical to those described in the randomized controlled trial as previously described; however, a welcome sheet specific to this cohort study will be included in the package.

Participants who have not completed their surveys within one week of initial email asking to complete surveys will be reminded by phone, text message or email by Emory study staff. Emory study staff will send up to 6 reminders to participants who have not completed their surveys

If men in the HIV positive group distribute the test kits to others, persons who receive the test kits will be considered "Guests of HIV-positive group": See next section.

***Guests of HIV-positive group (social and sexual network testers)*:** People who receive test kits from men with known HIV access the same system in the same way as people who receive test kits from men with negative or unknown HIV status in the intervention arm. Each test and related packaging and instructions is identical to those previously described, and accordingly comes with the same instruction booklets and educational brochure with study information (i.e., study website, referral support system phone number). Guests will also have access to online written test instructions in both English and Spanish and instructional videos for each test. Guests will have access to the study web site where they can log on as a "guest" (i.e., not as a study participant, and no registration is required) and sign a consent form indicating they are at least 18 years old, agree to use the test kits as part of a study, and agree to participate in the study (Appendix I). Consenting guests will be prompted to complete a survey that includes background information and rapid results reporting. They will receive messages based on their results (positive, negative, not working, or invalid) that will direct them to the study referral support system for access to care and supplemental HIV testing (if one or more tests is positive) or additional resources (if the test result is negative) (Appendix I).

11. INTERACTION WITH PARTICIPANTS: SURVEYS

A. Randomized Trial

After consenting, all men are prompted to take the eligibility screener (Appendix D). The eligibility screener verifies that the potential participant meets all inclusion criteria, specifically, that he is: at least 18 years old; lives in the US or Puerto Rico; was male at birth and currently self-identifies as male; has not participated in an HIV vaccine trial; is not taking PrEP; has had anal sex with at least one man in the past year; and does not have known HIV.

Men who consent to participate and complete the registration process will be prompted to access the website to take surveys. Prompts and reminders will be issued by text and/or email, depending on participants' preferences. All eligible men who have completed the registration process will be prompted to take a baseline survey (Appendix G),

All surveys will be accessible through the study website to men who log in with their username and password. Men also must enter a 4-digit pin code sent to his cell phone each time he logs in, for dual authentication, every time he logs in.

The baseline survey collects information on demographic characteristics, HIV testing history, and sexual risk behavior. After kits are shipped, men in the intervention arm will be asked to use the study website to enter results of their rapid HIV home-tests that they received and conducted at home (Appendix I; see below). All men will be prompted to take follow-up surveys (Appendix H) online. The follow-up surveys will collect information on HIV testing results and behaviors and sexual activities.

***Intervention arm participants*:** After registration, men in the intervention arm will complete the baseline survey (Appendix G). Upon completion of the baseline survey they will be informed that a welcome kit including 4 HIV rapid home-tests: 2 oral fluid tests (OraQuick), 2 finger-stick blood tests (Sure Check) is being sent to the shipping address they provided. They will be asked that if they use any of the test kits to test themselves that they use the study website to report their results. At 3, 6, 9 and 12 months men will receive a follow-up survey (Appendix H) that will include questions on HIV testing activities and results (either home-testing or testing in other settings), kit distribution to members of their social or sexual networks, and details of the relationship (i.e., sex partner, friend) with the people they gave kits to. Following the completion of the follow-up survey at 3, 6 or 9 months, men in the intervention arm will have an opportunity to order up to 4 kits (depending on the number used or distributed).

At month 12, participants in the intervention arm who have not had a positive HIV test result will be asked to participate in the performance assessment, in which they will be sent a package containing 1 oral fluid HIV test kit (OraQuick) and 1 finger-stick blood HIV test kit (Sure Check) and a DBS specimen collection kit and be asked to test themselves and take a survey on the study website to report their results and answer follow-up questions.

Intervention arm participants who report a preliminary positive HIV test result by reporting home-test results (Appendix I) or through follow-up surveys (Appendix H) will immediately asked to participate in the performance assessment (instead of at month 12) and be sent the performance assessment package containing 1 oral fluid HIV test kit (OraQuick) and 1 finger-stick blood HIV test kit (Sure Check) and a DBS specimen collection kit. If they decline the performance assessment at this point, they will be offered the performance assessment package again at 12 months. Intervention arm participants who report a preliminary positive HIV test result will no longer be eligible to receive additional test kits (other than the performance assessment package) and will be considered "censored" for the purposes of assessing HIV testing frequency and kit distribution; however, they will continue to receive follow-up surveys that will include questions about access to and retention in HIV care (Appendix H).

When the kits are ordered, participants will be contacted by Emory or MANILA study staff to let them know that their package is being shipped to them. Study staff will tell the participant when to expect the package. If the participant has any questions regarding study activities, they will be connected with Emory study staff. Emory staff will handle any research related questions or issues with the participant.

***Comparison arm participants*:** After completing the baseline survey (Appendix G), comparison arm participants will be linked to a welcome greeting and HIV prevention information. The online information will cover the importance of testing, links to AIDSVu and resources to locate HIV testing services and prevention information in their area. At 3, 6, 9 and 12 months men will receive a follow-up survey (Appendix H) and report on HIV testing activities and results.

Comparison arm participants who report a positive HIV test result through follow-up surveys (Appendix H) will immediately be invited to participate in the performance assessment (instead of at 12 months). They will be sent the performance assessment package containing 1 oral fluid HIV test kit (OraQuick) and 1 finger-stick blood HIV test kit (Sure Check) and a DBS specimen collection kit. If they decline the performance assessment at this point, they will be offered the performance package at 12 months. Comparison arm participants who report a positive HIV test result will be considered "censored" for the

purposes of assessing HIV testing frequency; however, they will continue to receive follow-up surveys that will include questions about access to and retention in HIV care (Appendix H).

When the performance assessment package is ordered participants will be contacted by Emory or MANILA study staff to let them know that their package is being shipped to them. Study staff will tell the participant when to expect the package. If the participant has any questions regarding study activities, they will be connected with Emory study staff. Emory staff will handle any research related questions or issues with the participant.

B. ***HIV positive group participants*:**
After consenting, all men are prompted to take the eligibility screener (Appendix D). The eligibility screener verifies that the potential participant meets all inclusion criteria, specifically, that he is: at least 18 years old; lives in the US or Puerto Rico; was male at birth and currently self-identifies as male; and has had anal sex with at least one man in the past year; and has been diagnosed with HIV infection.
As in the intervention arm, all surveys will be accessible through the study website to men who log in with their username and password. Men who consent to participate and complete the registration process will be prompted to access the website to take surveys. Prompts and reminders will be issued by text and/or email, depending on participants' preferences.
After registration, men in the HIV-positive group will complete the baseline survey (Appendix G). At 2 months, men will receive a follow-up survey (Appendix H) and report on kit distribution, and details of the relationship (i.e., sex partner, friend) with the people they gave kits to.

When the kits are ordered, participants will be contacted by Emory or MANILA study staff to let them know that their package is being shipped to them. Study staff will tell the participant when to expect the package. If the participant has any questions regarding study activities, they will be connected with Emory study staff. Emory staff will handle any research related questions or issues with the participant.

C. Guests
Persons may receive a study test kit from one of the intervention arm or HIV positive group participants. These guests to the study will be prompted through kit packaging to go online to report their results, and will have access to a study consent form, instructional videos, and a results reporting survey. Guests do not register, complete only one survey, and no compensation will be given if they choose to report their results on the study website.

12. Interaction with Participants: Focus Group Discussions

Focus groups are small groups of between 6-12 participants. The aim is to create diverse groups of participants who do not know each other, and to promote free flowing discussion among group members. Each focus group is led by a moderator (Sullivan, Winskell, Mustanski, Newcomb, Greene, Gravens Sharma or Sineath) with a note-taker (Gravens, Sharma or Sineath) present to record key themes as they arise.

Due to the geographic distribution of study participants, all focus groups will be conducted online to increase probability of representation from more geographic locations. All FGDs will be conducted with men who were randomized to the intervention arm and did not report a positive HIV test by the end of the study. Three sets of FGDs will be conducted: a) men who never ordered additional tests; b) men who tested themselves and ordered additional tests but did not distribute test kits to others; and c) men who

tested themselves and ordered additional test kits and distributed test kits to others. FGDs will be conducted online. Prior to interview, study staff will ensure that individuals are offered participation in the appropriate FGD using study records. Following obtaining verbal informed consent (Appendix K), a focus group guide (Appendix L) will be used to discuss the decision making process involved in home testing. The discussion will examine a) decisions to receive home test kits, b) decisions of where and when to use the test kit, c) reactions to the results, d) sharing information with friends or sex partners, and e) decision to use home test kits again in the future. . For online FGDs, participants will be sent an email containing the consent form to review prior to participation. Online informed consent will be obtained before the FGD. All FGD will be recorded and saved in password protected files in secure network drives as MS Word or PDF files with identifying information redacted.

13. Interaction with Participants: In-Depth Interviews

IDIs will be used for HIV-positive individuals, including both prevalent positives (i.e., men with known HIV at baseline who participated in the cohort study) and incident positives (i.e., men who enrolled in the randomized trial and seroconverted). A group setting such as a FGD is not appropriate for HIV-positive participants as a group environment risks revealing serostatus; therefore, we will perform IDIs. Separate interview schedules will be used for prevalent and incident positives. Prior to interview, study staff will ensure that they are offered participation in the appropriate IDI using study records. Following obtaining verbal informed consent (Appendix M), IDIs will be conducted using an interview guide (Appendix N). IDIs for men with known HIV at baseline who participated in the cohort study will focus on decision making during the study, including the decision to receive home test kits, the decision on whom to give home test kits to, how these decisions were made, the use of home test kits by sex partners, the timing of testing in their relationship with sex partners, and the sharing of results from home test kits. For men who enrolled in the randomized trial and seroconverted, the IDIs will focus on establishing the time line of activities after their HIV positive result, examining linkage to care and disclosure.

All IDIs will take place via telephone. A time will be coordinated with the participant once they inform the study staff of their interest and study staff verify that they meet the inclusion criteria. The telephone interview will be conducted by study staff (Sullivan, Winskell, Mustanski, Newcomb, Greene, Gravens, Sharma or Sineath). Telephone interviews reduce the time and transportation burden on the respondent. All telephone interviews will be recorded and tapes will be stored in locked cabinets in locked offices

14. Study Referral Support System

The study referral support system that was implemented and piloted in Part 3 will also be used in Part 4. This system will support the immediate needs of participants who have difficulty with home-testing, who have concerns after testing, or who have a new preliminary positive test result. It begins with a toll-free phone number which participants can use to call in with any study-related concern. The number will be attended by a voice-recognition system which will allow participants to: (1) get pre-recorded information about frequently asked questions; (2) request to ask a question of study staff (answered during business hours, or transferred to voicemail after hours); and (3) request immediate consultation with a counselor for crisis support and triage. Immediate consultation will be available 24 hours a day, 7

days a week and will be provided by trained Emory staff Monday through Friday from 9:00am to 5:00pm Eastern time, by trained HIV counselors at the Center on Halsted from 5pm-11pm EST Monday through Friday, and 9am to 11pm EST Saturday and Sunday, and crisis hotline counselors at Mental Health Association – New York City LifeNet at all other hours. Counselors at LifeNet, Center on Halsted and Emory staff that will be part of the study referral support system will have completed training about the study procedures and in the fundamentals of HIV prevention counseling.

For study participants and social and sexual network members who have a new preliminary positive result as part of the study, we will arrange referral to supplemental testing and care at a l facility in the city where the participant lives using AIDSVu, state and local health department contacts, and an existing database from Sullivan's HIV Minority Testing Initiative study that was developed to link new preliminary HIV positive persons to services. In conversation with the participant, the counselor or study staff will help determine the type of setting (community-based, medical setting, university setting, etc.) and the neighborhood which will best suit the participant. Counselors or study staff will build on pre-established relationships with providers to develop a suitable referral to a health care provider for supplemental HIV testing and, if necessary, linkage to HIV care services. They will have the option to request a written document (via mail or email) with their preliminary positive test results that they can take to their own healthcare provider (Appendix O).

Counselors will also make an assessment to determine other resources that the participant may benefit from such as medical case management, mental health care, or comprehensive risk counseling and services. Newly preliminary positive persons will be directly linked to medical care by connecting them with a medical care contact, if necessary. Emory staff will follow-up with them on the next business day to ensure that contact was made with a local facility in the city where the participant lives or with a medical care agency. The Emory staff will first attempt to contact the participant by phone, and if unsuccessful after six attempts, an email or text message will be sent asking the participant to call the counselor. The participant would be contacted at least three times: (1) to confirm an appointment was scheduled; (2) to confirm the appointment was attended; and (3) to report confirmatory results. Confirming appointment attendance from the participant will be used to document a successful linkage to care. Documentation includes: (1) date of the visit to a local facility; (2) location of facility and/or name of provider; and (3) verification of visit using self-report.

For persons reporting an invalid test result, Emory staff will discuss with the participant how the test was conducted to try to understand the reason for the invalid result. Study staff will provide counseling to the participant regarding what this test result means and next steps for determining the participant's serostatus.

15. HIV Test Kit Tracking System

All study test kits will be affixed with a barcoded sticker to enable the kit to be tracked. Kits will be scanned prior to distribution to study participants, which will link the test kit information (the type of test and the specific individual test) with the ID number of the participant it was sent to. Participants will be required to scan or enter a test kit barcode number into the study website before reporting their test results. MANILA study staff will keep a log of the test kit lot numbers, the barcode number and participant ID the test kit was sent to for each test kit. MANILA study staff will monitor the delivery and the tracking/fulfillment system.

16. Reporting of HIV Positive Results

The CDC and the Council of State and Territorial Epidemiologists have established a policy which requires state health departments to report cases of selected diseases to the CDC's National Notifiable Disease Surveillance System. HIV is a nationally notifiable disease per CDC, and it is a requirement by law to report HIV positive test results to state health departments. Because state and local public health officials rely on health care providers, laboratories, and other public health personnel to report the occurrence of notifiable diseases, participants who are determined to be HIV positive by laboratory testing of their DBS specimen in this study will have their contact information provided to the state health department in the state where the participant resides by Emory study staff. Participants will have previously been told in the informed consent document that confirmed positive HIV test results will be reported to the relevant state health department as required by law.

Participants in the intervention and comparison arm who participate in the performance assessment either immediately after reporting a positive test result or in month 12 of the study will receive 1 oral fluid test kit, 1 finger-stick blood test kit, and a DBS specimen collection kit. They will be instructed to test themselves and report their results on the study website. After the CDC receives a participant's DBS specimen it will be tested with Avioq, Western Blot (both approved for DBS testing) and either a 3rd generation IA or a 4th generation IA. The preference will be to use a 4th generation IA if indicated with DBS samples. Otherwise, a 3rd generation IA that has been validated in the CDC laboratory will be used (Appendix P).

Participants with discordant home-test and laboratory test results (the participant reported their home-test results as negative but the result of the CDC laboratory DBS specimen testing was positive, or the participant reported their home-test results as positive but the result of the DBS specimen testing was negative), or positive results on either a home-test or a laboratory test will be contacted by Emory study staff. Emory study staff will make up to 10 attempts to reach the participant by phone, email or text message. The text or email message will not contain any information about HIV or the participant's test results. Emory study staff will arrange referral for the participant to receive supplemental HIV testing and care at a local facility in the city where the participant lives as appropriate.

17. Storage of Specimens

The consent process will include permission to freeze part of the DBS specimen for an indefinite time for future testing. These specimens will be stored at the CDC in Atlanta, GA. No links to personal identifiers will be kept with the specimens. Tests that might be done include tests for HIV, other viruses, or immune function tests. Specimens will not be tested for genetic problems or used for cloning or commercial purposes. Participants who decline to have their specimens stored are still eligible to be part of this study.

18. Token of Appreciation

Men will be provided a token of appreciation for their time and participation on completing specific tasks during Part 4. These amounts are based on prior research experience in conducting studies with this population by the Principal Investigator. A token of appreciation is necessary to ensure recruitment and retention of a stigmatized population who are at greatest risk of becoming infected with HIV.

Men participating in the randomized controlled trial could be provided up to $90, and men participating in the evaluation of home test kit distribution by HIV-positive MSM component of Part 4 could be provided up to $30. Upon completion of the baseline survey, all men will be provided $20. All men will be provided $10 for completing each follow-up survey (men in the intervention and comparison arms at months 3, 6, 9 and 12, and men in the HIV-positive group at month 3), and men in the intervention and comparison arms will be given $20 for returning the DBS specimen. The tokens of appreciations will be provided by PayPal or by Amazon.com gift card.

Focus group and in-depth interview participants will receive $50 as a token of appreciation.

19. RESPONDENT BURDEN

The estimated burden for participants depends on the group they are in and the activities they participate in.

Intervention arm participants: The estimated burden for participants in the intervention arm is up to 6 hours and 5 minutes. Reading the basic study information and consenting will take approximately 10 minutes, completing the online eligibility screener will take approximately 3 minutes and the registration process will take approximately 5 minutes. Completing the baseline survey will take approximately 15 minutes. The OraQuick test will take approximately 5 minutes to perform and 20 minutes to wait for the results. The Sure Check test will take approximately 5 minutes for the finger prick and 15 minutes to wait for results. If the participant conducts all 4 tests included in the welcome kit, this could add up to 25 minutes x 2 tests plus 20 minutes x 2 tests for a total of 90 minutes. Completing the follow-up survey at months 3, 6, 9 and 12 will take approximately 10 minutes. If the participant requests and uses up to 2 additional test kits to home-test at months 3, 6, and 9, this could add up to 25 minutes x 2 tests x 3 times. For the performance assessment, the OraQuick test will take approximately 5 minutes to perform and 20 minutes for the results. The Sure Check test will take approximately 5 minutes for the finger prick and 15 minutes for results. The DBS collection will take approximately 5 minutes and packaging for mailing will take approximately 2 minutes. If an individual receives a preliminary positive test result, he is welcome to speak to a trained HIV counselor through the study referral support system and receive a referral for supplementary testing and linkage to care at a local facility in the city where he lives, if appropriate.

Comparison arm participants: The estimated burden for participants in the comparison arm is up to 2 hours and 5 minutes. Reading the basic study information and consenting will take approximately 10 minutes, completing the online eligibility screener will take approximately 3 minutes and the registration process will take approximately 5 minutes. Completing the baseline survey will take approximately 15 minutes. Completing the follow-up survey at months 3, 6, 9 and 12 will take approximately 10 minutes. For the performance assessment, the OraQuick test will take approximately 5 minutes to perform and 20 minutes for the results. The Sure Check test will take approximately 5 minutes for the finger prick and 15 minutes for results. The DBS collection will take approximately 5 minutes and packaging for mailing will take approximately 2 minutes. If an individual receives a preliminary positive test result, he is welcome to speak to a trained HIV counselor through the study referral support system and receive a referral for supplementary testing and linkage to care at a local facility in the city where he lives, if appropriate.

HIV-positive group participants: The estimated burden for participants in the HIV-positive group is up to 43 minutes. Reading the basic study information and consenting will take approximately 10 minutes, completing the online eligibility screener will take approximately 3 minutes and the registration process will take approximately 5 minutes. Completing the baseline survey will take approximately 15 minutes. Completing the follow-up survey at month 3 will take approximately 10 minutes.

Focus group participants: The estimated burden for the FGD participants is approximately 120 minutes. Registration, study overview, and consent process is approximately 15 minutes; focus group is approximately 90 minutes.

In-depth interview participants: The estimated burden for the IDI participants is approximately 75 minutes. Registration, study overview, and consent process is approximately 15 minutes; interview is approximately 60 minutes.

20. COSTS OF PARTICIPATION

There will be no costs to participants, and all men will receive a token of appreciation for their time and participation upon completing specific tasks during Part 4.

21. BENEFITS OF PARTICIPATION

Subjects will learn their current HIV status based on a home-test and from the results of a laboratory-administered IA. Although study staff believe that knowledge of one's HIV serostatus is beneficial, this opinion may not be shared by participants. There are no additional direct benefits to participants for participating in activities in Part 4. We will provide links on the web pages after the surveys to websites such as AIDSVu, CDC's National Prevention Information Network, and Act Against AIDS, with accurate information on HIV, sexually transmitted infections, and national HIV prevention resources for MSM.

22. RISKS TO PARTICIPATION AND PROCEDURES TO REDUCE RISKS:

Surveys: Some survey questions may be considered sensitive, and men who complete the surveys may be uncomfortable answering some questions. Men will have the option for all questions to not answer.

Disclosure of participation in a research study: Participants in Part 4 will provide their email address, shipping address, and phone number as well as a nickname or preferred name as part of the study registration process. Because participants are providing these pieces of identifiable information, there is a possibility that their participation in a research study could be disclosed in the following ways: (1) if someone other than the participant sees the package containing HIV home-test kits when it arrives at the provided shipping address; (2) if someone besides the participant reads the email sent with the link to the follow-up survey; (3) if someone besides the participant sees the participants' results being entered online; or (4) if someone besides the participant sees the study text or email messages, online surveys on participants' computer.

The risk of disclosure of participation in a research study by email, receiving a package containing HIV home-test kits, receiving text messages, or interacting with the participants' online survey will be

minimized in the following ways: (1) the package containing HIV home-test kits is a plain, unmarked, cardboard box with no reference to its contents; there is the possibility that an individual other than the research participant may open the box and see the contents; however, we are requesting that participants provide a shipping address where they would be most comfortable having the package arrive; (2) emails with links to follow-up surveys will not make any reference to the nature of the health survey; for online surveys, participants will be required to login to the study website with the username and password that they created as part of the registration process before beginning the survey, and they will then be asked two security questions; (3) participants will be encouraged to delete any emails or text messages received as part of the study to protect them from an unauthorized individual viewing the messages, and to interact with the study web site when in private.

Home HIV testing: Risks of the actual HIV testing are minimal. The oral test only requires the participant to obtain an oral swab and the finger-stick blood test only requires a single finger prick to provide enough blood to fill the sampler tip of the testing device (2.5 µL). For DBS collection the participant needs to perform a single finger prick to provide enough blood to fill 5 circles (each about the size of a dime) on the specimen collection card. There may be minor discomfort from the finger-stick HIV tests and bruising may occur. Receiving a preliminary positive/reactive HIV test result may lead to distress for some participants who believe their HIV status to be negative. If a participant has a positive laboratory-tested IA result, his contact information will be reported by Emory study staff to his state health department via telephone. Participants whose test results are positive on laboratory-testing with IA, but who do not report their test results online, will still have their contact information reported to their respective state health departments. Because the state health department will have participants' identifiable information and their HIV test result, there is a very slight risk that an unauthorized individual could gain access to the state's records containing this information. However, this risk is extremely rare and we do not anticipate this to be a problem.

If participants have difficulty with home-testing, have concerns after testing, or have a new preliminary positive test result they can call the study referral support system which is available 24 hours a day, 7 days a week. As previously noted, counselors at the crisis hotline and Emory study staff will have completed training about the study procedures and in the fundamentals of HIV prevention counseling. For participants who have a confirmed new HIV positive test result as part of the study, Emory study staff will report their contact information to their respective state health department and arrange referral to care at a local facility in their city. Participants will be informed that all testing should be voluntary and persons younger than 18 years of age should not use these tests.

Focus groups and in-depth interviews: There is only a minimal risk of discomfort for FGD and IDI participants. It will be made clear to participants that the research team will be available after the FGD or IDI should any participant wish to ask confidential questions or receive more information on local HIV/AIDS services.

23. PROTECTION OF HUMAN SUBJECTS

The following procedures will be used to ensure protection of human subjects:

1. Contact information used to confirm participation will be held in a password-protected database on a MANILA (contracting company) secure server, accessible only by study staff. Remote study staff will not be able to download data from the MANILA servers. This contact information will be held separately from focus group data, in-depth interview data,

baseline survey data, follow-up surveys, and participants' HIV test results, which will contain only the participants' study identification number. The database will be backed-up to a hard drive housed in another location, also accessible only by select study staff. MANILA staff will be able to access and download information. The linkage to care coordinator(s) and retention coordinator(s) will be able to access but not download data that will enable them to perform linkage to care and retention activities. The contact information (name, email address and phone number) in the database will be kept for at most two (2) years after the end of the study, as per FDA regulation and then will be destroyed. Emory study staff will notify MANILA when to destroy the information in the database; MANILA will use Norton CleanSweep software to delete the database file from the secure server and the back-up file(s) from the separate hard drive.

2. The consent procedure outlines the voluntary nature of the research and explains the potential benefits and disadvantages of the research.
3. The participant will be provided a copy of the consent form that includes contact information for the research team members and the IRB. Participants can use this contact information to report adverse events or unanticipated problems.
4. The study referral support system will support the immediate needs of participants who have difficulty with home-testing, who have concerns after testing, or who have a new preliminary positive test result. Immediate consultation will be available 24 hours a day, 7 days a week and will be provided by trained Emory study staff Monday through Friday from 9:00am to 5:00pm Eastern time, trained HIV counselors at Center on Halsted from 5pm to 11pm Monday through Friday and 9am to 11pm Saturday and Sunday, and by crisis hotline counselors at Mental Health Association – New York City LifeNet at all other hours.

24. DATA ANALYSIS

Rationale for proposed number of subjects

Randomized controlled trial: 3,200 HIV-negative or unaware participants are required to determine the prevalence of testing behaviors among men in the intervention arm compared with men in the comparison arm. The sample size of 3,200 is based upon a binary outcome of success as having ≥3 HIV tests per year and the chi-square test at the 5% significance level, with having a 90% power to detect a difference between the comparison and intervention groups if the success rates in these groups are 5% and 10% respectively. We inflated the sample size to allow for a maximum 40% attrition rate. Including 1,600 HIV-negative or unaware participants in the intervention arm will allow us to identify an estimated 94 new HIV diagnoses. To allow for appropriate analytical comparisons, at least 20% of men will be black, and at least 15% Hispanic. We will be consenting participants before the eligibility screener and kit ordering process. Therefore, we will need to consent more than 3,200 persons in order to reach 3,200 participants who are eligible, enroll in the study and order a test kit. We expect to consent 16,000 persons in order to reach 3,200 participants who are eligible, complete the baseline survey and order kits.

Test kit distribution evaluation: Although men in the HIV-positive group are already aware of their serostatus, 150 HIV-positive participants will be included to assess men's willingness to distribute the kits to their social and sexual networks, and the willingness of men who receive the tests to test themselves. We will be consenting participants before the eligibility screener and kit ordering process. Therefore, we will need to consent more than 150 persons in order to reach 150 participants who are

eligible, enroll in the study and order a test kit. We expect to consent 750 persons in order to reach 150 participants who are eligible, complete the baseline survey and order kits.

Focus groups and in-depth interviews: We are employing the rule of saturation, which is standard for qualitative data collection. We aim to have 16-18 FGDs and 24-30 IDIs. In our experience of working with this population, saturation has been achieved in 10-14 FGDs and approximately 25 IDIs; thus the proposed sample is sufficient to achieve saturation for this population.

Plans for data management and statistical analysis

Exposures and enrollment: We will monitor exposures (the number of people exposed to the banner advertisement), click-through rates (the number of people who click the banner advertisement and are taken to the informed consent site) weekly.

Analysis of testing frequency: The primary outcome will be the proportion of HIV-negative MSM tested for HIV at least 3 times during the study year and linkage to care among men diagnosed with HIV in the study. The primary outcome will evaluate whether men in the randomized trial were tested 3 or more times in the study year. Bivariate analyses will be performed to describe the associations between being a frequent tester and key demographics (age, race, education) and behaviors (patterns of sex partnering and sexual risk behaviors). Multivariable analyses will be conducted using logistic regression to describe factors associated with frequent testing; a variable for study arm will be included to allow assessment of the effect of study intervention on the outcome of testing frequency. Secondary outcomes will include kit preference, satisfaction with at-home testing, and yield from the distribution to social and sexual network affiliates stratified by HIV status of the participant.

Focus groups and in-depth interviews: The FGDs and IDIs will be recorded. FGDs will be recorded via digital audio recorder while the IDIs will be recorded via telephone recording equipment standard to telephone interviewing. Online FGDs will have the online transcript recorded. Tapes of the FGD and IDIs will be transcribed by a professional agency. All tapes will be destroyed within 4 weeks of the completion of the transcription. The resultant text files will be loaded into a qualitative analysis software. No identifying information other than participants' city and state will be included in the transcripts. In the consent process and the introductions to the FGD and IDI participants will be asked not to refer to themselves or others by name.

25. DATA SECURITY PRECAUTIONS

All participants will be assigned a unique identification number for the study. Consent forms and all confidential data (i.e., phone numbers and email addresses) collected regarding study participants will be maintained on the MANILA server, separated from the focus group data, in-depth interview data, baseline survey, follow-up surveys, self-reported rapid test results, and DBS specimen test results. A master list linking the identifiers and names will be stored on the MANILA server. Electronic audio files will be stored on password protected computers accessed only by MANILA study staff, and the original recording will be deleted once receipt at MANILA has been confirmed.. Access to confidential files is managed by the Project Director and is limited to study staff directly involved in this research on a need-to-know basis. Personally identifying information will not be stored at study sites. No confidential data will be permitted off site.

26. CONFIDENTIALITY

As noted above, eligible men who consent to participate will provide their email address, phone number and shipping address as well as a nickname or name of choice. This identifying information and survey responses will be held in a password-protected dual-authentication database accessible only by study staff. Shipping information is held in a separate computer and database not associated with or linked to the online reporting system. At the end of the study this information will be destroyed per protocol. If a participant's HIV test result is confirmed positive, their contact information will be reported to their state health department as required by law. Their information remains confidential when it is reported to the state health department. Participants agree to this when they sign the informed consent document (Appendix C).

During the FGD and IDI process, nicknames or name of choice, email addresses and phone numbers previously collected will be used to provide contact information to confirm participation, but names are not used during data collection nor associated with collected data. This will be emphasized during the introduction to the FGD. Contact information used to confirm participation will be held in a password-protected database accessible only by study staff. This contact and other identifying information will be held separately from focus group notes, and will never be associated with the study data collected.

27. INFORMED CONSENT

For Part 4 randomized trial and cohort study, we will use documentation of informed consent obtained through electronic agreement to the informed consent form presented online. The written informed consent document will explain: (1) what is meant by consent; (2) why we need to obtain consent; (3) the purpose of the consent form and (4) what an investigational device is and the alternatives if participant does not want to consent. Participants will be required to view the informed consent document before indicating whether or not they consent; this will be enforced by requiring participants to scroll through the entire consent before they can choose to consent to participate. Consent or lack thereof will be documented in the electronic database by the stored variable indicating consent or lack of consent. A button to allow participants to print the consent form for their records will be located at the end of the consent form document. The consent process will take approximately 5 minutes per individual.

All test kits will have a label on the box indicating that it is a test kit being distributed as part of the study, and by opening the test kit package the person agrees to use this product as part of a research study. The label will also request that the user report their results and will provide the study web site address and study support number to call if assistance is needed with the testing process or for assistance with linkage to services if the tester receives a positive rapid HIV test result. The label will also contain language indicating that persons should not feel pressured into using the test kits, and if testing under these circumstances occurs to contact the study support number to report the incident. The label on the Sure Check box will also contain the FDA's caution message, informing the user that the test is an investigational device.

Study staff will be available during business hours by phone or by email to answer any questions that participants have prior to consenting. Participants will be informed that the Sure Check® HIV 1/2 Assay is FDA approved for professional use, but not home use. Therefore it is being used in this study as an investigational device under an exemption from the FDA and with permission from the Emory University

Institutional Review Board for research purposes only. Participants will be informed that if they are found to be preliminarily HIV positive on any of the home-tests they are welcome to call the study referral support system and request immediate consultation with a counselor for crisis support and to obtain referral information on where to get supplemental testing and care. If the laboratory-administered IA tests labeled for use with DBS specimens are positive, Emory study staff will contact participants to provide them with referral information for supplemental testing and care in their respective cities of residence. Persons with a confirmed HIV-positive result will have the option to request a written document (via mail or email) with the test results that they can take to their own health care provider (Appendix O). Participants will be told through the informed consent document that the contact information of persons with confirmed positive HIV test results will be reported to the relevant state health department as required by law. The consent form has a Flesch-Kinkaid Reading Level of <8.5.

Verbal informed consent will be obtained for both the FGDs (Appendix K) and IDIs (Appendix M). Men who participate in either a FGD or IDI will be given basic information about the purpose of the study, will be emailed a consent form prior to the interview, and will be asked to ensure they have read it once the call begins before any data are collected. For Part 4, we request a waiver of written documentation of informed consent for the qualitative data collection. This is because the written consent document would be the only identifying document once voice recordings have been destroyed. Therefore, relying on verbal consent will reduce risk of loss of privacy for the participants. Participants will be emailed an informed consent form prior to the call, and the interviewer will begin the call by asking the participant if they have questions and ensuring they have comprehended the informed consent document. Each consent form has a Flesch-Kinkaid Reading Level of <8.5. Study staff will answer any questions that participants have and will document verbal consent.

28. APPENDICES

APPENDIX A Banner Advertisement Example
APPENDIX B Basic Study Information
APPENDIX C Study Consent Form
APPENDIX D Eligibility Screener
APPENDIX E AIDSVu
APPENDIX F Registration
APPENDIX G Baseline Survey
APPENDIX H Follow-Up Survey
APPENDIX I Reporting of Home-test Results
APPENDIX J Messages for Different Self-Reported Test Results
APPENDIX K Focus Group Consent Form
APPENDIX L Focus Group Discussion Guides
APPENDIX M In-Depth Interview Consent Form
APPENDIX N In-Depth Interview Guides
APPENDIX O eSTAMP Participant Home-test Referral Sheet
APPENDIX P Lab Algorithm and Data Analysis Plan
APPENDIX Q HIV+ Group Basic Study Information
APPENDIX R Study Consent Form (HIV+ Cohort)