

**Web-based Approaches to Reach Black or African American and
Hispanic/Latino MSM for HIV Testing and Prevention Services**

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Section B: Supporting Statement

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1. Respondent Universe and Sampling Methods

The population for this comparative effectiveness trial will be black or African American and Hispanic/Latino men with the following further inclusion criteria:

- Black/African-American race or Hispanic/Latino ethnicity
- Male sex at birth
- Currently identify as male
- Anal sex with at least one man in the past 12 months
- Aged 18 or over
- Has an Android or Apple mobile phone with currently active service
 - Currently resides in a study State and does not plan to move out of the State within 4 months: NC, SC, GA, AL, MS, LA, CA, NV, TX, NY, FL
- Willing to download a study mobile app
- Willing to provide valid contact information so that study HIV testing kits and other materials (condoms, lubricants, STI testing kits) can be mailed to participants.
- Successful completion of baseline survey

No vulnerable populations will be included in this study. Exclusion criteria are the following:

- Currently participating in another HIV prevention research study or program
- Has a bleeding disorder preventing use of dried blood spot testing
- Has previously participated in an HIV vaccine study.
- Currently taking PrEP for HIV prevention
- A previous HIV diagnosis

The study also excludes men who are currently taking PrEP as people who take PrEP are required to receive regular HIV testing. Components of the trial will be delivered via an Android or iOS smartphone application or a mobile-optimized website; therefore, participants are required to own an Android or iOS smartphone with which the app is compatible. According to 2018 survey data from the Pew Research Center (<http://www.pewinternet.org/fact-sheet/mobile/>), smartphone ownership is as follows: 80% among all men, 94% among those aged 18-29, 89% among those aged 30-49, 73% among those aged 50-64, 77% among Hispanic individuals, and 75% among black individuals.

Males aged 17 years or younger are excluded from the study because: (1) effective HIV preventive interventions for adolescents are likely to differ markedly from those focusing on young adults and adults,

both in content and presentation; (2) the individual, socio-cultural and developmental factors associated with HIV risk in MSM under 18 are different from those for MSM 18 and up; and (3) the research questions and issues of relevance for MSM aged 18 and up may not be relevant or appropriate for MSM under age 18.

Women are excluded from the study because: (1) effective HIV preventive interventions for women are likely to differ markedly from those focusing on men (particularly MSM), both in content and presentation; (2) the individual, socio-cultural and developmental factors associated with HIV risk in MSM are different from those for women; (3) the research questions and issues of relevance for MSM are not relevant or appropriate for women; (4) several effective HIV prevention interventions for women have already been developed, evaluated, and disseminated.

Study procedures and data collection will take place in North Carolina, South Carolina, Georgia, Alabama, Mississippi, Louisiana California, Nevada, Texas, New York, and Florida. The site where study recruitment will be conducted is Emory University, Atlanta, Georgia. Recruitment will be conducted in all study states by Emory University. Virtual HIV counseling will be available upon request provided by University of Michigan study staff to all participants. All study participant, regardless of assigned arm, who reports a preliminary positive test result will be contacted and offered virtual HIV counseling and linkage to care.

2. Procedures for the Collection of Information

Participants will take surveys and upload images of test devices through an online survey portal using secure webpages, accessed through the SMART app or through personalized links, which encrypt when sent and decrypt when received by the hosting server. These data will be collected and stored directly on the private server. These data will be identified in the system through a Study ID and a second identifier such as initials. The link between survey responses and contact information for participants is held by Emory study staff. For images of test results, we will use a secure survey form to transmit the upload of the image file, and it will be treated under the same confidentiality protections as other study data (e.g. stored on a secure server). The image data will be stored on the same server as the assessment data, subject to the same physical and procedural security measures described below for survey data.

Survey Assessment Contents: The baseline assessment collects information on topics which include: demographic characteristics, sexual behaviors, HIV testing, HIV prevention behaviors such as condom and PrEP use, HIV testing intentions, HIV treatment and care service history, other health service history, internet and mobile application

usage, intentions to seek care, mistrust, health literacy, and costs. Men will be prompted to take follow-up surveys after the end of the 4-month period, which will cover the same domains as the baseline survey, with scope limited to the post-baseline period. The assessments may be delivered in modular format to improve response rate and allow participants to take breaks while completing the surveys. Additionally, participants who were assigned to the HealthMindr arm will also answer additional questions in the follow-up surveys which ask about experiences using the app or websites. Individuals who use the video prevention counseling option will be asked about their experiences using this service. A participant will be able to connect with study staff if they have any questions regarding study activities, and study staff will handle any issues or research-related questions. Follow-up survey links will be provided to the participant, with unique SurveyGizmo.com survey links coded with participant study IDs and assessment. This process will authenticate that the correct participant will be taking the correct assessment. The survey will also verify his identity using three letter initials and date of birth. These assessments should take no longer than 30 minutes to complete. Participants will have an opportunity at the beginning the study to indicate if they are interested in future research projects. If they are, and they grant permission, Emory will keep their contact information in a separate database for persons interested in participating in future studies.

Study Management Mobile Application (SMART): As participants interact with the SMART app, data about features used, pages visited, functions used, and time spent may be captured and stored in the administrative portals of the SMART app. Data are stored with alphanumeric identifier strings unique to participants. Emory study staff hold the link between alphanumeric strings and contact information for participants.

HealthMindr: Participants assigned to the HealthMindr arm will receive access to a mobile app. As participants interact with HealthMindr app, data about features used, pages visited, functions used, and time spent will be captured and stored in the administrative portals of the app. Data are stored with alphanumeric identifier strings unique to participants. Emory study staff hold the link between alphanumeric strings and contact information for participants.

Video Prevention Counseling: Participants can use a HIPAA-compliant videoconferencing platform to interact with trained HIV counselors. As participants interact with the platform, data about length of sessions will be captured and stored in the administrative portal of the platform. These data will not contain any identifying information about the participant.

Reporting HIV Self-Test Results: Participants will be mailed up to four study HIV self-test kits. They will be informed that these tests are for their use and to give to other people, such as sexual partners or friends, hereafter referred to as “guests.” Participants will be reminded to tell the guest that the tests are being distributed as part of a study. Participants will be asked to upload an image of their completed test device and asked to report their test results through the reporting survey (**Attachment 3d**) or (**Attachment 3f**). The image and survey will be linked to the participant’s study record via their unique study ID.

Guests of Trial Participants: Participants may elect to give mailed-out HIV self-tests to guests. Guests will have access to online written test instructions and instructional videos. Guests will have access to a separate survey where they can log on as a “guest” (i.e., not as a study participant, and no registration is required). There, they can review the consent form (**Attachment 4c**). Guests who proceed past the consent form will be prompted to complete a survey that includes background information and rapid results reporting (**Attachment 3h**). 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.

DBS and Microtainer Test Results: Participants who consent to provide DBS and Microtainer samples for research purposes at the end of the 4-month study period will use study-provided collection kits. An instructional video will be provided for participants through an online video application. Using provided instructions, participants will mail the DBS card to Emory University for testing. DBS cards will be delivered pre-labeled and will not require registration. Microtainer samples will be mailed directly to CDC. Microtainer will be delivered pre-labeled and will not need to be registered (name and contact information will not be provided).

Emory staff will transport DBS samples to the CDC laboratory weekly. After laboratory processing and testing, laboratory personnel will upload results for all tests in a password-protected Excel spreadsheet onto a secure Emory server, and only designated study staff will be provided with access.

HIV Test Result Verification and Reporting: Participant HIV test result verification will depend on the type of HIV testing, as well as how the HIV test is reported. We will look to a variety of data sources to attempt to validate test results.

For all participants, instructions will be sent via email or through the SMART app concurrently with the mailing of the HIV self-test kits.

These instructions will ask participants to upload a picture of the completed test device through a secure SurveyGizmo link. Upon enrollment, participants will be made aware that they can receive a \$10 token of appreciation (limited to one per participant) for providing evidence of testing for HIV (e.g. a picture upload) during the study period, regardless of where or how they test.

To attempt to validate HIV testing results resulting from tests conducted outside of or as part of the study, we will look to a variety of different data sources. For men who report that their test results were negative, we will explore the use of CDC data sources to the extent possible, including evaluation data from public counseling and testing clinics. One process we will attempt to use to verify reported information is to liaise with CDC's Evaluation Web. Using participant-reported information about the specifics of the test, we will ask the CDC evaluation program to confirm if a person with matching de-identified data (date of birth, ZIP Code, race, month of testing) was reported through their system.

To attempt to validate both preliminary positive test results and initial linkage to care from participant-reported surveys, we will look to a variety of different data sources. We will explore the use of CDC data sources to the extent possible, as well as individual agreements with state departments of health. Emory has used this process most recently with the EngageMENT study (R01AI112723-04). After obtaining participant consent to do so, Emory may request HIV surveillance data from the state Departments of Public Health (SDPH) following the end of a person's participation in the study. By law, SDPH receives all reports of HIV western blot tests, CD4 counts and viral load tests performed on patients in their jurisdictions. In this other study, Emory obtained conditional approval from the Georgia Department of Public Health (GDPH) to obtain individual-level HIV surveillance data and included, at the request of GDPH, the contact information for the GDPH IRB on the study consent/assent. Emory will work to establish these arrangements with states. For the EngageMENT study, Emory provided GDPH with a list of names (a subset of participants) for whom specific HIV surveillance data was desired (e.g., first HIV positive test, CD4/VL in a date range).

For this study, Emory may serve as a case reporter to all states, reporting the results of study HIV tests to state health departments. This creates the reporter relationship required for data to care agreements. Where states agree, we will also request that they check the names and dates of birth of all participants in their states, which might help us identify participants who confirm HIV test results or enter care for HIV infection, even if they do not report an initial positive result to study staff.

Rapid HIV self-tests: The rapid HIV self-test to be used in this project is the OraQuick® In-Home HIV Test (OraSure Technologies, Inc.), an oral fluid test that is approved for HIV self-testing by the US Food and Drug Administration (FDA).

The study mobile app (SMART) or personalized emails will remind the user to report their results and will provide the study mobile app 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.

All items will be shipped to participants using a service such as Amazon Fulfillment Services, through which kits would be shipped and arrive in an Amazon labeled box though Amazon's usual shipping methods within 2 days. Nothing on the box will identify it as related to HIV, sexual health, or MSM. Amazon's shipping services will also provide confirmation of delivery to facilitate documentation of kit delivery.

DBS and Microtainer Testing: Additionally, at the end of the 4-month follow-up period, all participants will be mailed a dried blood spot (DBS) collection kit that participants can use to collect a sample of blood. For DBS collection, the participant must perform a single finger prick to provide enough blood to fill 5 circles (each about dime-sized) on a collection card. This may cause minor discomfort and bruising. 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. 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 through the SMART app and online.

Participants who return the DBS card and report taking PrEP or ART will be sent a microtainer collection after they return their DBS card.

The microtainer collection kit includes: an instruction booklet in English, a microtainer collection tube, a plastic bag, an alcohol wipe, two gauze pads, two safety lancets (BD, 2 mm), a bandage and a return envelope. Microtainers will be pre-labeled with the participant ID and do not need to be registered by the participant. Microtainers will be returned directly to CDC.

For the microtainer collection, the participant will perform a single finger-stick to provide enough blood to fill at least half (250 uL) of the microtainer. The participant will return the microtainer in the provided mailing envelope. The packaging will not contain identifiable information and it will be mailed to the CDC DHAP lab.

All participants will receive instructions through their study app or email to indicate whether they received the DBS and microtainer collection kits and report when they mailed it back to Emory.

Participants who within 1 week of receiving the package 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. The participant will receive a token of appreciation worth \$10 for sending in their DBS specimen. Similarly, for the microtainer collection kit, participants will receive \$10 for sending in their specimen.

Laboratory Testing: The CDC laboratory in the Division of HIV/AIDS Prevention will conduct HIV and drug testing. After the CDC receives a participant's DBS and/or microtainer specimen, staff will sort the DBS cards and microtainers based on the labeling provided by Emory to be tested in one of two ways:

- For MSM who report an HIV positive result (with the self-test or other HIV testing), the DBS specimens will be tested for viral load. If there is sufficient sample and participant self-reported being on ART on their follow-up survey, they will be tested for the presence of antiretroviral drugs to assess treatment adherence and compliance. The priority is viral load for HIV diagnostics, rather than drug levels.
- For MSM who do not report an HIV positive result, their DBS specimen will be tested for HIV infection with a laboratory-validated algorithm that includes using an Ag/Ab HIV screening test, and, if reactive, followed by an HIV-1/HIV-2 antibody differentiation supplemental test, and nucleic acid testing. This will be done to discover infections missed by the rapid HIV self-test or to discover any PrEP breakthrough infections. If there is sufficient sample and the participant reports being on PrEP on their follow-up survey, the DBS specimens will be tested for the presence of tenofovir-diphosphate (TFV-DP) and emtricitabine triphosphate (FTC-TP) as a measure of adherence to daily oral Truvada.

Once the CDC Laboratory processes the DBS and microtainer samples, the laboratory will generate an excel spread sheet containing the unique box ID associated with the mailed-out kit and the CDC-generated testing IDs. The results of the testing will be merged into this spreadsheet. Laboratory personnel will upload the spreadsheet onto a secure Emory server, or via another secure data transfer method, and the spreadsheets will be password-protected and only accessible to trained, CITI-certified study staff at Emory University and CDC. The unused DBS cards and punches will be stored for future HIV testing and available for additional research investigations.

Return of Test Results: HIV testing of DBS specimens will be conducted by the CDC laboratory using the following laboratory-validated assays for use with DBS specimens:

1. Ag/Ab test: GS HIV Combo Ag/Ab EIA (Bio-Rad Laboratories)
2. HIV-1/HIV-2 antibody differentiation supplemental test: Geenius HIV-1/2 Supplemental Assay (Bio-Rad Laboratories)
3. HIV-1 Viral Load

These assays are not approved by FDA to be used with DBS specimens and therefore it is not possible to return these results to study participants. However, if a participant not known to be HIV-positive has results indicative of HIV infection from testing with the validated laboratory assays, trained study staff will notify the participant via phone that "HIV infection is suspected but not confirmed and please seek further testing". This message of suspected HIV infection will be communicated to the participant within 6-8 weeks from receipt of the DBS card to the CDC laboratory. Viral load, antiretroviral, and TFV-DP/FTC-TP results will not be returned to participants. DBS cards will be delivered pre-labeled and thus do not need to be registered online.

By law, for all participants with positive laboratory-confirmed results, Emory will report that positive test to the relevant state Department of Public Health for purposes of statistics and service planning.

Preliminary Positive HIV Test Results: At any time during the study, study participants who report a positive test, a test that is not working, or an invalid test result (and have not already contacted the study referral support system using the toll-free number) will be contacted by trained study staff within 3 business days. 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, 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, study staff will contact the participant to organize the mailing of another kit.

STI Testing: Participants in the HealthMindr arm will have the ability to order up an STI testing kit (CareKit) in the first 3 months of study participation. The STI kit tests are for syphilis, gonorrhea, and chlamydia. Syphilis will be tested using a blood sample collected through a finger prick. Gonorrhea and chlamydia will be tested at three anatomical sites including rectal, pharyngeal, and urethral by collecting a rectal and throat swab and a urine collection.

Once completed STI kits will be sent to the Emory Clinical Virology Research Laboratory and CDC laboratory. Samples will be mailed using a USPS pre-paid, pre-labeled bubble mailer. Once labs process samples, results will be uploaded to a password protected excel file stored on a secure Emory network. After the results have been checked for quality, Emory University study staff will contact participants with results and provide STI testing and treatment referrals as needed.

3. Methods to Maximize Response Rates and Deal with No Response

The study retention plan will incorporate multiple strategies to achieve a target retention of at least 70%. Contact information, including email, mobile phone number, and mailing address, will be collected from and verified for each participant and may be able to be updated from the SMART mobile app (see a. below). Electronic notification reminders will be sent to the participant up to 3 times (24 hours after, 48 hours after, and 72 hours after) if a survey remains uncompleted. If the survey remains uncompleted after the 3rd notification, then study staff will attempt to make contact based on the participant's primary and alternative contact preferences provided at enrollment. These can include email, phone, SMS. Each contact attempt will be logged in an electronic retention system. If contact with participants is lost, study staff, using obtained informed consent, will attempt to use public-use databases to locate participants. These databases may include: LexisNexis, jail or prison entry records, and vital records.

- a. **SMART Participant Management System:** The study will use a HIPAA-compliant web-based platform entitled Study Management and Retention Toolkit (SMART), which is a SaaS (Software as a Service) based mobile application aiding studies with various aspects of participant recruitment, study implementation, and retention. The application can securely manage participant information across multiple studies and customers simultaneously, stratifying participant information by study and site. SMART may include a participant facing mobile app, which allows for secure messaging, study calendar management, self-scheduling by participants, secure photo uploads, and longitudinal tracking of participants from screening to study completion. These features encourage maximum response and retention among study participants.

4. Tests of Procedures or Methods to Be Undertaken

Our team includes experts with the target population, as well as with qualitative and quantitative research methods, including screening, instrument development, and pilot testing.

5. Individuals Consulted on Statistical Aspects and Individuals Collecting and/or Analyzing Data

The table below lists the project team members who were consulted on the study population, and aspects of the research design, as well as those who will be collecting and analyzing the data. CDC staff are primarily responsible for providing technical assistance in the design and implementation of the research; assisting in the development of the research protocol and data collection instruments for CDC Project Determination and IRB reviews; working with investigators to facilitate appropriate research activities; and analyzing data and presenting findings at meetings and in publications. The CDC staff will neither collect data from nor interact with research participants. Data will be collected by members of contractor project staff listed below at Emory and University of Michigan. No individual identifiers will be linkable to collected data, and no individually identifiable private information will be shared with or accessible by CDC staff.

Name	Affiliation	Role in data collection/analysis	Contact
David Benkeser	Emory University	Statistician: will conduct data analyses. Determined sample size calculations for Emory University prior to award of funds.	benkeser@emory.edu 404-712-9975
Craig Borkowf	CDC	Statistician: will conduct data analyses. Determined sample size calculations for CDC prior to award of funds.	cborkowf@cdc.gov 404-639-5325
Robin MacGowan	CDC	Analyst: will conduct data analyses after data collection.	Rmacgowan@cdc.gov 404-639-1920
Heather Saul	CDC	Analyst: will conduct data analyses after data collection.	Nud5@cdc.gov 404-718-3388
Arin	CDC	Analyst: will conduct	Gpo4@cdc.gov

Freeman		data analyses after data collection.	404-639-8432
Pollyanna Chavez	CDC	Analyst: will conduct data analyses after data collection.	Geo5@cdc.gov 404-639-1742
Patrick Sullivan	Emory University	Analyst: will conduct data analyses after data collection.	pssulli@emory.edu 404-727-2038
Ruth Dana	Emory University	Analyst: will conduct data analyses after data collection.	ruth.m.dana@emory.edu 404-712-9997
Annie Lockard Thorne	Emory University	Analyst: will conduct data analyses after data collection.	annie.lockard@emory.edu 404-727-2134
Kevin Weiss	Emory University	Analyst: will conduct data analyses after data collection.	kvnweiss@gmail.com 802-399-6773
Lisa Hightow-Weidman	University of North Carolina	Analyst: will conduct data analyses after data collection.	lisa_hightow@med.unc.edu 919-843-0033
Rob Stephenson	University of Michigan	Analyst: will conduct data analyses after data collection.	rbsteph@umich.edu 734-615-0149