Leveraging mHealth and Peers to Engage African-Americans and Latinxs in HIV Care (LEAN)

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1. Abstract

Baltimore's HIV prevalence rate (586/100,000) is among the top 5 in metropolitan areas in the US, and disparities are profound.[i] African Americans have an HIV prevalence that is 5 times higher than among whites, and they account for 78% of all HIV cases. Latinxs also have a higher prevalence of HIV than whites and are at the highest risk for late HIV diagnosis among all racial/ethnic groups.[ii] In addition, HIV viral load suppression, which is the best predictor of long-term survival among HIV-infected patients, is substantially lower among minority populations in Baltimore.

The hypothesis of this study is that an mHealth-enhanced Linkage to Care and Retention (mLTCR) intervention can improve HIV outcomes among HIV-infected African Americans and Latinxs compared to standard linkage and care support protocols. The mLTCR intervention consists of two smartphone applications (app), one for patients and one for support staff such as linkage officers or patient navigators, to help facilitate communication. Communication will focus on issues related to HIV care (e.g. appointment scheduling, need for laboratory tests), as well as patient-directed requests. Using HIV surveillance data (e.g. dated HIV viral load), support staff will be automatically alerted if a patient has a high viral load or has not had labs done in > 4 months and prompted to contact the patient. In addition to appointment and laboratory reminders, patients will receive positive reinforcement behavioral text messages.

This is a pragmatic randomized controlled study comparing existing linkage and care support (LTC) services to an mHealth-enhanced linkage to care and retention (mLTCR) protocol.

According to modelling studies, improvement in linkage and retention in care indicators is the single most important component to achieve the 2020 National HIV/AIDS Strategy targets and substantially reduce the burden of HIV in the United States.[iii] The results of this randomized study will contribute to the evidence on the effectiveness of mHealth-enhanced LTCR initiatives implemented by the local health department and clinics. Evidence supporting the feasibility and effectiveness of this intervention will be important for HIV clinics, the BCHD and other health departments as they allocate limited resources to address the HIV epidemic in their jurisdictions. The information will also be relevant to Ryan White officials responsible for allocating federal dollars to support clinical and ancillary services to improve HIV outcomes, particularly among patients who are uninsured or underinsured.

2. Objectives

Aim 1: To compare virologic suppression and retention in care between HIV-infected individuals who are randomized to receive standard of care linkage and care support services versus mHealth-enhanced LTCR (mLTCR) services. The primary outcome measure will be virologic suppression

at 12 months of study enrollment, and secondary outcomes will include retention in care at 12 months.

Aim 2: To examine the implementation of mLTCR services using a mixed-methods approach to determine the intervention's feasibility, acceptability, coverage, fidelity, sustainability, and patient satisfaction.

3. Background

HIV Disparities among African Americans and Latinos. African Americans represent 12% of the population but account for 43% of people living with HIV in the US and are less likely to receive ART or achieve virologic suppression compared to whites.[iv] HIV rates among Latinos are 3 times higher than among whites, and Latinos are at high risk for delays in diagnosis and linkage to care.[v,vi] Delayed initiation of ART is associated with increased morbidity and mortality.[vii] In addition, high viral load is the most important predictor of HIV transmission and drives the risk of HIV infection among sexual networks.[viii, ix,x] In Baltimore City, efforts to curve the HIV epidemic have led to a reduction in new HIV diagnoses but disparities persist. In 2016, 78% of new HIV diagnoses were among African Americans, whose rate of HIV infection is 5 times higher than among whites. In addition, linkage to care is lower for African Americans and only a third of HIV-infected African Americans from Baltimore have suppressed HIV viral loads (VL), dramatically short of the 80% goal outlined by the National HIV/AIDS Strategy (NHAS).[i, xi]

Health Department Response and Linkage to Care Initiatives. To address the HIV epidemic, health departments across the US have operationalized the Center for Disease Control and Prevention's (CDC) Data–to-Care initiative to optimize the HIV care cascade.[xii]Using routine HIV surveillance data, health departments, including the BCHD, systematically identify HIV-infected people who are newly diagnosed or out of care, and reach out to them to facilitate linkage to care.[xiii] In 2017, BCHD linkage officers engaged 1942 HIV-infected patients who needed linkage services. However, loss to follow up after initial engagement in care is a persistent problem. Under current BCHD Linkage protocols, linkage officers do not follow up patients after linking them to a clinic. Patients may be identified as out of care at a later point if they do not follow up with appointments. However, re-engaging patients in care is challenging because linkage officers do not have ongoing relationships with patients and contact information obtained from surveillance databases is often out of date, especially for those living in poverty and in unstable housing conditions.

Clinic-Based Retention in Care Initiatives. Health departments have traditionally focused on linkage to care, while clinics have mostly been responsible for retention of patients in their practice. Many HIV clinics have retention protocols, but these vary widely, ranging from simple automatic reminder calls to systematic review of patients to identify those who have fallen out of care.[xiv] Evidence suggests that increased contact with the clinic can improve retention in care but may not be enough. A randomized controlled trial conducted in six HIV clinics in the US showed that among patients who were newly diagnosed or had missed at least one appointment in the past year, enhanced contact with a clinic worker improved retention in care. In this study, patients who met with a clinic worker at study enrollment and maintained contact throughout the year by phone (personalized reminder calls and follow up for missed appointments) were more likely to keep appointments than those receiving automated appointment reminder calls (56% vs. 46%).[xiv] The intervention, however, was less effective among patients with at least one unmet need or active substance use disorder.

Unmet Needs and Linkage and Retention in Care. The Data-to-Care experience has shown that a significant proportion of individuals out of care are homeless, transitionally housed, transient, and without working phone numbers.[xv] Interviews with patients out of care contacted by the San Francisco Health

Department identified several personal and structural barriers to care. The top unmet needs included difficulty with transportation to the clinic and lack of practical support in navigating the system.[xvi] Participants expressed willingness in engaging with health department staff to receive assistance with ancillary services and HIV engagement in care. In Los Angeles, HIV-infected patients reported that the main reasons for not accessing HIV services were lack of information (do not know where to go or who to call), agency barrier (system too confusing, wait list too long), or financial/practical barriers (too expensive, transportation problem). In this study, African American were 3 times more likely to report unmet needs compared to whites.[xvii]

Integrating Retention Services into Health Department Linkage Protocols. Implementing homogenous retention to care services in all HIV clinics is neither feasible nor advisable, as clinics should be able to tailor their approach based on their resources and their clients' needs. This is where health departments can leverage routine HIV surveillance data and provide an additional layer of support to patients and clinics independent of clinic-based services. In most linkage protocols, contact with linkage officers is limited to one or two interactions, as linkage officers primarily assist with facilitating the initial appointment for engagement or reengagement in care. This model may be efficient for patients who are linked to care without additional support. However, for many patients, engagement in care occurs within a spectrum of frequent engagement and disengagement cycles due to complex personal and structural barriers. An evaluation of the San Francisco Health Department LTC model found that rather than being truly out of care or never in care, many patients were in intermittent HIV care, and were willing to accept health department assistance to help them stay in care.[xvi]

An alternative to one-time linkage services is to provide ongoing support to maintain continuity of care, particularly among minority populations that face multiple contextual challenges, such as poverty, substance use disorder, or housing instability. Providing linkage and longitudinal retention (LTCR) services from the health department that complements existing clinic-based retention efforts has not been systematically evaluated. This model assumes that a significant proportion of individuals will require not only linkage services but also retention support during their HIV care trajectory, and that providing longitudinal support may enhance timely linkage to care and facilitate future re-engagement attempts, if needed.

Enhancing Efficiency through Tailored mHealth Interventions. A health department or clinic-based LTCR approach could be enhanced with the use of evidence-based mobile health (mHealth) strategies that leverage mobile phones to improve health outcomes. Systematic reviews have found that mHealth interventions can promote engagement in care, adherence to ART, and virologic suppression.[xviii, xix, xx] These platforms can be programmed to send tailored messages, reminders, and alerts to patients and providers (such as linkage officers) using algorithms that leverage existing data (e.g. surveillance data) and patient input (e.g. response to prompts). A distinct advantage of mHealth platforms is the ability to facilitate patient-centered approaches to LTCR efficiently and without overburdening providers (alert for action to providers can be designed to focus on areas that truly require provider input).

Our team has previously partnered with emocha Mobile Health (https://www.emocha.com) to develop evidence-based HIPAA compliant mHealth applications to facilitate engagement in care.[xxi,xxii, xxiii] The miLINC platform, for example, facilitates direct communication and linkage between outreach workers, patients, and providers and has been used to link patients to tuberculosis services and improve coordination of care and timely treatment for patients with multi-drug-resistant tuberculosis in South Africa. A video directly observed therapy application (miDOT) has been evaluated and adopted by public health departments in the US for tuberculosis, hepatitis C, and opioid use disorder treatment. These emocha platforms have shown acceptability and feasibility of implementation in Baltimore City, including African American men who have sex with men, people who inject drugs, and foreign-born Latinos, and in diverse settings.[xxiv,xxv]

4. Study Procedures

a. Study design, including the sequence and timing of study procedures.

This is a pragmatic randomized controlled trial comparing Standard BCHD and HIV clinic-based linkage and care support services to mHealth-enhanced LTCR services described below.

Description of usual care and comparator arm:

Standard BCHD Linkage Services. The 2007 Maryland HIV/AIDS Reporting Act requires that HIV cases be reported by name. Laboratories are required to report HIV positive tests within 48 hours to the BCHD through PRISM, a morbidity and case management software. Data from PRISM is used to identify new HIV diagnoses and refer cases to a BCDH Disease Intervention Specialist for contact investigations and referral to linkage services. In addition, the Maryland Department of Health (MDH) HIV Surveillance Branch receives laboratory-based reports with results indicating HIV infection (including HIV diagnostic tests, CD4, HIV viral loads, and HIV genotype and phenotype tests) through the enhanced HIV/AIDS Reporting System (eHARS). Using this data, MDH generates weekly "Never in Care" and "Out of Care" lists for BCHD. Guided by these data, the BCDH linkage team contacts patients by phone or in person to connect them to care. Providers can also request assistance from the BCHD LTC program to link patients newly diagnosed or re-engage those lost to HIV care by contacting the LTC team. Therefore, the BCHD linkage officers attempt to contact and provide linkage services to all Baltimore residents newly diagnosed with HIV or who are presumed to be Out of Care or Never in Care, as identified through surveillance data or by referral from providers. Patients who agree to be linked to care by linkage officers are provided a same-day appointment and warm handoff to clinical care (the outreach worker drives the patient to the clinic of his or her choice). After the patient is seen by a provider, the linkage officer can assist with retention to the second appointment, but after the two initial appointments, the LTC officer is no longer involved in the case unless the patients appears again in the MDH Out of Care report at a later time or is referred by a provider. Linkage officers record patient encounters, and linkage attempts and outcomes in PRISM.

Clinic-based Linkage and Retention Services. In response to the "End the HIV Epidemic" strategy, many HIV clinics have strengthened their HIV Linkage and Retention Services. The Johns Hopkins Bartlett Clinic, for example, has implemented a Rapid ART initiation (RART) protocol where patients who are newly diagnosed with HIV in the Emergency Department and linked to the clinic within 1 business day with same-day ART initiation at the time of visit. In addition, the clinic uses "Data-to-Care" to identify patients who are out of care (no visits for > 8 months) or whose viral load is not suppressed, and provides them patient navigation services, appointment reminders, and pharmacy/adherence support.

mHealth-enhanced LTCR (mLTCR). This approach leverages the existing BCHD and clinic-based LTC and support protocols to identify newly diagnosed patients, those out of care, and those in need of retention services to provide ongoing linkage and retention to care services for 12 months. The intervention has an mHealth LTCR application based on an existing evidence-based HIPAA-compliant mHealth application facilitates direct communication and linkage between support staff such as outreach workers or patient navigators and patients, allowing for two-way communication to improve coordination of care and timely treatment. The app allows support staff and patients to communicate over time. In contrast to standard BCHD Linkage services, where linkage officers provide two-time support to link patients to care, the mLTCR approach will promote ongoing engagement between support staff and a patient over a period of 12 months. This allows for repeated doses of support (patient and algorithm-driven) and provides more opportunities for patients to develop a trusting relationship with support staff. The communication between patients and support staff will be driven by the patient's needs. Patients will be assigned a specific support staff member to allow for relationship-building, with backup as needed for support staff absences,

vacations, and sick leave. The BCHD linkage officers and clinic-based patient navigators are representative of the community served (primarily African American or bilingual Latino) and have long-standing experience working with the community.

mHealth Application for mLTCR arm**.** The mHealth application is designed to facilitate communication between the patient and support staff, and to automate certain tasks/alerts/reminders, so that support staff can focus their efforts on patients at high risk of falling out of care (such as calling a patient with a high viral load), rather than on time-consuming tasks not specifically targeted to high risk patients (like general appointment reminders). The patient application will be available in English and Spanish. Spanish-speaking limited English proficiency patients will be assigned a bilingual support staff person who will communicate with them in their preferred language. The study team has experience with cultural and linguistic adaptation of interventions and will elicit feedback from the Steering Committee (see below) to ensure messages are tailored to the health literacy and language proficiency of the target population. Tasks, alerts, and action prompts are outlined in Table 1 for the patient application and in Table 2 for the mHealth application.

Table 1. emocha mHealth-enhanced Participant Application

Task	Description	Support Staff Action
Laboratory Alerts	Participant in the intervention arm contacted by Support staff if he/she has not had a viral load in > 4 months or if the viral load is detectable (> 200 copies/ml)	Support staff contacts participant if alerted (see Table 2)
Appointment Data	Tab to record date/time/place of upcoming HIV appointment (entered by participant)	
Appointment Reminder	Participant automatically receives reminders about upcoming appointments (3 and 1 day prior). Day after scheduled appointment, participant receives prompt "Did you go to your appointment yesterday?" (Yes/No) If "Yes" receives message saying "Great job keeping your appointment" If "No" receives message "Do you need help rescheduling your appointment?"	Support staff contacts participant if alerted (see Table 2)
Ability to Directly Message Linkage Officer	Participant can click on prompts (eg "I need help with making appointments" or can free text message to Support staff)	Support staff contacts participant if alerted (see Table 2)
Control Over Messages	Participant has the option to type STOP if he/she prefers not to receive messages	

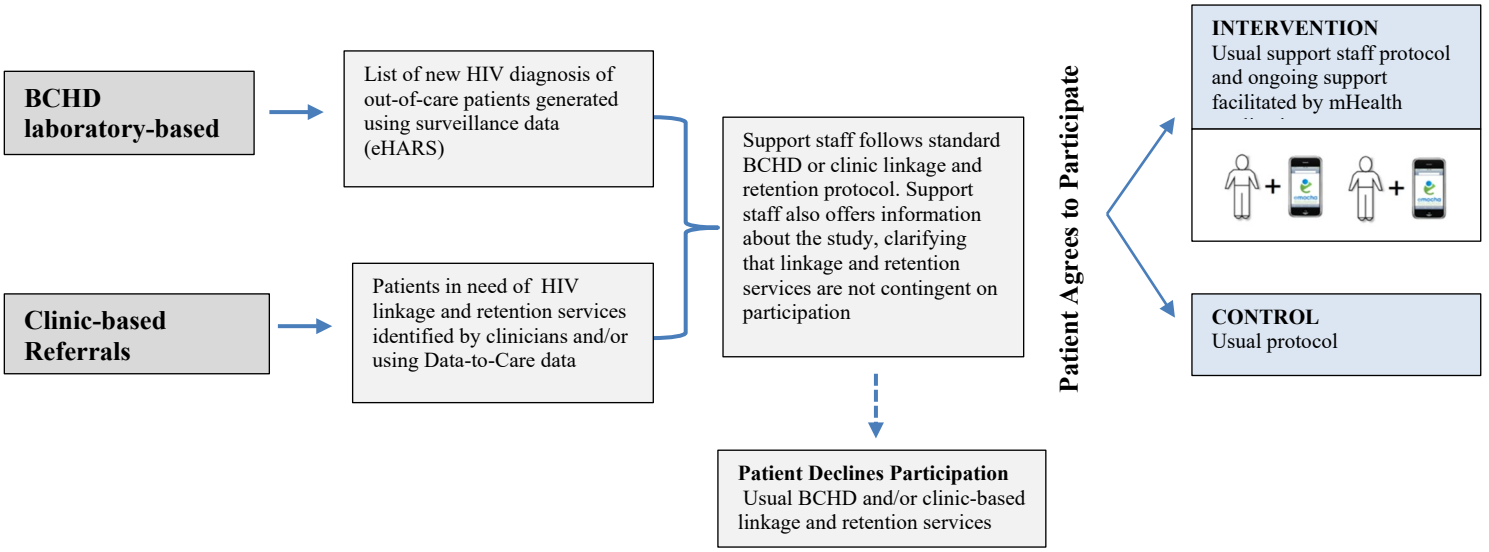
Note: To protect participant confidentiality no alerts will specify HIV.

Table 2. emocha mHealth-enhanced Support Staff Application

Task	Description	Support Staff Action
Laboratory Data	HIV surveillance data (Viral load and date) is provided by the BCHD and uploaded to emocha platform	
Laboratory Alerts	Support staff is alerted if participant in the intervention arm has not had a viral load in > 4 months or if the viral load is detectable (> 200 copies/ml)	Support staff contacts participant if alerted
Appointment Alerts	Support staff alerted if no upcoming appointment is documented in the emocha app or the patient responds "No" or does not respond to the question "Did you go to your appointment yesterday" or patient requests help rescheduling appointment	Support staff contacts participant if alerted
Patient initiated messages	Support staff alerted when participant sends message	Support staff contacts participant if alerted

Study Design.

This study is a pragmatic individual randomized trial comparing standard BCHD linkage services or clinic-based linkage and retention and care support services to mLTCR services. The study will not be masked to participants or support staff due to practical considerations, but all data analysis related to Aim 1 will be conducted in a blinded fashion. Figure 2 describes the study design.



The BCHD identifies newly diagnosed patients with HIV or those who are out of care based on laboratory-based HIV surveillance report. In addition, clinics and providers can identify patients in need of retention services and refer patients to their clinic's patient navigators or the BCHD linkage to care program. HIV Clinics can also get assistance from study team members in identifying patients by sharing the "Data-to-Care" report. Using the report, study team members will identify patients in need of retention services and alert their providers. Providers can then refer the patients to their support staff, clinic's patient navigators or the BCHD linkage to care program. Support staff reach out to the patient identified through surveillance or referred by providers to offer linkage and retention and care support services. When support staff meet or talk with the patient, he/she will tell them that they may be eligible for a study and ask them for permission to be contacted by a study research assistant (RA). All patients, regardless of their interest in the study, will be linked to care by warm handoff per BCHD protocol or receive standard linkage and retention and care support services provided at the clinic. Support staff will call the study RA to let him or her know that there is a potential participant. The RA will meet or call the potential participant to go over the study. After obtaining and documenting written informed consent (for in person enrollment) or oral consent (for over-the-phone enrollment) of participants who wish to enroll in the study, the participant will complete a baseline questionnaire and the RA will use a randomization program that will electronically assign the patient to the control or intervention arm. Patients randomized to the control arm will have no further interaction with the study team other than receiving a satisfaction survey and potentially being invited to an in-depth interview (which they can decline). Participants randomized to the intervention arm will be instructed to download the app to their personal phones (or study phone if participant does not own a compatible phone) and practice using the app by messaging the support staff, ideally in the presence of the RA (this can be done by phone or videoconference), who can trouble shoot any issues and show the patient how to use the various features of the app. Participants in the intervention arm will continue to be in touch with support staff for 12 months using the app, and by phone or in person, depending on the participants needs and Covid-19 situation (as identified through the app algorithms and patient-generated messages).

HIV Surveillance Data Flow. HIV laboratory data (dated viral load) will be used to drive emocha app alerts and for evaluation of primary outcomes. A list of the individuals who have consented to the study (including those recruited in the clinics) will be provided to the BCDH on a weekly basis. The BCHD will send this information to the Maryland Department of Health HIV Surveillance Branch. MDH will generate a weekly report of HIV viral load test results and dates and send this information to the BCHD. The BCHD will share this information with emocha so that it can be uploaded to the emocha platform. Alerts to participants will not include HIV-specific information. HIV surveillance data will be uploaded to the

emocha platform for all participants (intervention and control) and used for data analysis. However, this data will be integrated into the emocha algorithms and alerts only for participants in the intervention arm. Data on all participants will be exported from emocha to JHU secure servers for data analysis.

A backup system will be implemented in the event the MDH or BCHD is unable to generate and/or share the weekly HIV viral load test results. Study team members will access viral load data through health provider records and upload data directly from JHU secure servers to the emocha platform.

Laboratory Assessments. There will be no study-associated laboratory assessments. All laboratory assessments will be conducted as part of clinical care and reported to BCHD HIV surveillance databases (eHARS and PRISM). We will consider those with a suppressed viral load (HIV RNA <200 c/mL) to be fully engaged in HIV care. While some individuals are able to maintain immune control of HIV in the absence of ART, this occurs in <1% of infected persons.

Randomization plan. The study Statistician will generate a randomization schedule to assign 250 participants to each of the study arms with an arbitrary labelling of the arms. All but the data manager will be blinded to the arm assignment to the arbitrary labels initially. When a linkage officer makes the initial contact with an eligible participant /patient, they will introduce the study and if consent to participate is obtained, the officer will telephone the data center to obtain an arm assignment and proceed to enroll the participant. All data analysis will be conducted in a blinded fashion, but the linkage officers and participants cannot be masked from the intervention.

Mortality Assessment. Participants will be cross referenced with the Center for Disease Control and Prevention's National Death Index, a database for all deaths in the United States, to determine if there is a known date of death and cause of death.

Implementation Assessment

RE-AIM Framework. Using a hybrid study design, we will also incorporate implementation science evaluations to assess important implementation questions while also assessing effectiveness. Hybrid designs are efficient approaches to obtaining information that can help understand research findings in terms of internal validity and external generalizability, and provide data to facilitate translating research into real world policy and programs. We propose using the well-established RE-AIM Framework for implementation science research to provide methodological specificity for Aim 2. This framework was created to encourage consideration of program elements that can improve the sustainable adoption and implementation of effective, generalizable, and evidence-based interventions.

A summary of how the 5 components will be assessed in this proposal is shown below.

Summary of mHealth-enhanced LTCR implementation evaluation using the RE-AIM approach

Component	Research Question	Assessment Method(s)	Outcome(s) of Interest
Reach	Who received the intervention?	Program Data	Proportion of out of care or newly diagnosed HIV-infected patients contacted by linkage officers.
Effectiveness	What impact did the intervention have on outcomes?	End-of-study viral load	See Aim 1.
Adoption	Did the community and providers adopt the intervention?	Program data, In-depth interviews	Frequency of contacts between support staff and patients. Services provided/received.
Implementation	Was the intervention delivered as intended?	Program data, In-depth interviews	Roll-out program fidelity.
Maintenance	Was the intervention sustained over time?	Program data, In-depth interviews	Consistent implementation and effectiveness over time. Retention.

Support staff and patient navigators in-depth interviews. In an effort to measure the intervention's feasibility and degree of fidelity, we will conduct in-depth interviews (IDIs) with support staff (N=5) before and 12 months after the implementation of the mLTCR intervention to allow for sufficient time for staff to acclimatize to service delivery and to give ample time to adapt services based on feedback. Interviews with support staff will examine: the nature of service delivery; client interactions and how this differs from standard linkage and retention activities; barriers and facilitators of engaging out-of-care patients; challenges and solutions to the mLTCR service delivery; and recommendations for service delivery improvements and expansion of reach. Additional interviews with patient support staff may be requested beyond 12 months if and when additional feedback would be useful to further adapt services.

In-depth interviews with participants randomized to the intervention arm and the control arm. In order to examine feasibility and acceptability, IDIs will be conducted (in person or by phone due to Covid-19) with study participants randomized to standard linkage and retention and care support services (n=20) and to mLTCR services (n=20) to assess program fit and appropriateness of mLTCR services. Participants will be asked what they liked/disliked about the linkage/retention/care and mLTCR services they received as well as recommendations for additional services. Participants randomized to the intervention arm will be asked if the text message topics and materials in the patient portal were important to them, their motivation for engaging the support staff-delivered text messages, and their suggestions for other ways the mobile phone may facilitate HIV retention in care and adherence to medications. We will also assess facilitators and barriers to program participation. IDIs will take place in a private location and will last 45-60 minutes and participants will be paid $50 for their time (remuneration may be revised by the Steering Committee during planning phase).

Client satisfaction survey. All participants (control and intervention, n= 500) will be asked to complete a brief client satisfaction survey using a validated Client Satisfaction Questionnaire (CSQ-8). Participants in the intervention arm will be asked to complete the validated System Usability Scale (SUS) to assess acceptability and ease of use of the mHealth application.

Intervention fidelity We will monitor support staff-participant contacts weekly using phone records. This will allow an assessment of the level of intensity of support staff-participant contact that may be associated with clinical outcomes (retention in care, virologic suppression), as well as inform the appropriate caseload for support staff. Fidelity and quality assurance feedback will be provided during monthly meetings or more frequently if necessary.

Key-informant interviews with BCHD and clinic officials. In order to examine the mLTCR acceptability and sustainability, study investigators will conduct key-informant interviews with program managers and executives at the city health department and Bartlett Clinic. Interviews with BCHD and clinical staff will explore how the mLTCR intervention has affected the flow and efficiency of surveillance work at the BCHD and Bartlett clinic, any observed changes in the number of patients linked to care and time to engagement in care, and recommendations for service delivery improvements. These interviews will provide insights about policy, acceptability, political buy-in for the intervention, and potential for adoption in other settings going forward.

b. Study duration and number of study visits required of research participants.

Study Duration: 4 years

Number of visits:

Participants in the RTC: One baseline visit (can be done by phone). This is a pragmatic implementation trial with outcomes (such as retention in care) that could be influenced by frequent study-related interactions, so we will minimize study contact to a baseline visit. During the baseline visit, support staff or patient navigator will obtain basic demographic and contact information as is routinely done for LTC and patient navigator operations.

Participants in qualitative in depth interviews: One visit (can be done by phone) for study participants and BCHD stakeholders, two visits for support staff (12 months apart)

c. Blinding, including justification for blinding or not blinding the trial, if applicable.
This is a non-blinded pragmatic randomized trial. Blinding is not feasible with this design.

d. Justification of why participants will not receive routine care or will have current therapy stopped.
Not applicable

e. Justification for inclusion of a placebo or non-treatment group.
The control group will receive usual linkage and retention to care services provided by the BCHD or the participant's clinic. The objective of the trial is to determine the benefit of delivering mHealth enhanced, longitudinal linkage to care and retention services.

f. Definition of treatment failure or participant removal criteria.
Not applicable

g. Description of what happens to participants receiving therapy when study ends or if a participant's participation in the study ends prematurely.
Participants randomized to the intervention arm will receive mHealth-enhanced LTCR services for a year. Following the 12 month follow up, patients will receive usual BCHD LTC services or clinic-based retention and care services. The BCHD or clinics may decide to continue to provide mHealth-enhanced LTCR services beyond the patient's 12 month enrollment in the study based on the studies interim analysis of effectiveness, patient satisfaction and cost.

5. Inclusion/Exclusion Criteria

Enrollment criteria for RTC:
Eligibility criteria include:
1. ≥ 18 years of age
2. Ability to provide consent
3. Identified by BCHD Linkage protocol to be a new HIV diagnosis or HIV-infected and "out of care" or referred by HIV clinic-based patient navigator, nurse, or provider.

Exclusion criteria include:
1. Excluded due to insufficient facility using a smartphone based upon participant and/or study staff assessment during enrollment process.

Enrollment criteria for in-depth interviews
Participant meets one of the following criteria:
1. Participant in the RTC, OR
2. Linkage to care officer, OR
3. Patient navigator, OR
4. Other support staff members, e.g. nurses
5. Stakeholders at the Baltimore City Health Department (BCHD) who has administrative or programmatic input on HIV services

6. Drugs/ Substances/ Devices

a. The rationale for choosing the drug and dose or for choosing the device to be used.
Not applicable

b. Justification and safety information if FDA approved drugs will be administered for non-FDA approved indications or if doses or routes of administration or participant populations are changed.
Not applicable

c. Justification and safety information if non-FDA approved drugs without an IND will be administered.
Not applicable

7. Study Statistics

a. Primary outcome variable. Virologic suppression: Viral load < 200 copies/cc within a 6-month window of 12 month follow up period (i.e. 3 months before or after 12 month follow-up).

b. Secondary outcome variables.
   1. Retention in care: Viral load or CD4 count reported in eHARS within a 6 month window of 12 month follow up period (i.e. 3 months before or after 12 month follow up)
   2. Mortality: Death occurring within a 6 month window of 12 month follow up period (i.e. 3 months before or after 12 month follow up)
   3. Implementation outcomes will include:
      a. Proportion of out of care or newly diagnosed HIV-infected patients contacted by support staff.
      b. Frequency of contacts between support staff and patients.
      c. Qualitative assessments from in-depth interviews with support staff, BCHD/clinic officials, and study participants
      d. Client satisfaction surveys

c. Statistical plan including sample size justification and interim data analysis.

Statistical Analysis. For the study's main outcome, we will conduct a test for the equality of proportions of virologically suppressed/not suppressed or missing VL individuals at 12 months between the two study arms, in line with the randomized design of the study. Secondary to this, and to adjust for any residual confounding, we will conduct a logistic regression using individual outcomes (yes/no suppressed) with study arm as a main predictor and adjusting for patient demographic characteristics, socio-economic status at baseline, and other factors. A subgroup analysis will be conducted to assess the effects of the intervention among African-Americana and people of Hispanic/Latino descent.

Secondary outcomes analysis. An evaluation of the differences in retention in care and participant mortality will follow the same analytical approach as for the main outcome. That is, we will test for the difference in proportions between the 2 arms and a logistic regression will be conducted adjusting for study arm and patient characteristics.

Qualitative data analysis. Qualitative data analysis involves the search for patterns in data and for ideas that help to explain the presence of those patterns. Transcripts from in-depth interviews and key informant interviews will be entered and managed in Atlas.ti. Separate coding schemes will be developed for HIV-infected patients (control and intervention arm) and the other groups of BCHD staff (Linkage officers and BCHD officials). An iterative coding process in Atlas.ti will be used to conceptually name the data and reduce it to manageable units of information that cover broad and general categories. Codes will be informed by the questions in the qualitative

guides, and new themes that emerge from the data will be analyzed through a grounded theory approach, allowing for themes to emerge and ensuring that the knowledge assembled from the observational data is not subjected to the themes solely established through the interview guide. Two coders will conduct open-coding on three transcripts to develop initial coding schemes. After discussion and development of a combined draft scheme, two more interviews will be coded, and these will be further discussed and inform a final coding scheme under the guidance of Dr. Grieb. Through weekly meetings, a team approach to data analysis will be employed, whereby different analysts provide feedback on emerging interpretations and check emerging categories against the raw data. In this way, an "audit trail" will be used to help ensure trustworthiness of findings, gather input from multiple perspectives, and enhance reliability.

Power Calculations. The reported virologic suppression or lack of a VL measurement rate under standard of care among HIV-infected African Americans and Latinos in Baltimore City is 33%.[xxvi] In order to detect an improvement of 13%, such that 46% of the mHealth enhanced LTCR group have a VL and achieve virologic suppression, with 80% power at an alpha=5% level of significance, we require a total sample size of 442 (221 per arm). We plan to enroll 500 participants to the study to account for withdrawals.

d. Early stopping rules.
Not applicable

4. Risks

a. Medical risks, listing all procedures, their major and minor risks and expected frequency.
There are no direct medical risks associated with the intervention arm. There is a risk to confidentiality in the use of the mHealth application.

b. Steps taken to minimize the risks.
After obtaining consent, all participant data (such as basic demographics and contact information) is entered into the emocha platform. In addition, HIV surveillance data is imported into the emocha platform from the BCDH (see above). Risks to confidentiality will be minimized by storing all data in encrypted format on an emocha web-server that is password protected. Data collected by the LTCR emocha app will be sent in real-time to a secure server, where LTCR activities and data can be accessed through a simple web interface. Only authorized study personnel will have access to this data. A triple level of data encryption will be used to ensure confidentiality of data and HIPAA-compliance. LTCR phones, and access to the LTCR and participant emocha apps will be password protected. To further protect participants' confidentiality, messages to the participant will include non-specific terms without mention of HIV or other personal health information. Electronic research data will be exported from emocha to central storage (JHU) via secure, encrypted transmission. The National Center for Health Statistics is required by law to maintain the confidentiality of identifying information it collects including information on individuals supplied by research groups to the National Death Index for the purpose of matching study participants to death records.

c. Plan for reporting unanticipated problems or study deviations.
The research staff and support staff will report problems or study deviations to the study supervisor (Jane McKenzie-White). Ms. McKenzie-White with discuss problems and event with the study PIs (Drs. Page and Chang) at weekly study meetings (or sooner) depending on the severity of the event. The PIs will report unanticipated problems or study deviations that involve risks to participants or others promptly to the JHM IRB in accordance with Organization Policy. Minor problems and protocol deviations (which pose no risk to subjects or others) will be reported in annual protocol continuing review.

d. Legal risks such as the risks that would be associated with breach of confidentiality.
There are risks that confidential information could be revealed to people not involved in the research such as a friend, relative, or an outside organization. This could be embarrassing to the participant if the participant wanted to keep participation in the study secret. The legal risks are limited because we are not collecting any additional data than is collected during routine BCHD activities. Thus, the risks associated with participating in this study are no greater than the risks associated with routine psychological examinations or tests.

e. Financial risks to the participants.
This study entails no financial risks to participants.

5. Benefits

a. Description of the probable benefits for the participant and for society.
The study has the potential to benefit society if the tested intervention (nHealth LTCR) is found be effective in improving virologic suppression by reducing HIV transmission risk in the community.

6. Payment and Remuneration

a. Detail compensation for participants including possible total compensation, proposed bonus, and any proposed reductions or penalties for not completing the protocol.

Participants will receive $50 for completing the baseline enrollment and $20 for completing client satisfaction surveys. Participants randomized to the intervention arm who do not own a phone will be provided a study phone with a pre-paid data plan.

Participants in the in depth interviews will be compensated $50 for their time.

7. Costs

a. Detail costs of study procedure(s) or drug (s) or substance(s) to participants and identify who will pay for them.

There will be no costs to participants for any services or treatment provided in this study. The study procedures will be financed by a PCORI grant.

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