**Project Title:** Telemedicine for PrEP throughout Mississippi (Tele-PrEP-MS)

## SPECIFIC AIMS

**To overcome barriers of access to Pre-exposure prophylaxis (PrEP) services in underserved areas, this project will develop a telemedicine PrEP program for use by community based organizations (CBOs) that provide STI/HIV testing. The study will collect data on factors related to feasibility, acceptability and implementation.** The **premise** of this project is that underserved populations in the South have high rates of HIV but are not engaged in PrEP care because access to academic centers, where PrEP is prescribed, is limited. Telemedicine could be a promising approach for use in CBOs that provide STI/HIV testing and could improve linkage to PrEP care for underserved communities.

Despite PrEP's efficacy and advances in its availability, uptake of PrEP in the southern United States has been slow, especially in areas at distance from academic medical centers. PrEP-related services in the South have been confined to academic centers, even though HIV is of particular concern in the region.[(1)] Mississippi (MS), the site of this proposed project, has the seventh highest incidence of HIV of any state[(2)] and CBOs that provide HIV/STI testing outside of urban areas report that very few of their at-risk individuals use PrEP. Unfortunately, physicians outside of academic centers are often reluctant to prescribe PrEP because of a lack of training and support necessary to provide comprehensive HIV prevention care. Those at-risk do not seek PrEP from academic centers due to stigma, travel burdens, and financial concerns.

**Telemedicine is a promising, but previously untested mode for delivering PrEP care.** Although there is no report of telemedicine being used for PrEP care, it has been used successfully in other areas of healthcare. Reviews indicate it is as impactful as in-person care, cost-effective, and acceptable to patients and providers.[(3-6)] Particular benefits are its capacity to reach those at a distance, increased access to subspecialty care, and greater efficiency of physicians. In this project, we will evaluate the barriers and facilitators to training CBO staff to screen patients for PrEP and the use of telemedicine to link PrEP specialists with the CBO. We will assess whether this strategy can provide CBOs with the capacity to deliver quality PrEP assessment, counseling and care. This project could allow patients to receive the highest level of HIV prevention from trusted CBOs within their local communities. Telemedicine for PrEP care could also enhance the CBO's mission of providing high-quality services to the local community.

The program, to be called **Tele-PrEP-MS**, will be developed in collaboration with medical specialists at the University of Mississippi Medical Center (UMMC) and local CBO stakeholders (providers, administrators and patients). A mixed-methods assessment will assess the feasibility, acceptability and preliminary rates of PrEP uptake and use in local and trusted CBOs and the barriers / facilitators to its implementation. If successful, this program can be disseminated to other HIV/STI testing centers/CBOs in the South and factors related to its effectiveness can be further studied. Because telemedicine services can be reimbursed in MS, this developed program could be financially viable. The aim is to increase the availability of PrEP for at-risk individuals in underserved area and ultimately reduce the rate of HIV infection in the Southern US. **This proposal is consistent with the NIH HIV/AIDS research priority to reduce the incidence of HIV/AIDS by developing, testing, and implementing a strategy to improve entry into prevention services.**

The **specific aims** of this project are to:

1. **Develop a PrEP telemedicine program for CBOs that provide HIV/STI testing in underserved areas and document the procedures and protocols.** The program, to be called Tele-PrEP-MS, will be developed through a collaborative development approach with UMMC specialists and local CBO stakeholders (CBO agency staff, administrators and patients).
2. **Implement Tele-PrEP-MS in CBOs that conduct STI/HIV testing for an underserved area in MS**
3. **Determine the acceptability and feasibility of Tele-PrEP-MS, and examine the individual, organizational and structural factors associated with its acceptability and feasibility during its implementation in the CBOs.** This aim uses a mixed methods approach that includes an online survey of 25 - 50 patients and in-depth interviews. The interviews will include approximately 20 patients who initiated PrEP via telemedicine (recruited from our current TelePrEP study and from UMMC associated clinics), 5 PrEP-eligible patients from our study who did not receive PrEP, and 5 providers / staff who are involved in telemedicine for PrEP.

**We are utilizing DocuSign, a HIPAA-compliant electronic signature software, to obtain written consent for the online survey of 25 -50 patients from CBOs in Aim 2 of this proposed project. The survey portion of this study is observational and is considered minimal risk. Participants will not be assigned to an intervention group, and the assessments will not collect any PHI. The three surveys will assess knowledge, attitudes, and behaviors related to Pre-exposure prophylaxis (PrEP) over six months among adults presenting for HIV testing at community based organizations (CBOs).**

## SIGNIFICANCE

**HIV is a significant problem in the Southern US. Pre-exposure prophylaxis (PrEP), if delivered to underserved communities, could help address disparate care.** The **premise** of this project is that underserved populations in the South have high rates of HIV but are not engaged in PrEP care because access to academic centers (where PrEP is prescribed) is limited. Many individuals in Mississippi (MS) are at high-risk for HIV acquisition, have sought HIV testing, and engage in services at CBO testing sites, but do not access health care in urban academic centers that can provide PrEP counseling and treatment. Stigma, travel burdens, and financial concerns limit their engagement in PrEP-related care despite having had HIV testing at their local CBOs. Telemedicine is a promising approach for use in CBOs to improve linkage to PrEP care in these underserved communities. This project will assess telemedicine delivery of PrEP care in local CBOs that are already performing HIV testing. The CBO HIV testing staff will be trained to use a checklist to screen all clients for HIV risk. Those with significant risk will be able to discuss prevention options with the CBO staff and with the UMMC specialist/clinician, and will be able to begin and continue PrEP, if indicated, via the webcam link to the CBO within a week of the HIV testing.

PrEP has received considerable attention and holds tremendous promise because it is efficacious and safe.[7-13] Despite the advancements supporting PrEP and its availability, **uptake of PrEP by those at high risk has been slow, particularly in the Southern United States**.[14-19] This is a significant issue because of the growing and high HIV rates in the South. Eight of the ten states with the highest rates of new HIV infections are located in the South, and estimates suggest that BMSM in the South are five times more likely than white MSM in the South to become infected.[20-22] The site of this proposed project, Mississippi (MS), has the highest prevalence of HIV infection among MSM and the second highest estimated prevalence of undiagnosed HIV in the U.S. (28.2 and 6.3 per 100 MSM respectively).[23]

**Uptake of PrEP in underserved areas outside of academic centers has been slow, leaving many high-risk individuals without access to this efficacious HIV prevention strategy.**[7, 24] HIV infection in the Southern United States is not limited to dense urban areas near academic medical centers, non-metropolitan Mississippi is at special risk because of the lack of local services, poverty and stigma.[22, 25] Studies have found that MSM living in the rural South are more likely to have sex on their first date than urban men, possibly due to long travel distances and concern that the next sexual encounter may be a long time away. Additionally, rural venues where MSM openly socialize are scarce, resulting in men seeking sex partners via the Internet and by regularly traveling to higher seroprevalence areas. Our physicians at the University of Mississippi Medical Center (UMMC) are prescribing PrEP in their HIV/STI clinics in Jackson, MS but this only reaches 18% of the State's population. **PrEP is unavailable elsewhere in Mississippi, so 72% of the State is essentially underserved.**

**Reaching this greatly at-risk population and evaluating effective methods for prevention of HIV infection is critical**. PrEP clinical care follows a cascade that is similar to the HIV treatment cascade. The **PrEP cascade** includes screening a high-risk population, identifying candidates for PrEP, linkage to PrEP care, initiation of PrEP, retention in PrEP care, and adherence and persistence in PrEP clinical care.[7, 24, 26, 27] Gaps arise at each step of the PrEP cascade and this proposed project will focus on addressing **identification, linkage, initiation, and adherence over 6 months** through a creative telemedicine/CBO link. Numerous studies indicate that many at-risk individuals will agree to, and successfully, take PrEP if it is easily available.[9, 28] Unfortunately, many underserved populations have not yet been reached. By working with local CBOs, this project will reduce the barrier of distance and reach the underserved.

**Local organizations are disinclined to prescribe or counsel patients about PrEP because they lack the needed resources and training**. Previous research, clinical reports and the CDC have identified steps to introduce PrEP, provide counseling in risk reduction, and engage patients in continuing care.[29,30]

These procedures are followed at the University of Mississippi Medical Center (UMMC) STI/HIV testing clinics and other academic multidisciplinary HIV clinics. At UMMC, high-risk patients engage in a discussion with their clinician about their risk behavior, are given a PrEP fact sheet, and are shown a brief PrEP video to improve motivation and acceptance.[29] However, this model is not maintained outside of the UMMC academic setting where local organizations are often reluctant to prescribe or counsel patients about PrEP because they lack the training and expertise necessary.[22, 25, 30] This project will identify the necessary training and resources.

**Telemedicine is a promising mode for delivering PrEP care because it has been effective in other healthcare areas.** Although there is no report of telemedicine being used for PrEP care, it has been used successfully in other healthcare areas. Telemedicine, defined in this application as the use of video/internet connections to link patients, agency staff, and physicians for medical care visits, has been most extensively studied in mental health care, pediatric services and consultation by specialists to community emergency departments.[5, 6, 31] It has been successfully implemented to extend care to underserved areas and reduce costs.[32, 33] For example the Indianapolis Veterans Administration Hospitals conducted 23,267 telemedicine visits in 2013 to reach rural populations with a 96% satisfaction rating by patients.[33] Several reviews and meta-analyses indicate that telemedicine is feasible and patients and providers rate it favorably and equally with in-person care.[3-6] For many clinical outcomes, telemedicine does not differ from traditional in-person care.[3-6] Particular benefits are its capacity to reach those at distance, increased access to subspecialty care, and greater efficiency of physicians. These attributes make it promising for PrEP care in the South.

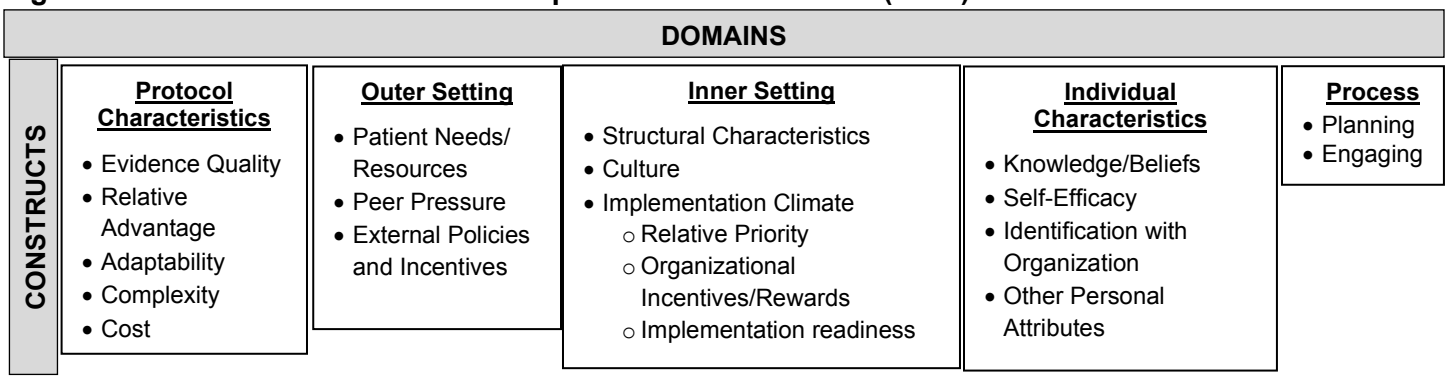
**But potential barriers to using telemedicine to provide PrEP care to those most at risk for HIV need to be assessed and addressed. Providing PrEP services by telemedicine will likely differ from providing routine medical care (e.g. for hypertension). The provision of PrEP care carries unique privacy concerns and the physician – patient relationship is of great import when discussing sexual risk behavior.** Additionally, there are important caveats to the above summary of telemedicine that have bearing for this proposed project. First, African Americans, compared to other groups, may be more concerned about privacy issues with the technology. For example, one qualitative study found that African Americans were worried that their identity would be stolen with telemedicine and their health information would be "floating around for everyone to see."[34] This finding may reflect a distrust with institutions and large medical care systems. Patients may also worry about the privacy of their personal health information because same sex, or other "high-risk," behavior is highly stigmatized in their community. Additionally, some physicians indicate that telemedicine changes the quality of the clinical interaction by making it more difficult to ask questions and to "connect with patients."[35, 36] Relatedly, studies of clinician – patient communication indicate that, during telemedicine, physicians are less likely to ask open-ended questions and patients talk less than during in-person care.[37, 38] Rural patients may have a different cultural and racial context than the urban telemedicine physicians, which could create a potential divide in expectations, and hamper collaborative communication.[39] These findings need to inform training of providers as will be done through provider training in this project. Finally, Telemedicine needs to be easily sustainable for the CBOs for providers to use it. Sustainability depends on many factors including finances, available personnel, continued availability of providers, and acceptability by the community.[6, 32] Telemedicine is reimbursable in Mississippi, so telemedicine for PrEP is theoretically viable. All of the above factors will be examined during this study through in-depth interviews with patients, providers and CBO staff to inform protocol development.

**The project will collect needed data on the feasibility, acceptability of telemedicine for PrEP in CBOs and the barriers / facilitators to its implementation.** Factors that potentially affect feasibility, acceptability and implementation exist for at-risk individuals, care providers, and the CBOs.

**A Consolidated Framework for Implementation Research (CFIR)**, will guide our exploration of barriers and facilitators to Tele-PrEP-MS.[41] CFIR is a logical, evidence-based typology that was developed by synthesizing 19 existing theories and models to identify common constructs and processes related to protocol effectiveness and dissemination. The project team will select the constructs most relevant to this study and its context in order to inform protocol development and assessment of its impact. The PrEP-related outcomes of participants are of critical importance in determining the impact of Tele-PrEP-MS. It is equally important to examine the broader context of the attitudes, behaviors and policies of the providers and CBOs. These data will help inform the development of the Tele-PrEP-MS protocol, and understanding of the processes necessary for Tele-PrEP MS efficacy and the potential barriers to be overcome in a later, multisite implementation study. CFIR identifies five major domains: the protocol to be implemented, its Outer Setting, its Inner Setting,

Individuals Involved, and the Process of Implementation. Within each domain, there are several clearly defined constructs. For example, protocol domain constructs relevant to Tele-PrEP-MS are its Adaptability, Complexity, Relative Advantage and Cost. A relevant Outer Setting construct is Patient Needs and Resources, and Implementation Climate is a relevant Inner Setting construct. Knowledge and beliefs about the protocol and Self-efficacy are important constructs in the Individual domain. Developing Tele-PrEP-MS will concentrate on the Planning and Engaging activities identified in the Process of implementation domain. These constructs, supported by a growing number of instruments, will inform the project's development and assessment. In addition, CFIR has templates for use by researchers to assist with qualitative data collection and analyses. The templates can be modified to fit the specific project and also contain definitions and organizational patterns. In addition to informing the adaptation of Tele-PrEP for use by a CBO, this framework provides an excellent structure for our mixed-methods assessment of the PrEP cascade outcomes. We will examine the factors associated with the acceptability and outcomes of Tele-PrEP-MS, as these factors will influence protocol development future implementation. The figure below contains the CFIR domains and the constructs that are the specific focus of this proposed project.

**Figure: Consolidated Framework for Implementation Research (CFIR) for Tele-PrEP-MS Interviews**




**Multilevel influences on engagement in PrEP care.** Factors that potentially affect feasibility, acceptability and implementation exist for at-risk individuals (e.g. knowledge, motivation, stigma, mistrust of medical systems, poverty), care providers (e.g. training in new procedures and roles, motivation), and the CBOs (e.g. climate, capacities, mission, policy, and reputation in community). Broad structural elements (e.g. healthcare access, stigma) are barriers to PrEP use and will be assessed by participants, providers and CBOs. Tele-PrEP-MS is uniquely positioned to address many of these barriers to PrEP care as described below. The project will assess each of these areas in Aim 1 in order to inform staff training and implementation.

**1. Factors of those at-risk *to be* examined and addressed**

**a. To date, knowledge and access to information about PrEP remains low for those at-risk for HIV.** Studies indicate low awareness and initiation of oral PrEP has greatly restricted PrEP's effectiveness at the community level.[14-18, 40-43] An analysis of pharmacy claim data found that fewer than 4,000 PrEP prescriptions were written in the US in 2014, and a cohort study reported that only 75% of those with risk behavior that indicated a need for PrEP initiated PrEP.[18, 43] Uptake of PrEP has been slow nationwide, but data supports that awareness and engagement in PrEP care is lowest among those who are most at risk for infection with HIV.[40] Only 8 percent of participants who were part of a PrEP demonstration project conducted in three major U.S. cities between 2012 and 2013 were black [43] and studies show that awareness about PrEP among black men remains particularly low in the Southern United States.[40-42] Among, 436 BMSM surveyed in Atlanta, GA, from January 2012 (6 months prior to PrEP approval) to March 2014 (20 months after approval), 20.5% were aware of PrEP before approval and only 23.4% were aware of PrEP after approval.[40, 42] In addition to lack of awareness, Brooks et al. found that heightened concerns over potential side effects to PrEP may pose a particularly significant barrier to uptake among BMSM.[17] Improving knowledge about PrEP is critical for successful, universal PrEP implementation in the South. HIV/STI testing and Tele-PrEP-MS at CBOs is likely to increase knowledge and access to information about PrEP.

**b. Those most at-risk are often mistrustful of medical care and providers.** Those who are at highest risk of HIV infection are historically underserved by healthcare.[44-47] Therefore, engaging patients in care is challenging and requires reinforcement and support for doctors and patients.[47, 48] In the Southern

United States, homophobia, stigma, and medical caregiver/ patient communication pose a particular challenge to uptake of PrEP.[49-51] Eaton et al. surveyed 398 HIV uninfected BMSM at a Black Gay Pride event in the South Eastern US. Among this sample, 60% agreed that they were uncomfortable with talking to a health care provider about having sex with men. Race-based medical mistrust also was identified as a barrier to engaging in PrEP. Believing that "people of my race don't receive as good of care as people of other races" was frequently endorsed. A substantial number of participants reported that "people of my race cannot trust doctors and health care workers" (21%) and "people of my race should be suspicious of information from doctors and health care workers" (19%).[42] Strengthening communication and trust between medical caregivers and those at-risk are crucial components to improving PrEP uptake.[42, 45, 51, 52] In this project, patients will be screened for HIV at a trusted, local CBO. Any concerns by patients will be assessed and addressed by the local CBO staff.

**c. Decreasing stigma about PrEP and HIV can improve uptake and engagement in care.** Participants in PrEP demonstration studies have reported feeling stigmatized by their decision to use PrEP by medical providers, friends, and sex partners.[27, 47, 48, 53-56] Likewise, PrEP-related stigma could act as an important barrier to PrEP uptake in the South and at CBOs. Gay men have reported a fear of being labeled as "Truvada whores" by others. This phrase, intended as a stigmatizing label, infers that the use of PrEP leads to "unbridled" sex. Labels like these may be contributing to PrEP's slow uptake.[48, 53, 54, 56] Furthermore, the only currently available PrEP method, Truvada, is the same medication used to treat those infected with HIV. In settings, such as the Southern U.S., where HIV and same sex behavior stigma is high, being seen with Truvada can lead to an additional stigma and is a disincentive for HIV-uninfected persons to start PrEP.[47, 56] Stigma and discrimination can profoundly impact service utilization by those at risk for HIV.[48] Relatedly, stigma has been shown to be a deterrent to HIV-testing, disclosure of serostatus, and linkage and retention to ART in HIV infected persons.[26, 47, 57, 58] HIV-related stigma is particularly widespread in the South among black men and might pose a particular challenge in MS.[41, 42, 48-50, 59] Local CBOs, using Tele-PrEP-MS can address negative community attitudes about PrEP by creating positive impressions of PrEP-users as individuals who keep themselves and their community safe.[60]

**d. Addressing access and economic barriers to receiving PrEP-related care is imperative**. Studies indicate that MSM in southern suburban and rural towns will travel for sexual encounters, but do not travel for medical care or HIV testing.[21, 61, 62] This poses unique challenges to HIV prevention efforts and increases the spread of HIV through sexual networks. PrEP care at a local CBO can address this issue. In addition, effective interventions to improve PrEP must assist individuals when navigating insurance companies, signing up for medication co-pay assistance, and receiving any needed assistance for the payment of PrEP.[63] In 2012, approximately 19% of African Americans did not have health insurance, compared to 11% of whites.[19, 64] The situation is particularly concerning since Mississippi (the site of this proposed project) has the highest poverty level (28%) in the US and this directly impacts health care access. Southern states also have the most restrictive Medicaid eligibility criteria and provide fewer Medicaid benefits than other regions in the country.[19] Interventions that help individuals navigate the economics of getting on PrEP, such as the PrEP co-pay and full medication assistance programs through Gilead, are essential to the successful implementation of PrEP in the South, where poverty is highest. Staff at community CBOs will become knowledgeable and able to assist those at-risk for HIV through challenging economic and structural issues (just at staff at UMMC are able to do).

**2. Provider Factors to be examined and addressed**

**a. Physicians:** The few studies that have focused on PrEP implementation by healthcare providers suggest that physicians in academic medical centers prescribe PrEP, but providers in community-based settings are less knowledgeable about PrEP.[65] In addition, physicians outside of subspecialty centers have less familiarity with the HIV risk assessment that must accompany the initiation of PrEP care, are concerned about PrEP side effects, and are ambivalent about prescribing it.[66, 67] This lack of training in risk assessment and engagement in PrEP care limits the identification of individuals who could greatly benefit from PrEP treatment. For example, procedures at the UMMC STI/HIV testing clinics are similar to other large city multidisciplinary HIV clinics and follow CDC guidelines for introducing PrEP, continuing care and counseling in risk reduction.[68] High-risk patients engage in a discussion with their clinician about their risk behavior, are given a PrEP fact sheet, and are shown a brief PrEP video to improve motivation and acceptance.[29] However, this model is not maintained outside of UMMC where local organizations are often reluctant to prescribe or counsel patients about PrEP because they lack the training and expertise necessary.[22, 25, 30] Persons at risk

for HIV who live away from urban academic medical centers are rarely introduced to PrEP or screened for risk. Telemedicine can address this barrier to PrEP initiation and care. Utilizing MDs with PrEP expertise from UMMC in order to deliver PrEP via telemedicine will address physician knowledge and motivation barriers in extending specialty care to rural areas. Telemedicine (although widely used and favorably rated by patients and providers in numerous studies) will be a new medium for patient care for these physicians. Physicians will undergo training in telemedicine via the UMMC Center for Telehealth to have the necessary technical skills. Because physician – patient relational factors are also important, Tele-PrEP will be developed with consideration as to how to enhance and maintain the important aspects of the Patient-Provider Alliance (i.e., collaborative goals, tasks and trust).

**b. CBO staff:** Several CBOs in rural communities currently provide HIV testing but none deliver other health care. HIV testing staff at the CBOs provide pre- and post-HIV test counseling as part of their current duties, however, the procedures and risk assessment screenings are not standardized. Accurate and consistent risk assessment by CBO staff is needed to identify those who will benefit from PrEP. Staff will also require training in the initial PrEP counseling in order to improve the knowledge and motivation of patients, and to decrease mistrust and stigma. Training and support will need to be provided for CBO staff to assist individuals with potential financial barriers (e.g. enrollment in assistance programs for PrEP and healthcare). Although the healthcare objective is consistent with the mission of such CBOs, these tasks will be new for the CBO staff and their attitudes and skills in these areas are unknown. The staff's knowledge, motivation and skills in identifying those who can benefit from PrEP will likely impact their effectiveness in improving patients' motivation for PrEP and linkage to PrEP care. This proposed project will gauge CBO staff's knowledge, motivation and skills at identifying and linking clients to PrEP care via telemedicine and will also provide needed training. Because relational factors are also important, there will be training in building the principles and techniques of the Patient-Provider Alliance (collaborative goals, tasks and trust).

**3**. **CBO factors to be examined and addressed:** CBOs that provide HIV testing have as a mission to improve the health and welfare of an underserved, at-risk community. Without access to a physician or nurse practitioner, they are unable to provide medical services other than health screening. As in other areas of health care dissemination, many CBO factors will influence implementation of this new service including organizational climate, structure, leadership, division of responsibilities, ability to change staff duties, relevant resources, standing in the community, and capacity to sustain the service. Because this project will develop the proposed telemedicine protocol in collaboration with two identified CBOs, their initial motivation and enthusiasm is assured. However, many of the factors listed above (e.g. capacities, leadership, climate) are not known and may change over the course of the implementation of Tele-PrEP.

## INNOVATION

This proposed project is innovative because:

1. It will use and assess telemedicine as a way to link experienced PrEP providers at an academic medical center to patents and staff in CBOs in underserved areas. Telemedicine uses a secure Internet connection to provide specialty care, which otherwise would be unavailable. We are unaware of any other example of the use of telemedicine for PrEP.
2. It will target underserved areas in the South for PrEP care. Areas at distance from academic centers have not been the focus of PrEP care outreach. Mississippi, has the highest prevalence of HIV infection among MSM and the second highest estimated prevalence of undiagnosed HIV in the U.S.(23) and non-metropolitan Mississippi is at high risk because of the lack of services, poverty and stigma.
3. It will operate in local, trusted CBOs, which are already providing HIV testing. However, very few at-risk individuals obtain PrEP because of barriers to accessing care in academic, urban locations. The project will study if the trusted reputation of CBOs can be leveraged to improve linkage and initiation to PrEP care.
4. It will increase access to PrEP. We will examine if telemedicine provided at CBOs, will reduce the wait time, travel burden, and motivational barriers to accessing PrEP care.

## PRELIMINARY STUDIES

**Project Investigators.** This project will involve clinicians and scientists from the Departments of Psychiatry at Rhode Island Hospital and Brown University, and the Division of Infectious Diseases at the University of Mississippi Medical Center (UMMC). Our research team is composed of experts in biobehavioral

HIV prevention, PrEP and STI/HIV medical care, and the utilization of technology to promote adherence to ART and PrEP care. Drs. Brown, Brock, Seifer and Whiteley have a successful history of excellent collaboration and communication on other NIH studies (R34MH104068, R34MH111342, RO1HD074848). Dr. Brown and Dr. Brock will serve as **Multiple PIs** with complementary expertise. **Larry Brown, MD**, Professor of Psychiatry at Rhode Island Hospital and Brown University, is a psychiatrist with expertise in HIV prevention, adherence to care, clinical intervention relevant to HIV, and the use of technology programs. **He has developed efficacious HIV-related interventions for agency use** in an iterative, collaborative manner .[69] [70, 71] He is also the Director of a NIMH T32 HIV Biobehavioral Research Training Program**; James B. Brock MD** is an assistant Professor of Medicine at the University of Mississippi Medical Center (UMMC) and an infectious disease physician with research and clinical expertise in HIV/STI screening and delivery of PrEP services; **Ronald Seifer, PhD,** Research Director at Bradley Hospital, has expertise in the design and analysis of qualitative / quantitative longitudinal studies including implementation science studies with provider training; **Laura Whiteley, MD** is a psychiatrist at Brown University with expertise in the use of technology for behavior change and mPI with Dr. Brown on two NIMH R34 PrEP engagement and adherence development trials (no overlap with Aims of this proposed project).

**Clinical Settings – CBOs and University of Mississippi Medical Center (UMMC)**

**Only 18% of the State's population is within reach of the UMMC HIV/STI testing clinics.** UMMC patients come from the Jackson metropolitan area, which has a population of 340,000. Mississippi has a population of 3 million, so 72% of the state does not have effective access to PrEP. For those few out-of-town patients at the UMMC clinics, PrEP uptake is hampered by the travel and scheduling barriers of having to return to see the MD. The STI/HIV testing clinics serve more than 9,000 patients annually. HIV rates are very high, with 15% already infected with HIV at time of testing. In addition, HIV risk behavior is prevalent - 75% of those non-infected are PrEP-eligible. For example, in a recent clinic survey, 80% of MSM report recent condomless receptive anal sex and 39% more than 6 male partners. Only a third of patients return to initiate PrEP because wait times and distance are often barriers. The CBOs report a similar risk pattern for their patients, and very few use PrEP because of the travel and lack of local providers.

**Two CBO HIV testing sites,** one on the Gulf Coast and one in Hattiesburg, will be the sites for this trial (see letter of support). The sites are sponsored by a non-profit agency, **My Brother's Keeper, Inc. (MBK)** and sites have separate directors and staff. MBK is a private, nonprofit, 501c3 organization, founded in 1999, with headquarters in Jackson and HIV testing sites throughout MS. MBK's mission is to reduce health disparities. It provides a wide array of services including outreach, community mobilization, technical support, and collaboration with other organizations. Although the two testing sites refer clients to medical care (and MBK sponsors a medical care clinic for MSM near the UMMC), the testing sites do not have the licensed medical staff to provide care other than screening. Because MBK has an extensive collaborative network with other CBOs, it will be able to assist in disseminating Tele-PrEP-MS.

*** Due to slow recruitment from initial study delays and the COVID-19 pandemic, the following additional recruitment sites were approved by the UMMC IRB: AIDS Services Coalition, Test to Know, and Express Personal Health. These community organizations, like MBK, provide HIV testing in MS and refer patients to PrEP care.**

**Recent experience with Tele-PrEP-MS:** Since our initial application, we have piloted Tele-PrEP-MS at one CBO on Mississippi's Gulf Coast. In less than two months, 19 individuals who were tested for HIV were determined to be eligible for PrEP, and 78% (15/19) attended a Tele-PrEP-MS session. Over 90% (14/15) returned for follow-up care and all 14 were taking PrEP. Also, CBO staff were trained by UMMC HIV/STI testing clinic case managers in dealing with financial and logistical barriers experienced by patients in PrEP care (access to health or social care services, including transportation for appointments). CBO and UMMC staff collaborated to resolve these issues and all patients returned for a Tele-PrEP-MS session within a week of testing. The CBO was able to schedule patients for any day of the work-week because five UMMC physicians were available to schedule Tele-PrEP-MS for a half-day each per week. This arrangement will continue for this proposed project. CBO staff reported that "patients said they were really comfortable seeing the provider via live video chat and felt as if the provider was actually present." They also said "it felt private because it wasn't set up like a typical doctor's office." The staff also approved of Tele-PrEP-MS because "patients receive care from an expert who is culturally competent." This initial experience, combined with

UMMC and MBK data and experience, informs our plans and our estimates of Tele-PrEP-MS use and rates of PrEP uptake and adherence. A goal of this study is to more precisely determine the PrEP cascade rates and their associated factors.

**The UMMC Center for Telehealth** provides high quality telemedicine to more than 100 clinical sites in Mississippi, allowing the state to be a leader in telemedicine. The Center was begun in 2003 and it is estimated to have delivered a diverse range of medical services to a half a million individuals. It will support healthcare access needs of the two CBOs by using state of the art technology to deliver healthcare that meets the same standard of care as an in-person visit. This system provides HIPPA-compliant, secure access to the statewide UMMC Telehealth video network using a desktop webcam. UMMC Telehealth and My Brother's Keeper, Inc. have drafted and agreed to a letter of understanding for the service with negotiated rates.

## APPROACH

The **specific aims** of this project are to:

1. **Develop a PrEP telemedicine program (Tele-PrEP-MS) for CBOs that provide HIV/STI testing in underserved areas and document the procedures and protocols.**
2. **Implement Tele-PrEP-MS in two CBOs that conduct STI/HIV testing for an underserved area in MS**
3. **Determine the acceptability and feasibility of Tele-PrEP-MS, and examine the individual, organizational and structural factors associated with its acceptability and feasibility.**

**Project Overview:** Tele-PrEP-MS will examine the delivery of PrEP in underserved areas by using technology to link patients to Infectious Disease specialists at the University of Mississippi Medical Center (UMMC). The **UMMC Center for Telehealth** will link **Mississippi CBOs** to **UMMC PrEP specialists** via a HIPPA compliant, secure network (see **Environment** for description of the Telehealth Center and the CBOs). The CBO HIV testing staff will be trained to screen all clients for degree of HIV risk and assist with structural barriers (e.g. finances, schedules). Those with significant risk will be able to discuss prevention options with the CBO staff and with the UMMC specialist, who will be able to begin and continue PrEP via the webcam link to the CBO within a week of HIV testing. **Outcomes:** This project will collect important data on the participant, provider and CBO factors associated with acceptability of telemedicine and PrEP-related outcomes to inform later, wider implementation. If Tele-PrEP-MS shows promise in this pilot development study, it can be implemented in other CBOs and factors related to its wider impact can be further examined.

**Tele-PrEP-MS Timeline:** The proposed study is projected to begin on 07/01/2018 and end on 06/30/2021.

| | **Year 1** | | | | **Year 2** | | | | **Year 3** | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Tasks / Quarters** | **1** | **2** | **3** | **4** | **1** | **2** | **3** | **4** | **1** | **2** | **3** | **4** |
| Startup / Interviews | X | X | | | | | | | | | | |
| Protocol Development | | | X | | | | | | | | | |
| Training | | | | X | | | | | | | | |
| Enrollment | | | | | X | X | X | X | | | | |
| Assessments | | | | | X | X | X | X | X | X | | |
| Analyses / report | | | | | | | | | | | X | X |

**Protocol Development (Aim 1 - Year 1): Develop a telemedicine program for CBOs that provide HIV/STI testing and document the procedures and protocols.**

**Tele-PrEP-MS will be developed with individual interview input from stakeholders.**

**Subjects:** Approximately 4 CBO HIV testing staff, 4 CBO administrators, 3 PrEP specialists at UMMC and 10 to 20 HIV testing clients will be consented for individual interviews. CBO staff and administrative participants will be drawn from four CBO HIV/STI testing sites to ensure generalizability of our study. All genders and sexual orientations will be represented in the patient interviews and participants will be drawn from the two participating CBOs. All development interviews will be conducted by Dr. Brown, Whiteley, or a trained senior research associate, who have experience with interviews used to develop behavioral interventions and

healthcare provider training. Interviews will be digitally recorded and recordings uploaded to a secure file location on the Rhode Island Hospital server, which will only be able to be accessed by project staff.

The Consolidated Framework for Intervention Research (CFIR), as described above, will guide interviews, data collection and organization. In the interviews, we will probe for inner and outer context factors most relevant for protocol development including organizational characteristics, culture and climate; dynamics of the CBO team; individual characteristics and attitudes; training needs; monitoring and support; potential protocol fit; technology issues, and fiscal viability and needs. **Patients/client interviews** will target outer setting constructs such as patient needs and resources (e.g. "To what extent do you feel the staff at CBO is aware of your needs and preferences?" "What barriers will you face prior to participating in the study?"). Individual characteristics and domain constructs to be assessed include knowledge and beliefs about PrEP, self-efficacy to use PrEP, experiences with lack of provider knowledge, mistrust of medical system, stigma surrounding PrEP, and telemedicine experience). **Staff members and CBO administrators** will be assessed on key constructs such as the protocol's design and quality (e.g. "What supports, such as online resources, marketing materials, or a toolkit, would need to be available to help you implement and use the protocol?"); project setting (e.g. "To what extent is staff aware of the needs and preferences of the individuals served by your organization?"); organizational infrastructure (impact of age, maturity, size, or physical layout on the project); and individual characteristic constructs of knowledge of PrEP and telemedicine, possible provider training methods, perceived stigma of clients, and perception of the use of technology and its safety.

**Analysis** of these interviews will occur using Rapid Approach methodology [72], which utilizes key probes in the construct areas to elicit the major themes to be examined, which in this case are the organizational requirements and the barriers or facilitators to implementation, as described by patents, PrEP specialists, CBO staff and administrators. Other themes not directly related to protocol adaptation, training or clinic procedures (e.g. organizational structure, climate, reputation in the community) will be retained to inform the later post-study interviews.

**Protocol and training development** will occur with iterative refinement of current materials and procedures for PrEP initation and maintenance (e.g., flyers, risk assessments, informational brochures, and follow-up questionnaires) used by the UMMC PrEP clinic and the Center for Telehealth. Regular meetings will occur between UMMC and RIH research staff to discuss how to best adapt the materials for CBO use. Interviews, guided by the CFIR constructs and the Patient-Provider Alliance, will inform our protocol development and training. The Patient-Provider Alliance is supported by considerable research indicating that an effective working alliance is based on collaborative goals, tasks, and trust. [74] An effective alliance between patient and provider has been shown in many health disorders to influence important patient outcomes such as adherence to medical care and satisfaction with treatment. Based on previous examinations of HIV/STI prevention delivery, likely constructs that will be identified include: knowledge, skills, expectations of PrEP and the use of telemedicine.[75] For example, in this project a person at-risk for HIV must learn information that is directly relevant to their HIV risk and understand how treatment with PrEP might be protective for them. Similarly, staff at the CBO will need to know how to assess HIV risk, counter mistrust in patients, improve motivation for care, and establish collaborative goals. For example, modeling of techniques to establish collaborative tasks and goals could be provided through live role plays and written vignettes of potentially difficult discussions about HIV testing, risk reduction counseling, the risks and benefits of PrEP, and improving motivation for care. CBOs and their providers will need methods / training to address patient mistrust of the security of telemedicine and concerns about the expense of PrEP. UMMC specialists will need to overcome any future barriers to continuing to offer Tele-PrEP-MS five days a week. They will be trained on effective videoconferencing communication techniques to enhance the quality of the provider/ patient interaction needed for an effective working alliance.

The acceptability of the developed strategies for the protocol, training and implementation procedures will be reviewed by RIH, UMMC, and CBO research staff to ensure that chosen strategies are aligned with the CBO, provider, patient and technology needs, and that methods are sufficiently refined. If the team needs further input, additional interviews will occur.

**Tele-PrEP-MS Training of CBO Staff** (pending modifications from interviews). Effective, standardized training is crucial for later dissemination of the protocol and is planned to be done via video-conference. We will create a training manual and list of resources for staff. Techniques for all procedures will emphasize the patient-provider alliance and the necessity of establishing collaborative goals, tasks and trust.

**Specific procedures for the CBO staff** are anticipated to be:

1. Screening: CBO staff will identify people who are at high-risk for HIV acquisition using consistent instruments, provide individualized feedback, provide accurate, tailored information about prevention strategies, and improve their motivation for prevention. So that all clients receive an accurate risk assessment, CBO HIV testing counselors will be trained in the use of a risk checklist, which includes behavior items to be applicable to all. This checklist queries patients about the number of sexual partners in last 12 months, transactional sex, the number of partners with HIV, presence of STIs in last 12 months and injection drug use.
2. Risk feedback: CBO staff will be trained to assess participants' unique risk behavior by using a standardized version of a risk checklist, similar to ones currently used by UMMC. At-risk individuals are counseled on more intensive HIV prevention strategies and are shown an informational / motivational video that shows a patient discussing their sexual risk with a physician and discussing HIV prevention options that include PrEP.
3. Prevention counseling: Training will address other barriers to HIV risk assessment such as patient and provider discomfort with discussions about sexual orientation and behaviors and substance use. [77-79] Training will address the principles of Patient-Provide Alliance. It emphasizes the need to collaboratively establish goals, assign tasks, and establish trust to establish an effective alliance. Strategies include eliciting personal concerns, reviewing options, and enhancing motivation for health care. [80] Drs. Whiteley and Brown have successfully trained providers in these collaborative alliance-building principles in other HIV-related projects. [81, 82]
4. Resources (financial and logistic barriers): CBO staff will be trained in procedures, similar to those at UMMC, for insurance navigation (enrollment, copayment cards, etc.), access to Gilead's PrEP program, and access to other health or social care services, including transportation for appointments. UMMC and CBO staff will collaborate to resolve these issues for patients and to schedule the Tele-PrEP-MS session within the same week as testing.
5. Lab testing: CBO staff will also be trained in Point-of-Care Creatinine testing and the collection and transport of samples for STI screening, which will include staff-collected blood for syphilis, and Hepatitis serology (for those without HBV immunization) and patient-collected urine and urethral, rectal and vaginal swabs for CT/GC to be assisted by detailed instructions and graphic handouts. Samples will be sent to the County Health Department for testing and any needed treatment.
6. HIV testing: Rapid testing will be used. Those preliminarily positive will have confirmatory testing and be immediately linked to care if HIV is confirmed. All CBO HIV testing counselors will attend HIV pre- and post-test counseling training as per CDC and state guidelines.
7. Telemedicine technology: CBO staff will be trained by staff from UMMC Center for Telehealth in the use of the webcam / computer and the UMMC Telehealth Network. The service is secure and reliable with a connection failure rate of less than 2%. A second computer and webcam will be available at each CBO, in case of an equipment malfunction.

**Quality and fidelity of protocol delivery. Training:** CBO staff will complete assessments of HIV/PrEP knowledge (see Measures) and knowledge of PrEP counseling (developed to reflect understanding and mastery of the project activities above). Scores greater ≥ 80% correct will be deemed passing. Training using educational material and role-play vignettes will continue until CBO staff demonstrate to Drs. Brock and Brown procedural competence similar to UMMC staff and attain passing scores on the knowledge measure. **Fidelity:** To capture project fidelity, the project will assess elements of protocol delivery (e.g. use of Risk Checklist), protocol acceptability, and patients' perception of their working alliance with staff and physicians. (See Measures, Aim 3, Primary Outcomes) A goal of the project is to determine the degree to which CBOs are able to implement Tele-PrEP-MS.

**Tele-PrEP-MS Protocol** (pending modifications from interviews). Based on the CDC guidelines [83](2014) and successful methods used at UMMC, Tele-PrEP-MS will 1) systematically screen for HIV risk behaviors using a Risk Checklist, which is reviewed by CBO staff (see above), 2) provide HIV/STI testing and STI screening and/or treatment with the help of the UMMC specialist, 3) discuss HIV prevention strategies including PrEP with a UMMC specialist via UMMC Telehealth Network within a week of testing, as done in our recent Tele-PrEP-MS experience 4) prescribe PrEP at the initial visit or at follow-up, 5) provide Point-of-Care

Creatinine testing if PrEP is started, and 6) follow all on PrEP for routine medical care at 3 month intervals via Telemedicine. The UMMC specialist, CBO HIV testing staff will have defined but flexible roles. For example, CBO staff will provide individual feedback to the patient about their negative HIV test and the patient can watch an informational / motivational video showing a patient discussing their sexual risk with a physician and discussing HIV prevention options that include PrEP. A videoconference can be scheduled within the week between patient, and UMMC specialist, who can further assess the client's current risk behavior, review treatment options, and plan for decreasing HIV risk. The UMMC specialist could begin PrEP care at that visit and further patient-specialist teleconferences could review the barriers and facilitators to HIV-safe behavior and PrEP adherence in order to determine care plans.

**Tele-PrEP-MS Trial (Aim 2 - Year 2): Implement Tele-PrEP-MS in MS CBOs**.

**Recruitment and enrollment** (see Human Subjects): All PrEP-eligible adult clients who present for HIV testing in the participating CBOs (not near UMMC) during the months of Aim 2 will be eligible to be enrolled in the online feasibility, acceptability and implementation survey. As noted in Aim 1, CBO staff will be trained in procedures to assist clients in obtaining necessary financial, transportation, and logistic resources for PrEP. They will collaborate with UMMC staff to resolve these issues for participants as they did in our recent Tele-PrEP-MS experience at a CBO.

**PrEP Care Cascade estimates:** Based on data from the CBO testing sites, UMMC HIV screening clinics, and our recent Tele-PrEP-MS experience in a CBO (see Preliminary Studies), it is estimated that a total of 600 adults (both sites combined, 25 per month at each month for 12 months) will present for HIV testing during Year 2. It is estimated that 300 (50%, which is less than the UMMC rate) will be PrEP-eligible (not HIV infected and with elevated risk scores). Because of COVID, the CBOs have discontinued the in-person events that led to most of their HIV testing. With permission of our NIMH program officer, Dr. Stiratt, our survey recruitment goal was reduced from 240 PrEP-eligible to 25-50 and Aim 3 (qualitative assessment) was enhanced We will **enroll 25-50** (80%) of the PrEP-eligible in the assessments [(84)]. The sample will be **75% male (mainly MSM), 85% will be nonwhite, with mean age of 26 years**. Of the 25-5- enrolled participants, 75%, which is less than our recent experience, will attend Tele-PrEP-MS with UMMC specialist, and 66.6%, which is less than our recent experience and more than the UMMC rate, will return within three months and will be taking PrEP. Adherence at 6 months will also be assessed.

**Determinations of Tele-PrEP-MS acceptability and its associated factors (Aims 2 & 3, Year 3):**
**Aim 3: Determine the acceptability and feasibility of Tele-PrEP-MS and to examine the individual, organizational and structural factors associated with its acceptability and feasibility.**

**Analyses will occur with a mixed methods approach** that includes interviews of stakeholders (clients, staff, and administrators), an online survey of clients obtained during the implementation phase in Aim 2, and aggregate clinic records.

**Stakeholder interviews** will provide in-depth data from the perspective of each stakeholder group. **Subjects**: After the end of Aim 2, in-depth interviews with a sample of approximately 20 patients who initiated PrEP via telemedicine (recruited from our current TelePrEP study and from UMMC associated clinics), 5 PrEP-eligible patients from our study who did not receive PrEP, and 5 providers / staff who are involved in telemedicine for PrEP will yield data on the acceptability and feasibility of the protocol and the facilitators and barriers to wider implementation of Tele-PrEP-MS. Patients that did not participate in the TelePrEP study will be selected through medical record review of eligibility criteria. These individuals will be contacted by research staff to determine interest and consent. Interviews will continue until redundancy is reached. All interviews will be done by phone at the end of the study by a trained staff in RI unknown to the stakeholders. Interviews will be digitally recorded and kept in a secure file location on the Rhode Island Hospital server. The Consolidated Framework for Intervention Research (CFIR) as described above will guide our interviews and analyses. In the interviews, we will probe for factors including community context; organizational characteristics, culture and climate; leadership; dynamics of the CBO team; individual characteristics and attitudes; training monitoring and support; protocol fit; and fiscal viability. We all also probe for the perceived utility, feasibility and acceptability of the protocol and barriers to longer-term implementation (e.g. finances, staff resistance, technology issues). We will pay particular attention to the influence of patient and provider demographic variables (e.g. race, gender, sexual orientation) and degree of match in patient/provider characteristic on acceptability and quality of the

alliance. Also, the project interviews will document any challenges for the UMMC specialists in providing Tele-PrEP, including the technology and providing appointments in the same week as testing. Quantitative data on these issues will also be obtained through self-report (see Primary Outcomes, below).

**Interview Analysis:** Framework analysis,[85] in conjunction with the data collection, organization and association templates provided by CFIR, will be used as it is systematic and dynamic approach to interview data that produce analyses focused on specific research questions. Consistent with Framework analysis and recommendations of CFIR, we will first review interview content. Our probes in each domain and construct area will provide the initial coding framework. CFIR also provides definitions for each construct, although probes are altered to fit the project and its context. A subset of transcripts will be double coded to assess inter-rater reliability. Discrepancies will be resolved through discussion. Relevant themes will be extracted by review and consensus of Investigators. Specific sections, often from the detailed probes, will be indexed in their relationship to particular themes. Next we will chart and map the data by refining the relationships between indexed data and the thematic framework. We will then interpret the resulting themes that impact the acceptability and feasibility of Tele-PrEP-MS (e.g. patient – provider racial / sexual orientation match, working alliance), and contextualize their meaning within and across stakeholder type and CBO. CFIR provides templates and definitions to quantify ratings of the strength of participant attitudes about barriers and facilitators. We will examine the utility of such ratings, while recognizing that Aim 3 is to provide descriptive associations of factors related to the acceptability / feasibility of the Tele-PrEP-MS, to inform later adaptations to the protocol, its implementation and its assessment.

**Quantitative assessments:** A repeated online survey of PrEP-eligible clients tested for HIV will provide quantitative data to complement the interview data gathered above.

**Subjects:** All adults over the age of 18 presenting for HIV testing at the CBO sites who are PrEP-eligible during the implementation phase (Aim 2) will be approached. Interested patients will be introduced to a member of the research staff who will explain the study in more detail and will email the participant a consent document via DocuSign to review upon the subject's willingness to participate. Those who electronically sign will be enrolled in the study and will then be asked to complete a brief survey, using REDCap, to assess PrEP behaviors and demographic, structural, and personal factors that may be associated with Tele-PrEP-MS. We estimate that at least **25-50 of** available PrEP-eligible adults will enroll. [84] Participants will complete online surveys three and six months after their HIV screening visit to assess satisfaction with Tele-PrEP-MS and their HIV and PrEP-related behaviors. With participant's knowledge and signed HIPAA authorization via DocuSign, their attendance at Tele-PrEP-MS sessions and adherence to PrEP will be obtained from clinic records. Online **assessments** will be done with REDCap [86], which is a free, secure, HIPAA compliant web-based application designed to support data capture for research studies. Our research team currently uses REDCap in our other research collaborations in Jackson, MS (See Human Subjects). A REDCap survey will be emailed to each participant's unique email address after the HIV/STI testing visit (at time of enrollment), and at 3- and 6-months follow-up so they can complete assessments online. I **Tracking and Retention:** Techniques to be implemented by the Retention Coordinator and outreach staff include maintaining updated participant contact information, frequent reminder cards, phone calls and emails, and obtaining the name and telephone number of another relative or family friend who would know of the patient's whereabouts. The retention rate in Dr. Brown's previous community study (U01 MH066785) was 85% after 18 months.

**Measures.** A computer self-interview using REDCap will assess behavior since it is confidential, allows for complex branching/skip patterns.[86] Measures from our on-going NIH HIV and PrEP research will be used. All measures will be relevant to themes derived from the Phase 1 work as grouped in CFIR constructs. Constructs are likely to represent information, motivation, behavior, and attitudes about PrEP, the CBO, medical care, and the quality of the patient – provider alliance.

**Primary outcomes**

**PrEP-related outcomes**: The project will assess at 3 and 6 months: attendance at Tele-PrEP-MS session, receipt of PrEP, and adherence to PrEP by participant self-report and, with participants' knowledge and signed HIPAA authorization via DocuSign, abstraction from the electronic medical record. Because of travel and structural barriers, virtually no one will begin PrEP at another location, although the project will also assess this occurrence by participant self-report.

**Protocol acceptability and patient – provider relationships:** The Acceptability of Tele-PrEP-MS by clients, CBO staff, administrators and UMMC physicians will be assessed with modified versions of the

Session Evaluation Form (SEF) and the Client Satisfaction Questionnaire (CSQ-8), which have good reliability and validity.[87, 88] These 21 items assess study procedures, quality and quantity of service, outcome, and general satisfaction using Likert-style items. In addition, patients and providers will complete two assessments focused on their perceived working relationships. The 12- item Working Alliance Inventory (WAI) measures perceptions of collaborative goals, tasks.[89] Another 5-item Likert scale, PrEP Collaboration, using items modified from the ART Adherence intervention, assesses mutual trust and understanding.(90) These quantitative data will supplement the analyses of the interviews of representative stakeholders to examine protocol acceptability and association of patient – provider relationships with demographic factors and PrEP outcomes.

**Secondary outcomes** (pre/post and follow-up assessments)

**PrEP knowledge:** Because there is no PrEP knowledge scale with published psychometrics, we will use a 15-item questionnaire to assess knowledge (true/false/don't know) based on facts from the CDC and the San Francisco AIDS Foundation websites concerning PrEP. The items will be tested for readability and relevance with the target population in the qualitative phase of the study. Items will be revised, if needed, for the RCT.

**Motivational readiness for PrEP and PrEP-related care:** Rollnick's Readiness Ruler(91) will be used to assess motivation for engaging in PrEP care using two items from 1 (not ready) to 10 (ready to engage).

**Barriers / facilitators for PrEP and PrEP-related care:** Participants will also complete the 10-item, Likert-style IMB PrEP Motivation Scale.[92] It has been modified to assess personal and social factors for PrEP, rather than ART, and is used in our on-going study of PrEP adherence study (1R34 MH104068).

**PrEP & appointment self-efficacy:** The IMB PrEP Behavioral Skills Scale has 14 Likert-style items that assess perception of ability for adherence to care and has an internal consistency of 0.9 among adults living with HIV.[92] It has been modified to address PrEP, rather than ART, and is used on our on-going PrEP studies.

**Perceived risk for HIV scale** has 8 items that evaluate various dimensions of perceived HIV risk (e.g. cognitive assessment, intuitive feelings, salience HIV infection). This scale demonstrates good internal consistency (α=0.88) when used with adults attending HIV testing and prevention services. [93]

**Moderators**

In addition to demographic factors, a number of psychosocial factors might influence adherence, so the project will assess these factors for exploratory analyses in order to further characterize the sample. Some factors, such as the quality of the relationship with health care providers could function as moderator or could be influenced by the Tele-PrEP-MS program.

**Demographic** variables to be assessed include age, gender identity, sexual orientation, and structural factors such as insurance, housing and literacy.

**Patient – provider relationships:** See scales in Primary outcomes, above.

**Social Support for Medication Adherence:** This six-item measure assesses social support for taking medications, going to medical appointments and other tasks related to adherence using Likert-style items with a four-point scale. It is being used in AIDS Clinical Trials studies. A single score for social support can be generated or single items can be analyzed, such as support for medical appointments.[90]

**The Risk Behavior Assessment:** The RBA (used in Dr. Brown's other federally-funded projects) is a reliable and valid computer-assisted structured interview assessing self-reported sexual behaviors. It assesses type of sexual behavior (i.e., anal, oral, vaginal) in the past 3 months, frequency of sex, use of condoms, and number and gender of partners. Additional questions cover sex with high-risk partners, exchanging sex for drugs, and frequency and quantity of substance use and having sex while using alcohol/drugs.[94] These items can also be used to compute the PrEP Risk Stratification Scale.

**Design Considerations:** (1) Ethical concerns that preclude random assignment: CBOs that provide HIV testing outside of Jackson MS do not offer medical care, so PrEP-eligible patients are referred and seldom follow-up. We decided not to randomly assign high-risk patients to a referral-only condition that rarely results in obtaining PrEP. (2) CFIR is an appropriate model for a study of effectiveness and a simultaneous focus on implementation factors: PrEP is effective and telemedicine has been shown to be as efficacious as in-person medical care in many disorders. Therefore, this project will focus on the acceptability and feasibility of Tele-PrEP-MS for patients, providers and CBOs because there are likely to be unique considerations for PrEP telemedicine. The project will carefully assess participants' experience with CBO staff and Tele-PrEP-MS physicians using interviews and self-report. It will not match participants and providers by race or sexual

orientation, since the project is meant to provide data to examine the influence of these and other factors (e.g. patient characteristics) on protocol acceptability and PrEP cascade outcomes. Approximately half of the CBO and medical staff are of racial and sexual orientation minority groups. (3) Alternative designs: Because the project will work with CBOs, we considered using a step design in which one CBO implements TelePrEP 6 months earlier than the other. However, each CBO requires 18 months for the enrollment and follow assessments and the short R34 project period does not accommodate such a design (see Timeline). The project will have data from the CBOs on HIV testing rates and referral to PrEP prior to Tele-PrEP-MS implementation and from UMMC on the PrEP care cascade rates throughout the study period. These data will provide context for the outcomes observed in this study.

**Quantitative Data Analytic Plan:**

**Aim 2: Determine the acceptability of Tele-PrEP-MS and to examine the factors associated with its acceptability.** The Client Satisfaction Questionnaire (CSQ), the Session Evaluation Form (SEF) and the Working Alliance Inventory (WAI) will quantitatively assess acceptability according to patients attending Tele-PrEP-MS. In addition to scale scores, individual item mean scores and standard deviations will be reviewed to determine if there are specific elements of the protocol that are lacking in feasibility, appeal, relevance, or utility. Other scale scores (e.g. Motivation for PrEP) will be computed and non-scale items topically grouped (e.g. health literacy, housing).

**Aim 3a: Examine PrEP-related outcomes over six months** (proportions screened for PrEP eligibility; attending a PrEP medical evaluation; taking PrEP at 3 and 6 months) **to compare the academic medical center and the CBOs** (Exploratory). The UMMC HIV/STI screening clinics test 9,000 patients each year and approximately 65% are at high-risk for HIV (according to on-going analyses of the Risk Stratification data). Only one third return to initiate PrEP because wait times and distance are often barriers. These rates will be updated at UMMC for the trial year of this study and will be used to gauge the efficiency PrEP outcomes observed in Tele-PrEP-MS at the CBOs. As this is an exploratory aim, direction of effects is not predicted and the comparison is largely descriptive and to provide context for the results. Comparisons of proportions will be made using Chi Square analyses.

**Aim 3b: Examine any factors related to these outcomes** (Exploratory aim). Only the CBOs will have patient-level data to examine factors related to patients' PrEP outcomes. Relevant scale scores (e.g. Motivation for PrEP) will be computed and non-scale items topically grouped (e.g. health literacy, housing). Outcomes include Tele-PrEP-MS visit attendance (yes/no; clinic and self-report data), PrEP prescription accepted (yes/no; clinic and self-report), and adherence to PrEP (yes/no; clinic and self-report). For the enrolled PrEP-eligible group multiple logistic regression will be used to examine the predictive association of demographics (e.g. race, sexual orientation), baseline scales (e.g. motivation, skills), scale change scores (e.g. PrEP knowledge), and screening visit acceptability (CSQ, SEF, WAI scores) on each outcome.

**Inclusion of Women, Minorities, and Children**

**Women.** Participants in this study will be comprised of both females and males. It is anticipated that 25% of the sample will be females, reflecting the population of the HIV testing clinics from which the sample will be recruited, so women will be adequately represented.

**Minorities.** The aim of our recruitment strategy is for the resulting program materials to be appropriate for racial minorities in the South. We anticipate that in terms of race 73% of the enrolled participants will be Black/African American, 22% will identify as White, and 5% will identify as More than one race. Ethnically, 2% will self-identify as Hispanic or Latino.

**Children.** No children will be included in this project. PrEP was recently FDA-approved for youth under that age of 18 but the CDC has not yet released guidelines for its use. The aim of this study is to examine the use of telemedicine for PrEP among adults who are eligible for its use according to the FDA and using CDC guidelines.

**Protection of Human Subjects and Safety Monitoring Plan**

**Human Subjects Involvement, Characteristics and Design**

The proposed research study is comprised of two phases: a formative phase to develop Tele-PrEP-MS and a trial phase to test the protocol. In the **formative phase** of the project (year 1), the telemedicine program for community based organizations will be developed using an iterative, collaborative development approach with University of Mississippi Medical Center (UMMC) specialists and local stakeholders (CBO agency staff, administrators, and patients). Interviews will be conducted with approximately 10-20 HIV testing clients, 4 CBO HIV testing staff, 4 CBO administrators, and 3 PrEP specialists at UMMC to inform development of the protocol. Protocol and training development will occur with iterative refinement of current materials and procedures for PrEP initiation and maintenance (e.g., flyers, risk assessments, informational brochures, and follow-up questionnaires), used by the UMMC PrEP clinic and the Center for Telehealth. Regular meetings will occur between UMMC and RIH research staff to discuss how to best adapt the materials for CBO use.
In the **implementation phase** (year 2-3) a trial of Tele-PrEP-MS will be conducted to determine the acceptability and feasibility of Tele-PrEP-MS and to examine the individual, organizations, and structural factors associated with its acceptability and feasibility among 25-50 PrEP-eligible individuals. At the end of the trial phase, we will conduct stakeholder interviews to collect data on the feasibility and acceptability of the Tele-PrEP-MS program from approximately 20 patients who initiated PrEP via telemedicine (recruited from our current TelePrEP study and from UMMC associated clinics), 5 PrEP-eligible patients from our study who did not receive PrEP, and 5 providers / staff who are involved in telemedicine for PrEP.

**Inclusion Criteria**. Eligibility criteria for patient participants in all phases of the project will be: 1) at least 18 years of age; 2) Presenting for HIV testing at the two CBO sites during the trial months; and, 3) ability to read and speak English. Exclusion criteria will be: a) known HIV-infection (staff will facilitate entry into care if needed). Other interview participants (CBO staff and UMMC physicians) will be eligible by virtue of their employment at the respective organizations.
Participants will be recruited from participating CBOs (not near UMMC). There will not be overlap between subjects in the formative phase and the implementation phase. Retention techniques for the study include maintaining updated participant contact information, frequent reminder cards, phone calls and emails, keeping records of friendship contacts, and obtaining the name and telephone number of another relative or family friend who would know of the patient's whereabouts. The retention rate in Dr. Brown's previous community study (U01 MH066785) was 85% after 18 months.

**Rationale for Including Special Classes of Subjects.** N/A Special classes are not included in this project.
**Sources of Material**

**Research Material Obtained from Living Human Subjects**
Research material obtained from participants includes: 1) questionnaire data; 2) audio-tapes from interviews with patient participants, CBO staff, and UMMC physicians; and 3) Point-of-Care HIV test results.

For the formative phase, participants (patients, CBO staff, and UMMC physicians) will partake in interviews and will be asked questions regarding their perception of barriers or facilitators to implementation of telemedicine. These interviews will take place in private offices at the CBOs or UMMC. The audio-taped interview and written notes of the interview will be the sources of material for this phase. Additional interviews will occur after the trial phase. Interviews will be digitally recorded and kept in a secure location on the Rhode Island Hospital server. Interviews will inform the development of the protocol and provider training.

For the implementation phase of the study, patient participants will complete brief online questionnaires about their demographic, structural, and personal factors that may be associated with Tele-PrEP-MS. At baseline and follow-up, participants will complete an online survey about their knowledge around PrEP, protocol acceptability, motivational readiness for PrEP, PrEP & appointment self-efficacy, and perceived risk for HIV.

Questionnaires will be completed online via REDCap at entry to the study, and at 3-months and 6- months post-enrollment. PrEP-related measures (telemedicine PrEP visit, receipt of PrEP, and taking PrEP) will be obtained at the follow-up assessment time points from the electronic medical record.

After the end of the implementation phase, in-depth interviews with a random sample of stakeholders: 20 patients who initiated PrEP via telemedicine (recruited from our current TelePrEP study and from UMMC associated clinics), 5 PrEP-eligible patients from our study who did not receive PrEP, and 5 providers / staff who are involved in telemedicine for PrEP will occur to yield interview data on acceptability and feasibility of the protocol and the facilitators and barriers to wider implementation of Tele-PrEP-MS. These interviews will focus on similar factors including community context; organizational characteristics, culture and climate; leadership; dynamics of the CBO team; individual characteristics and attitudes; training monitoring and support; protocol fit; and fiscal viability. All interviews will be done by phone at the end of the study period by a trained staff in RI. Interviews will be digitally recorded and kept in a secure location on the Rhode Island Hospital server.

**Clinical Trials Registration and Results Dissemination Plan.** This study will be registered on ClinicalTrials.gov in accordance with NIH policy. Consent forms will include language informing participants of the project's registration and submission of results to ClinicalTrials.gov. No participant identifying information will be submitted.

**Linkages to Subjects and Access to Subject Identities**

For each stage of the research study, participant names and contact information will be maintained in a recruitment/enrollment database. Once individuals enroll in the study, names will be linked to a participant ID number in this database, which will be kept in a restricted access folder on a secure server. All name/ID number files will be assigned a code name unrelated to the name of the study. Signed consent to contact forms will also be kept in a locked file cabinet, separate from any other project data. Once data collection is completed, the corresponding recruitment/enrollment database will be deleted as it is unnecessary to maintain the link between participant identity and study data. Destruction of these databases must be witnessed and documented on the Master List Verification of Destruction document, which will be maintained in a regulatory file. Furthermore any information collected as part of this study will be accessible only to research staff that has completed mandatory training in the protection of human subjects.

**Potential Risks**

The risks for this study for patients are considered minimal. Every effort will be made to ensure that study participants are protected from risks. The risks are as follows: 1) potential coercion; 2) loss of confidentiality; 3) emotional discomfort during the assessments; and 4) risk associated with learning they have HIV, if that is diagnosed during the course of the study. The protection against each risk is described in detail below under Adequacy of Protection Against Risk.

The risks for this study for other stakeholders such as CBO staff and PrEP clinicians are also considered minimal. Every effort will be made to ensure that study participants are protected from risks. The risks are as follows: 1) potential coercion; 2) loss of confidentiality; and 3) emotional discomfort during the interview. The protection against each risk is described in detail below under Adequacy of Protection Against Risk.

**Adequacy of Protection Against Risk**

**Recruitment and Enrollment.** The risk of possible coercion will be minimized by following standard procedures for recruiting and enrolling participants. All PrEP-eligible adults over the age of 18 presenting for HIV testing at the CBO sites during the trial will be approached for recruitment and given a Consent to Contact form for the online surveys. The Consent to Contact form will include: name, email address, and phone number. Consent to contact forms will be securely faxed to University of Mississippi Medical Center (UMMC) staff, who will follow up with interested parties by phone or email. Similar procedures are already being used by CBOs to send forms containing PHI to the Jackson UMMC site. Those who wish to participate will receive a

DocuSign consent form via email from the UMMC RA, which will outline study aims and procedures, and language regarding the risks/benefits of participating in a research study. It will also state that by electronically signing, they are allowing UMMC study staff to view their medical records relevant to PrEP and to contact them after the last survey for participation in a phone interview. Participants can decline the phone interview but still participate in the surveys. This online survey data will be de-identified and kept on a password protected participant log on a secure drive. Participants will be given ample time to consider risks of participation and have the option of talking to research staff by phone to discuss any questions. Participants will also be reminded that study participation is voluntary and that refusing to participate or withdrawing from the study at any time will not result in any negative consequences.

Recruitment of stakeholders (i.e. staff members at community based organizations and PrEP specialists) in the formative phase or post-implementation phases of the study will involve being contacted by investigators to participate in interviews. Stakeholders will be reminded that they are not obligated to participate in this project by virtue for their employment and they are free to withdraw at any time without jeopardy to their position.

**Protections Against Risk**

**Breach of Confidentiality.** Potential risk will be minimized by strictly adhering to the guidelines for research outlined by the site IRB, state laws, the Federal Health Insurance Portability and Accountability Act of 1996 and its regulations ("HIPAA"), and the DHHS Federal Policy for the Protection of Human Subjects (45 CFR Part 46 Subpart D). This will include identifying participant research data by numeric ID only and maintaining any records containing potentially-identifying information separate from any research data. All research data (written records and audiotapes of program sessions) will be kept in a locked file and electronic data will be password-protected. All of these study-related materials will only be accessible to research staff. No names, only identification codes, will be used in presenting data in lectures, seminars, and papers. Information will be released only with written consent of the participant.

Participant confidentiality will be breached only to protect the safety and welfare of research participants and only in accordance with state and federal law. If abuse is reported, a report will immediately be filed with the appropriate state department or agency. See "Emotional Distress" below for more details on the available clinical services.

Questionnaire data collection for the implementation phase will include a baseline assessment (completed upon enrollment) and assessments at 3- and 6- months post-enrollment. Participants will receive the three assessments, as online REDCap surveys, via email. **No PHI will be collected in these assessments. REDCap online survey software will be utilized for the collection of data from participants,** from which data are easily extracted for entry to statistical programs (e.g., SPSS)**. The research team will develop documentation for each survey measure, including appropriate branch and skip logic, as well as a codebook with documentation for each variable. Staff will program surveys using the REDCap survey platform. Basic survey content will be programmed first and then survey flow and logic will be programmed after content has been reviewed and edited. Survey-based reporting mechanisms will be programmed, including automated invitation and reminder emails for participants as well as triggered emails to staff for the purposes of monitoring and reporting. Usability testing by trained staff will be conducted and will include checks for basic grammar, spelling, sequence, and comprehension. Further advanced testing will be conducted in order to test the survey's logic and flow; this advanced testing phase will include the generation of test data to ensure all branch and skip logic works as planned within the variable codebook. Throughout the course of the project, regular data downloads will be conducted to check the quality and accuracy of the data, to ensure no data are missing, and to regularly report on the sample characteristics. REDCap meets or exceeds all HIPAA and HITECH requirements for security and privacy**. Following data transfer, syntax will be developed to arrange the data for quantitative analysis. Directories describing data files, variable label codebooks, and data routines will be

developed during the year-2 trial. Following that, data will be extracted and archived on a monthly basis. Routines for assessing data integrity will be developed, with procedures established for accepting, correcting, or rejecting data. All data will reside on servers behind firewalls (with access restricted to study personnel) and on computers with hospital security enabled. All servers are routinely backed daily (to off-site locations), and the project will create its own weekly backups on secure external drives kept both on and off site. Any transfer of data among the study sites will be done using secure methods (e.g., secure FTP).

All study personnel names on this application have completed training and received certification in Human Subjects Research Protection (CITI Program) and HIPAA regulations. They will continue to renew this training in compliance with hospital policies.

For the formative interviews in PY01 and the post-implementation interviews in PY3, participants will be asked to provide informed written consent to audiotaping at the time of study entry. To assure confidentiality and protection of the participants, interviews will be digitally recorded and kept in a secure location on the Rhode Island Hospital server. Only research staff will have access to the audio files for review of the interviews.

**Emotional Distress.** We will minimize distress by presenting questions in a supportive manner, assuring participants that they may refuse to answer any questions that make them uncomfortable, and may terminate participation in the study at any time. All participants may receive medical or mental health treatment at any time during the study. Clinical need will determine whether it is appropriate for the participant to stop continuation in the study. If stakeholders experience distress or concerns, they will be able contact one of the PIs to discuss any concerns for themselves for their role in the project. They will be able to discontinue participation in the project at any time if desired.

All patient participants will be HIV negative as tested by the CBO and we anticipate that very few participants will later test positive for HIV; however, those who test positive may feel extreme distress when learning of their diagnosis. For those who test positive to HIV, they will be counseled by clinic staff in private by in accordance with CDC's HIV testing and counseling guidelines. The diagnosis and counseling provided will involve first reviewing the type of test that was administered, giving them their test results, explain the meaning of the test result, ask if they have any questions, comments or concerns, talk about resources, discuss the participant's feelings and assess their readiness to leave the location, secure additional support and resources for the youth if necessary, and provide them with additional information if necessary. All participants will be linked to the University of Mississippi Medical Center HIV clinic to ensure they get confirmatory testing and that they are enrolled in HIV treatment services. If an appointment in the HIV clinic is not immediately available, then clinic staff will maintain contact with the subject until they have been evaluated by the HIV clinic. The result will be reported to the Department of Health as per state regulations. Dr. Brock and staff are expert HIV medical care providers and are experienced in assisting those newly diagnosed with HIV.

If a participant reports feeling distressed, or has any acute concerns, as a result of their involvement in any phase of the research project (i.e. enrolling, baseline assessment, interview session, Tele-PrEP-MS session, follow-up), clinical resources will be offered. If a participant contacts study staff because of distress or concern due to participation in the study or directed activities that occur away from the clinical space, he will be assessed first over the phone, and then, if needed, as described below.

During any phase of the study, if research staff determines that a participant is an acute medical or psychiatric risk, Dr. Brock or a licensed designee will meet with them individually for further assessment. Acute risks would include severe medical illness, or the development of any other severe psychiatric symptoms or disclosure of sexual or physical abuse. Any participant who exhibits acute risks will be evaluated immediately by emergency room clinical staff or if less acute, by an independent clinician that day. Less severe medical needs or distress can be managed by staff or Dr. Brock over the phone or with an individual interview. Dr. Brock and/or staff will meet with participants and/or families to review concerns and to make referrals for continuing care as needed. Of note, members of the proposed research team have substantial prior clinical (medical and psychiatric) and

research experience in care of PrEP-eligible and HIV-infected individuals as evidenced through their biographical sketches.

**Potential Benefits of the Proposed Research to the Subjects and Others**

**Importance of Knowledge to be Gained.** All phases of the proposed study will provide important information for the development of Tele-PrEP-MS protocols for PrEP-eligible individuals in underserved areas. We hope that our study will be successful in overcoming barriers of access to PrEP services in these areas and think that the clear examination of these questions outweighs the previously mentioned risks. Given the significant risk of HIV infection in the Southern United States and the lack of easily accessible PrEP services in Mississippi, the knowledge to be gained from this research is significant. The risks to participants are reasonable in relation to the importance of the knowledge to be gained.

**Reimbursement for Time and Effort.** Participants (10-20 HIV testing clients) will be reimbursed with a $40 gift card for focus group participation. Stakeholders (4 CBO HIV testing staff, 4 CBO administrators, 3 PrEP specialists) will be reimbursed with a $40 gift card for focus group participation. Participants in the Tele-PrEP-MS Trial (240 HIV testing clients) will be reimbursed with a $25 electronic gift card for the baseline assessment, and $30 electronic gift cards for both the 3-month and 6-month follow-up assessments. In Year 3, stakeholders (25 patients, 5 CBO HIV testing staff/, CBO administrators/ UMMC PrEP specialists) will be reimbursed with a $40 electronic gift card, for their time and effort..

**DEPARTMENT OF HEALTH AND HUMAN SERVICES (DHHS) "REQUIRED EDUCATION IN THE PROTECTION OF HUMAN RESEARCH PARTICIPANTS"**
Since October 1, 2001, Lifespan, which is the nonprofit health care system of which Rhode Island Hospital is a part, has required that researchers and IRB members read Protecting Study Volunteers in Research (Dunn & Chadwick) and complete the related exam. This process has served as initial certification between 10/2001 and 5/2005. In June 2005, the Office of Research Administration contracted with CITI, a Collaborative Institutional (modular) Training Initiative program, for our Human Subjects protection and HIPAA training for all research personnel. Currently this program offers our researchers a basic human subject's protection course as well as a refresher course, which is required every three years. Documentation of successful completion is automatically generated and is printed directly by the researcher. For further information regarding Lifespan's Human Subject's Protection course go to: http://www.lifespan.org/research/IRB/MandatoryEdguidance.asp. Additional and continuing education opportunities for clinical researchers include the Office of Research Administration newsletter that is circulated to > 900 recipients every 6 weeks. Relevant information concerning research review is available on the ORA web page at www2.lifespan.org/research/. In addition to standard institutional research information, the web page contains links to other sites such as CenterWatch, NIH, PRIM&R/ARENA. Investigators and staff at all sites receive similar training and certification.

**Resource and Data Sharing Plan.**

Sharing of data generated by this project is an essential part of our proposed activities and will be carried out in several different ways. We will make our research available to the community of researchers interested in this topic to avoid unintentional duplication of research. After the results are analyzed, the information and results will be made available through presentations at national scientific meetings. We will distribute the results through the Center for AIDS Research Social and Behavioral Sciences Research Network for investigators who are interested in this topic. The results will also be made available through publications in scientific journals appropriate to the project's subject area. If the results appear promising, we will share the protocol and training manual with other relevant and interested clinics and community based organizations and it can be distributed through the Centers for AIDS Research and AIDS Trials Networks. We will also distribute the manual and procedures to other relevant community based organizations with the assistance of My Brother's Keeper (MBK), the organization working with us on this project. MBK has connections and affiliations with similar community organizations throughout this South and will facilitate dissemination of the findings.

**Clinical Trials Registration and Results Dissemination Plan**

Investigators at Rhode Island Hospital (RIH) will be responsible for the registration and submission of results for this project on ClinicalTrials.gov as outlined in the NIH policy (NOT-OD-16-149). The senior research assistant will work with the department research administrator and the P.I. to ensure that this project is registered within 21 calendar days of enrollment of the first participant. Results will be submitted to ClinicalTrials.gov within one year of the trials' primary completion date. Additionally, all consent forms, will include standard language related to posting of project results on ClinicalTrials.gov. Consent forms, containing the language below, will be submitted and IRB-approved prior to participant enrollment.
*"Additionally, a description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time."*
The senior research assistant will confirm with the RIH Office of Research Administration (ORA) when the clinical trial registration and project result submission have been completed to ensure compliance with internal policies and procedures.

**Data and Safety Monitoring Plan**

The nature of the population warrants the development of a Data Safety and Monitoring Plan.

**Roles and Responsibilities:**
To address the NIH policy for Data and Safety Monitoring, Drs. Brown and Brock have developed a system for oversight of the proposed study and its participants. The Data and Safety Monitoring Plan for this application will begin by implementing standard procedures for day-to-day monitoring of the study. Weekly meetings with the research team will be conducted to evaluate the progress of the trial and to review data quality, recruitment, study retention, and examine other factors that may affect outcome. Drs. Brown and Brock will meet to ensure subject recruitment, enrollment, and enrollment targets are all in accordance with our planned targets in this protocol. Participant experiences with the study procedures and the rates of adverse events will also be reviewed to determine any changes in participant risk. The project will designate two Independent Safety Monitors (one in Jackson, MS and one in Rhode Island) will review all Adverse events with the PIs quarterly or more frequently as indicated. The Independent Study Monitors will be academic researchers with experience in psychosocial intervention trials with adolescents.

**Trial Safety:**
Description of any specific events that would preclude a participant from continuing the study: Specific events that will preclude a participant from continuing the study include acquiring HIV and if a clinician determines it is not appropriate for the participant to continue the study based on his or her emotional distress. During any phase of the study, if research staff determines that a participant is an acute medical or psychiatric risk, Dr. Brock or a licensed designee will meet with them individually for further assessment. Acute risks would include severe medical illness, or the development of any other severe psychiatric symptoms or disclosure of sexual or physical abuse. Any participant who exhibits acute risks will be evaluated immediately by emergency room clinical staff or if less acute, by an independent clinician that day. Less severe medical needs or distress can be managed by staff or Dr. Brock over the phone or with an individual interview. Dr. Brock and/or staff will meet with participants and/or families to review concerns and to make referrals for continuing care as needed. Of note, members of the proposed research team have substantial prior clinical (medical and psychiatric) and research experience in care of PrEP-eligible and HIV-infected individuals as evidenced through their biographical sketches.

Description of any procedures in place for managing any medication related issues: N/A

Description of the potential risks and the measures in place to protect participants against foreseeable risks:
See Human Subjects section above

Description of the consent/assent procedures: See Human Subjects section above

Description of the mechanisms in place to protect subject privacy: See Human Subjects section above

Description of the trial stopping rules for the study: None, given the aim of the study, which is to study factors related to the use of Telemedicine for PrEP. PrEP is approved and telemedicine has been used widely in health care. There is not a control or comparison condition in this study. Of course, occurrence of serious adverse events could necessitate a change in procedures, design, or termination of the study. See Reportable Events below for details.

Description of the plan for management of incidental findings: Incidental findings will be managed by staff or Dr. Brock. Patients will be referred to the appropriate clinical resources.

Description of the process for the disclosure of any conflicts of interest that may potentially challenge participant safety or bias the data and how the conflict will be managed: Rhode Island Hospital has a policy in place for disclosing any potential conflicts of interest before a grant is submitted. Researchers must report any equity interest in anon-publicly traded entity and any income from intellectual property rights. Special rules are in place for PHS funded investigators. Investigators are required to disclose financial interests related to their institutional responsibilities (teaching, research, clinical, and administration). Training regarding financial conflicts of interest is now mandatory.

Description of the procedures for ensuring compliance with the monitoring plan including requirements for data reporting across study sites: N/A

Description of the data security in place to protect the confidentiality of the data and any limits to confidentiality: See Human Subjects section above

**Reportable events:**

1. Serious Adverse Events: The NIH defines a serious adverse event as “any untoward medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject’s participation in the research study that: 1.) results in death; 2.) is life-threatening (places the subject at immediate risk of death from the event as it occurred; 3.) results in inpatient hospitalization or prolongation of existing hospitalization; 4.) results in persistent or significant disability/incapacity; 5.) results in congenital anomaly/birth defect; or, 6.) based upon appropriate medical judgement, may jeopardize the subject’s health and may require medical or surgical intervention”. The PIs will immediately report any serious adverse events (SAEs) to the UMMC IRB and the Rhode Island Hospital IRB immediately by telephone and by written report within 24 hours of our receipt of information regarding the event; SAEs will also be reported in writing to NIH. Actions taken by the IRB in response to SAEs will also be reported to NIH, as will reports of changes or amendments to the protocol as a result of an SAE. Reports of changes or amendments to the protocol in general must be requested first in writing to the Lifespan IRB, which then will grant or deny permission to make the requested change or amendment in protocol. Modifications to study aims or design will also be submitted to NIH for approval prior to instituting them. Finally, if significant medical or mental health risks occur during the study period evaluation by the site’s hospital emergency department will be immediately initiated to determine whether hospitalization or urgent care is needed. In the event that a research participant either withdraws from the study or the investigator decides to discontinue a research participant due to SAE, the research participant will be monitored by the investigator via ongoing status assessment until either a resolution is reached (i.e. the problem requiring hospitalization has resolved or stabilized with no further changes expected), the SAE is determined to be clearly unrelated to the study, or the SAE results in death. Outcome of all SAEs will be periodically reported to NIMH. A summary of the SAEs that occurred during the previous year will be included in the annual progress report to NIMH.

2. Any other adverse events (e.g., causing interference with usual activities or requiring treatment) and which appears definitely, probably, or possibly related to study participation will be reported to the IRB as indicated under #1 above in writing within 10 working days.

We will inform NIH of actions, if any, taken by the IRBs, or changes in our protocols as result of any of the reviews.