Title: A Mobile Intervention to Improve Uptake of PrEP for Southern Black MSM

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## SIGNIFICANCE

The strategy of using anti-retrovirals as a form of HIV prevention, also known as pre-exposure prophylaxis (PrEP), has received considerable attention and holds tremendous promise (1,2). Despite the advancements supporting PrEP efficacy and its availability, uptake of PrEP by many men who have sex with men (MSM) has been slow. In particular, uptake has been slow for young Black MSM (BMSM) that live in the Southern United States (23-27,130). This is a significant issue because BMSM living in the South have particularly high rates of HIV. 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 5 times more likely than white MSM in the South to become infected with HIV (15). The site of this proposed project, Jackson, MS, has the highest prevalence of HIV among urban MSM living in the U.S. (39.5 per 100 MSM) (15). The premise of this project is to develop a targeted mobile messaging intervention to improve linkage to PrEP care for young BMSM in Jackson, MS who are at high risk for HIV infection. Interventions that improve linkage to PrEP care are urgently needed for BMSM in the South.

**Knowledge and access to information about PrEP remains low in many MSM communities.** This has restricted linkage and uptake of PrEP, and ultimately the effectiveness of PrEP, at the community level (19-21,23-28). To use PrEP, individuals must have accurate knowledge, understand its risks and benefits, and be willing to take it. Studies show that many high-risk individuals who would be excellent candidates for PrEP have not taken it simply because their knowledge about it is limited (19,20). In one study conducted among young MSM in 2013, only 27% of study participants were aware of PrEP (20). Knowledge about PrEP has increased recently (28,29), however, some studies show that awareness remains markedly lower among men of color, those that live in southern and rural areas in the U.S., and those whose primary care providers are not aware that they have sex with men (129). Among, 436 BMSM surveyed in Atlanta, GA, from January 2012 (6 months prior to PrEP approval) to March 2014 (20 months after approval), only 20.5% were aware of PrEP before approval and only 23.4% were aware of PrEP after approval (23). Improving Southern, young BMSM's knowledge about PrEP is critical for successful linkage to PrEP care.

**Strengthening the relationships young BMSM have with providers is critical for successful PrEP uptake.** Young BMSM who are at highest risk of HIV infection are historically underserved by healthcare (31- 33,41). Therefore, engaging patients in care is challenging and requires support for doctors and patients (41-42). Brooks et al. found that heightened concerns over potential side effects to PrEP pose a significant barrier to engagement and linkage to PrEP care for BMSM (26). In the Southern US, homophobia, stigma, and clinician/ patient communication all influence initiation of PrEP (10-12). Eaton et al. surveyed 398 HIV- BMSM at a Black Gay Pride event in the South Eastern US (23). 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 was also identified as a barrier to engaging in PrEP. Around one-in-five participants reported that "people of my race cannot trust doctors and health care workers" (21%), "people of my race should be suspicious of information from doctors and health care workers" (19%), and "people of my race should be suspicious of medicine" (19%). Strengthening communication and connection between medical caregivers and the young BMSM community are crucial components to improving linkage and initiation of PrEP care in the South (12,21,29,33). Accurate information about PrEP and issues such as potential side effects will need to be shared in a method that considers a history of mistrust to effectively to allay concerns among Southern BMSM (33).

**Addressing structural/economic barriers to receiving PrEP related care is imperative for BMSM.** Effective interventions to improve PrEP must assist individuals when navigating insurance companies and enrolling in medication co-pay assistance. In 2012, approximately 19% of African Americans did not have health insurance, compared to 11% of whites (17,30). The situation is particularly concerning for southern BMSM since some of the highest levels of poverty in the US are in the South. Six of the ten states with the highest poverty levels are located in the South (30). 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 (30). Interventions that help navigate the economics of getting on PrEP, such as the PrEP co-pay and full medication assistance programs, are essential to the successful implementation of PrEP in the South, where poverty is highest.

**Decreasing stigma about PrEP and HIV can improve linkage and initiation of PrEP related care for BMSM.** Participants in PrEP demonstration studies have reported that stigma effects their decision to initiate PrEP care (36-42). Gay men have reported a fear of being labeled as "promiscuous" by doctors and "Truvada whores" by friends These stigmatizing labels, infer that PrEP is associated with "unbridled" sex and may be a barrier to care (37,38,40,42). Furthermore, the only currently available PrEP method, Truvada, is the same medication used to treat those infected with HIV. In the South, where HIV-associated stigma is high, and HIV is prevalent, being seen with Truvada can be perceived as being HIV infected, which is a further barrier (40-41). HIV-related stigma is particularly widespread in the South (10,11,16,20,21,42). Interventions must replace negative community attitudes about individuals using PrEP with positive impressions of PrEP users as individuals who take care of themselves and others (63).

**PrEP and HIV Prevention Interventions for young BMSM need to be interactive, cost-effective, and easily integrated into existing clinical care.** We will use interactive, tailored text messaging and appealing free web content (publicly accessible educational websites and YouTube videos) to promote linkage to PrEP care and decrease HIV preventative behaviors. A cost effective, interactive intervention that utilizes mobile technology is particularly compelling for use with young MSM. MSM make greater use of cell phone technologies than heterosexuals (50) and there is evidence that mobile phone teledensity (i.e. number of phones per person) in black Southern communities has outpaced black communities in the Northeast (48-52). On a monthly basis, young Black adults in the U.S. spend nearly 56 hours using smartphone apps or Internet browsers and 2.5 hours watching videos on their smartphones (45,46). With such widespread use of mobile technologies, it is not surprising that data supports the use of mobile technology to improve health (126-128). Meta-analyses have shown that mobile interventions are most effective when they are interactive and tailored (126-128). The widespread appeal and use of smart phones and promising data supporting mobile messaging interventions for health promotion create a unique opportunity. Information about PrEP and HIV prevention can be delivered to young, southern BMSM during their leisure time, outside of the STI/HIV clinic, and in a manner that is cost effective and easily scalable (44-49,53-55).

**Interventions to decrease behavioral risk for STIs are still needed in the era of PrEP.** Although there is great optimism about PrEP, a concern is that persons who choose to utilize PrEP might take more sexual risks or decrease traditional risk reduction strategies (such as condom use and HIV/STI testing of partners) (56,57). Behavioral models (Behavioral Disinhibition and Risk Compensation) suggest that risk could increase by loosening of self-imposed constraints or by decreasing individuals' perceptions of HIV risk. This, in turn, could lead to increased incidence of STIs (57-59). Evidence is mixed regarding the actual impact of PrEP on risk-taking and STIs among young BMSM. Some surveys and studies find that most MSM do not anticipate any change in their condom use while on PrEP, although many perceive little risk for acquiring HIV from unprotected anal sex (60,62) (60,64). However, other studies suggest that it would be difficult to take PrEP daily and still consistently use condoms (60,65). Increases in risk behaviors have been documented in the context of microbicide trials, vaccine trials, and among patients living with HIV on antiretroviral therapy (61,71,72). Therefore, HIV prevention counseling and testing remains clinically relevant and should accompany PrEP related counseling, as recommended in guidelines (67), especially in the South, which is disproportionately affected by sexually transmitted diseases (STDs) (66). In this project, text messaging and theoretically- informed publicly accessible web content will be used to promote HIV/STI prevention behaviors (e.g. condom use, STI testing).

**The Information-Motivation-Behavioral Skills (IMB) model is a well-established conceptualization for improving engagement in care as well as decreasing HIV risk behaviors.** HIV prevention interventions and linkage / engagement in care interventions based on the IMB Model have demonstrated efficacy (75,77). Reviews have suggested that interventions guided by theory are more efficacious than those not driven by theory (75-78). According to the IMB model, health information, motivation, and behavioral skills are the fundamental determinants of health behavior. In order for a PrEP-related intervention to be successful, a person must learn information that is directly relevant to HIV prevention and treatment with PrEP. Knowledge is a necessary but not sufficient condition for change. Personal motivation to engage in HIV preventative behavior or engage in treatment regimens (attitudes about health) and motivation (perceived social, cultural, and structural support for performing these acts), are essential for change. Finally, skills for performing healthy behaviors and a sense of self-efficacy must be easily applied to an individual's cultural, social, and structural setting (75-78). Engagement in PrEP care can be facilitated by accurate knowledge of medication benefits, self efficacy for care, and structural support (88,89). Our intervention will address these factors within the IMB Model and the local/geographic, structural and racial context. The IMB model is broadly applicable and can be used to organize and guide theoretically consistent and culturally, structurally informed intervention content (73).

## INNOVATION

This project is innovative because it will develop and test a targeted, tailored intervention that:

1) Makes use of free, already existing, publicly available Internet content to deliver a theoretically informed intervention.
2) Improves attendance at a PrEP Services Appointment in order to improve linkage and engagement in PrEP care. No other published study has attempted to improve this important step of the PrEP cascade for Southern BMSM.
3) Uses carefully selected online content to begin to address cultural barriers (such as stigma) and structural barriers (such as payment) to initiating engagement in PrEP care. Structural barriers will continue to be addressed at the PrEP Services Appointment.

## APPROACH

**Our CFAR Developmental Project found that free web content decreased HIV risk behavior in young adults in Providence, RI.** We tested the preliminary efficacy of utilizing easily accessible, educational YouTube videos and online material for HIV prevention in a small grant from the Center for AIDS Research (CFAR) (PI: Whiteley). The

project enrolled 80 diverse young adults (mean age 18.6, 62% male, 52% Black/African American, 36% Hispanic, 47% non-heterosexual). Qualitative interviews with 20 of these diverse young adults provided data and feedback on publicly available HIV prevention Internet content (80). After choosing content that was considered culturally relevant and appealing by the young adults, a new set of diverse young adults (N=60) were sent 8 of the most highly rated, appealing and informative websites as links over 4 weeks as part of a Mobile/Internet HIV prevention Intervention. The links included publicly available online YouTube videos and websites (81). Participants were randomized to the Mobile/Internet Intervention (n=31) or to an assessment only condition (n=29). There were no significant differences in demographic factors (age, race, ethnicity, sexual orientation) between conditions. All the young adults in the study reported a history of vaginal and/or anal sex. Retention for the three-month post-intervention assessment was 85%. An analysis of co-variance (controlling for baseline scores) found a significantly greater improvement in reported HIV self- efficacy (F= 5.71, p=0.021) for those in the intervention compared to the control condition at 3 months follow up. There was also a significant reduction in unprotected vaginal or anal sex, 6.6% (internet intervention) vs. 47.6% (control) (AOR= 7.77, p=0.033, adjusting for baseline scores). Nearly half of the sample identified as MSM, and restricting the analyses to that sub-group, the results were very similar. At the three-month post- intervention assessment, MSM (50% African American) in the intervention group reported greater HIV self- efficacy (F=3.84, p= 0.063) and less unprotected sex (18.2% vs. 50.0%, AOR= 12.85, p=0.089) (79). The method of using carefully selected publicly available Internet content was highly acceptable and feasible for this diverse group of young adults. Participants in the intervention provided detailed comments about the relevance of the publicly available online content in qualitative interviews at study end, after the last assessment. Participants stated that they "liked the mix of videos, and stuff to read." BMSM participants stated, "I learned a lot, the way I like, with videos, and online." Participants also stated, "It's good being able to view stuff any time I want, on my phone," and "I liked getting the texts a couple times each week." Of note, 89% of the young adults in this small study in Providence, RI had smart phones (80).

**This method of texting publicly available links was preliminarily tested for acceptability in Jackson, MS.** Thirty-three young, PrEP eligible BMSM, seen in the STI/HIV testing at UMMC during one week (October 12th-16th, 2015) were asked if they owned a smart phone, and if they wanted to receive links to web content about PrEP on their smart phones. Of the UMMC sample (n=33), 100% had smart phones (30 iPhones, 3 Androids), and 28 wanted to receive links about PrEP, and none had started PrEP. We texted the following link to these 28 young BMSM: https://www.youtube.com/watch?v=aVvhMsFRa-M&feature=youtu.be&app=desktop. Participants received the following text: "The link above is a video about PrEP. Let us know what you think of this link (by replying back to this text)." We chose to identify the link as PrEP-related so that participants would know the subject material prior to opening the link in a public setting. Participants were asked to text back with a rating of the likeability of the link on a scale from 1 (hated it) to 10 (loved it) and the mean rating was 8.9 by the 25 who responded. Participants also rated how much they learned from the link on a scale from 1 (a little) to 5 (a lot) and the mean rating was 4.8. We also found that participants were more likely to reply to texts when the texts were sent in the afternoon, on weekdays between 3-5pm.

**Qualitative Work is Necessary to Make a PrEP Linkage to Care /HIV Intervention that is Relevant for Young BMSM living in the South.** Through formative qualitative research we will carefully select publicly available online content, and design interactive text message queries, that are tailored to BMSM living in Jackson, MS. Our team's expertise in qualitative methods will ensure that stigma and structural barriers, often overlooked in brief HIV prevention/PrEP interventions, are addressed in order to measurably improve PrEP knowledge and linkage to care. Dr. Brown has utilized qualitative methods to tailor HIV prevention interventions in four NIH-funded RO1 RCTs (82-87,91). One intervention outcome paper, with an impact lasting for up to 9 months, received the Reiger Award for Scientific Achievement from the American Academy of Child and Adolescent Psychiatry (120). Dr. Operario has published multiple research papers involving MSM communities, documenting the co-occurrence of HIV infection, sexual risk behaviors, and substance use. He has particular experience conducting qualitative research and using qualitative and quantitative findings to develop behavioral HIV prevention interventions with MSM (92-95). Dr. Operario has completed and published formative qualitative work exploring PrEP knowledge, willingness to use PrEP, and risk compensation beliefs among MSM living in Providence RI. In a qualitative focus group, at-risk MSM identified potential benefits of PrEP as increased intimacy, and reduced anxiety, but expressed concerns about side effects, cost, insurance coverage, availability for low-income men, FDA approval, and PrEP's potential behavioral impacts on the MSM community. Efficacy was of paramount concern; some reported that they would not use PrEP without certainty of benefit (92). Dr. Operario's other qualitative research has investigated PrEP message framing in the US and PrEP experiences of MSM and female sex workers in Kenya (94,95). Dr. Operario's expertise will guide the proposed qualitative interviews in this project to understand individual, community, and structural barriers relevant to PrEP uptake. These interviews will ensure that the IMB-consistent content and texts chosen for this intervention are engaging, acceptable, and address unique community and cultural barriers.

**Design**

This research includes:

(1) a **Development Phase** in which we will assemble a preliminary PrEP Mobile Messaging Intervention based on our preliminary work and the expertise of our investigators during months 1-6.
(2) a small, pilot **Controlled Trial Phase** (n= 70) in which we will evaluate the preliminary efficacy of the PrEP Mobile Messaging Intervention in Jackson, MS.
(3) a post-RCT Phase (n=20) in which we will assess the acceptability and relevance of the intervention material among RCT participants.

**Development Phase**

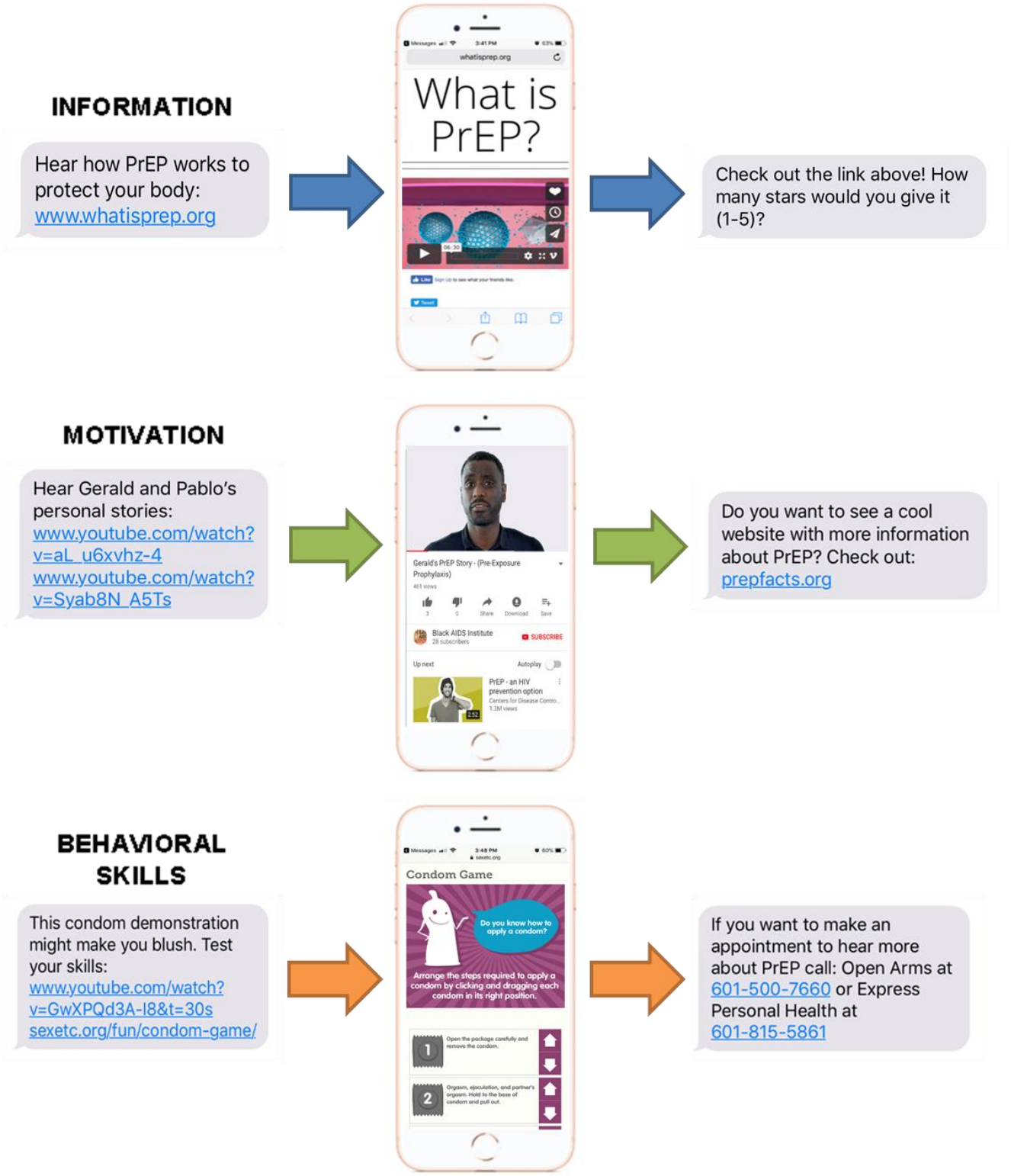
The goal of the development phase is to assemble the IMB PrEP Mobile Messaging Intervention from publicly available online content and design messages that will improve engagement in care.

**The Preliminary PrEP Mobile Messaging Intervention (Figure 1 below, and Appendix A).** The preliminary rough draft of the PrEP Mobile Messaging Intervention employs graphics, characters, and video content specifically chosen to be appealing to young Black MSM. Texted publicly available web content will target IMB constructs: information, motivation and behavioral skills. These IMB-consistent messages aim to: 1) increase knowledge about PrEP, 2) increase motivation and skills to improve attendance at a PrEP Services Appointment following STI/HIV testing, 3) decrease structural barriers to engaging in care, 4) decrease HIV risk behaviors. Intervention text messages will have links to web information, videos, quizzes and games focused on providing factual information about PrEP and HIV transmission, HIV prevention, and correcting misperceptions about HIV and PrEP. As currently drafted, young Black role models are used to convey basic information about PrEP. Role models will also address motivation, such as one's personal values for safety, health care, peer rejection, perceived stigma, and community norms. Intervention material will reduce PrEP misconceptions that fuel stigma. Textable online and video material shows Black MSM discussing how PrEP has decreased their anxiety about infection and how they have handled discussions with partners.

**Inclusion Criteria.** All young BMSM ages 18-35 years old who visit the STI/HIV testing clinics at UMMC, and who are eligible for PrEP according to current treatment guidelines (67) will be eligible for enrollment in each phase of study according to the following criteria: 1) English speaking, 2) eligible to receive prophylactic antiretroviral treatment, 3) not enrolled in another PrEP related study or HIV prevention study, and 4) able to give consent/assent and not impaired by cognitive or medical limitations as per clinical assessment. There will not be overlap between subjects in the Development and Controlled Trial Phase. We are enrolling only BMSM between the ages of 18-35 because they are the sub-group most at risk for acquiring HIV in Jackson, MS. Limiting the study to young BMSM will allow for the development of a mobile intervention that is targeted, acceptable, and engaging for this specific population. Enrollment of participants for this study will only be in Mississippi. There will not be any participants enrolled in Rhode Island.

Intervention material also addresses behavioral skills such as talking the doctor about PrEP, using condoms while on PrEP, and strategies to receive support around PrEP and medical care. The intervention content will also address structural barriers. Mobile information will be sent to help participants navigate health insurance, medication assistance programs and co-pay assistance programs. **Importantly, the major goal of this intervention is to provide motivation and skills to help people attend a PrEP Services Appointment after their HIV/STI testing.** At this follow-up appointment, **the clinic care coordinator** will meet with participants to further discuss structural barriers. The PrEP clinics already have a care coordinator to help with scheduling, transportation, and engagement with assistance programs during the PrEP Services Appointment. Clinic Care Coordinators also help with access to additional primary care/health care services. (Note: The Clinic Care Coordinator is an integral part of care provided at the clinics and is available to participants in both conditions)

**Figure 1: Sample Interactive Text Messages with Potential IMB Mobile Content**




**The Intervention will be interactive and tailored to participants.** Meta-analyses indicate that tailored messaging and bidirectional communication are two elements of effective text message interventions (126- 128). The text

message platform will be a HIPAA compliant text message service with secure data capture. Participants will be texted questions following receipt of intervention material of such as, “Check out the videos above! How many stars would you give them (1-5)? Please reply with a count for each video!” Prompts like this will allow the intervention to be interactive and the content is tailored to the informational, motivational, behavioral skills, and structural needs of individual participants. The platform will also help participants contact the Clinic Care Coordinator to discuss any questions or concerns about the intervention material, and assist them in making an appointment. After receipt of each text with intervention material, participants will be texted “If you want to make an appointment to hear more about PrEP call: Open Arms at 601-500-7660 or Express Personal Health at 601-815-5861.” Above, (Figure 1) are sample interactive text messages and pictures of accompanying IMB web content that could be used in the Intervention. Appendix A has more examples of possible web content and texts that could be used in the Intervention. Qualitative interviews with BMSM in Jackson, MS, will ensure that the IMB material and texted queries are relevant and appropriate to community context (e.g., stigma, structural barriers).

**Iterative development of the PrEP Mobile Messaging Intervention.** During months 1-6 a thorough review of available PrEP and HIV prevention web content will occur and potential intervention content will be selected. We completed a review of publicly available, existing websites that indicates the existence of an abundance of PrEP-related Internet content. This scholarly review categorized 62 websites and 89 videos by their Informational, Motivational, Behavioral Skill building components and also rated their quality and interactivity (125). The investigators will continue to search for new online material and sort material for appeal, understandability, utility, and enjoyment for young black MSM, as well as consistency with the IMB Model. Additionally, web material will also be assessed for addressing structural barriers (e.g. web material on payment for PrEP, enrollment in assistance programs, insurance).

**Qualitative interviews** will focus on the relevance and utility of the presented content and its appeal, and will solicit suggestions for potential improvements. Feedback will be elicited after exposure to mobile material in a secure clinical space at the UMMC STI/HIV testing clinics. All qualitative interviews will be audiotaped. We will ask about general reaction to the preliminary web content and texted all texted queries. Participants will be asked about the acceptability and relevance of texts and mobile content, actions and graphics as they relate to race, culture, and structural factors. We will also concentrate on deeper, or more complex, emerging themes. For example, if there are particular barriers to engagement in PrEP care, such as misconceptions about the perceived risk of HIV, more content will target this misperception (87,121,122). If other barriers to engagement in PrEP-related care, such as misinformation about side effects or mistrust of the medical community, more content will target these issues. For example, participants will be asked “As a black, gay male, how worried are you about getting HIV? How effective do you think PrEP is at preventing someone from getting HIV?” “How comfortable do you feel talking to your doctor about sex, HIV and PrEP?” After viewing preliminary web content, participants will be asked, “Which parts of this website or YouTube video would influence how concerned you are about HIV?” “Do any parts of this website or video help you feel prepared start on PrEP?” “Do any parts of this website help you to know how to pay for PrEP?” “How could these messages be made more relevant to you, your friends, and your partners?” Major topics and sub-topics from the interviews will be coded. Additional codes will be generated for topics that invariably arise and that may have significance to the project. We will perform interviews on a sufficient number of each relevant sub-group defined by age (divided at 25 years), level of interest in starting PrEP, identifying as gay bisexual, or neither, until there is redundancy in themes and general feedback. All interviews will focus on how sexual orientation, race, stigma, culture, age and structural factors influence information, motivation and behavioral skills for the major targets of the intervention.

After the first 15 qualitative interviews, a preliminary PrEP Mobile Messaging Intervention will be assembled. This preliminary intervention will be assessed with another 15 young BMSM using the similar qualitative procedures until thematic redundancy is achieved. These iterative design efforts will provide an intervention that is culturally acceptable, as well as theoretically informed. Throughout the development phase, members of the research team will iteratively review, re-review, and assess the clinical utility of all intervention components via the BMSM participants’ qualitative feedback, and audiotaped session materials. We will use the Rapid Approach to examining all interview data, which is appropriate when interview topics are tightly focused (130). The team will assess the strengths and weaknesses of intervention components and indicate revisions. Specifically, we will assess the intervention content’s suitability, the ability of the intervention content to engage MSM, and its ability to target STI/HIV-related behavioral change with material and techniques consistent with the IMB model. Additionally, the team will review the Intervention material for relevance, conceptual clarity, and potential technological problems. The qualitative interviews will be a major focus for Drs. Whiteley, Operario, and Brown, who have a specialized interest and experience in this area. For example, Dr. Brown completed a qualitative and quantitative study of a culturally tailored STI/HIV prevention campaign for African American teens with a TV/radio media component (IMPACCS, U01 MH066785) (87). Dr. Operario is the PI on an R21 that examines PrEP feasibility, acceptability, and appropriate PrEP-promotion content using qualitative methods. Our team’s preliminary ethnographic and qualitative experience, and the information gained from the qualitative interviews will ensure that a refined and culturally targeted mobile PrEP/HIV prevention intervention is assembled.

**Quantitative assessment.** Throughout the development phase, participant's satisfaction with the PrEP Mobile Messaging Intervention materials will be surveyed using a modified version of the Client Satisfaction Questionnaire (CSQ-8). This is an 8-item measure with good reliability and validity (103). Participants will also complete a modified Session Evaluation Form (SEF), which has 13 items that reflect areas of feasibility and perceived utility of the intervention (102). Responses to items on these questionnaires will also help determine feasibility and acceptability of all potential intervention material. Web material that consistently receives low CSQ-8 or SEF scores (< 24 on the CSQ and < 30 on the SEF) will be replaced with higher scoring content.

**Randomized Controlled Trial Phase**

**Overview.** During months 18 to 30 we will evaluate the impact of the IMB Mobile PrEP/HIV Intervention, compared to Enhanced Standard of Care (ESC) in a randomized controlled trial with 70 newly recruited black MSM with the same eligibility criteria as in the Development Phase. We will compare conditions on attendance at a PrEP Service Appointment at 16 weeks using data from the electronic medical record as well as by self- report. Conditions will also be compared by self-report on PrEP and HIV-related knowledge attitudes, skills and risk behaviors at baseline, 4 weeks (immediate post-intervention) and at 16 weeks.

**The PrEP Mobile Messaging Intervention.** The PrEP Mobile Messaging Intervention will employ graphics, characters, and video content tailored to young Black MSM living the Southern United States. Qualitative interviews (See Development Phase above) will ensure that the assembled content is culturally, racially, and gender relevant and appropriate for our target population. This condition will make use of interactive mobile technologies, thus enhancing appeal. **Procedures.** After consent and assessment, each participant will receive texted messages with intervention content and follow-up queries over 4 weeks, on their mobile phones, or email address if he does not own a phone. The preliminary intervention is composed of 26 texts with links to web content and queries about content. Texts will be sent twice a week over 4 weeks. Immediately after receipt of intervention material, participants will receive follow up queries asking them to rate the content they received (on a scale of 1 – 5 stars). The preliminary timing and length of the texts and web activities are based on the timing and length of the efficacious CFAR HIV prevention project reviewed in preliminary studies (PI: Whiteley) (79). Participants in the Development phase offered important feedback about the timing and number of texts that has been incorporated into the RCT. Participants will receive all intervention content in the afternoon. Separate texts will be sent to ask for a rating and with Clinic Information. Intervention content will address information, motivation, and skills for engagement in PrEP-related care, structural barriers to care (such as enrollment in assistance programs), and HIV/STI preventative behaviors. Each mobile link sent to participants will take between 5-10mins to read, listen to, or interact with. Participants can engage the text message material on their phones, at any place that is convenient and comfortable. Participant's weekly text messages will be sent from a HIPAA compliant web-based platform. (See Protection of Human Subjects).

**Technology for measuring fidelity and dosage.** The mobile platform will track the number of texts each individual participant receives and how each participant answers texted queries. The resources of the study will not allow for more detailed participant data such as if a participant views material multiple times, cuts a video short and watches it later, or searches the web outside of the mobile platform we are using.

**Enhanced Standard of Care (ESC) condition.** The impact of the IMB Mobile PrEP/HIV Intervention will be compared to Enhanced Standard of Care (ESC). At both UMMC STI/HIV testing clinics, Dr. Mena and his staff assess patients for PrEP eligibility and HIV risk (as defined by the CDC guidelines) (67) and feedback is given to each patient on their current risk behavior and future plans (personal risk summary). Patients are given contact information for the Clinic Care Coordinator. This is consistent with CDC guidelines for PrEP. Patients in both conditions will receive the ESC clinical encounter described here and be followed for assessments. The Clinic Care Coordinator has always been available to all patients seen in the HIV/STI and PrEP clinics, and will continue to be available to both conditions. Only patients in the IMB Mobile Messaging Intervention will receive the additional 26 text messages and interactive queries.

**Other Design Considerations**

**Intervention contamination.** BMSM participants will continue to have Internet access outside of the IMB PrEP/HIV Mobile Intervention and it is possible for them to navigate off the page that holds their texted mobile assignment or module. It is also true that BMSM might peruse other online or mobile materials other than the assigned intervention activity. Similarly, we cannot prevent young BMSM from talking to others in or out of the project about what they have learned about PrEP or HIV prevention. This type of contamination is often difficult to fully control, even with face-to-face interventions, because participants can continue to pursue knowledge from the Internet, books, magazines, friends, and other health professionals outside of any intervention. However, we are very interested the differences in the number of interactions that young BMSM have with the intervention activities and this will be measured and monitored at assessments and using HIPPA compliant data from our text message service (see Fidelity and Dosage above). Cross talk between conditions also be assessed and adjusted for in the analyses, if needed.

**Choice of comparison condition.** We considered several alternative comparison conditions. Because the mobile messaging intervention is meant to add on to and improve ESC and **enhance** linkage and engagement in PrEP-

related medical care, a no-treatment or delayed-treatment condition seems inappropriate. CDC guidelines exist for PrEP medical care (67) but we are aware that providers may have differing interpretation of the guidelines and that the clinical encounter could vary between patients. These factors make "real-world," naturalistic care difficult to monitor and describe. We considered scripting PrEP related encounters at the time of STI/HIV testing, training clinicians, and audiotaping the encounters but, because there is no "state of the art" evidenced-based medical script for PrEP and this approach is restrictive and creates a medical care condition with unknown validity. We also considered sending general health promotion texts (not PrEP-related) to the comparison group to control for time, attention, and the novelty of seeing texted information. However, this project aims to collect data on the feasibility, acceptability and preliminary impact of the IMB PrEP Mobile Messaging Intervention at a time when a proven enhancement to linkage to PrEP related care does not exist. These factors make a Health Promotion comparison premature. With the chosen design, the project will be able to describe the enhanced standard of care for all patients in the UMMC clinics and the IMB messaging intervention that adds on to current clinical care, but does not replace or modify it.

**Access to Mobile Phones and Tracking.** Our previous work in Jackson MS has shown that all, or nearly all, of participants will own smartphones (See Preliminary Studies). Although data suggest that young BMSM have access to mobile phones on a daily basis, in some instances young BMSM might not have access to a phone, or their access could be limited or lost. In these instances, BMSM will be provided with an email version of the intervention, and/or access to a computer in the UMMC clinics to view intervention links. We anticipate that some will change phone service. We will gather detailed contact information on participants that includes all modes of contact (email, all phones, social media accounts) and secondary contacts (family and friends). We will use this information to get new phone numbers if needed. We have used this detailed contact information in our other NIH studies to maintain contact with participants for as long as three years.

**Measures and Assessments**

**Assessments.** Assessments will occur at baseline, immediately post intervention (4 weeks), and three months post intervention (16 weeks) and will take approximately 20 minutes to complete. The enrollment will take place in a quiet room in the HIV/STI testing clinics at UMMC and the baseline assessment completed through REDCap (123). REDCap is a free, secure, HIPAA compliant web-based application designed to support data capture for research studies (See Human Subjects). Our research team currently uses REDCap in our other research collaborations in Jackson, MS. The 4 and 16-week assessments will be done via emails or texted links. A REDCap survey will be emailed or texted to each participant's unique phone or email address. If patients cannot complete assessments online, by computer or phone, they can utilize a computer at the UMMC STI/HIV testing clinics. Clinic records will also be coded for attendance at the PrEP clinic for a PrEP Services appointment or receipt of a PrEP prescription at 16 weeks. We will use tracking procedures (See Sample and Recruitment) to maintain contact with each participant.

**Measures.** A computer self-interview using REDCap will be used to assess behavior since it is confidential, allows for complex branching/skip patterns, and detects greater rates of risk behavior (123). Standard items will be administered to gather demographic data (including age, educational level, sexual orientation, SES, race, ethnicity and stability of housing). The measures below will be used to evaluate HIV and PrEP-related knowledge, attitudes, and behavior (See Table 1 below for linkage between constructs and intervention).

Table 1. Linkage between constructs, intervention foci, and assessment instruments

| IMB Constructs | Intervention Foci | Assessment Instruments |
|---|---|---|

| | | |
|---|---|---|
| Information: PrEP and HIV risk knowledge | Increased HIV/PrEP knowledge, perceived vulnerability to HIV/STIs | HIV/PrEP Knowledge Scales |
| Motivation: Risk attitudes, intentions and self-efficacy for starting PrEP and engaging in PrEP related medical care | Improved motivation for PrEP and related medical care, Increased motivation for safer sex, Decreased perceived structural and stigma barriers | IMB PrEP Care Motivation Scale, Self-Efficacy for PrEP Care, Rollnick's Readiness Ruler |
| Behavior: Attendance at PrEP prevention appointment, sexual risk | PrEP prevention appointment, safer sex skills | Attendance at PrEP Services Appointment, receipt of PrEP prescription, and sexual risk self- report |

**Primary outcome**

**Attendance at a PrEP Services Appointment:** With participant consent, staff at the STI/HIV testing clinic will abstract from the electronic medical record any PrEP Services Appointment, and any PrEP related care, at 16 weeks. This study is occurring in PrEP clinics in Jackson which are affiliated with UMMC. Participants are recruited from the STI/HIV clinics run by the same medical staff, including Dr. Mena. Virtually no one will begin PrEP at another location.

**Secondary outcomes**

**PrEP knowledge:** The PrEP Knowledge Questionnaire: Because there is no PrEP knowledge scale with published psychometrics, we will use selected items from 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 portion of this study (See Appendix B).

**Personal and social motivational readiness for PrEP care:** Rollnick's Readiness Ruler (108) will be used to assess motivation for engaging in PrEP care. Respondents rate how ready they are to: (1) attend at PrEP Service Appointment, (2) begin PrEP and (3) go to PrEP related medical appointments on items from 1 (not ready) to 10 (ready to engage). Participants will also complete the 10-item, Likert style IMB PrEP Motivation Scale from the LifeWindows Project Team. It has been modified to assess personal and social (culture and structure) motivations for PrEP, rather than ART, and is used in our on-going study of PrEP adherence study (1R34 MH104068) in consultation with Dr. Jeffery Fisher, one of the developers of the IMB Model. (See Appendix B) (109).

**Risk Behavior and Perceived Risk:** Selected items from two scales will be used. The Risk Behavior Assessment (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 types of sexual behavior (i.e., anal, oral, vaginal) in the past 3 months, frequency of sex, age of sexual debut, and number and gender of partners. Additional questions cover use of barrier method contraception, sex with high-risk partners, exchanging sex for drugs, reasons for condom nonuse, frequency and quantity of substance use and having sex while using alcohol/drugs (124). The second scale is the 10-item Perceived Risk of HIV Scale (Napper, Fisher, and Reynolds, 2012). The instrument consists of Likert style items and assesses how participants think and feel about their risk of HIV infection. The scale has excellent internal consistency (0.88).

**Receipt of a PrEP Prescription:** With participant consent, staff at the STI/HIV testing clinic will abstract from the electronic medical record any prescription written for PrEP at 16 weeks. This study is occurring in the only two PrEP clinics in Jackson and both are affiliated with UMMC, and directed by Dr. Mena. Virtually no one will begin PrEP at another location.

**Connor-Davidson Resilience Scale (CD-RISC):** Selected items from the CD-RISC (Campbell-Sills and Stein, 2007) will be used to measure participants' resilience and ability to cope with adversity. Questions are answered on a 4-point Likert scale with responses ranging from 0=not true at all to 4=true nearly all the time. The 10-item version of the scale has an alpha value of .85, indicating that the revised scale has good reliability.

**Coping with Homosexuality:** Selected items from the Identity Management Strategies Scale will be used to assess participants' coping and identity management strategies regarding their homosexuality (Button et al., 2004). This measure has four subscales (counterfeiting, avoidance, acknowledging, and advocating) and consists of Likert style items. The current study will also ask three questions relating to the social support for each of the participants. This scale has an internal consistency of .78 (Choi et al., 2016).

**Response to Links:** Participants' satisfaction with the PrEP Mobile Messaging Intervention materials will be surveyed using a modified version of the Client Satisfaction Questionnaire (CSQ-8). This is an 8-item measure with good reliability and validity (103). Participants in the intervention arm will also be asked about if they have shared the links with anyone. Participants in the enhanced standard of care arm will be asked if anyone has shared any PrEP-related websites or videos with them.

**Moderators**

In addition to demographic factors, a number of other factors might influence linkage to care, 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 intervention.

**Demographics:** Participants will be asked 12 general demographic questions (birthday, gender, race, education level, etc.).

**Comfort receiving PrEP care:** Participants will be asked about their comfort level about receiving PrEP and other health-related services at six different locations (e.g. STI Clinic, Mobile Clinic, etc.). Responses will be on a Likert scale ranging from *1=Very comfortable* to *4=Very uncomfortable*.

**DSM-5 Self-Rated Level 1 Cross-Cutting Symptom Measure (DSM):** For further clinical evaluation and research, the APA is offering a number of "emerging measures" in Section III of *DSM–5*. Participants will answer two Likert-style questions from the scale about depressive symptoms (2013, American Psychiatric Association).

**The Alcohol, Smoking and Substance Involvement Screening Test (ASSIST V2.0):** The ASSIST is an eight-item questionnaire that screens for all levels of problem substance use. The instrument covers tobacco, alcohol, cannabis, cocaine, amphetamine-type stimulants (including ecstasy), inhalants, sedatives, hallucinogens, opioids and "other drugs." The ASSIST V2.0 demonstrates significant concurrent, construct, predictive and discriminative validity. The ASSIST scores are comparable with other measures of substance use and the ASSIST is able to discriminate between low, moderate and high-risk use (114).

**Internalized Homonegativity (IHNI):** The IHNI was developed as a valid and reliable measure of negative attitudes towards homosexuality among gay men. The instrument consists of three subscales, personal homonegativity, gay affirmation, and morality of homosexuality, and 23 items, each rated on a six-point Likert scale from strongly disagree to strongly agree (98). Additional items are taken from Ross and Rosser's (1996) Reactions to Homosexuality Scale. This study will use items from the "Perception of Stigma Associated with Being Gay" subscale. This subscale has 6 items scored on a 7-point Likert scale. The overall consistency for the scale was 0 .84, and 0.56 for the selected subscale.

**Internalized Homophobia:** Selected items from Meyer's (1998) Internalized Homophobia Scale. The scale has Likert style items that measures negative attitudes around one's sexual orientation (e.g. "I would like to be completely heterosexual."). Reported alphas range from 0.79 – 0.83.

**Experiences of homophobia, racism, and poverty:** Adapted from Diaz's Homophobia Scale has Likert style items that measure experiences of homophobia both as children and as adults (e.g., "As you were growing up, how often did you feel that your homosexuality hurt and embarrassed your family?"), 4 of these items focus on experiences of verbal harassment and physical assaults in relation to both perceived sexual orientation and gender nonconformity (e.g., "How often are you hit or beaten up for being homosexual or effeminate?"), and 10 items measure experiences of racism as children and as adults (e.g., "How often have find that men pay more attention to your race or ethnicity than to who you are as a person?") (99-101).

**Trauma History Screen (THS):** The THS is a brief, 14-item scale that that asks participants about their history with traumatic events (Carlson et al., 2011). Responses are dichotomous, with respondents answering "Yes" or "No." This scale has good reliability and validity in a diverse sample.

**Intervention Dosage:** The number of texts received, replies sent, and sites visited will yield count data for each participant (See Fidelity and Dosage above).

## Data Analytic Plan

**Hypothesis One:** The PrEP Mobile Messaging Intervention, developed with participant feedback, will be judged by 30 participants to be feasible, appealing, relevant, and useful. Intervention links that receive a mean score on the Session Evaluation Form less than 30, or less than 24 on the Client Satisfaction Questionnaire will be discarded.

**Hypothesis Two:** 70 participants will be randomized to two conditions. Those in the IMB PrEP Mobile Messaging Intervention condition will show improvements in each of the IMB domains: Information (HIV and PrEP knowledge), Motivation (motivational readiness for PrEP and medical care, improved self-efficacy and improved attitudes for PrEP care), and Behavior (HIV risk behavior score and engagement in PrEP).

Information, motivation and HIV risk scores will be evaluated at 4 and 16 weeks using linear mixed-effect models, which will account for the three assessments (0, 4, & 16 weeks) being nested within individuals (115,116). We will test for differences in linear change over time between intervention and control groups on each outcome variable. For our primary

outcome, attendance at a PrEP Services appointment, we will evaluate the difference between conditions in attendance rates. Secondarily, we will examine rates of receiving a PrEP prescription or self-report of starting PrEP. Propensity scores (i.e., inverse probability of treatment weighting) will be used to account for any imbalance in baseline characteristics between conditions (119). Dose response, which is likely to be skewed account data, will be examined by dividing dose into quartiles, exploring the relationship with outcomes graphically, and testing them using dose as a moderator in the above analyses.

**Power.** As this is an intervention development study and the impact of the experimental intervention is not known, there may not be adequate power to determine the efficacy of the IMB PrEP Mobile Messaging Intervention and pilot studies are not designed to provide accurate estimates of effect sizes upon which to base large trials (117). Nevertheless, the small pilot RCT may provide a "signal" of impact on its outcomes. We conservatively assume that retention of 70 participants over 16 weeks is 85%, based on previous clinic trials.

Power analyses were run with Optimal Design 3.01 (118). The model assumed 3 assessments nested within cases. Hierarchical Linear Modeling analyses with alpha of 0.05 and power 0.80 will be able to detect an effect size .38 SD for change in the IMB outcomes. If the alpha is 0.1 (as is appropriate in exploratory research), then power is 0.80 to detect an effect size of .34 SD. Power to detect a difference in the proportion of participants attending a PrEP Services Appointment after their HIV/STI screening is 0.80 if attendance is 20% in ESC group (similar to our preliminary studies) and 40% in the intervention. The project will also collect data on the proportion receiving a prescription for PrEP during the study period as a secondary outcome.

### Post-RCT Phase

**Post-RCT Qualitative interviews (n=20)** will examine the relevance and acceptability of the intervention content among RCT phase participants (focusing on those aged 18-early 20s), and suggestions for future improvements. Feedback will be elicited after their completion of the RCT. Interviews will occur either in a secure clinical space at the UMMC STI/HIV testing clinics after successful COVID-19 prescreening or remotely via phone or a video conferencing platform. All qualitative interviews will be audiotaped and stored-on a digital recorder for in-person or Zoom for those conducted virtually. These recordings will be erased when the study is completed. We will ask about reactions to intervention content and recommendations for improving content for the future-to increase engagement, interest level, relevance for the target demographics, and to address any unmet concerns. Specific emphasis will be placed on better tailoring the content for younger individuals (18 to early 20s).

## PROTECTION OF HUMAN SUBJECTS AND SAFETY MONITORING PLAN

### Human Subjects Involvement, Characteristics and Design

The proposed research study is comprised of three phases. Firstly, a Development Phase (n=30,18-35 yrs.) in which we will conduct formative research to guide the development of the IMB Mobile Messaging Intervention. Secondly, a Controlled Trial Phase in which we will evaluate the preliminary efficacy of the IMB PrEP Mobile Messaging Intervention compared to a comparison condition (n=70,18-35 yrs.). Lastly, a post-RCT Phase (n=20) in which we will assess the acceptability and relevance of the IMB PrEP Mobile Messaging Intervention content among RCT participants. Subjects will be recruited from two STI/HIV Testing Clinics (Open Arms and Crossroads) at the University of Mississippi Medical Center in Jackson, Mississippi. Dr. Leandro Mena directs both of these clinics.

**Inclusion Criteria.** All black MSM (18 -35 yrs.) presenting to the UMMC STI/HIV testing clinics who are eligible for PrEP by CDC guidelines, are eligible for enrollment in each phase of study according to the following criteria: 1) English speaking, 2) eligible to receive prophylactic antiretroviral treatment, 3) not enrolled in another PrEP related study or HIV prevention study, and 4) able to give consent/assent and not impaired by cognitive or medical limitations as per clinical assessment. There will not be overlap between subjects in the Development and Controlled Trial Phase. We are enrolling only BMSM between the ages of 18-35 because they are the sub-group most at risk for acquiring HIV in Jackson, MS. Limiting the study to young BMSM will allow for the development of a mobile intervention that is targeted, acceptable, and engaging for this specific population. Enrollment of participants for this study will only be in Mississippi. There will not be any participants enrolled in Rhode Island.

**Rationale for Including Special Classes of Subjects.** The age, gender, and race of our participants are dictated by the need for research in the area of HIV prevention for black MSM living in the south.

### Sources of Materials

**Research Material Obtained from Living Human Subjects.** Research material obtained from participants include the following 1) all questionnaire data, 2) audio-tapes from qualitative interviews, 3) medical chart review to measure initiation of PrEP related care 4) subject engagement with the IMB PrEP Mobile Messaging Intervention material. For the Development Phase, subjects will complete qualitative interviews in-person regarding their reactions to the IMB

informed publicly available web material. These interviews will be recorded and they will take place at The UMMC STI/HIV Testing Clinics (Open Arms and Crossroads). The audio-taped interviews and written surveys of participant reactions to the IMB links will be the sources of material for this phase. The same procedures will be used for the post-RCT interviews, except that interviews will take place either in-person at the UMMC clinics pending a successful COVID-19 prescreening and temperature check prior to entry, or remotely via phone or a video conferencing platform. For the Randomized Controlled Trial study phases, participants will complete questionnaires about their demographic information, sexual behavior, PrEP initiation, and attitudes. Questionnaires will be completed at entry to the study, and at 4 weeks (immediate post-intervention), and at 16 weeks. In addition, data will be abstracted from the electronic medical record of any visit to receive PrEP or receipt of a PrEP prescription (PrEP clinics are located in the STI/HIV testing centers at UMMC) at 16. The 4 and 16 week assessments and the collection of PrEP clinic medical record data will be done in the UMMC clinical care areas, in designated clinical spaces that are HIPAA compliant. The study will use a HIPAA compliant web-based platform to send out weekly text messages to participants in the intervention arm of the study.

**Linkages to Subjects and Access to Subject Identities.** For each stage of the research, participant names and contact information will be maintained in a recruitment/enrollment database during the course of the study. Once individuals enroll in the study, names will be linked to 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 and assent forms will be kept in a locked file cabinet, separate from any other project data. The baseline, 4 and 16 week assessments will be done through REDCap. REDCap 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. A REDCap survey can be emailed to each participant's unique email address so they can complete assessments online. If patients cannot complete assessments online they can utilize a computer at the STI/HIV testing clinics. 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 the Master Participant Lists must be witnessed and documented on the Master List Verification of Destruction document, which will be maintained in the site's regulatory files. 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**

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/or program sessions. The protection against each risk is described in detail below under Adequacy of Protection Against Risk.

**Adequacy of Protection Against Risk**

**Recruitment and Informed Consent.** The risk of potential coercion will be minimized by following standard procedures for obtaining the informed consent. Study personnel will fully explain the study procedures, risks, benefits, and alternatives to participants. 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 for two phases of the project (Development Phase and Randomized Controlled Trial Phase) will involve the same screening procedures. Research staff will search for participants who are eligible for the study in the clinical setting of their routine care at UMMC STI/HIV testing clinics. Subjects will be assured that their routine clinical care will not be disrupted, or negatively affected, by their choice to participate or not participate in the study. Subjects approached about the study will be approached and consented regarding the phase of the study that is relevant at that time (i.e. qualitative interviews or randomized controlled trial). Participants in the intervention arm of the RCT will be contacted by phone and given the option to participate in post-RCT interviews. In all cases above, participants will be assured that they are free to withdraw from the study at any time and that if they do withdraw any data collected up to that point will be destroyed/stripped from any data files (see Protection Against Risk for data handling procedures).

**Protections Against Risk**

**Breach of Confidentiality.** Potential risk will be minimized by strictly adhering to the guidelines for research outlined by the Lifespan and UMMC IRBs, Rhode Island and Mississippi state law, 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 parent/guardian.

All data collection will take place in secure and supervised clinical settings or with HIPAA compliant software (REDCap). All study personnel 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.

Participants will be asked to provide informed written consent to audiotaping at the time of study entry if they are participating in the qualitative interviews during the Development Stage or Post-RCT phase. To assure confidentiality and protection of the participants during audiotaping, all tapes will be stored in locked file cabinets in a secured office. Only Drs. Whiteley and Mena will have access to the audiotapes so that ongoing guidance can be provided as to the conduct and design of the study.

To further protect the privacy of the study participants, we will obtain a Certificate of Confidentiality from the U.S. Department of Health and Human Services (DHHS). With this Certificate in place, the researchers cannot be forced to turn over identifying information about a study participant in any federal, state, or local criminal, administrative, legislative, or other proceedings. This Certificate does not prevent a study participant from volunteering to turn over their research information nor does it prevent researchers from providing research-related information to others when requested by the study participant.

**Emotional Distress.** We will minimize distress by presenting questions/program techniques in a supportive manner, assuring participants that they may refuse to answer any questions that make them uncomfortable, and may terminate participation in the intervention at any time. All subjects 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 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. consenting, baseline assessment, interview session, follow-up, collection of biological data), clinical resources will be offered on-site. The clinical locations used in this study are ideal as they each provide easy access to medical and mental health clinicians. If a subject contacts study staff because of distress or concern due to participation in the study or directed activities that occur away from the clinical space (such as a concern that phone use or activities led to a dispute), the subject 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, the PI or licensed designee will meet with the participant individually for further assessment of any clinical needs. Acute risks would include severe medical illness, or the development of any other severe psychiatric symptoms or disclosure of sexual or physical abuse. Any subjects who exhibit acute risks will be evaluated immediately by emergency room clinical staff at UMMC, or if less acute, by an independent clinician that day. Less severe medical needs or distress can be managed by staff or PIs over the phone or with an individual interview. The PIs and/or staff will meet with participants 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 young adults and adults 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 PrEP related intervention development. We hope that our intervention will be successful in improving PrEP uptake and reducing HIV in our subject population and think that the clear examination of these questions outweighs the previously mentioned risks. The effectiveness of a novel, scalable, technology driven, intervention integrated to improve PrEP uptake is understudied. Given the significant health sequelae associated with HIV infections, and the paucity of data on PrEP uptake/engagement in care and behavioral intervention programs, 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.** Subjects will be reimbursed $50 for each qualitative interview during the Development phase and Post-RCT phase. During the RCT phase subjects will be reimbursed $50 for baseline, and $40 for the 4 week and 16 week assessments. Participants who confirm their research appointment prior to the 4 week assessment and their contact information prior to the 16 week assessment will receive an additional $10 at each appointment.

## Data and Safety Monitoring Plan

The nature of the population warrants the development of a Data Safety and Monitoring Plan. To address the NIH policy for Data and Safety Monitoring, the PIs 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. Participant experiences with the study procedures and the rates of adverse events will also be reviewed to determine any changes in participant risk. The PIs will immediately report any adverse events that are observed to the Lifespan Internal Review Board (IRB) and NIMH. Serious adverse events (SAEs) will be reported to the Lifespan 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 NIMH. Actions taken by the IRB in response to SAEs will also be reported to NIMH, 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 and UMMC IRBs, 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 NIMH for approval prior to instituting them. Finally, if significant medical or mental health risks occur during the study period evaluation by the UMMC 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 intervention, 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.

**Educational Training**

Lifespan/RIH and UMMC requires that researchers and IRB members read Protecting Study Volunteers in Research (Dunn & Chadwick) and complete a related examination. This process has served as an initial certification. The Offices of Research Administrations (Lifespan and UMMC) both contract with CITI, a Collaborative Institutional (modular) Training Initiative program, for Human Subjects Protection and HIPAA training for all research personnel. Currently this program offers researchers a basic human subject's protection course as well as a refresher course that is required every three years. Documentation of successful completion is automatically generated and can be printed directly by the researcher

Additional and continuing education opportunities for clinical researchers include the Office of Research Administration newsletters that are circulated to recipients every 6-12 weeks. Relevant information concerning research review is available on the ORA websites at www.lifespan.org/research/ (Lifespan/RIH) and https://www.umc.edu/Research/Office_of_Research.aspx (UMMC). In addition to standard institutional research information, the web pages contain links to other sites such as CenterWatch, NIH, PRIM&R/ARENA.