OnPOINT RCT Protocol Summary (IRB Approved 2/29/2024)

A. SIGNIFICANCE

HIV in the United States (US) disproportionately affects young men who have sex with men (YMSM),[14,15] yet nearly half of YMSM are unaware of their HIV infection.[16] MSM accounted for 86% of HIV incidence among males in the US in 2016.[14] Despite decreasing rates of overall incidence nationally,[14] HIV incidence among MSM continues to rise.[155] Between 2010 and 2014, more than 70% of HIV infections affected YMSM (≤ 24 years old),[15] and an estimated 49% of YMSM are unaware that they are infected with HIV.[16]

Barriers to HIV testing can prevent YMSM from using facility-based testing centers. YMSM experience many barriers to HIV testing, including worries about sexual orientation or same sex behavior disclosure, actual and/or perceived HIV- and gay-related stigma, low perceptions of HIV risk, difficulty communicating with healthcare providers, and confidentiality concerns.[17-21] Some barriers to facility-based HIV testing can be particularly difficult for YMSM, including issues of testing access (e.g., concerns about parental consent for minors) and unfriendly testing environments (e.g., crowded/non-private testing centers).[20,21]

HIV self-testing (HIVST) is one mechanism to engage YMSM early in the prevention cascade. Approved by the US Food and Drug Administration (USFDA) in 2012, rapid-HIV test kits are accessible at local pharmacies without a prescription.[22] HIVST has been found to be an acceptable method of HIV testing,[23-58] including among MSM.[35-49,51-58] In fact, HIVST was the most preferred option of HIV testing among MSM, with more men favoring HIVST over couples-based, expedited, and other facility-based testing options.[40] Benefits of HIVST include convenience, confidentiality, privacy, and avoidance of HIV clinic stigma.[3,21,26,32,38-40,46-48,58]

Many HIV-negative YMSM would benefit from pre-exposure prophylaxis (PrEP). Engaging YMSM in HIVST offers a unique opportunity to participate in other prevention strategies along the HIV prevention cascade,[156] including biomedical HIV prevention. Adherent PrEP use is effective[72-75,157] and approved by the USFDA for daily oral use,[158] yet uptake among YMSM has been minimal. PrEP uptake was reported as low as 4.2% and as high as 12.2% among YMSM in larger US cities between 2014 and 2016,[76-78] even though as many as 64% of MSM meet Centers for Disease Control and Prevention (CDC) guidelines for PrEP.[64,65,159] US PrEP uptake trends indicate differences by race/ethnicity, with fewer minority YMSM using PrEP compared to White YMSM.[76] Research is needed to develop a single, comprehensive intervention for HIVST *and* PrEP.

The Information-Motivation-Behavioral Skills (IMB) model[79-82] offers an intervention framework. The IMB model posits that individuals must be highly informed, motivated, and behaviorally skilled to initiate HIV prevention behaviors.[79-82] This model has been well-tested and empirically supported for HIV prevention with many diverse populations and HIV prevention behaviors.[1,79-104] Several formative studies provide rationale for using the IMB model to understand barriers and facilitators to HIVST[3,21,46,47,53,105] and PrEP uptake.[4,5,76,106-144] Integrating findings from prior studies among diverse populations, barriers to HIVST included lack of information and worries about result accuracy.[3,21,47,49,105] Individuals reported motivational factors for HIVST including convenience, confidentiality, avoiding negative implications of clinic stigma, and removing insurance barriers to HIV testing.[3,21,46,47,53,105] Despite these motivating benefits, the need for behavioral skills were also identified, including the ability to administer self-testing and cope with a potential HIV-positive result.[47,105] Regarding PrEP, low knowledge and awareness of PrEP is a plausible barrier to uptake[112,116,122,145] and amenable to intervention.[145,146] Motivational components associated with the IMB model include attitudes, norms, and intentions,[79-82] and researchers have documented these as motivational components—in addition to perceived risk of HIV and stigmatization—as barriers and facilitators to PrEP use.[76,106-142] Behavioral skills relevant to PrEP uptake and adherence include self-efficacy to discuss same-sex sexual behavior and PrEP with a healthcare provider, to mitigate perceived risks associated with PrEP use (e.g., side-effects, PrEP stigma), to discuss PrEP use with their main partner, and to manage the PrEP maintenance activities (e.g., dosing adherence, quarterly HIV/STI testing).[4,5,113,125,137,143,144] As such, the robustness of prior work supports use of the IMB model to guide intervention development.

A mobile health (mHealth) intervention is a promising platform for YMSM, especially since YMSM already report seeking sexual health information online.[162-164] Prior research has shown that many in-person interventions can be adapted for successful mHealth delivery (e.g., motivational interviewing common in HIV prevention research[165-169]). Guiding YMSM through interactive activities and material relevant to specific IMB model constructs (e.g., multimedia, written material, decisional tools, and virtual situations) offers a platform to promote engagement and retention in mHealth activities. *Notably, a recently published intervention "Keep It Up!" found YMSM were responsive to an mHealth intervention, with YMSM in the experimental arm reporting a 40% decrease in bacterial STIs compared to the control arm 12-months post-intervention.[170]* While in-person intervention strategies have several benefits (e.g., building rapport), mHealth HIV prevention

interventions can provide access to individuals not linked to prevention and treatment care[147,148] and offer several key advantages including *confidentiality,* intervention *scalability,* and delivery *efficiency*.[149]

Development of mHealth interventions to increase HIV prevention behaviors among YMSM is ongoing, but further research is needed to identify crucial targets for intervention. In addition to published IMB-guided mHealth interventions for YMSM that showed acceptability and preliminary impact,[48,122,168,169,171-174] additional interventions are currently under development or being evaluated for efficacy among MSM using the full or partial IMB model, including several online or app-based interventions to promote HIV testing and/or PrEP uptake (e.g., *healthMpowerment, HealthMindr*, *LYNX, MyChoices*, and *P3*). Despite plausible evidence of the utility of IMB-guided interventions, we currently lack empirical evidence to determine which IMB model construct(s) are most important for supporting HIVST and PrEP uptake. mHealth interventions are designed to increase intervention reach and efficiency;[149] however, the current "kitchen sink" approach to promote HIVST and PrEP uptake may result in scaling *inefficient* interventions if certain constructs or intervention components could be dropped due to lack of intervention effect. Empirical evidence on condom use suggests some IMB model constructs are more important[1,79-104] and importance could differ by demographic characteristics and sexual health care history.[84,85,91,93,96-98,100,101] In reviewing online HIV/STI prevention interventions for YMSM in a systematic review, Knight et al.[175] identified the need for assessing intervention effects by subgroups of YMSM rather than a "one-size-fits-all" approach. Research is needed to determine *which* IMB model construct(s) are most important—and for *whom* (in future powered study)—to promote HIVST and PrEP uptake among YMSM in a scalable, efficient, and targeted manner.

We propose an mHealth intervention to promote HIVST and PrEP uptake among YMSM using a factorial randomized experimental design[150] to determine key intervention targets of the IMB model. Responsive to NIMH and OAR funding priorities (e.g., PA-18-278; PA-18-281; NOT-OD-15-137), the proposed research will "develop, test, and implement innovations in HIV testing" and "promote pre-exposure prophylaxis (PrEP) uptake among individuals at substantial HIV risk." The main objective is to pilot a two-group randomized controlled trial (RCT) with 132 YMSM nationwide using a factorial experimental design. The two arms of this attention-matched RCT will be *information-only* (I), *and information + motivation* (M) + *behavioral skills* (B) representing the *full IMB model* (IMB). All YMSM will be offered an HIVST kit to be sent to their home (or alternative location) for post-intervention HIVST. We will assess self-report outcomes of HIV testing and PrEP uptake 3-months post-intervention. Feasibility, acceptability, and preliminary impact data will support an R01 application.

B. INNOVATION

First, development of an mHealth intervention to increase HIVST and PrEP uptake offers long-term potential for *scaling* an evidence-based intervention nationwide. *Using previously developed intervention content through publicly available sources whenever possible, this intervention will incorporate and build upon past successes to promote HIVST and PrEP uptake, while developing new intervention content with YMSM involvement*. **Second**, combining HIVST and PrEP in a single intervention package (opposed to two individual interventions) provides a comprehensive intervention package for HIV prevention for YMSM. Engaging YMSM in HIV testing could provide the necessary cue to action for PrEP uptake, and our intervention will prepare them for their next steps toward biomedical prevention.

C. RCT APPROACH

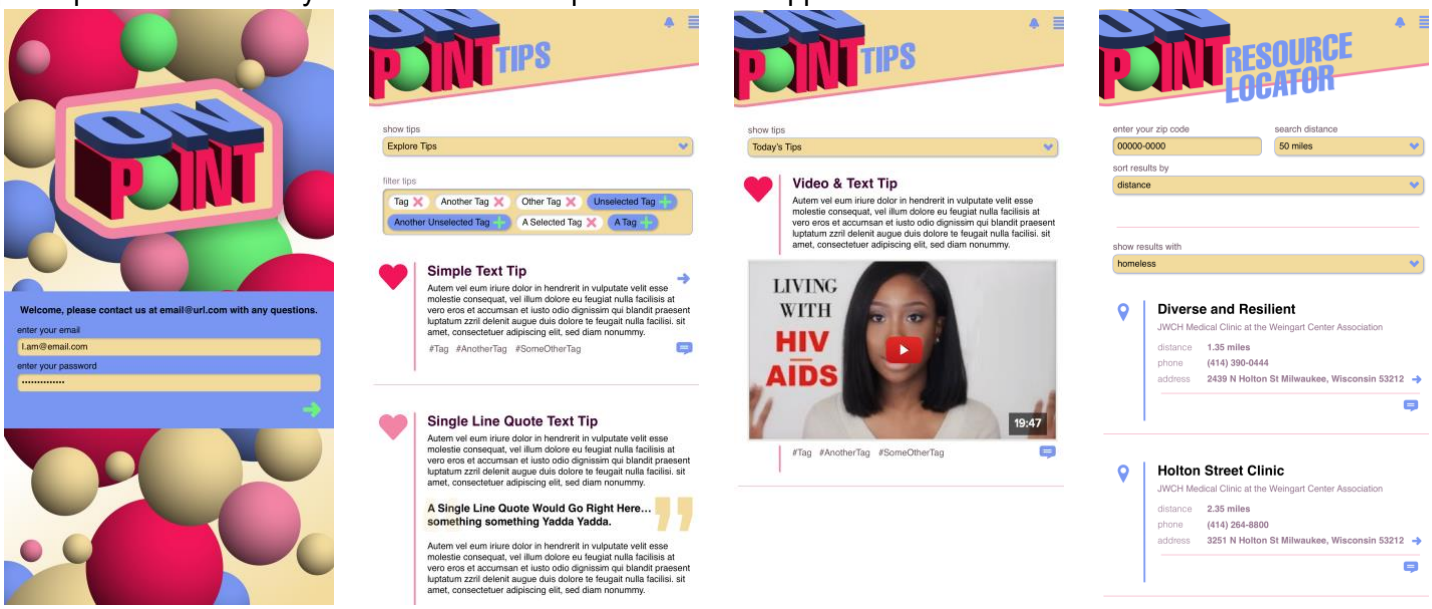
C4a. Participants, Eligibility, Recruitment, Sample Size, & Incentive Payments: YMSM (17-24 years old) who meet CDC criteria for PrEP use but are not currently taking PrEP (see **C2a**) will be eligible for this pilot RCT. Specifically, individuals must meet the following eligibility criteria:

1. 17-24 years old;
2. Individuals who self-identify as male (including transgender men);
3. Report one or more male sexual partners in the past 6 months;
4. Resident of the US;
5. HIV-negative or unknown status based on self-report; and
6. Self-reported risk for HIV (based on CDC criteria for PrEP use) defined as reporting any of the following in the past six months:
    a. Bacterial sexually transmitted infection;
    b. Condomless anal sex (CAS) with a casual male sexual partner;
    c. CAS with an HIV-positive or unknown status main partner; or
    d. CAS with an HIV-negative main partner who reports CAS with other male partners.

We will recruit 132 young men who have sex with men (YMSM) via email from individuals selected from the data bank in companion IRB protocols [i.e., screening survey (PRO00036424) and data bank (PRO00036416)]. Eligible participants will be selected using a purposive sampling strategy to ensure balance by age, race/ethnicity, and geography and invited via email. Participants will complete a baseline survey and then be given provided access to the intervention. The intervention is access to a secure, password protected website designed for compatibility with smartphones. The goal of the intervention is to provide participants access to content to support decision-making around HIV testing and prevention. Participants will be provided content designed to be consumed within 45-60 minutes over the course of the study. Participants will be texted prompts to their phones over the course of the project, which will direct them to a specific "Tip" on the study website. Tips include ~2-3 sentences of content with embedded videos, links, and avatar-based role-play scenarios. Participants will each be provided 30 Tips over the course of the project. Content is arranged by behavioral constructs (information, motivation, and behavioral skills). Individuals will be randomized to 2 attention-matched groups: (1) info only, and (2) info + motivation + behavioral skills. Participants will have access to intervention content aligned with the constructs included in their randomized group. Participants will also receive a free HIV self-testing kit (FDA-approved Oraquick In-Home HIV Test available for purchase without a prescription from pharmacies). Follow-up surveys will then be conducted at 1- and 3-months post-baseline survey. All surveys will cover topics related to sexual health and HIV prevention. Constructs include demographics, sexual partners and behavior, HIV testing and associated behavioral constructs, biomedical HIV prevention and associated behavioral constructs, substance use, mental health, and barriers to health care engagement (e.g., stigma, self-efficacy, social support, discrimination, medical mistrust, and health literacy). We will also assess intervention acceptability and tolerability via the follow-up survey, and we will conduct Zoom or telephone-based exit interviews with 12 YMSM to gain user feedback on our study procedures and assess intervention acceptability. Intervention participants will be provided $75 electronic gift card for completing the baseline assessment and intervention components, with follow-up survey incentives of $50 electronic gift cards at 1- and 3-month post-baseline. Exit interview participant will be provided $50 electronic gift cards.

Informed Consent/Assent & Baseline Assessment: All participants will complete a procedure for providing informed consent/assent (with a waiver of parental consent), which will include a guided procedure using Qualtrics that describes the study's purpose, procedures, and other critical components. Participants will then complete a brief quiz to ensure adequate comprehension of the critical components, including the voluntary nature of the study, risks and benefits to participation, and confidentiality of all data collected. After providing consent, participants will complete a baseline survey in Qualtrics.

Randomization, Experimental Design, & Intervention Delivery: Participants will undergo a randomization procedure using Qualtrics, and participants will be randomly assigned to one of two attention-matched study arms: (1) *information-only,* and (2) *full IMB model* (IMB). All participants will be offered a free HIVST kit with no incentive for HIVST. After completion of the baseline survey, participants will be enrolled into the mobile app, which will deliver intervention content. The app will be password protected to help support participant confidentiality. Below is a mock-up of the mobile app of the intervention.



Post-Intervention Assessments & Exit Interviews: All participants will complete follow-up surveys at 1- and 3-month follow-up timepoints. We will also assess intervention acceptability and tolerability[173,225] at the final assessment, and we will conduct virtual exit interviews with 12 YMSM to gain user feedback on our study procedures and assess intervention acceptability.

Data Analysis & Evaluation: The pilot study will be evaluated for *feasibility* (i.e., enrollment & retention), *acceptability* (i.e., survey, exit interview feedback), and *preliminary impact* by experimental group. The intervention will be considered feasible if we are able to enroll 120 YMSM (in 18 months) with at least 80% retention at each follow-up assessment. We will transcribe and analyze exit interview data to assess acceptability of the intervention and procedures, allowing us to refine as necessary for the R01 study. Preliminary impact will be assessed using within- and between-subjects analyses. First, we will test the performance of randomization by chi-squared comparisons and ANOVAs for categorical and continuous variables, respectively. Second, we will test for differential attrition by treatment group at 1- and 3-month follow-up assessments. Third, we will assess post-intervention HIV testing and PrEP uptake using factorial logistic regressions to determine between-group differences, adjusting for any breakdowns in randomization or differential attrition. Fourth, we will test for changes in stage of change indicators by randomized group, time, and group*time interaction, with similar adjustment procedures, using GEE; this analysis will help us determine a trend towards HIVST or PrEP uptake were we to extend the length of follow-up. Power: Our study has 80% power to detect a ½ stage *average* difference (d = 0.68; α = 0.05) on the PrEP cascade comparing the three experimental groups combined to the information-only control (M = 1.59, SD = 0.74)[159,200] assuming 80% retention. Finally, we will conduct within-subjects tests comparing baseline and follow-up IMB construct scale scores stratified by group as an evaluation of internal validity (i.e., *did the interventions influence constructs?*).