Title: CHALO! 2.0: A Mobile Technology Based Intervention to Accelerate HIV Testing and Linkage to Preventive Treatment

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***Background***

India has the 3rd largest population of HIV infected persons globally, with an estimated 2.1 million infected persons, 62,000 AIDS-related deaths, and more than 80,000 new infections annually.[1] Overall HIV prevalence in India is 0.3%, but prevalence in MSM is 3-9%.[1] Although MSM make-up less than 2% of the Indian population, they comprise over 20% of HIV infected individuals[1,2] and are designated a key priority population for HIV interventions by the Indian Health Ministry.[2]

Prior studies, that recruited Indian MSM through in-person approaches, report that 18-49% of MSM have never been HIV-tested. Recent studies that recruited MSM online report that 23-47% have never been HIV-tested,[3,4] and that 75% of sexually active MSM are unaware of their current HIV status (i.e. were never HIV-tested or were last tested more than 12 months prior).[5] Reaching the first "90" in UNAIDS 90-90-90 paradigm (90% of those with HIV aware of their status, 90% of those aware linked to HIV care, and 90% of those linked to care having undetectable HIV viral loads) is key to ending the HIV epidemic, and HIV serostatus awareness remains the major barrier to HIV linkage-to-care and treatment in India.[6]

HIV testing interventions and care models for MSM are often limited in their reach and impact, in part due to social stigma associated with same-sex behaviors.[3,4,7] In Mumbai, **The Humsafar Trust** (**HST**), a well-established, large LGBTQ community-based organization and our community partner on this study, provides comprehensive MSM-sensitive clinical and social services in safe environments, including several testing sites in Mumbai. However, a key challenge faced by HST and addressed by this study is how to engage individuals who fear being seen at MSM-identified spaces due to stigma associated with attending a LGBTQ or HIV center (e.g., general voluntary testing/counseling centers) or other logistical challenges. Our recent online survey of over 1,000 Mumbai-based MSM found that 81% were aware of HST, but only 28% had ever visited HST for any reason. Of those respondents who had been HIV-tested, only 10% were tested at a HST site. Thus, traditional interventions that rely on in-person outreach model may not address barriers that prevent individuals from seeking care, and may also fail to reach MSM who do not frequent physical meeting venues, do not identify as a sexual minority, or are unlikely to go to LBGTQ- or HIV-affiliated settings.[8-13]

Additionally, MSM globally and in India frequently lack both access to accurate information about HIV and support for accessing services (e.g., navigation, awareness of MSM friendly testing sites). [5,14-16] Coupled with community-level stigma, lack of knowledge and support reduces awareness of the need for HIV testing, and also reduces motivation to seek HIV testing and subsequent care. Evidence suggests that mass media HIV awareness campaigns, information provision, linkage to support services, stigma reduction, and reducing structural barriers may all improve HIV testing rates and subsequent linkage-to-care;[17,18]

Social media technologies (SMT) (e.g., mobile phones, multimedia message) could be an extremely helpful tool to deliver the mass media HIV messages. Globally and in India, the gap in disparities to access to SMT is closing due to declining costs and growth of SMT infrastructure. India is experiencing exponential growth in SMT adoption, with younger individuals leading this curve (the same age group most at risk for HIV). In 2016 in India, the cost of mobile data fell 96%,[19] which has meant that now mobile phones are ubiquitous, and incoming calls and SMS are free. There are over 400 million Internet users in India, and 78% access the Internet primarily through mobile devices.

The growth in SMT infrastructure has been followed by an increase use of the technology by MSM to socialize and seek sexual, romantic, or transactional partners.[20] In fact, the HST reports that most MSM reached at physical outreach sites use smartphone-based messaging applications such as WhatsApp. HST staff also note decreasing MSM traffic at historical and new physical spaces, and attribute this to the ease with which MSM find community and partners online. While this shift in how MSM socialize makes it more challenging to conduct face-to-face outreach, SMT allows new options for engaging historically hard-to-reach populations in health interventions. In Mumbai, the setting for this study, there are over 700 new profiles registered monthly on an MSM-specific SMT dating platform[21] and at least 65,000 MSM are estimated to be reached by Facebook advertising. The number of SMT users in India is expected to exceed 730 million by 2021, during the course of the study. Such widespread use of SMT by all segments of Indian society creates unprecedented opportunity to develop and test SMT-based health interventions and have a population level impact.

In addition, SMT could be leveraged to circumvent stigma by linking MSM to an acceptable testing strategy that might or might not be an HST site.[22] Other potential HIV testing strategies include private laboratories or self-testing, and our recent online studies found that over half of individuals received HIV testing through a private lab or clinic.[23,24] Studies of HIV testing preferences in low-and-middle-income countries have found that no single HIV testing approach meets the needs of most individuals, that preferences and decisions for HIV testing vary based on numerous factors,[25-27] and that multiple testing options should be available, including self-testing.

Prior studies of HIV testing preferences, including HIV self-testing, have been primarily hypothetical (e.g., using discrete choice experiments or surveys).[25-33] Real-world data are lacking regarding what stigmatized populations such as MSM choose for initial HIV testing, given multiple testing options. Additionally, prior intervention studies have focused on single testing strategies to understand uptake. In the proposed pragmatic RCT, MSM in all 3 arms will be provided with multiple testing options. Their choices will provide insights about actual preferences for HIV testing, information policymakers and service providers can use to inform resource allocation for scale-up and determination of how to achieve UNAIDS target of 90% serostatus awareness.

Around the world, SMT-based interventions have been feasible and acceptable for diverse MSM populations.[34-41] Among Indian MSM, our own studies found that SMT-based interventions are feasible and acceptable,[24,42,43] and provide preliminary evidence suggesting that offline health behaviors may be changed by online intervention.[24] However, few studies have tested whether SMT can increase HIV testing among MSM in low-middle income countries,[36,44-48] and none were conducted in India or other South Asian countries. Prior studies have largely been single-arm pilots, with none that we could identify evaluating whether SMT-based interventions lead to movement along the HIV care continuum (e.g. STI testing/treatment, PrEP, risk reduction counseling, antiretroviral treatment).

Furthermore, though SMT-based interventions are promising, prior platforms have been limited by several factors. These include: (1) reliance on less interactive technology (e.g., static informational websites or 1-way SMS communication); (2) reliance on a single media format (e.g., text-only SMS messages) rather than leveraging the strength of diverse media; (3) intervention components that are not integrated into participants' natural usage patterns (e.g., having to visit study-specific platforms and devote substantial time to receive adequate doses); (4) multimedia content that works for television/desktop computers, but is incompatible with how individuals process information (e.g., videos that are too long);[49] and (5) interventions that are too complex and resource intensive to develop and sustain (e.g. Apps), or are unlikely to be adopted and implemented at scale (e.g., a CBO being unable to implement an intensive app-based behavioral intervention for a large population).

***Objective and Rationale***

Our objective is to test whether an SMT intervention will accelerate HIV testing and linkage-to-care by delivering consistent information, motivational, and behavioral skills content from a reputable source (i.e., HST) along with facilitated access to multiple HIV testing strategies.

To fill the gap presented by previous SMT-based interventions, this RCT will determine the efficacy of **CHALO! 2.0** for increasing HIV testing and care engagement for MSM. **CHALO! 2.0** builds on prior interventions by integrating effective elements to increase HIV knowledge, enhance motivation for testing and linkage-to-care, and confer skills to access testing and care, while addressing structural factors by providing digital coupons for multiple free testing options. We propose to test this model in a pragmatic RCT with two comparison conditions: (1) an attention control condition including a digital coupon for free testing at a site of the participant's choice, and (2) digital coupon alone, without online SMT-based intervention.

If **CHALO! 2.0** is even modestly effective, it could have a large population level impact given its rapidly scalable design. **CHALO! 2.0** is designed to address the limitations presented by previous SMT-based interventions, by using a widely adopted existing technology medium (WhatsApp) that is already integrated into individuals' daily routines, delivering contents that are incorporated into typical use patterns and pushed to users, using diverse digital media (brief video clips, pictures, infographics, text messages, website links) to facilitate behavior change and allow heterogeneity in learning, allowing participants to message peer-counselors 'just-in-time' to obtain information or support as desired, and drawing on evidence from social media marketing to develop contents specific to how individuals process SMT information to maximize behavior change.[50-53] Finally, **CHALO! 2.0**'s design features protect against shifting use of online technology, making findings from this study applicable for the future. For example, **CHALO! 2.0** will use a generalizable communication system (WhatsApp) with core contents and design features that are easily scalable to other messaging platforms (e.g., Viber, Facebook Messenger, multimedia SMS, Apple watch). This will help ensure relevancy, acceptability, and feasibility for future scale-up, increasing likelihood of impact.[36,37,54-56]

**Aims:**

1. To determine whether CHALO! 2.0 increases HIV testing compared to control conditions, and to identify factors associated with HIV testing.

2. To determine whether CHALO! 2.0 increases linkage-to-care (both HIV prevention through counseling

and use of PrEP, and HIV treatment with antiretrovirals), and to identify factors associated with linkage to care.

## *Methods*

**Research Sites:**

While Einstein is the coordinating site for the study, all research related activities will take place at the international site, The Humsafar Trust (HST), in Mumbai, India. The activities conducted at HST include recruitment, informed consent, enrollment and follow-up, as well as intervention delivery. The HST site will responsible for all data collection. The Einstein team provided assistance building study protocol and will provide consultation for the development of study materials including survey questionnaires. Both research staff from Einstein and HST will participate in data analysis. Einstein staff, including the PI (Viraj Patel) will not have access to any identifying information.

**Participants:** Researchers at HST will recruit 1000 individuals who meet the following eligibility criteria: (1) ≥18 years old; (2) live or work in the Mumbai metropolitan area, including Thane; (3) fluent in Hindi or English, (4) identify as cis male, (5) anal sex with men in past 1 year; (6) (a) report that they have either never tested for HIV, (b) are unaware of HIV test results, or (c) are HIV-negative with last HIV test ~~>6 months ago~~ at any time and anal sex since last test; (7) able to provide and verify a WhatsApp mobile number and email address; (8) willing to answer online surveys for 18 months; and (9) have not participated in a prior HIV research study (by self-report).

**Procedures**

1. **Description of 3 trial arms.**

**1.1 CHALO! 2.0 (intervention arm):** MSM randomized to this arm will receive 2x-weekly digital media messages for 12 weeks (24 messages total) about HIV, HIV-testing, and HIV prevention and treatment. Messages will target information, motivation, and behavioral skills, as we did for the **CHALO!** pilot. Digital media will combine text messages, infographics, and brief videos (<30 seconds), with each message containing a link to the study specific webpage listing testing resources and MSM specific services offered by HST. Messages will convey information (HIV knowledge, logistical information about testing/care, PrEP), enhance motivation (i.e., brief video clip creating a social norm for HIV testing), and build behavioral skills (i.e., brief video clips demonstrating how to how to request and obtain a HIV test at HST or the private lab using the digital coupons), and provide interaction with online peer counselors (who will be reachable by the same Whatsapp channel/number that participants receive intervention contents). The study team will guide finalization of exact messaging contents, based on input from HST's two community advisory boards. Researchers at HST will use WhatsApp Business App[57] to deliver prescheduled messages and collect process data.

**1.2 Attention matched control (AMC):** MSM randomized to this arm will receive informational messages also sent out 2x-weekly using the WhatsApp Business App. Message formats and delivery will be matched to the **CHALO! 2.0** arm (i.e., same number of video clips, infographics, text messages, sent in the same pattern), but contents will differ from **CHALO 2.0** and will focus on the top health priorities identified by participants in our 2017 online survey: diabetes, hypertension, obesity, nutrition, and stress management.

**Table 1. Overview of study arms and components.**

| Components | CHALO! 2.0 | Attention matched control | Digital coupon only |
|---|---|---|---|
| Contents of digital-media sent 2x/week for 12 weeks | *HIV, testing, prevention, treatment, linkage-to-care* | *general health information* | -- |
| Personalized digital coupon for free testing | ✓ | ✓ | ✓ |
| Webpage listing testing/care sites, contact information for online peer-counselors | ✓ | ✓ | ✓ |

**1.3 Digital coupon only control:** MSM randomized to this arm will receive, at study entry, the digital coupon and a resource webpage link, and then will receive follow-up study assessment surveys. They will be eligible for prize drawings based on completion of assessments.

2. **Components common to all trial arms**

**2.1 Personalized digital coupon for free HIV testing:** All participants, after verifying contact information, will receive a personalized digital coupon consisting of a number (linked to their study id), and a personalized link to an arm-specific webpage listing HIV testing locations where the coupon can be used (HST and private laboratory sites). This approach has been used previously,[36] including in a recent feasibility pilot by our private laboratory partner, Suburban Diagnostics. The coupon will also be linked to participants' mobile numbers, and will be scanned or entered into an online system by testing staff (at HST or the private laboratory).[58] Each coupon can only be used once every 4 weeks. All participants who check in will also receive an automated message with a link for a pre- and post-test counseling video, and contact information for HST's community health worker (who can provide additional counseling and linkage-to-care/navigation for prevention and treatment, blinded to participant's study condition). These steps will help ensure confidentiality of test results and linkage of valid test results to each participant.

**2.2 Informational webpage:** All participants will receive a personalized link (e.g., using Bit.ly link shortened)[59] to an identical informational webpage (one webpage per arm) listing testing sites where digital coupons can be used, contact information for online peer counselors, and other MSM-specific health services offered by HST (e.g., counseling, crisis support). The use of personalized links and study arm-specific webpages will enable us to collect process data on website visits, linked to participants and outcomes.

**2.3 Online peer counselors:** All participants will be able to use SMT to contact HST's online peer counselors to receive support, have questions answered, or obtain referrals for linkage services. Online peer-counselors are currently supervised by HST's existing peer outreach infrastructure. For each online peer, collect communication-related process measures will be collected by downloading their message- and voice-call history to examine potential associations with study outcomes. Peers will not be informed of study hypothesis.

**2.4 Choice of HIV testing strategy:** All participants will be able to use digital coupons for free testing using a strategy of their choice: (1) standard counselor-based finger-prick rapid testing at any of 3 HST testing sites across Mumbai, (2) Oraquick self-testing in a private room at any of the 3 HST testing sites, accompanied by an instructional video and brief post-test self-administered survey, or (3) 4$^{th}$ generation HIV antibody/antigen test at any of the 41 private laboratory sites. Those testing at HST via counselor or self-test will undergo standard pre- and post-test counseling, and those testing at the private lab will be sent pre- and post-test counseling video links. HST currently collects and verifies mobile phone numbers for clients presenting for testing (now a requirement by the health ministry), and these phone numbers will be used to determine whether any study participants received counselor-based testing at HST but forgot to show the digital coupon. Study participants will only be able to receive free self-tests at HST or test at the private lab if they show the coupon.

**2.5 Linkage-to-care based on HIV testing strategy:** Specific protocols will be used for HIV-positive results, based on testing strategy. For standard counselor-based testing, HST will use current protocols for linkage and monitoring after a positive test. For private HIV self-testing at HST, a brief post-test self-administered survey will ask participants to indicate test results; we expect (based on prior non-India based studies) that the majority of those testing positive will indicate results on the post-test survey or inform the on-site HST counselor.[60-62] Post-test survey results will be visible to counselors, with participants informed of this disclosure. Once participants inform counselors of positive self-tests, participants will be linked and monitored using HST's existing protocols. We anticipate that most of those who do not immediately disclose a positive result immediately will contact HST for support. The post-test video link sent to all participants (both positive and negative) will also provide information about options for care, including free and private sector care. Finally, participants choosing private lab testing who test positive and do not contact HST within 24 hours will be contacted by the HST study healthcare worker, who will deliver results via face-to-face or live voice or video call (if face-to-face is not feasible for participant). The researchers at HST will use HST's current standard protocols to deliver positive HIV test results and provide counseling. All participants testing HIV-positive or HIV-negative will be offered linkage to care services.

3. **Exit interviews.** To provide insight into why **CHALO! 2.0** may or may not work to increase HIV testing and linkage-to-care and obtain data to inform intervention scale-up, the team of researchers at HST will perform phone-based exit interviews with 5-10 randomly selected participants from each of the following groups: never HIV tested, tested only once, tested multiple times, linked to HIV treatment, linked to HIV prevention care (e.g. PrEP, counseling), and not linked to care.

4. **Risk.** Possible risk faced by the participants include: confidentiality issues, inconvenience and discomfort associated with interviews, stigma and confidentiality concerns in terms of HIV testing, being outed as a sexual minority. More detail information about the potential risk and precautions against those risks can be found on the Protection of Human Subjects document below sections A3 and B1.
5. **Benefits.** The potential benefit to participants in this study could be linkage-to-care, access to HIV/STI prevention and testing services otherwise difficult to obtain, and access to credible information on new and existing HIV prevention tools. But all participants may not realize these benefits and there will be no other direct benefits to participants. However, if effective, CHALO! 2.0 could be implemented broadly and rapidly diffuse information on available HIV prevention tools and improve linkage to HIV testing and linkage to care services for MSM, a hard-to-reach population. Additionally, CHALO! 2.0 could have significant public health benefit by reducing the HIV burden in MSM and the broader population. More information about the Risk/benefit ratio can be found in the Protection of Human Subjects document below section C.

***Procedures***

6. **Recruitment.** The researcher staff at HST will use similar procedures for recruitment as we have used in prior studies: online ads will be displayed on MSM dating apps in Mumbai (Grindr, Blued, others if a new popular app emerges) and by targeted ads on Instagram to men in Mumbai with LGBTQ/gay interests associated with their profiles. All ads will contain links directing potential participants to a webpage with further information about the study and an eligibility screener. Eligible participants will be directly linked to an informed consent page (including an audio-video version of the informed consent) on Avegen's Health Machine (HM), a web-based survey platform,[63] and non-eligible participants will be directed to an exit page thanking them for their interest. Eligible participants who agree to participate after reading the informed consent will be directed to a baseline survey. All potential participants will provide a phone number associated with their WhatsApp account and an email address, and reply to a confirmation code (sent immediately to confirm the individual is real and not a bot or a computer program). Phone numbers will be checked against HST's registry by research staff to ensure participants aren't already receiving services through HST. Eligible participants will receive their incentive and be considered fully enrolled within 48 business hours.
   - **6.1 Feasibility of recruitment:** In prior studies of MSM in Mumbai, HST enlisted community members to help design ads to recruit MSM at high risk of HIV. For the **CHALO!** Pilot, HST enrolled 244 MSM in Mumbai over 3 weeks, and for Zero Meters Away online survey, we enrolled 1036 sexually active MSM from Mumbai in over 4 weeks (46% of whom would have met inclusion criteria for the proposed study and provided mobile numbers). Recruitment for this trial will be enhanced because all participants will receive an incentive (unlike our 2017 online study) and because of the continual increase in SMT use by Indian MSM. We plan to enroll approximately 100 participants per month (which will be controlled by the frequency of online recruitment ads); this rate will ensure that study staff can verify participants and that HST's testing sites and counselors are not overwhelmed by potentially large influxes of individuals needing services in a short time.
   - **6.2 Unique Participants and non-fraudulent data:** Fully online studies risk enrolling fraudulent participants, [64-68] and] precautions will be taken to avoid such participants. First, the only way individuals will learn about the study and start the screener will be by clicking on a direct link from an MSM networking app or social media site with ads only displayed in Mumbai. Based on our prior experiences in India and the US, the likelihood is exceptionally low of fake accounts "trolling" MSM dating apps or having a Facebook or Instagram profile with attached LGBTQ interests, then being invited into a research study and successfully "guessing" the enrollment criteria. Second, our screening survey will be able to block multiple submissions from the same device.[69] Third, eligibility screener will contain attention questions and include items beyond the inclusion criteria (e.g., smoking, substance use, other health issues) to prevent individuals from "guessing" eligibility criteria. Fourth, participants will verify their mobile number and email address (found to be acceptable to Indian MSM).[23,24,43] Fifth, baseline and follow-up surveys will also include attention questions. Finally, study staff will manually review all flagged surveys for suspicious responses, check for duplicate emails and mobile numbers, compare responses from the same IP addresses, and examine those from proxy-IP addresses.[70] These protocols are based on what we and others have used (NIH K23MH102118, NIH UG3AI133675).[23,67,71]
   - **6.3 Tracking and retention:** The research team at HST will collect information at baseline about whether and how peer-counselors should identify themselves when calling or texting (e.g., by name, "the research study," or the

"**CHALO!** project"), particularly for participants who test HIV-positive. Participants will receive automatic reminders for completing the pre-specified follow-up surveys at 3, 6, 12, and 18 months.

**6.4 Regular incentives:** Participants will receive increasing incentives for each complete assessment at months 3, 6, 12 and 18; the research team at HST will ensure acceptability of incentives by offering choices (PayTM – e-cash widely used in India and connected to mobile number,[72] or Amazon.co.in gift-code) (see Table 1 for amounts).

**6.5 Drawing:** In addition to the small incentives above, the research staff at HST will use a prize Drawing to reinforce study assessment completion and minimize attrition.[126-128] The drawing will be contingent on completing post-baseline assessments, and not on testing or linkage-to-care. After completing each online survey, participants will be automatically entered into a drawing to win 1 of 20, 1,000 Rupee incentives. Additionally, participants will be entered into similar drawings at months 9 and 15 for 1,000 rupees, based on verifying contact information (to aid in retention). Participants in all 3 arms will thus be contacted every 3 months, which has been shown to improve engagement and retention in online longitudinal studies.[73]

**6.6 Retention and attrition:** Though we conservatively estimate 15-20% attrition at 12 months, we have a strong record of retention in online studies. In the **CHALO!** pilot, retention was 82% at 3 months, despite no rigorous procedures for verifying phone numbers or emails and only using one incentive option. In our US.-based E-PrEP trial, we used verification procedures at enrollment, provided choice of incentives and have had >90% retention at 6 months, with 100% of retained participants consenting to be contacted at 12 months. We also anticipate high retention rates for the proposed trial because incoming mobile voice calls and text-messages are free in India, because the research team at HST will use an increasing incentive structure coupled with prize drawings, and provide choices for incentives. If participants do not respond to a survey, they will to receive follow-up surveys for subsequent assessments unless they request to stop receiving follow-up messages.

**6.7 Snowball Recruitment:** If a participant requests a screening/enrolment link to share with their network at any time, we will share a customized link to the Chalo!2.0 study information page. They can request this link either by texting/WhatsApp on the study phone number or by contacting our VPeers on a recruitment platform. If a participant does not request a link by the 3-month mark of enrolment in the study, we will proactively ask participants whether they are willing to share a customized link among their network, via WhatsApp or SMS. All links lead to the Chalo! 2.0 study information page. Rationale: Participants may already be sharing screening/enrolment links among their network. This strategy allows us to monitor when participants refer other individuals to the study. We will not provide any monetary benefits/ support for sharing the link.

**7. <u>Randomization and blinding.</u>** Subjects meeting all eligibility criteria will be randomized to one of three study arms. Participants will be assigned either to **CHALO! 2.0** (intervention), to an Attention-Matched Control, or to a Digital Coupon for free HIV testing only arm. After baseline survey completion, The research team at HST will use random blocked design, with a fixed block size, to stratify randomization by prior HIV testing history (never tested vs. not tested in >6 months). To further minimize bias in group allocation and analysis, a data manager who has no contact with study participants will (1) assign them to study group (intervention or controls), (2) notify our technology consultant of group assignment by providing the consultant each week with a list of mobile numbers and which set of contents each number should be programmed to receive, and (3) store allocation sequences in a password-protected encrypted file. Participants will be unaware of arm assignment and will receive automated messages to complete online surveys. Study staff collecting HIV testing and linkage-to-care outcomes will also be blinded to study arm. Finally, HST's online peer counselors and navigators will not be informed of study hypothesis.

**8. <u>Data Collection.</u>**

**Table 2: Data sources and measures**

| Measure | Study Instrument | Assessment Month | | | | |
|---|---|---|---|---|---|---|
| **Outcomes: HIV testing and linkage to care** | | **0** | **3** | **6** | **12** | **18** |
| HIV testing | Lab report (via digital coupon); self-report | ● | ● | ● | ● | ● |
| Linkage to prevention/treatment (PrEP, counseling, ART) | HST's healthcare worker log; HST clinic record; self-report | ● | ● | ● | ● | ● |
| **Covariates** | | | | | | |
| Sociodemographic characteristics | Zero Meters Away[23] | ● | | | | |
| Sexual behaviors, partners, condom, PrEP, and PEP use | Zero Meters Away[23,42] | ● | ● | ● | ● | ● |

**8.1 Online study assessments**: The researchers at the international site at HST will use Avegen HM online surveys to collect self-reported data on sexual behaviors, prior HIV testing, HIV knowledge (transmission, treatment, and prevention), self-efficacy for HIV-testing and care, stigma, and other covariates listed in Table 2. The survey will be in Hindi and English, and will also ask questions to assess potential contamination between study arms. At each assessment point, subjects will receive 3 automated reminders, 48 hours apart if surveys are not completed. After the 3 automated attempts, study staff will be notified if surveys are not completed, who will then reach out to participants.

| | | | | | | |
|---|---|---|---|---|---|---|
| Anticipated, perceived, and community HIV stigma | India HIV Stigma Scale[75,76] | ● | ● | ● | ● | ● |
| MSM internalized and community stigma | MSM Stigma Scale[77] | ● | ● | ● | ● | ● |
| Identity disclosure | Sexual Identity and Presentation[23] | ● | ● | ● | ● | ● |
| HIV knowledge, risk perception | HIV Knowledge Scale[78] | ● | ● | ● | | |
| HIV testing attitudes, intentions | Attitudes Towards Testing Scale[79,80] | ● | ● | ● | | |
| Self-efficacy (testing, coping, care linkage) | Self-Efficacy scales[80,81] | ● | ● | ● | | |
| Knowledge of free MSM-sensitive HIV testing sites | Zero Meters Away[23] | ● | ● | ● | | |
| Social support | MPSS,[82] Counselor Support[60] | ● | ● | ● | ● | ● |
| Alcohol/substance use | WHO ASSIST[83] | ● | ● | ● | | |
| Depression/Anxiety | CES-D[84]; Beck's Anxiety scale[85] | ● | ● | ● | | |
| Contamination assessment | Content Recall questionnaire[86,87] | | | ● | ● | ● |
| **Process measures, SMT engagement (paradata[88,89])** | | | | | | |
| Message delivery and view statistics | Whatsapp Business App analytics[57], YouTube analytics | | ● | ● | ● | ● |
| Peer-Counselor interaction via SMT | Downloaded message and call log from HST Peer smartphones | | ● | ● | ● | ● |
| Website visits | Google, Bit.ly analytics | | ● | ● | ● | ● |
| Participant Incentives (in USD $) | | 6.20 | 7.75 | 8.52 | 8.52 | 9.30 |

**8.2 HIV testing digital coupon data:** When participants present the coupons at any testing site, the tester-counselor (at HST sites) or lab technician (at the private lab sites) will enter the coupon code using an online coupon form. This system will register the coupon as being used, with time, date, and location of usage. Once test results are available, they will be entered in a manner specific to the testing site. At HST, the tester-counselor will enter test results directly into an Avegen HM form. If the coupon is used at the private lab, the data manager will retrieve results from the lab's secure online portal (along with the coupon use data) and enter it into the Avegen HM database. Two strategies will be used to capture testing data if a participant does not use the digital coupon provided by the trial. As described above, counselor-based testing that occurs at HST will be identified when the data manager cross-checks mobile phone numbers and emails for clients obtaining HIV tests against participant contact information. (At HST, contact information is provided by >99% of clients,[90] as required by Indian guidelines.[91]) Second, testing that occurs outside both HST and our private lab partner is expected to be rare, as subjects will receive free tests through the private lab (41 sites across Mumbai) or through HIV self-testing only if they use the digital coupon provided. Further, HST's 3 sites are the only MSM-specific free testing sites in Mumbai. In the very rare event that a participant does report testing elsewhere, this will be captured in the online survey, which will ask for the name and location and for the participant to upload a picture through secure link of their test completion result.

**8.3 Clinical outcomes data from HST computerized information system (CIS):** The HST CIS contains data on all services used by clients, linked to their mobile-phone number and includes both services at HST and services at sites outside HST. The HST data manager will cross-check data weekly and merge it with the study's Avegen HM database. On-site HST services include clinic use (counseling, HIV testing, PEP, and PrEP prescribing, STI testing/treatment) and healthcare worker navigation logs (HIV treatment referral/linkage in both public centers and the few preferred private clinics, antiretroviral treatment status, and PrEP referral). In addition, the HST CIS includes data on linkage-to-care and outcomes from public ART centers for all referred clients, because HST is an official voluntary testing-counseling center under the Indian Health Ministry. Finally, because of reporting requirements and the mandate to provide choices to clients, HST refers to a small number of vetted MSM-competent private HIV treatment providers with whom there are linkage agreements for HST to obtain client follow-up and ART use data (confirmed with clients themselves) and entered the data into HST's CIS. For study participants who self-report linkage-to-care anywhere outside HST or HST's partners, questions about care status (ART treatment, counseling, STI testing, PrEP use) and request permission (via an emailed statement) will be asked to have study staff from HST verify the information. Due to privacy concerns, not all participants may be willing to share this level of information.

**8.4 Process measures:** Process measure data will include messaging frequency, online peer counselor interactions, and study website visits. Whatsapp Business Analytics will be used to assess whether messages were received and

viewed by each participant. The assessment of online peer counselor interactions that occur via Whatsapp, SMS, and voice-call will be done by downloading HST's peer counselors' message- and voice-call history, cross-matching it to participant phone numbers, and merging the matched data to the study Avegen HM database. Finally, we will assess study website visits using Google analytics to monitor traffic and visits. The use of personalized links and study arm-specific webpages will enable the HST and Einstein teams to assess overall web traffic by study arm, and to determine frequency of clicks on individual links (though link data cannot accurately be attributed to one individual, due to current technology limitations).

9. **Data Security.** All data collected online will be maintained in encrypted, password protected computer systems. The web-based Avegen Health Machine (HM) software database will used by the HST team to hold study data – this system uses the latest encryption data and in the U.S. meets all regulations for security and privacy of participant information. Avegen HM will also be used to collect web-based survey responses – which also use the latest security protocols for transmission and receiving online data. All data can only be accessed by logging into the online Avegen HM database and different study staff can be given different levels of access as required – all of which facilitates security, privacy. All offline data, if it exists, (which we expect there to be minimal to none) will be stored in secure locked cabinets at HST. All data will be deidentified prior to analysis and reports. Only members of the HST's research team who are in charge of follow-up and the HST site investigators will have access to the data of participants who agree to be a part of the follow-up. Their identifying information will be destroyed at the conclusion of the project by HST staff. More detail information regarding data security can be found in the Protection of Human Subjects below sections B3 and B4.

**Analytic Plan**

10. **Outcome variables.**

Aim 1 is to determine whether **CHALO! 2.0** increases HIV testing compared to control conditions, and to identify factors associated with HIV testing.

- *Primary outcome*: dichotomous measures (yes/no) of receipt of a verified HIV test within 6 months of randomization.
- *Secondary outcomes:* frequency of HIV testing within 18 months of randomization, receipt of a verified HIV test within 12 and 18 months of randomization, and receipt of a self-reported HIV test within 6 months of randomization.

Aim 2 is to determine whether **CHALO! 2.0** increases linkage-to-care (both HIV prevention through counseling and use of PrEP, and HIV treatment with antiretrovirals), and to identify factors associated with linkage to care.

- *Primary outcome*: dichotomous measure of linkage-to-prevention (yes/no), which will be defined as a composite of either counseling or PrEP use. We consider any counseling as prevention because of evidence that non-HIV specific counselling for MSM in India and elsewhere may confer HIV preventive behaviors directly or indirectly.[92-94]
- *Secondary outcomes*: HIV treatment linkage (yes/no) and ART initiation (yes/no) for those testing HIV positive, each variable individually in the primary composite outcome (i.e. counseling, PrEP), sexual behavior (consistent condom use, number of partners).
- *Exploratory Outcomes*: include alcohol/substance use, PEP use, STI testing/treatment, and type of prevention or treatment care site accessed (i.e. HST vs. other).

Finally, the following outcomes will be reported by study arm: HIV knowledge, HIV- and MSM-stigma, risk-perception, self-efficacy, social support, intention to obtain HIV test in next one month, and SMT engagement by arm (proportion of all messages viewed, website visit, and any communication with online-peer counselors).

11. **Plans to identify contamination across study arms.** Contamination will be assessed by using a content recall questionnaire[86,87] to measure any diffusion and sharing of **CHALO! 2.0** and attention matched control contents, determining whether participants report sharing messages or website links. Participants will also be asked if they knew anyone participating in the study and if they received any contents from them.[95]Members from the HST and Einstein research teams will assist in building research instruments.
12. **Randomization checks and missing data.** A member from either the Einstein or HST team will first review and summarize data using descriptive summaries and graphical analyses to ensure that reported values are within appropriate ranges, check for outliers and abnormal values, and verify that distributions of measures meet

assumptions of planned statistical tests. The Einstein and HST research teams will also explore whether **CHALO! 2.0** and the 2 control groups are equivalent on potential confounders (e.g., sexual identity, income, age, education, intention to test, and sexual behaviors. If these variables differ between groups, we will include them as covariates in multivariable analyses (see Section C.7.4). For missing categorical data, we will use multivariate multiple imputation using the fully conditional specification method.[96] We will repeat imputations 5 times, and then compare statistical results using datasets that include imputed values and the dataset that drops missing values. This will guide interpretation of our assessment of the impact of missing data on our study findings, as well as our interpretation of overall results.

13. **Specific analyses by study aim.** All of the analysis will be done by members of both Albert Einstein College of Medicine and the HST. All primary analyses will be intention to treat, including participants who are lost to follow-up. In secondary analyses, we will conduct per-protocol analyses to ascertain outcomes among participants who actually viewed messages and identify exposure levels ("dosage") that may be associated with outcomes. We will conduct additional exploratory analyses on a per-protocol basis to assess factors such as participant satisfaction.

13.1 **Aim 1 analyses:** To test the hypothesis that **CHALO! 2.0** participants (vs. controls) will be more likely to be HIV-tested, the proportion of HIV testing at 6 months between **CHALO! 2.0** ($n_1$=300) and attention-matched control ($n_2$=300) participants will be compare. We will also compare **CHALO! 2.0** participants to digital coupon only participants. Both analyses will be 2-sample comparisons of proportions, using chi-square tests. Although this is a randomized trial, to account for possible confounders we will also perform logistic regression with HIV testing at 6 months as the dichotomous outcome and intervention type as the primary predictor, adjusting for the covariates in Table 2. In secondary analyses, we will repeat these analyses with HIV testing at 12 months and 18 months as outcomes, and with the outcome of self-reported HIV test within 6 months.

To test the hypothesis that **CHALO! 2.0** participants (vs. controls) will obtain HIV tests more frequently, we will compare the frequency of HIV testing by 18 months between **CHALO! 2.0** ($n_1$=266) participants and attention-matched control ($n_2$=266) or digital coupon only participants, using Poisson tests. We will repeat this analysis comparing **CHALO! 2.0 to**. We will account for possible confounders by performing Poisson regression with frequency of HIV testing as the outcome and intervention type as the primary predictor, adjusting for confounders in Table 2. In exploratory analyses, we will report proportions (with 95% confidence intervals) of initial HIV-testing strategies (counselor based testing at HST, self-testing, or private laboratory testing) within each intervention condition, and assess differences between arms if other participant characteristics are associated with the initial testing strategy used.

**Table 3. HIV testing proportion at 6 months***

| Power | CHALO! 2.0 ($n_1$=300) | attention-matched control ($n_2$=300) | Digital coupon only ($n_2$=300) |
|---|---|---|---|
| >99% | 0.5-0.75 | 0.2-0.5 | 0.15-0.45 |
| >93% | 0.5-0.6 | 0.35-0.45 | 0.35-0.45 |
| >59% | 0.5-0.6 | 0.4-0.5 | 0.4 |
| >15% | 0.5 | 0.45 | 0.45 |

*power is for CHALO! compared to each control separately

13.2 **Aim 1 sample size considerations**: With a total of 1,000 participants, we expect at least 900 participants at 6 months, and 800 participants at 12 months. This will provide a total of 300 participants per arm at 6 months, and 266 participants per arm at 12 months. Based on findings from online intervention studies of HIV testing showing 1.7-2.2 increases in odds of testing in intervention vs. control conditions (across low and high income countries and heterogeneous online interventions),[97-100] we estimate the proportion HIV testing at 6 months to be 70% for **CHALO! 2.0** ($n_1$=300) vs. 35% for attention-matched control ($n_2$=300) and 30% for digital coupon only ($n_2$=300). With the expected sample, the study's 2 main effects (**CHALO! 2.0** vs. attention-matched control and **CHALO! 2.0** vs. digital coupon only) have >99% power (Table 3). We also provide power estimates based on a wider range of parameters in Table 3, showing that we have sufficient power to detect between-group differences in the primary outcome with smaller effect sizes. Power was calculated using PASS software V15.0, with all analyses conducted with a two-tailed alpha of .025, resulting in a family-wise error rate of at most 0.05 for the primary outcome.

13.3 **Aim 2 analyses:** To test the hypothesis that **CHALO! 2.0** participants will be more likely to be linked to care (vs. controls), we will compare rates of linkage-to-prevention (i.e. counseling, PrEP-initiation) at 12 months among HIV-uninfected participants between study arms. As for Aim 1, we will perform 2-sample comparisons of proportions using chi-square tests, and will also perform logistic regression with linkage-to-prevention by 12 months as the outcome and study arm as the primary predictor, adjusting for covariates in Table 2 as required. We will repeat these analyses with linkage-to-care outcomes at 18 months, and with the outcome of self-reported linkage-to-prevention by 12 months. Additionally, using the entire study cohort, we will explore

**Table 4. Proportion linked to HIV prevention by 12 months**

| Power | CHALO! 2.0 ($n_1$=247) | attention-matched control ($n_2$=139) | digital coupon only ($n_2$=108) |
|---|---|---|---|
| >99% | 0.15-0.4 | 0.05-0.1 | 0.03-.01 |
| >98% | 0.3-0.4 | 0.1-0.2 | 0.03-0.1 |
| >90% | 0.3 | 0.15 | 0.1-0.15 |
| >70% | 0.2 | 0.1 | 0.08 |
| >49% | 0.3 | 0.2 | 0.2 |
| >21% | 0.15 | 0.1 | 0.1 |

*power is for CHALO! compared to each control separately

whether participant factors and testing strategy predict HIV prevention (counseling or PrEP use) and treatment (ART initiation). For secondary and exploratory outcomes (defined in C7.1), we will repeat analyses as above, using ANOVA for or chi-square tests as appropriate.

**13.4 Aim 2 sample size considerations**: We anticipate that there will be no higher than 7% prevalence of undiagnosed HIV. Combined with expected HIV testing rates by 12 months of at least 75%, 45%, and 35% in the three arms, we anticipate the available sample size of HIV-uninfected participants for Aim 2 to be **CHALO! 2.0** ($n_1$=247), attention-matched control ($n_2$=139), and digital coupon ($n_2$=108). Based on HST's current linkage-to-care rates for HIV- negative individuals (30%),[90] we expect the rate of linkage-to-prevention care at 12 months to be 30% for **CHALO!** vs. 15% for attention-matched control vs. 5% for digital coupon only. The study's 2 main effects (**CHALO!** vs. Attention-matched control and **CHALO! 2.0** vs. digital coupon only) have >90% and >99% power, respectively (Table 4). We also provide power estimates for smaller effect sizes. The power was calculated using PASS software V15.0., with a two-tailed alpha of .025, resulting in a family-wise error rate of at most 0.05 for the primary outcome in the Aim 2. Due to an expected overall small number of individuals testing HIV-positive, we will not have power to detect potential differences between arms.

**PROTECTION OF HUMAN SUBJECTS**

**A. RISKS TO HUMAN SUBJECTS**

A1. HUMAN SUBJECTS INVOLVEMENT, CHARACTERISTICS, AND DESIGN.

A1a. Proposed human subject involvement. The protocol will include a 3-arm parallel, single blind, pragmatic randomized control trial of an online HIV digital messaging intervention (CHALO! 2.0) compared to an Attention-Matched Control, or a Digital Coupon only. Through online surveys, HIV testing utilization and results, and clinic visit data tracked by HST healthcare workers during the 12-week intervention period, and during the 15 months of follow-up, we will evaluate the outcomes for CHALO! 2.0.

A1b. Subject population characteristics. The 1000 MSM in the proposed trial will be composed of a diverse sample of individuals unaware of their current HIV status (e.g. never tested or tested >6 months ago and have been sexually active with men) recruited via MSM specific dating apps (Blued, Grindr), and via the most used general social media sites (Instagram) in an urban area with high rates of HIV (Mumbai, India). Currently, HIV rates for online-person recruited MSM in Mumbai are estimated at 5-7%, based on our recent studies (the only

such data available). All participants are expected to identify as Asian Indian and male.

A1c. Description and justification of sampling plan, recruitment and retention strategies and eligibility criteria. Recruitment will be passive via online advertisement displayed to individuals on MSM dating apps (Grindr and Blued, and will include others if we find a new app emerging in popularity) or by targeted advertisements on Instagram to men who have LGBTQ/gay interests or keywords associated with their profiles. Due to technological advancements, the ads will be geographically limited to those potential participants accessing these sites from Mumbai or those who have indicated a Mumbai address on their social media profile. All advertisements will contain links directing potential participants contain links directing potential participants to a webpage with further information about the study and an eligibility screener. Eligible participants will be directly linked to an informed consent page (including an audio-video version of the informed consent),[63] and non-eligible participants will be directed to an exit page thanking them for their interest. Eligible participants who agree to participate after reading the informed consent will be directed to a baseline survey. All potential participants will provide a phone number associated with their WhatsApp account and an email address, and reply to a confirmation code (sent immediately to confirm the individual is real and not a bot or a computer program). Phone numbers will be checked against HST's registry by research staff to ensure participants aren't already receiving services through HST. Eligible participants will receive their incentive and be considered fully enrolled within 48 business hours.

Retention will be enhanced by (1)utilizing Whatsapp for intervention and online survey delivery since all incoming mobile phone calls text messages are free in India, which will allow participants to receive all study communications and will remove the burden for participants to appear go to a study site to complete the surveys (2) collecting information in the baseline assessment about whether and how peer-counselors should identify themselves when calling or texting (e.g., by name, "the research study," or the "CHALO! project"), particularly for participants who test HIV-positive, (3) providing incentives completing online surveys (at 0,3,6,12, 18 months) in increasing amounts ($6.20, $7.75, $8.52, $8.52, and $9.30 respectively), (4) providing participants choices of incentives to broaden acceptability of incentives (PayTM – e-cash widely used in India, and connected to mobile number, or Amazon.co.in gift-code) (5) utilizing a drawing prize system of one in twenty $15.50 incentives to reinforce online study assessment completion and minimize attrition (at 3,6,12,18 months) and being entered into a drawing at months 9 and 15 (for one of twenty $15.50 incentives) for verifying or updating contact information.

This protocol aims to recruit a diverse sample of men who do not know their current HIV status (i.e., report that they have either never been tested for HIV, are unaware of HIV test results, or are HIV-negative with last HIV test greater than or equal to six months ago, and have engaged in anal sex since last HIV test). Therefore, inclusion criteria will be

(1) ≥18 years old; (2) live or work in the Mumbai metropolitan area, including Thane; (3) fluent in Hindi or English, (4) identify as cis male, (5) anal sex with men in past 1 year; (6) (a) report that they have either never tested for HIV, (b) are unaware of HIV test results, or (c) are HIV-negative with last HIV test >6 months ago and anal sex since last test; (7) able to provide and verify a WhatsApp mobile number and email address; (8) willing to answer online surveys for 18 months; and (9) have not participated in a prior HIV research study (by self-report).

We will exclude individuals who (1) are unwilling to consent/ assent to the study, (2) do not verify their WhatsApp account, and (3) have used services at HST within the past year.

A1d. Special vulnerable populations. We will not include fetuses, neonates, children, pregnant women, prisoners, or institutionalized individuals in the proposed research. Men who have sex with men are vulnerable due to their status as a stigmatized population in society and further stigmatization could be possible if their status as a participant in an HIV prevention intervention is revealed. In the following sections, we discuss these risks and procedures to minimize them and believe that the risks to participation in the proposed study are minimal.

A1e. Study group assignment procedures, and rationale for intervention's dose, frequency and administration. Subjects meeting all eligibility criteria will be randomized to one of three study arms. Participants will be assigned either to CHALO! 2.0 (intervention), to an Attention-Matched Control, or to a Digital Coupon for free HIV testing only arm. Randomization will occur in a random blocked design, stratified by HIV testing history (never tested/unaware of results vs. previously tested). To minimize bias in treatment group allocation, the data manager will store the allocation sequence using a password-protected file, and has no contact with study participants. Participants will receive automated messages with online

survey links to complete study assessments, and study staff extracting medical record/log data to ascertain linkage-to-care outcomes, will be blinded to treatment group allocation and will have no contact with study participants.

During the 12-weeks intervention period, participants assigned to either CHALO! 2.0 (intervention) or the Attention-Matched Control (AM) arm will be exposed to twice-weekly digital messaged, including text, brief videos, inform graphics, etc. via an online messaging site. However, the digital message for participants in the CHALO! 2.0 arm will include information regarding HIV testing, accessing treatment and prevention care with a focus on targeting information, motivation, and behavioral skills, while the information in the AM arm will focus on general health topics (e.g., diabetes, obesity, nutrition, exercise). Participants in the digital coupon only arm will not receive any messages aside from the reminders to complete study assessments. We are providing twice weekly contents as this was determined in the past to be acceptable, not intrusive and higher frequency may actually be detrimental.

Participants in all three arms will receive a digital coupon for free rapid HIV testing or 4$^{th}$ generation serum testing (per participant choice), have access to a website listing the testing sites where the coupon is redeemable across Mumbai, care information for treatment and prevention, and have contact information to get in contact through SMT with HST's online peer counselors.

Through online surveys, HIV testing utilization and results, and clinic visit data tracked by HST navigators/health workers during the 12-week intervention period, and during the 15 months of follow-up, we will evaluate the CHALO! 2.0 exposure outcomes.

A2. SOURCES OF MATERIALS.

The HST team will collect online survey data (at baseline, 3, 6, 12, and 18 months), HIV testing utilization and results (throughout the 18 months), and clinic visit data tracked by HST navigators/health workers through existing linkage to care and tracking protocols at HST (over the 18-month tracking period).

Online Surveys. Avegen Health Machine (HM), an online web surveys software, will be used to collect self-reported data from participants on their sexual behaviors, sociodemographics, HIV testing history, how they self-identify with regards to sexuality, HIV knowledge, motivation for testing, intention to obtain HIV test, self-efficacy for testing and care, HIV and internalized sexual minority stigmas, and HIV prevention knowledge,

Personalized Digital Coupon use data (HIV testing data): All participants, after verifying their contact information will receive a personalized digital coupon consisting of a QR barcode and number through a Whatsapp message and email. The coupon will be linked to their study-id and mobile number, preassigned by the data manager. Once a client presents the coupon at any testing site, the tester-counselor (at HST sites) or lab technician (at the private lab sites) will scan the coupon or enter the coupon code using an online coupon management system, which will register the coupon as being used with time, date, and location of the scan saved by the coupon software in their online system. On a twice weekly basis, the data manager will download the coupon use data and merge it into the Avegen HM database.

This system will also alert study staff that a coupon was used with information about which coupon, so that study staff can follow-up with clients if needed about their results. If the coupon is used at HST, the tester/counselor will enter test results directly into a front-end HIV testing result form on Avegen HM (coupon-code and associated test result); if the coupon is used at a private lab, study staff will retrieve results from the lab's online portal, and then enter the test results into a front-end HIV testing result form on Avegen HM.

This approach has been generally used previously, including in a recent feasibility pilot by our private laboratory partner, and will enable real-time monitoring of test results, and accurate follow-up for clients.

Lab HIV testing data: Additionally, HST currently collects and verifies mobile phone numbers for clients coming in for testing to enable follow-up and linkage-to-care and as a requirement per Indian guidelines and requirements for testing. Subjects will only be able to receive the free test at the private lab or HIV self-test if they show the coupon. These steps will help ensure thorough assessment of our primary outcome and facilitate appropriate follow-up.

Linkage-to-care outcomes for HIV negative and positive individuals will be abstracted from HST's healthcare worker log, which contains information about linkage status and outcomes (HIV treatment registration, ART initiation, follow-up) or from HST's counseling and clinic utilization records which are housed on a computerized information system (CIS) at HST. Data from the HST healthcare worker log and the CIS can be linked to an individual's mobile phone number which will be how we match a participant's use of HST services. The data manager at HST on a monthly basis, will scan and match participant phone numbers to those in CIS; for any matches, that data will be extracted and merged into the Avegen HM database. The healthcare worker log also contains information about linkage/referrals to private HIV treatment clinics and for primary care/PrEP. Currently, HST refers clients interested in PrEP to two providers in Mumbai (vetted by HST to

provide MSM competent services). HST will also begin offering PrEP this summer to its patients, and will thus be available moving forward for all HST clients, including study participants.

Whatsapp Business Analytics Data. This platform will be used to preschedule the automated messages participants will receive in the CHALO! and attentional control arms and it enables us to download data from the Whatsapp business analytics platform to merge into the study database on Avegen HM. This data will contain information for CHALO! and attention matched control arms about if each message/content was received and if the message/contents was viewed. This will give us a crude measure of exposure (or engagement with intervention contents) to enable calculation of "dose received" and associate this data with outcomes. The data manager will download this data and merge it into the Avegen HM database.

Online Peer-Counselors Interaction data. Participants will be able to connect via Whatsapp to online peer-counselors at HST to receive support, answers questions, or referrals for linkage services. For each of the online-peer counselors, communication related process measures will be collected by downloading their message- and voice-call history and merge this data into the final study database in Avegen HM to examine potential associations with study outcomes as mobile phone numbers can be linked to individual participant data.

Study Webpage visit data (process data). All participants will be given a personalized link (e.g., using Bit.ly link shortener) to identical informational webpages (one webpage per arm) listing testing sites where the digital coupon can be used, contact information for the online Peer-Counselor, and other MSM specific health and wellness services offered by HST (e.g., mental health counseling, crisis support, hotline). The webpages will also have google analytics attached to the website to monitor traffic and visits. The use of personalized links and study- and arm-specific webpages will enable us to collect process data on website visits and assess overall web visit traffic by study arm as well as determine frequency of clicks on the individual links. While this individual link data cannot be attributed to one individual due to current limitations and privacy protections of tracking ability by Google Analytics and Bitly, allows for exploration of whether certain individual's links were clicked through more often than others and in exploratory analysis, compare this by study arm.

Exit Interviews. To provide insight into why CHALO! may or may not have worked to increase HIV testing and linkage-to-care for HIV+ and for HIV- individuals, and get additional insight to inform intervention strengthening and scale-up, research staff at HST will perform brief phone-based exit-interviews with 5 to 10 randomly selected participants from each of the following groups: never HIV-tested, HIV-tested only once, HIV-tested multiple times, linked to HIV treatment (if positive), linked to prevention care (e.g., PrEP, safer-sex counseling), and those not linked to care. In addition, the research team at HST will attempt to interview all participants who test positive to explore potential missed opportunities for prevention to inform future efforts. Data will be audio-recorded, but kept anonymous and not linked to any other data source. Interviews will be performed by the India Co-Investigators.

A3. Potential Risk to subjects

We believe that the risks posed to participation in our study are minimal and no greater than what individuals encounter in their regular use of the Internet and SMT services. The primary risks of this study are: (1) breach of confidentiality leading to embarrassment or "outing" of an individual's sexual orientation, (2) breach of confidentiality leading to disclosure of an individual's participation in a HIV prevention intervention, (3) inconvenience and discomfort associated answering questions about sexual health behavior, (4) stigma and confidentiality concerns when engaging in HIV testing

Confidentiality issues: The research team at HST will collect limited personal information from participants to facilitate follow-up and will be asking personal questions about substance use, HIV risk behaviors, and sexual identity. We have outlined procedures to address maintaining confidentiality below (**see section B3a**).

Inconvenience and discomfort associated with interviews: In all surveys, participants will be asked about HIV risk behaviors, sexual activity, and/or substance use. It is possible that such questions could produce anxiety in participants. Participants will be instructed that they may refuse to answer any question without providing justification and/or may withdraw from the study if this occurs.

Stigma and Confidentiality Concerns in Terms of HIV testing: Individuals make decisions about where and how to get HIV-tested by weighing multiple perceived and actual risks/benefits of each testing strategy in the real-world, such that no single testing approach likely meets the need of majority of MSM. CHALO! 2.0 uses a pragmatic approach by linking individuals to multiple exiting testing options. The coupon will be linked to participants' mobile numbers, and will be scanned/entered into an online system by testing staff (at HST or the private laboratory), at which time participants will immediately receive a code to provide to the tester to verify eligibility as a study participant. This will discourage sharing and use of the coupon aside from the participant, and help protect the participant's privacy. Each coupon can only be used

once every four-weeks at the most to minimize increased harm from potential false positive due to frequent testing and to discourage sharing the coupon. All participants who get tested, will also receive an automated message with a link for a pre- and post-test counseling video, a brief, bulleted Whatsapp message covering the central points of the counseling videos, and contact information for HST's community health-worker (who can provide counseling and linkage-to-care/navigation services for both prevention and treatment, and will be blinded to participant's study condition). These steps will help ensure confidentiality of participant test results, linkage of valid test results to each participant, and ensure data integrity.

Being Outed as a sexual minority. Participation in the study could theoretically out someone if another individual saw contents on the participants Whatsapp messages about MSM health and HIV testing. However, participation in this trial is voluntary, and is not likely to pose any greater risk than already experienced by potential participants who are using gay/MSM dating apps on their mobile phones, may be having text message conversations with other gay/MSM, or accessing LGBTQ related contents from their phones. Participants will only be receiving twice weekly messages/contents – which will only be sent during daytime hours. Additionally, participants will only be contacted by online peer-counselors or healthcare workers by the method the participant indicated during enrollment.

## B. ADEQUACY OF PROTECTION AGAINST RISKS.

B1. REGULATORY COMPLIANCE.

We will follow procedures as outlined by the National Institute of Mental Health (NIMH) Internet-based Research Interventions: Suggestions for Minimizing Risk (2007) and other evolving best practices in ethical conduct of social media and Internet research.[35,63,101-103] Additionally, the research team at HST will work with our social media consultants to ensure technical capacity of maintaining ongoing security and privacy.

B2. RECRUITMENT AND INFORMED CONSENT.

Members from the research staff at HST will first be conducting a quick screener that will not require potential participant to enter any identifiable information. Then, online informed consent will be obtained from eligible participants prior to providing the baseline self-administered online questionnaires and collection of any automated process data. Online informed consents will be provided in two ways: (1) A recorded video of the informed consent text and (2) the same information will be provided in an easy to read text format. A link for emailing or direct messaging and contact information with the PI and Research Assistant's office phone numbers will be displayed for potential participants to ask any questions participants might have. To indicate consent, an individual will then click a box attesting to their consent and then clicking a "submit" button. After consenting, participants will be taken directly to an eligibility screener which will continue seamlessly to the baseline survey (for eligible participants) or to an exit page thanking them for their interest. As part of the baseline survey and enrollment, potential participants will need to provide a phone number associated with their WhatsApp account and an email, and reply to confirmation code (sent immediately) to verify their information, subsequently receive their incentive, and be considered fully enrolled.

B3. PROTECTIONS AGAINST RISK.

B3a. Protection of confidentiality Questions pertaining to substance abuse, sexual activity and identities requires special sensitivity to issues of confidentiality. Participant confidentiality will be carefully protected. The researcher staff at HST will institute the following processes to ensure confidentiality is maintained:

1. Research staff at HST will be using Avegen Health Machine (HM) for data collection – this system uses Transport Layer Security (TLS) encryption (also known as HTTPS) for all transmitted data. Avegen HM hosts all data in in trusted data centers that are independently audited using the industry standard SSAE-16 method. Avegen HM deploys the general requirements set forth by many Federal Acts, including the FISMA Act of 2002, and they meet or exceed the minimum requirements as outlined in FIPS Publication 200. Avegen HM also institutes HITECH (Health Information Technology for Economic and Clinical Health Act) updated HIPAA rules to ensure that data are properly protected and best security practices followed and safeguards all customer data, and uses secure data centers to ensure the highest protection as per HITECH requirements. Additionally, Avegen HM allows us to assign individuals different levels of access to the system and data and allows monitoring of data access and flags/rules can be created for any potential suspicious activity (e.g. a user accessing the system outside expected working hours). The full dataset will only be accessible to the PI and study staff that need all such data (which will be rare).
2. Whatsapp will be the primary platform for intervention delivery and communication with participants. WhatsApp's uses an end-to-end encryption, which ensures only the study team and the participant with can read what is sent, and nobody in between, not even WhatsApp. This is because the messages are secured with a lock, and only the recipient and the sender have the special key needed to unlock and read them. For added

protection, every message sent on Whatsapp has its own unique lock and key, and all of this happens automatically. Thus, this messaging approach is the most secure way to deliver intervention contents and balance using a user-friendly platform that ensures engagement.

3. The research team will also consult with our social media technology consultants to provide ongoing advice on technical aspects of securing information over the Internet and social media and in particular Whatsapp, Avegen HM, and protecting participant data.
4. An electronic, password protected and encrypted system will be used to store analyses, and Whatsapp activity will remain private to study participants.[164] Research participants will be informed of how communications are recorded and stored during the online informed consent process. Due to the ever-changing and evolving nature of privacy issues on messaging platforms, smartphones, the Internet, the research team and our technology consultant will regularly review privacy settings for all online platforms used in the study at least every month and adjustments will be made to protocols if necessary to ensure security.
5. Data analyses and reporting will be conducted using de-identified data in so that no participants will be identifiable. In order to deliver electronic gift card incentives, participants will be asked to provide their mobile number and an e-mail address where we can send incentives (requirement for enrollment). However, researchers at HST will not request names (regardless, there is no way to ensure we are getting actual or alias names and so there is little utility in collection of information). All participant responses will be kept confidential. Only appropriate research staff, and *not* the Peers will be able to review raw survey responses and un-summarized web activity. At all times, data collected for the project will downloaded onto secure servers and stored in password protected encrypted files.
6. All research having any potentially identifying information such as this proposal, will have a Certificate of Confidentiality automatically issued by NIH, as data will be stored on secure servers at Albert Einstein College of Medicine.

B3b. Data Security and

B3d. Managing the matter of anonymity and/or false information of research participant/study: The research team at HST will conduct meetings with all supporting research staff to discuss site activity, messaging, and participant responses to scan content for false information. Email and mobile phone numbers will be verified by sending an email and Whatsapp message to each potential research participants and requiring a verification response via clicking a link in the email and responding to the Whatsapp message. To protect false information, participants will provide basic demographic information again when participating in the assessment surveys, and online gift-card incentives that will be provided for completing surveys can only be sent to the mobile number once each data collection wave.

B3e. Protecting participants from research "posers": Research participants will be provided with options for verifying the credentials of the researchers and approval of the study through provided contact information of the site PI, research assistant, and the local IRB(for international site) and approval number (phone number, email, institutional website); a signed certificate and SSL (Secure Sockets Layer) for all data transfer over the Internet will be used, provided by our technology partner; participants with be given the option to print or save the informed consent page for their personal records and receive it via email from the study team.

B3f. Monitoring the research participant's well-being and building trust: If a participant reveals symptoms of psychological distress via SMT interaction with the online-peer counselors, appropriate referrals and follow-up care and intervention will be made by the HST health workers and online peer-counseling staff in accordance existing protocols for online/phone counseling by HST outreach workers and with a developed resource guide. All efforts will be made to link the online participant to resources at the HST health resources or to one of HST's vetted partners.

B3g. Addressing the lack of in-person communication and possible needs of research participants: Graphics and video will be used for participants to help overcome limited literacy. Additionally, all participants, regardless of arm, will be able to communicate via SMT with online peer-counselors at HST. Participants will be able to directly contact the research team (site PI, PI, and Project Director) through email and phone, and this information will be readily accessible in the customized Website link.

B3h. Managing confusion among research participants and debriefing: Research participants will have the opportunity to leave comments and ask questions about the online assessments/surveys both before and after completion, and additional contact information of the research team will be made readily available to all participants.

B3. Data Security for Storage and Transmission: As outline above, all data collected online will be maintained in encrypted, password protected computer systems. Study data will be store in the web-based Avegen Health Machine (HM) software database to hold study data – this system uses the latest encryption data and in the U.S. meets all regulations for security and privacy of participant information. Avegen HM will be used to collect web-based survey responses – which also uses the latest security protocols for transmission and receiving online data. All data can only be accessed by logging into the online Avegen HM database and different study staff can be given different levels of access as required – all of which facilitates security, privacy. This system is used by Research centers across the world including in India (e.g., AIDS Society of India for a study with HIV positive individuals, Prashanti Cancer Center in Pune, KLE JN Medical College, etc.). All offline data, if it exists, (which we expect there to be minimal to none) will be stored in the cupboards at HST under lock and key. All data will be deidentified prior to any analysis and reports. Only members of the research team who are in charge of follow-up and the investigators will have access to the data of participants who agree to be a part of the follow-up. Their identifying information will be destroyed at the conclusion of the project.

B4. Additional Online Safety and Suicidal ideation protocol

The following protocol has been approved by our IRB and is being used in our current social media/online research studies[212]. Given that we cannot actually verify real-world identities of participants and will not be collecting residential address/location information (to encourage participation and help minimize perceived breaches of privacy), the following protocol will allow us to monitor and address safety concerns of participants in a timely manner to the extent possible. While our study poses no more than minimal risks already being encountered by potential participants, these measures and protocols will be in place to maintain adequate protection of participants in the event they are needed.

1. If online peer counselors' sees a status update display on study sites or receives email, phone calls that suggests suicidal ideation. Key words for example may include (but are not limited to) “kill myself,” “end it all,” “not be around anymore,” “better off dead” or themes alluding to these issues, including any description of an intended activity linked to suicide such as “I’m going to jump off a bridge,” “I’m going to shoot myself,” they will follow standard operating procedures at HST for such occurrences as HST deals with these issues regularly. Additionally, because subjects are volunteering for a research study, the HST research team will employ the following procedures:
    a. Peer-counselors notes date and time of reference
        i. Write down name and any available contact information for that profile owner on a document separate from the data collection sheet for this study.
            1. If reference is within the last 72 hours, calls Project Manager (TBD) and S. Rawat (Site PI) immediately. If for some reason they are not reachable by cell phone, or email within 4 hours, call the IRB.
            2. If reference is older than 7 days but no status updates since, call S. Rawat (Site PI) immediately.
            3. If reference is older than 7 days, read status updates since and note any references to “feeling better” or similar comments. If these are present, discuss with S. Rawat the next day during business hours.
            4. Peer-counselor will contact participant immediately upon noticing the information and provide telephonic counseling and will attempt to refer them to in-person services, per current HST protocols.
2. Protocol for acute SI noted on profiles (within last 7 days)
    a. Online peer-counselors will reach out to the individual by phone and then text messages and follow standard operating protocols for such situations that they currently employ.
    b. Additionally, Online peer-counselors will notify S. Rawat (site PI) and the Project Manager immediately.
    c. S. Rawat and the Project Manager will perform status check on the individual participant. The Site-PI and Project Manager will debrief with online peer-counselor and assess adequacy of response. If acute SI issue is resolved with a safe-plan, this will be documented and submitted to the IRB.
    d. For participants who do not have a resolution, participant will be called using the Whatsapp phone number they enrolled in the trial, emailed, and contacted with any other information they may have provided. If participant is not reachable within one hour, a member from HST’s research team will call any emergency contact they may have provided. This protocol will be made known to participants during the informed consent.

e. As per existing protocol and training at HST, online peer counselors will continue reaching out to the participant regularly as deemed necessary and linked to appropriate resources (i.e., professional counselor at HST or outside clinic).

## C. POTENTIAL BENEFITS OF THE PROPOSED RESEARCH TO HUMAN SUBJECTS AND OTHERS

The potential benefit to participants in this study could be linkage-to-care, access to HIV/STI prevention and testing services otherwise difficult to obtain, and access to credible information on new and existing HIV prevention tools. But all participants may not realize these benefits and there will be no other direct benefits to participants. However, if effective, CHALO! 2.0 could be implemented broadly and rapidly diffuse information on available HIV prevention tools and improve linkage to HIV testing and linkage to care services for MSM, a hard-to-reach population. Additionally, CHALO! 2.0 could have significant public health benefit by reducing the HIV burden in MSM and the broader population.
*Potential Benefits to control condition participants*: Participants in attention matched control condition will receive non-overlapping health information about general health topics as prioritized by MSM in Mumbai themselves based on a recent study by our team. This will include topics on physical fitness, diabetes, heart disease, and nutrition during the 12-week intervention period and a free HIV testing coupon. Both the attention matched control and the digital coupon only conditions will both receive digital coupons for free HIV testing to 41 private lab sites and 3 MSM community based testing locations throughout Mumbai, and a link to a Website with information about different HIV testing sites. The digital coupon addresses important structural barriers to testing. Thus, in this pragmatic study, all conditions are receiving some level of outreach, beyond what is currently available or standard of care. At the end of the follow-up period, after the final participant completes the final assessment survey, participants will be given access to all CHALO! 2.0 components if they choose to receive this information.

C1. Risk/benefit ratio. CHALO! 2.0 has the potential to increase reach of HIV prevention programs and services, increasing HIV Testing and linkage to care, and serostatus awareness. If effective, CHALO! 2.0 could be broadly implemented by health centers and community-based organizations, and reduce HIV transmission and promote healthy behaviors. Additionally, this level of outreach may foster social support and self-efficacy. Given the steps that the research team will take to minimize the chances of breach of confidentiality, participating in this study presents low risk and the risk/benefit ratio is favorable.

## D. IMPORTANCE OF THE KNOWLEDGE TO BE GAINED

This study will test an intervention to facilitate access to education about HIV, increased access to HIV testing, and linkage to both treatment and prevention care. The proportion of MSM who contract HIV each year is significant and the costs to society of this ongoing epidemic are high. Additionally, most prevention interventions do not reach this highly vulnerable population and contribute to the disproportionate burden of HIV. CHALO! 2.0 could help mitigate these disparities by promoting timely access to information and services. As a result of this study, we will have tested an innovative virtual outreach model. If effective, this intervention could be broadly implemented and help reduce HIV infection and associated health disparities.

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