A Technology-Based Intervention Among Young Men Who Have Sex With Men and Nonbinary People (The Conectad@s Project): Protocol for A Vanguard Mixed Methods Study

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Abstract

Background: In many parts of the world, including Brazil, uptake for biomedical interventions has been insufficient to reverse the HIV epidemic among key populations at high risk for HIV, including men who have sex with men. Young MSM (YMSM), particularly Black YMSM, have high HIV incidence, low viral suppression, and low preexposure prophylaxis (PrEP) uptake and adherence. Therefore, novel approaches to increase the HIV biomedical interventions uptake by YMSM are urgently needed.

Objective: We describe the Conectad@s Project, which aims to: (1) estimate the prevalence and incidence of HIV and other sexually transmitted infections, the onset of sexual risk behavior, and barriers to biomedical interventions among YMSM aged 18 to 24 years in Rio de Janeiro, Brazil; and (2) conduct a technology-based adherence intervention study to promote a rapid linkage of YMSM to HIV care or prevention, and support and sustain adherence.

Methods: A cross-sectional survey will be conducted with 400 YMSM recruited using respondent-driven sampling (RDS) adapted for social media-based sampling, preceded by a formative phase. HIV and sexually transmitted infections testing will be conducted, including early HIV infection biomarker detection. Behavioral, partnership, network, and structural measures will be collected through structured questionnaires. All individuals recruited for the survey will have access to HIV risk assessment, antiretroviral therapy (ART), PrEP, prevention counseling, and a technology-based adherence intervention. Those who accept the adherence intervention will receive weekly text messages via a social networking app (WhatsApp) for 24 weeks, with follow-up data collected over 48 weeks.

Results: The Conectad@s project has been approved by our local institutional review board (#CAAE 26086719.0.0000.4262) in accordance with all applicable regulations. Questionnaires for the RDS survey and intervention were developed and tested in 2020, formative interviews were conducted in January and February 2021 to guide the development of the RDS, and enrollment is planned to begin in early 2022.

Conclusions: The Conectad@s Project is a vanguard study that, for the first time, will apply digital RDS to sample and recruit YMSM in Brazil and rapidly connect them to ART, PrEP, or prevention counseling through a technology-based adherence intervention. RDS will allow us to estimate HIV prevalence among YMSM and measure HIV infection biomarkers in the context of the onset of risky behavior. The data will lay the groundwork to adapt and implement HIV prevention strategies, identify barriers to the earliest HIV infection diagnosis, immediate ART or PrEP initiation, and detect new clusters of HIV transmission.

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KEYWORDS
sexual and gender minorities; young MSM; Brazil; HIV prevention; technology-based adherence intervention; HIV

Introduction
Reported HIV cases in Brazil are increasing among gay, bisexual, and other men who have sex with men (MSM), particularly among the youngest, with a considerable disparity of infection for this population [1,2]. In 2020, 53% of reported male HIV cases were MSM [1]. Reported cases in Brazilian surveillance may be incomplete as MSM status is likely under-reported among men classified as heterosexual (30% of male cases) and those with unknown risk (14% of male cases) due to stigma [3,4]. National surveillance data show a 7-fold increase in the rate of HIV cases reported among Brazilian men aged 15-24 years between 2009 and 2019 [1]. A population-based survey in selected capital cities in Brazil found 18% HIV prevalence in MSM in 2016 [5], increasing from 12% seven years earlier [6]. In addition, MSM surveyed in 2016 were notably younger than those in 2009, while HIV prevalence rose [7].

Brazil was the first low-income/middle-income country to provide free antiretroviral therapy (ART) for HIV treatment, participate in clinical trials proving preexposure prophylaxis (PrEP) efficacy [8] and PrEP demonstration projects [9-12], and establish a national policy to provide PrEP at no cost within the National Public Health System (SUS). Nevertheless, uptake of these biomedical interventions has been insufficient to reverse or even slow the HIV epidemic among young MSM (YMSM).

Data from a national web-based survey of Brazilian MSM indicated higher HIV risk and lower use of biomedical prevention among YMSM aged 18-24 years compared to older MSM, including condomless anal sex, being unaware of PrEP, never testing for HIV, and not using PrEP [13]. Among 16,667 Brazilian MSM recruited in web-based studies, YMSM showed increased odds of binge drinking and condomless receptive anal sex and decreased chances of high perceived HIV risk [14]. Youth also had an increased probability of high-risk behaviors measured by the HIV Incidence Risk Index, even when adjusted by race, income, education, sexual orientation, steady partner, previously sexually transmitted infection (STI), and ever testing for HIV [15].

The data point to disparities for Black Brazilians, including late HIV diagnosis, not being on ART, low virological suppression rates, and low PrEP adherence [9,16]. Black Brazilians had over 50% increased odds of experiencing discrimination than White individuals, even after controlling for income, education, social status, and health problems [17]. In surveillance data, the proportion of HIV cases for Black and Pardo (mixed-Black) Brazilians rose from 51% to 63% from 2009 to 2019 [1]. MSM populations may face various forms of stigma, including internalized, perceived, experienced, and layered stigmas [18], and Black/Pardo MSM populations also face structural racism, which may increase their vulnerability to HIV infection in comparison to White MSM.

The Rio de Janeiro metropolitan area, with 13 million inhabitants and 22 municipalities, is the second-largest in the country and the 16th largest urban area in the world. Rio de Janeiro state accounts for 10% of HIV cases nationwide, 90% of them residing in the metropolitan area [1], where mortality due to HIV-related causes, particularly tuberculosis, remains persistently above the Brazilian mean [1]. The state also demonstrates high rates of late-stage HIV and death, which suggest poor engagement along the HIV care continuum, including late diagnosis, low ART use, and insufficient virologic suppression [1]. Emerging evidence points to resurging HIV among YMSM, including high case detection rates at HIV testing sites [19]. HIV prevalence among YMSM aged 18-24 years in Rio de Janeiro increased from 4.4% to 13.3% between 2009 and 2016 [20]. Drivers of HIV infection among Brazilian YMSM, likely to intersect in Rio de Janeiro, remain understudied and unaddressed. Therefore, we designed the Conectad@’s Project, a respondent-driven sampling (RDS)-based study to specifically reach and engage YMSM in Rio de Janeiro, Brazil. Our primary aims are: (1) to estimate the prevalence and incidence of HIV and other STIs, the onset of risky behavior, and barriers to biomedical interventions among YMSM aged 18 to 24 years, and (2) to conduct a technology-based adherence intervention study to promote a rapid linkage of YMSM to HIV care or prevention.

Methods
The institutional review board of the INI-Fiocruz reviewed and approved this protocol on February 27, 2020 (#CAAE 26086719.0.0000.4262) in accordance with all applicable regulations.

Study Design
RDS has gathered robust samples of MSM in studies worldwide, including in Rio de Janeiro [5,6]. To reach and engage YMSM in Rio de Janeiro, Brazil, we will conduct an RDS-based study at the National Institute of Infectious Diseases Evandro Chagas (INI)-Fiocruz. The RDS will be adapted to include social media-based methods. The approach builds on research on young transgender women aged 15-24 years in San Francisco, United States [21]. Starting with initial “seeds” (ie, initial participants who start recruitment chains), successive waves of referrals will reach diverse social networks of YMSM. We anticipate that peer referrals through social media connections will particularly appeal to Brazilian YMSM who spend much of their time on mobile-based apps (eg, WhatsApp) and digital social media. Despite the discussion around the generalization of their data, RDS-based studies provide estimates of HIV risk among hard-to-reach populations [22] and allow the recruitment of these populations into longitudinal studies (ie, observational or intervention). Subsequently, we will offer all recruited individuals a prospective 48-week technology-based adherence intervention study to promote a rapid linkage of YMSM to HIV care or prevention and support and sustain adherence.

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Eligibility Criteria

Individuals will be included if they (1) self-identify as men (cis or trans) or gender nonbinary, (2) report ever having engaged in anal sex with men or gender nonbinary persons with a penis, (3) are aged 18 to 24 years, (4) reside or spend most of the time in Rio de Janeiro metropolitan area, (5) did not previously participate in the study, and (6) possess an electronic referral coupon from a peer acquaintance participant. In this study, we collectively refer YMSM to young (18-24 years) cisgender men, transgender men, and non-binary or gender-nonconforming individuals. Exclusion criteria include individuals who self-identify as women (cis or trans).

Formative Phase

RDS-based studies require a formative phase to verify theoretical assumptions and identify logistical constraints and solutions [23]. These objectives are met through focus group discussions, key informant interviews, and pilot testing. The theoretical RDS assumptions are: (1) members of the population know each other as members, (2) social networks are interconnected within a few degrees of separation, (3) sampling occurs with replacement, (4) network size is reported accurately, and (5) people recruit approximately randomly from their network. RDS also depends on sufficient network density to make long recruitment chains [24]. Furthermore, the characteristics of social networks guide the selection of the number and type of “seeds.” The formative phase also identifies potential “bottlenecks” (ie, social and physical barriers between networks) and variables to track “equilibrium” (ie, stability in sample composition as the chains grow). Other logistical questions include study site acceptability, transportation, online and social media apps for electronic referrals, safety, confidentiality, and appropriate incentives for participation and recruiting peers. In addition, the formative phase will inform the development and pilot testing of the questionnaire, as well as the refinement of the technology-based intervention.

The formative phase has already been conducted, comprised of two focus group discussions (aged 18-19 and 20-24 years) of up to 10 participants each and individual interviews with up to 20 YMSM. Group discussions and individual interviews lasted 1-2 hours. YMSM were referred from HIV clinics, LGBTQIA+ (lesbian, gay, bisexual, transgender, queer/questioning, intersex, and asexual/aromantic/agender) nongovernmental organizations, and peer counselors at Instituto Nacional de Infectologia Evandro Chagas, Fundação Oswaldo Cruz (INI-Fiocruz). We used a maximum variation sampling approach to include a diversity of participants by place of residence, race/ethnicity, and age [25]. Group discussions and individual interviews were audio-recorded with field notes captured by the interviewer. Files were transcribed in Portuguese and translated into English. Content analysis using transcribed content is underway and will focus on RDS theory, logistics, and strategies to improve the study. The study team will analyze qualitative data and discuss the preliminary results related to the density of the social network and logistics to reach a consensus on strategies to improve the implementation of RDS in this study. If social networks appear weak or diffuse, we will develop an additional seed recruitment plan and alternative approaches to improve recruitment based on the findings within a theoretical probability-based sampling framework. Questions raised during the formative phase will be incorporated into the RDS study instruments to be quantified. A chosen subset of participants (approximately 10) will pilot the questionnaire. Participants will provide feedback regarding comprehensibility, missing and unnecessary constructs, wording, and timing.

Sample Size and Power Calculation

Within an acceptable margin of error, the sample size of RDS surveys is powered to measure key indicators of HIV risk and prevention in the population of YMSM (eg, HIV prevalence, PrEP awareness, willingness to use PrEP, and never testing for HIV). Assuming a design effect of 2.0 (typical for RDS) [26] and a 95% CI, 400 participants are sufficient to measure RDS-adjusted estimates within SD 5% over a wide range of point estimates (ie, 5%-40%). For example, 400 participants could measure HIV prevalence at 5%, SD 2.1% or being unaware of PrEP at 39%, SD 4.7%. A sample size of 400 also provides 80% power at a 95% CI to detect significant odds ratios for effect sizes of 1.9 or greater for key outcomes (eg, HIV infection, PrEP awareness, and willingness to use PrEP) and predictor variables (eg, race/ethnicity, perceived HIV stigma, and family support).

Recruitment Methods

RDS sampling begins similarly to “snowball sampling” (ie, with purposively selected “seeds” from diverse social networks who then refer peers to the study). Peer recruitment on RDS differs from snowball sampling on key procedural and theoretical factors that enable better estimates of disease prevalence [22]. Seeds will be chosen for their connections to other YMSM, enthusiasm for the research, and belonging to different social circles. As with all other participants, the seeds must be eligible and undergo all study procedures. After completion, the seeds will be trained to recruit their peers using a digital coupon. This process will create a link between the recruiter and recruits, providing information needed for statistical adjustment. Digital coupons (Figure 1) will be shared on mobile apps and web-based texting platforms [25,27]. Digital referrals significantly increased recruitment of a cohort of transwomen aged 15-24 years in San Francisco, United States [21,25]. Upon presentation of a digital coupon to the study site, recruits will undergo similar procedures if eligible. The process will continue until the sample stabilizes on key characteristics (“equilibrium”) and the sample size is met. RDS requires monitoring for “bottlenecks” (eg, chains that do not cross networks) and valid connection (eg, true acquaintances). The limited number of recruits per participant (typically 3) and incentives drive the propagation of long chains of referrals within and across social networks. Participants receive a “primary incentive” for their enrollment and a “secondary incentive” for each eligible participant they recruit. The value and type of incentives will be explored and determined in the formative phase.
**Figure 1.** Digital coupon for the Conectad@s Project recruitment. Legend: Coupon used by seeds to recruit peers to the project, with the name (Conectad@s) followed by “we are strong,” inclusion criteria (18-24 years) and invitation to participate in the project only if coupon was received from a friend or acquaintance. Phone number and WhatsApp contact information to schedule an appointment are provided with a statement that scheduling is required.

**HIV Diagnosis Algorithm**

All participants will be tested for HIV using an HIV rapid test and antibody/antigen 4th generation serology. Participants reporting recent anal condomless sex (<30 days) with a negative HIV rapid test will be screened for acute HIV infection through HIV RNA viral load (VL) testing.

**HIV Recency And Phylogenetic Testing**

We will also test for recent HIV infection with the limiting avidity assay [28] to identify seroconversions occurring in the last few months. Recency data can help to identify possible transmission clusters and permit the calculation of HIV incidence by providing the timing of seroconversion [28]. The detection of acute infections may contribute to identifying active clusters of HIV transmission. HIV VL reaches high levels in the short period after infection, increasing the risk of HIV transmission. Recent HIV acquisition events will allow the characterization of drivers of new infections and avoid recall bias because remembering sexual partners once in the last few weeks is easier than over a longer time.

We will perform HIV phylogenetic testing on specimens with detectable HIV VL. Phylogenetic data will identify HIV strain types, ART resistance mutations, and clusters of transmission.

**STI Testing**

The incorporation of biomarkers for acute and recent infection, as well as STIs, may be particularly valuable among YMSM, where the onset of behaviors leading to infection is more recent.
We will evaluate STIs as markers of HIV sexual risk and causes of morbidity using nucleic acid amplification tests for oropharyngeal, urethral and rectal *Neisseria gonorrhoea* and *Chlamydia trachomatis* (nontreponemal syphilis testing and if positive treponemal test), chronic hepatitis B (anti-HBs antibody, Hbs antigen, and total anti-HBc antibodies), chronic hepatitis C (anti-HCV), human papillomavirus testing and anal cytology. Participants diagnosed with STI will receive treatment according to Brazilian guidelines [29]. Participants screened positive for hepatitis B and C will undergo a complete diagnosis algorithm (ie, HCV viral load) [30] and will be referred to treatment. Participants without hepatitis B diagnosis and who have not been vaccinated will be referred for hepatitis B vaccination.

**Behavioral, Partnership, Network, and Structural Measures**

Trained staff will administer face-to-face questionnaires to participants using tablets. Due to the COVID-19 pandemic, all efforts will be undertaken to minimize SARS-CoV-2 transmission. Before study procedures, participants will be screened for COVID-19 symptoms, and visits will consider the safety of all participants and the study team. Our instrument will build upon questionnaires previously used for MSM in Brazil and the United States. Table 1 presents examples of measurements, hypotheses, and sources of questionnaires.

Biological data, particularly markers of recent HIV and STI infection, will permit closer linkage to the events, behaviors, partnerships, and social and structural conditions that lead to HIV acquisition. We will also identify whether there are infection clusters within specific racial/ethnic groups, as previously seen among Black MSM in the United States [31]. With robust biomedical markers of infection, we will be able to discern whether tight sexual networks constrained by racial bias and discrimination impact the spread of HIV among Black and *Pardo* Brazilians and whether this is a recent phenomenon or ongoing over the course of the Brazilian MSM epidemic.

**Table 1.** Behavioral, partnership, network, and structural measures for the RDS-based study.

<table>
<thead>
<tr>
<th>Timeframe</th>
<th>Level/domain</th>
<th>Examples of measures/hypotheses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute infection: within the last several weeks</td>
<td>Individual</td>
<td>Events of likely acquisition and transmission; missed opportunities for prevention; STI co-infection.</td>
</tr>
<tr>
<td></td>
<td>Partnership</td>
<td>Characteristics of most recent sexual partners (HIV status, disclosure, on ART(^c), PrEP(^d), and age) [32]; phylogenetic linkage.</td>
</tr>
<tr>
<td>Recent infection: within last 130-180 days</td>
<td>Individual</td>
<td>Missed opportunities for prevention; untreated STIs; HIV care cascade.</td>
</tr>
<tr>
<td></td>
<td>Sexual network, with a focus on Black/Pardo Brazilians</td>
<td>Characteristics of recent sexual partners; age and racial mixing, with a specific focus on sexual networks of Black/Pardo Brazilians [31]; phylogenetic clustering; partner concurrency.</td>
</tr>
<tr>
<td>Long-standing infection: since the onset of risk or last HIV test</td>
<td>Previously undiagnosed</td>
<td>Missed opportunities for testing, linkage to care, experiences, and attitudes towards care providers.</td>
</tr>
<tr>
<td>Long-standing infection: since the onset of risk or last HIV test</td>
<td>Previously diagnosed</td>
<td>Barriers to care, ART initiation, adherence [33-35], viral suppression; care cascade; care self-efficacy; perceived HIV stigma [36].</td>
</tr>
<tr>
<td>All (including and regardless of HIV status): since the onset of risk</td>
<td>Demographic</td>
<td>Racial disparities in risk, prevention, and care access (eg, race/ethnicity and socioeconomic status); homelessness, runaway; incarceration; digital health information.</td>
</tr>
<tr>
<td>Risk and prevention</td>
<td></td>
<td>Onset of sexual risk, lifetime risk; substance use and chemsex [37]; HIV testing; internet use for sex (eg, apps); PrEP awareness, willingness, use [10,12,13,38]; knowledge and willingness to use new prevention technologies [39]; HIV perceived risk [40]; knowledge of HIV [41,42].</td>
</tr>
<tr>
<td>Psychosocial, structural</td>
<td></td>
<td>Mental health [43,44], psychological distress, trauma [45], suicidality, and social support; testing, PrEP norms, and stigma [12]; peer support; family support; sexual orientation disclosure; experiences of discrimination [46,47], internalized homonegativity [48]; sexual compulsivity [49]; COVID-19 pandemic impact in personal life [50].</td>
</tr>
<tr>
<td>Health and social welfare systems</td>
<td></td>
<td>Care-seeking and medical mistrust; health care participation; avoidance of care; perceived care access; “<em>Bolsa Família</em>” (family grant or family stipend) program and other cash transfer programs; SUS(^e) experiences; food insecurity [51]; political context; digital health experiences.</td>
</tr>
</tbody>
</table>

\(^{a}\)RDS: respondent-driven sampling.  
\(^{b}\)STI: sexually transmitted infection.  
\(^{c}\)ART: antiretroviral therapy.  
\(^{d}\)PrEP: preexposure prophylaxis.  
\(^{e}\)SUS: Sistema Único de Saúde (Brazilian National Public Health System).
Technology-Based Adherence Intervention

All RDS participants will be invited to participate in a technology-based adherence intervention study. The intervention builds upon Health eNav, a text messaging HIV care linkage and retention intervention for young people living with HIV in San Francisco, United States, using an SMS-based platform to support ART adherence and provide HIV prevention counseling [21]. Based on a prior study, we anticipate 13% HIV prevalence [20] (N=52 individuals), 26 (50%) of whom will be newly diagnosed and 26 (50%) previously diagnosed (regardless of linkage to care). Therefore, we estimate that 65% (226/348) of HIV-negative YMSM, as previously described [15], will be interested and eligible for PrEP according to the Brazilian guidelines (eg, condomless anal sex, sex with HIV positive partner, and STI diagnosis in the last 6 months) [52].

HIV-negative participants enrolled in the intervention study will receive same-day PrEP, according to the Brazilian recommendations, plus a complete prevention package, including HIV/STI testing and treatment, counseling for HIV/STI risk reduction, hepatitis B vaccination, and condoms/lubricants distribution (Group 1: HIV-negative on PrEP). HIV-negative YMSM not eligible for PrEP or who do not accept PrEP may also be enrolled in the intervention study to receive the prevention package (including PEP, when indicated), risk assessments, and counseling (Group 2: HIV-negative not on PrEP).

HIV-positive YMSM enrolled in the intervention study will initiate same-day ART treatment according to Brazilian recommendations and will be further linked to care at the INI-Fiocruz HIV clinic (Group 3: HIV-positive on ART). HIV-positive YMSM previously diagnosed and who initiated ART prior to inclusion will also be invited to the intervention.

All participants enrolled will receive weekly reminders for 24 weeks via WhatsApp, the most common SMS platform in Brazil. Automatic messages will include scheduled medication reminders, if applicable, and posts. Periodic feedback from participants will adapt and improve the approach (eg, adjustments or modifications on the content of electronic messages). The weekly reminders will be personalized. Participants will be able to select the timing of reminders and choose between having explicit medication reminders or factoid messages (not specific to medication), such as LGBTQIA+ community events, health facts, or a combination of both types of messages. All messages sent will solicit a response, so we will have backend data (eg, time, date, message content, etc) on whether the message was received and reviewed by participants. For example, we may send a medication reminder text, such as “Did you take your medication today?” Responses will be recorded in our database, but more importantly, we will know whether the participant was exposed to the text message regardless of receiving a formal response.

After enrollment, follow-up visits will occur at 4 and 12 weeks and then quarterly (24, 36, and 48 weeks). Briefly, during follow-up visits, we will collect information on study outcomes, such as HIV seroconversion, PrEP continuum endpoints, and PrEP adherence (using dried blood spots for TFV-diphosphate concentration among HIV-negative participants); HIV viral load suppression among HIV-positive participants; and STI incidence among all participants. The intervention study baseline visit procedures are the same as those conducted during the RDS visit. A detailed schedule of events and procedures is depicted in Table 2.
### Table 2. Schedule of events for the Conectad@s Project.

<table>
<thead>
<tr>
<th></th>
<th>RDS Baseline</th>
<th>Week 4</th>
<th>Week 12</th>
<th>Week 24</th>
<th>Week 36</th>
<th>Week 48</th>
<th>Early Termination</th>
<th>HIV seroconversion visit</th>
<th>Unscheduled visit</th>
</tr>
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<tbody>
<tr>
<td><strong>Questionnaires</strong></td>
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<td></td>
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<tr>
<td>Behavioral, partnership, network, and structural measures</td>
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<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Technology-based intervention: inclusion</td>
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<tr>
<td>Technology-based intervention: acceptability</td>
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<td><strong>Laboratory procedures</strong></td>
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<tr>
<td>HIV antigen rapid test</td>
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<td>X_d</td>
<td>X_d</td>
<td>X_d</td>
<td>X_d</td>
<td>X_d</td>
<td>X</td>
<td>X_e</td>
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<tr>
<td>HIV RNA Pool</td>
<td>X_f</td>
<td>X_f</td>
<td>X_f</td>
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<td>X_f</td>
<td>X_f</td>
<td>—</td>
<td>X_e</td>
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<tr>
<td>HIV RNA viral load</td>
<td>X_g</td>
<td>X_g</td>
<td>X_g</td>
<td>X_g</td>
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<td>X_g</td>
<td>X</td>
<td>X_e</td>
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<tr>
<td>CD4/CD8</td>
<td>X_i</td>
<td>X_i</td>
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<td>HIV recency testing</td>
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<td>X_e</td>
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<td>HIV genotyping</td>
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<td>X_e</td>
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<td>Urine (CT/NG)</td>
<td>X</td>
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<td>X</td>
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<td>Oropharyngeal swab (CT/NG)</td>
<td>X</td>
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<td>X</td>
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<td>X</td>
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<tr>
<td>Anal swab (CT/NG)</td>
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<td>X</td>
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<td>X</td>
<td>X</td>
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<tr>
<td>Anal swab (HPV^o)</td>
<td>X</td>
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<tr>
<td>Anal cytology</td>
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<tr>
<td>Hepatitis B rapid test</td>
<td>X</td>
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<td>X_p</td>
<td>X_p</td>
<td>X_e</td>
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<tr>
<td>Hepatitis B serology</td>
<td>X_i</td>
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<td>—</td>
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<td>X_f</td>
<td>X_e</td>
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<td>X_i</td>
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<td>—</td>
<td>—</td>
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<td>X_s</td>
<td>X_s</td>
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<tr>
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<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
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<td>X_i</td>
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<td>Non-treponemal syphilis testing (VDRL)</td>
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<td>X_u</td>
<td>X_e</td>
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</tr>
<tr>
<td>DBS^v (PrEP adherence assessment)</td>
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<td>X_w</td>
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<td>X_f</td>
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<td>X_f</td>
<td>X_e</td>
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<tr>
<td>Complete blood count</td>
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<td>X_f</td>
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<td>X_f</td>
<td>X_e</td>
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</tr>
</tbody>
</table>

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*a* RDS: respondent-driven sampling.

*b* Withdrawn or discontinued participants before the final visit.

*c* Not applicable

*d* Only for HIV-negative participants in a prior visit.

*e* If necessary.

*f* Only for postexposure prophylaxis use.

*g* Only for HIV-positive participants or HIV-negative participants with recent HIV exposition according to INI-Fiocruz guidelines (HIV acute infection screening).

*h* Only for HIV-negative participants with recent HIV exposition according to INI-Fiocruz guidelines (HIV acute infection screening).

*i* Only to HIV-positive participants or to participants with HIV rapid test, HIV RNA Pool or HIV RNA viral load positive result.

*j* Only to participants with HIV rapid test, HIV RNA Pool or HIV RNA viral load positive result, with negative HIV rapid test in a prior visit.

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[^34885]: https://www.researchprotocols.org/2022/1/e34885
**Analysis Plan for the Technology-Based Adherence Intervention**

We will measure exposure to the intervention, including the number of received and read WhatsApp messages during the 24-week intervention period. Intervention exposure and outcome data will be analyzed using multivariable logistic generalized estimating equations (GEE) with exchangeable correlation structures to account for repeated measures over time for each participant. GEE models will assess the association between intervention exposure measures (e.g., receipt of intervention and intervention dosage) and primary outcomes related to the HIV care and PrEP continuum.

**Results**

To date, the Conectad@s Project has made significant progress despite the still ongoing COVID-19 pandemic. During 2020, we prepared the questionnaires for the RDS survey, intervention, and formative phase. We also discussed the best approach to move forward with the study in the context of the COVID-19 pandemic. The formative stage of the study started in January 2021. We conducted 20 individual interviews from January 12 to February 4, 2021, and three focus group discussions on February 4, 10, and 24, 2021. The study team prepared a COVID-19 plan that includes assessing COVID-19 symptoms, screening by phone prior to study attendance onsite before study visit, as well as a strong recommendation of facemask use and social distancing. Planned activities are indicated in Table 3.

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**Table 3. Planned activities for the Conectad@s Project.**

<table>
<thead>
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<th>Activities</th>
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<td>Dissemination of formative results</td>
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<td>Manual of operations approval</td>
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<tr>
<td>Training</td>
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<td>Investigators’ meetings</td>
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<td>RDS(^b) survey and intervention enrollment</td>
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<tr>
<td>Follow-up for intervention</td>
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</tr>
<tr>
<td>Dissemination of intervention results</td>
<td>___</td>
<td>___</td>
</tr>
</tbody>
</table>

\(^a\)Not applicable.

\(^b\)RDS: respondent-driven sampling.

**Discussion**

The Conectad@s Project is a vanguard study that will apply for the first time an RDS-based survey for YMSM in Brazil integrated with a technology-based adherence intervention. The results of the RDS survey will allow us to estimate HIV prevalence and incidence using recency testing and to measure HIV biomarkers near the onset of risky behavior among Brazilian YMSM. The intervention study will contribute to
developing intervention-based adherence strategies to support HIV care and prevention among a highly vulnerable population. Data will lay the groundwork to adapt and implement all strategies to identify the barriers to the earliest possible diagnosis, immediate ART initiation, PrEP uptake, and detecting new clusters of HIV transmission.

Acknowledgments
This study is sponsored by the National Institutes of Health (grant number 1 R01 AI149627-01) and Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq #404187/2019-6).

Conflicts of Interest
None declared.

Multimedia Appendix 1
Peer-review report by the Center for Scientific Review Special Emphasis Panel - RFA-AI-18-054 U.S.-Brazil Collaborative Biomedical Research Program (National Institutes of Health, USA).

References


**Abbreviations**

- **ART**: antiretroviral therapy
- **GEE**: generalized estimating equations
- **INI-Fiocruz**: Instituto Nacional de Infectologia Evandro Chagas, Fundação Oswaldo Cruz
- **LGBTQIA+**: lesbian, gay, bisexual, transgender, queer/questioning, intersex, and asexual/aromantic/agender
- **MSM**: men who have sex with men
- **PrEP**: preexposure prophylaxis
- **RDS**: respondent-driven sampling
- **STI**: sexually transmitted infections
- **SUS**: Sistema Único de Saúde (Brazilian Public health System)
- **VL**: HIV RNA viral load
- **YMSM**: young men who have sex with men

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