LETSYNC STUDY PROTOCOL NCT04951544

LetSync: Pilot Test of Mobile Health (mHealth) Intervention

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SECTION 1: OVERVIEW

1.1 Study Rationale

For *LetSync* to come to fruition so that it can be tested by a largescale randomized controlled trial, further developmental work to address a number of critical issues is required, which will be addressed in this study. First, in order to design *LetSync* to motivate, facilitate, and target dyadic processes in HIV care engagement, we must have a deeper, more contextualized understanding than we have currently of the potential mechanisms by which couple's resilience drive the capacity and opportunities for engaging in dyadic HIV care engagement.[10,11] Although the formative work has illuminated the potential role of black men who have sex with men (BMSM) couple's resilience in dyadic care engagement, the necessary next step for informing *LetSync* designs includes exploring how couple's resilience fosters joint problem-solving, and identifying successful joint problem-solving strategies and dyadic-coordination opportunities. Second, developing an mHealth intervention for successful adoption takes considerable time and resources during the design process.[75-77] mHealth intervention development requires that the research and design processes occur in tandem to allow the science and the designs to mutually inform each other—the definition of "iterative user-centered design."[75-77] Third, once a full version of *LetSync* is developed, it will need to be pilot-tested to examine its acceptability and feasibility, and to determine if it appears likely to be efficacious. Thus, this developmental R01 is needed for iterative mHealth development given the considerable time and resources necessary to develop and pilot *LetSync* to prepare it for a full efficacy trial.

1.2 Study Aims

Aim 1: Explore dyadic processes in retention in care and ART adherence. To inform mHealth components, we will also obtain feedback on app wireframes.

Aim 2: Develop and refine *LetSync* using an iterative process, drafting and refining wireframes based on feedback from the CAC.

AIM 3: Conduct a pilot RCT of *LetSync* to assess acceptability, feasibility, and preliminary efficacy using a waitlist control design.

1.3 Timeline

Table 2. Study timeline	Months											
Year 1	1	2	3	4	5	6	7	8	9	10	11	12
Aim 1: Investigate dyadic HIV care engagement												
Study set-up, preparation, recruitment	✓	✓	✓	✓	✓	✓	✓	✓	✓			
Conduct individual and couple qualitative interviews			✓	✓	✓	✓	✓	✓	✓	✓	✓	
Transcribe, analyze, and synthesize qualitative data						✓	✓	✓	✓	✓	✓	✓
Year 2	1	2	3	4	5	6	7	8	9	10	11	12
Aim 2: Development, refinement, and mini-pilots												
Establish *LetSync* CAC, convene CAC sessions	✓	✓	✓	✓	✓	✓						
Iteratively develop, refine *LetSync* v0.5			✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Develop User's Guide, study protocol and procedures										✓	✓	✓
Year 3	1	2	3	4	5	6	7	8	9	10	11	12
Mini-pilot *LetSync* v0.5 components, protocol, and procedures	✓	✓	✓									
Develop *LetSync* v1.0 components, protocol, and procedures			✓	✓								
Aim 3: Pilot RCT												
Recruit, set-up for pilot RCT			✓	✓	✓	✓						
Conduct intervention arm with *LetSync* v1.0							✓	✓	✓	✓	✓	✓
Year 4	1	2	3	4	5	6	7	8	9	10	11	12
Continue conducting intervention arm with *LetSync* v1.0	✓	✓	✓	✓	✓	✓	✓	✓				
Develop *LetSync* v2.0 based on feasibility and acceptability data	✓	✓										
Conduct waitlist control arm of *LetSync* v2.0			✓	✓	✓	✓	✓	✓				
Develop *LetSync* v3.0 based on feasibility and acceptability data									✓	✓	✓	✓
Analysis of primary outcomes, and synthesis of findings									✓	✓	✓	✓

1.4 A Useful Overview of Research

- Who is a research participant?
    - A research participant used to be referred to as a human subject. Human subjects are providers of information (i.e., data) that is used to advance scientific knowledge about a particular problem or research question. A research participant has rights beyond those of the private citizen that are stipulated in documents including the Belmont Report, which was part of the response to the atrocities and misconduct of scientists in "studies" involving Nazi prisoners, Tuskegee airmen and their families, Henrietta Lacks, to name just a few.
    - Here is a typical research protocol involving a research participant:
        1. Screening/intake
        2. Research informed consent and enrollment into the study as a research participant
        3. Research activities (e.g., participating in interviews, focus groups, surveys, blood draws)
        4. [For a community-based research project:] Involving the participants in the analyses of the data collected, sharing interim findings
        5. Publishing and disseminating study findings back to the community from which they came ← This is often the part that researchers do not always do and therefore destroy any subsequent relationship and trust from the community, and rightfully so.

- What is informed consent?
    - A research participant must give informed consent prior to participation. Giving informed consent means that they have been informed of their rights, the way the data will be collected and used, and what is offered in exchange for their participation. Their consent, in the form of verbal or written assent, MUST BE RECORDED AND DOCUMENTED.
- Who is a researcher?
    - A researcher is a person with a question about the world and then tries to find the answer following a set of rules, called the scientific method. Each and every one of you is a researcher if you have a question you want to find answers to.
- What is research?
    - Research is the situation set up by the researcher to be able to carry out to scientific method to find the answers to a question. Research involves articulating a research question, hypotheses, and the design of the research so that if X happens, we know that Y must be true under the conditions we set up.
- What are research data?
    - Research data are information donated by the research participant to answer a research question that solves a societal problem. In a utopian world where no one is arbitrarily privileged over another (e.g., based on one's skin color), research participation is never compensated, because information is donated and the research participant is "compensated" by participating in advancing knowledge for the good of everyone. This may seem trivial at first glance, but some of the biggest advancements in HIV, cancer,

and many many other diseases are due to these donated, volunteered information in the form of blood specimen, tissue, thoughts, beliefs, attitudes, feelings, etc.

- What are research incentives?
    - Commonly referred to as stipends or compensation, incentives for research participation have taken the form of money and data are assigned monetary value. There is nothing wrong with this, since we do not live in a utopian society but a real society that inherently disadvantages some at the expense of others and meritocracy is mostly a myth.
    - However, research incentives fundamentally introduces a problem because it changes the relationship between participant and researcher into that of **supplier and consumer**, where the participant supplies data and the researcher consumes it. This is problematic for obvious reasons.
    - Nevertheless, people have bills to pay, and when they offer their insights and time, they need to be protected, and a way researchers show appreciation is by giving a research incentive, a monetary token of appreciation, to **incentivize and facilitate** the act of donating and volunteering private information.
    - In donating a part of themselves, a research participant is no longer in control of how their donation is used. This is another reason why we give research incentives. **This is also why it is critical for researchers to disseminate the research findings back to the community from which they came.**
    - Over time, researchers have conflated and muddied up these important distinctions.

SECTION 2: PARTICIPANT SELECTION AND SCREENING

2.1 Study Population

BMSM couples who meet the inclusion and exclusion criteria will be eligible for participation in this study.

2.2 Eligibility Criteria

Inclusion Criteria (Index partner)

1. Self-identify as BMSM
2. HIV-positive or the primary partner of a Black man who is HIV-positive (HIV+)
3. Have a primary relationship partner, defined as *someone to whom the participant is committed above anyone else for three or more months*
4. Age 18 or older
5. English-speaking
6. Willing and able to provide informed consent
7. Use and own a personal Smartphone (**Aim 2 and 3 only)**

Inclusion Criteria (Primary partner)

For primary partners, eligibility will be determined using identical criteria, except for the following:

1. In serodiscordant couples, the primary partner will be HIV-negative (HIV-)
2. Primary partners may be of any race or ethnicity, or may be a trans male or female

Participants in earlier aims of the study may also participate in later aims of the study, except as described in the exclusion criteria section below.

Exclusion Criteria

1. Report fear of intimate partner violence (IPV) resulting from participation as assessed at screening
2. Unwilling or unable to disclose HIV status to primary partner
3. Present evidence of severe cognitive impairment that would prevent comprehension of study procedures assessed during informed consent

Additional Exclusion Criteria, Aim 3

1. HIV+ individuals who are unable or unwilling to provide small hair samples will be excluded
4. Couples who participated in the **Aim 2 mini-pilot** will be **ineligible** for Aim 3

2.3 Eligibility Exceptions

Exceptions to Eligibility

1. Dyad with family ID 885 has one smartphone between the 2. Both are African American/Black and HIV positive. They are allowed to participate with one smart phone and 2 accounts if randomized into the intervention arm.

2.4 Sample Size

Aim 1

We will conduct onetime individual interviews with 48 BMSM from 24 couples (12 seroconcordant-positive, 12 serodiscordant). To explore emergent couple-level themes from the individual interviews,

we will also conduct couple interviews with 12 couples where both partners will be present (6 seroconcordant-positive and 6 serodiscordant).

Aim 2

We will establish the LetSync CAC by recruiting 10-12 HIV-positive BMSM who are in couples using the same eligibility criteria and recruitment procedures. We will strive for diversity among CAC members in terms of age, relationship length, and socioeconomic status.

To obtain feedback on *LetSync* v0.5 features, functionality, and usability, as well as to pilot-test intervention protocols and procedures, we will recruit 10 BMSM couples (*n*=20) (can be recruited from Aim 1) and give them *LetSync* v0.5 to download and use for 1 week.

Aim 3

Using a waitlist control design, 110 couples will be randomized to either the intervention or waitlist control conditions (*N*=220).

2.5 Recruitment

2.5.1 Recruitment Strategy

For all three aims, we will develop and implement a multipronged recruitment strategy, as follows:

1. Advertisements and outreach: These will include print and online advertisements, dating apps, word-of-mouth referrals, organization listservs, and the creation of social media presence. The trained study recruiters will post study promotional materials and conduct in-person outreach at community-based organizations (CBOs; e.g., churches, AIDS-service organizations, single-room occupancy, etc.), bars, and spaces where black men socialize, as well as clinics that provide HIV/STI testing.
2. Established relationships with CBOs: Through CAPS Community Engagement Core, we will contact CBOs throughout the Bay Area and meet with care providers and CBO leaders to inform them of the study.
3. UCSF Clinical and Translational Science Institute (CTSI) Recruitment Service: We will use this service, which will search for and mail letters to UCSF patients found eligible by inclusion criteria in the electronic medical record.
4. For Aims 2 and 3, couples who participated in earlier aims of the study and selected "willing to be contacted for future research" on their consent forms may be invited to participate, except as described above in the exclusion criteria (Section 2.2).

2.5.2 Recruitment Log

Study staff will keep track of site visits and recruitment activites in the recruitment log (excel sheet tab inside of the Study Log, saved in the Box folder "Study Logs and Trackers"). The log will include the names of organizations contacted, contacts at these organizations, dates of contact, updates, and action items. The log will be completed by all staff members completing recruitment activities.

2.6 Screening

Participants who are interested will call the study line or express interest via the study website. The Recruitment Coordinator and Study Recruiter(s) will check the study website daily and update the phone screen "to call" list. All tracking attempts will be noted in the database.

Eligibility will be determined when individuals contact the study via a dedicated phone line. Upon establishing eligibility, study staff will collect contact information for the participant and his primary

partner. We will instruct the index partner to have his primary partner call the study line so that we can determine his eligibility and to verify partnership status. If the primary partner does not call within 3 days, we will call the index partner back to remind them.

HIV status will be verified at the first in person meeting during the consent visit by a letter of diagnosis, copy of pharmacy ART prescription, or a recent ART pill bottle with the participant's name on it.

Participant IDs (PIDs) will be assigned while completing the phone screen questionnaire. Everyone who completes the phone screen, even if they are not eligible, will receive a PID. See section 4.1, Participant ID Assignment, for information on how ID numbers are assigned.

Update August 2020: Due to privacy concerns, participants will no longer be asked to verify their HIV status.

The Phone Script for the Screening call may be found in Appendix A as well as in the Box "Protocol" folder.

The Screener Questionnaire may be found in Appendix B as well as in the Box "Screening Forms" folder.

2.7 Interview scheduling

Aim 1

Once both partners are confirmed eligible, the team member will attempt to schedule the interview with Partner #2 over the phone. If Partner #2 would like to discuss times with Partner #1 before scheduling, give them a call back the next day to check in and see if they have come up with an available day and time and preferred location (Oakland or San Francisco).

Both the individual and couple interviews will be scheduled for a day and time when both members of the couple are available to come to the interview site for a period of 1.5-2 hours.

Scheduled interviews will be tracked in the study calendar maintained by the study coordinator.

When the interview time and location are scheduled, the interviewer will email, text, or give over-the-phone instructions to the participant (as per their preference) the interview location address, time and date, and directions.

2.7.1 Reminder Calls

Interviewers will text and/or call the participant **3 days before** and **1 day before** the scheduled interview to remind and confim the location, date, and time of the interview. During this call, the interviewer will also remind the participant that both partners need to arrive at the same time in order for the interview to occur, as well as remind any HIV-positive participants to bring in their HIV status verification materials.

The interviewer will also re-send directions to the interview location to the participant at this time.

2.7.2 Confirming interview location space

The lead recruiter will work with the interview locations to keep an updated schedule of interview room availability to ensure that participant scheduling flows smoothly. When interviews are scheduled, s/he will contact the interview location to let them know as well as confirm availability.

SECTION 3: AIM 1 PROCEDURES

3.1 Interview Checklist

The day before the interview, the interviewer will check/confirm the following:

- Test recording equipment and check batteries
- Calculate time to arrive at interview location and review directions
- Consider bringing backup recording equipment
- Room availability at the interview location
- Participant availability via phone call or text

The interviewer will bring the following items to the interview:

- Recording equipment, extra batteries, and charger (ensure is charged, functioning, and has enough room to record the interview)
- Consent forms
- Interview guide
- Petty cash for participant reimbursement
- Receipt forms
- Writing pad and pen to take notes
- Participant contact info
- Clear directions to place of interview
- Snacks/refreshments

3.2 Consent Process

Individual Interviews, IN PERSON

The written consent process will occur during the first in-person meeting with the participant, right before the scheduled interview. The team member will hand the participant a copy of the consent form if they want to read or look at it and verbally review the consent form with the participant. Once this is completed, the team member will then briefly discuss it with and answer any questions from the participant, as well as ask a few questions of the participant to make sure that the consent form and study are understood.

The interviewer will always bring 2 copies of the consent form with them: one for the participant to take if they choose, and one for the study to keep. Any copies kept by the study or taken by the participant must be signed and dated by both the team member and participant.

Participants will all be consented separately and privately, in private rooms.

Individual Interviews, REMOTE

Due to SIP mandates caused by COVID-19, all consent procedures will occur remotely. UCSF IRB has authorized studies to acquire consent online through Qualtrics.

Once interviews have been scheduled with the participant, the Coordinator will send the link to the online Qualtrics consent form and questionnaire to the email address provided. The participant will be asked to read it in its entirety and contact study staff should any questions arise.

Participants will be asked to give consent by indicating ‘Yes’ or ‘No’ on the Qualtrics form.

3.3 Enrollment

After participants consent to participate in the study and sign the consent form, interviewers will ask them to complete a contact form to assist study staff with contacting partcipants for follow up. Not all sections of the contact form are required to be completed; just as much as the participant is able and willing to complete.

The interviewer will then hand the participant a tablet with the demographics questionnaire loaded up, which the participant will complete. The interviewer will have already entered in the PID into the survey for the participant.

Both partners will need to sign the consent forms and complete the questionnaire in order for enrollment to be considered complete.

Both the contact form and demographics questionnaire will be completed in the separate, private rooms in which the consent process occurred. Once these are completed, interviewers will then conduct the interview as described below.

For **Aim 3** only, participants will also be randomized to their pilot RCT group during this time.

3.4 Interview Procedures

Two research staff will be at the interview location to complete the separate participant processes.

3.4.1 Interview Procedures

Individual Interviews, IN PERSON

Participants will arrive at the predetermined and scheduled interview site. Study staff will greet the participant and accompany them to the private interview room. Staff will offer the participant refreshments. If one partner shows up before the other partner arrives, they will be instructed to wait until they are both there.

Participants will be placed in separate rooms so that staff can review the consent with them individually. Study staff will explain the overall study objectives, the participant's rights of as a research subject (including the right to stop participation at any time), answer any questions the participant has, and give a consent form approved by the UCSF IRB for him to read with ample time. Staff will then obtain a written informed consent. After both individuals consent to the study, study staff will conduct the interview privately with each individual at the same time.

The interviewer will set up the recorder by recording both voices and **playing back to make sure both voices record**.

S/he will record the ID number of the participants and date at the beginning of the recording.

Individual Interviews, REMOTE

Participants will complete the interview either over the phone or over Zoom, depending on their preference and capability. The same procedures apply for checking that recorders are functioning appropriately.

Field notes: Interviewers must take notes during the interview about their observations, interesting ideas the participant mentioned, new probes, and/or questions for the PI. This consists of jotting down key phrases as the participants mention them, new areas of inquiry or related ideas that come up during the conversation, as well as questions or probes that don't work or fail to elicit rich data. Remember that the most important thing is to maintain rapport, so note-taking must be brief and the participants should be aware that you are going to be writing things down during the interview itself so this does not come as a surprise to them. Keeping the flow of the interview, maintaining warmth, eye contact, and connection all are more important than taking thorough notes.

Once the interview is completed, the interviewer will turn off the recorder, reimburse the participant for any travel, collect receipts, and thank the participant for his time.

Couples Interviews
The Couples interviews will follow the same consent procedures as described above (e.g., partners are consented separately). Participants will arrive at UCSF Mission Hall or the alternative interview site, and study staff will accompany them to the private interview room. Study staff will explain the interview topics and answer any questions from the couple before commencing the interview.

The interview guides may be found in Appendix C, as well as in the "Interview Guides" folder in Box.

3.4.2 Post-interview checklist
After the interview is completed, the interviewer will complete the following steps:

- After the interview and before leaving space, transfer the audio file to a password-protected laptop and upload the audio file to an encrypted transcription service website (HomeRow).
- Label the file with Participant ID number(s) and date. Each file will be kept in the appropriate Box folder.
- If the interview did not record, sit down immediately and write up everything s/he can recall about the interview.
- Review field notes and add anything missing.
    - Create a summary of the interview. This includes the manner of the participants (i.e., were they on time, did they seem comfortable, etc), developing rapport, key themes that emerged during the interview, areas that were particularly rich (i.e., provider relationships, or couple dynamics) and also particular areas that should be explored in future interviews (noting any dynamics that are based on sero-status concordancy will be key). These field notes can almost be thought of as a diary for the interviewer, and will be used as a starting point for the analysis. These should be completed directly after the interview if possible, but no later than within 24 hours of the interview.
    - Save the field notes to the Box "Field Notes" folder. Make sure the file does not contain identifiable information. Save the file as "PID_Individual Interview Field Notes_Date.docx".
- After the recorded file is downloaded and backed up (double check that they backed up before completing this step), the interviewer deletes the file from the recorder.

3.5 Participant Reimbursement
Each participant will receive $60 cash per individual interview and $60 each per couple interview. The interviewer will fill out the receipt and have the participant sign that they received the payment. At least

once per week at UCSF Mission Hall, the interviewers will review their petty cash stock and receipts with the study petty cash handler to update and verify the petty cash balance.

Should it be deemed necessary to pay participants with gift cards, use National Gift Card Group, found in BearBuy. Log into MyAccess, then, under the search bar, click on Browse: Suppliers. Jump to page 6 (approximately) and select National Gift Card. Select the cards or e-cards you want to purchase and add to cart. Please note, if the denomination is not listed, email **customerservice@ngc-group.com** and request they add the denomination you need. It can take up to 30 days to get that added, so plan in advance. When checking out, if needed, ask Emelyn Ponce to change the delivery address if cards need to be send to someone's home.

SECTION 4. AIM 2 PROCEDURES

4.1. LetSync CAC

We will strive for diversity among CAC members in terms of age, relationship length, and socioeconomic status. Sessions will be audio-recorded and transcribed.

4.1.1 LetSync v1.0 development:

The CAC will engage in three sessions.

In Session 1, we will present potential intervention targets and mHealth approaches based on a synthesis of the prior K01 mHealth designs with Aim 1 findings. We will solicit the CAC's input on intervention targets and mHealth approaches.

Based on Session 1, we will work with School of Medicine Tech Services (SOM Tech) and Wow Labz (see *Letters of Support*) to incorporate the CAC's feedback and our observations in drafting wireframes to present in Session 2.

Based on CAC feedback in Session 2, we will refine wireframes and present them for final feedback in Session 3 to produce *LetSync* v0.5 for mini-pilots. The CAC will be able to view emergent intervention targets and approaches on a large TV screen during these sessions. The team will take notes during the sessions, adding any new constructs and approaches that emerge to inform the app designs.

4.1.2. Draft of intervention protocol and procedures:

In tandem with the app development, we will draft the pilot RCT procedures and protocol. We will also draft a script for the brief (5-minute) "User's Guide" video with instructions to using app features. It will automatically play when the app is first launched and may be re-watched anytime. We will present protocols, procedures, and User's Guide script in the CAC Session 2 and make revisions according to feedback. We will then also produce the video with a video production team.

4.2. Mini-pilots and Interviews

To obtain feedback on *LetSync* v0.5 features, functionality, and usability, as well as to pilot-test intervention protocols and procedures, we will recruit 10 **new** BMSM couples (*n*=20) and give them *LetSync* v0.5 to download and use for 1 week.

We will interview each couple to explore their perspectives on the product usability; ways in which they liked or disliked the prototype and the intervention framework; and ways in which they would customize them. We will also explore the extent to which men liked their information linked and accessible to each other.

We will show a rough cut of the **User's Guide** during the interview for feedback. Finally, we will ask how they would like to access and receive the app, i.e., whether they would like it prescribed by their provider, referred by friends, or simply via GooglePlay or iTunes.

Based on the couple interviews, we will work with SOM Tech/Wow Labz improve upon *LetSync* v0.5 to finalize *LetSync* v1.0 and the intervention protocol. We will also work to finalize the User's Guide video. Interviews will last 1-1.5 hours and will be audio-recorded and transcribed.

We will collect self-reported information from participants using questionnaires administered via computer-assisted self-interview (CASI) on encrypted and password protected tablets (i.e., iPads). We will collect demographic information such as age, gender, sexual orientation, highest education level attained, and race/ethnicity. We will also ask about incarceration history and experience in the foster care system, as these variables explain differences in outcomes related to health among BMSM. Validated survey measures will be administered pertaining to self-reported clinical outcomes of adherence to ART, retention in care, and viral suppression. In addition, we will ask for verification of HIV status via a letter of diagnosis from the participant's provider or a pill bottle. Other validated measures will pertain to psychosocial variables (e.g., stigma, stress, social support, experiences with racism, relationship satisfaction, social identity, minority stress) and app acceptability and usability.

4.3. Study Procedures, Materials, and Potential Risks

4.3.1. CAC Procedures

Individuals interested in the CAC will call a dedicated study phone line to a trained research staff. We will give an overview of the study before conducting a screening over the phone to determine eligibility. Upon determining eligibility, we will obtain informed consent individually using the same procedures in Aim 1.

We will enroll the participant as a member of the study's CAC comprising of 10 – 12 members. Three CAC sessions will be scheduled and will take place remotely – or, if/when it is safe to meet in person, take place at UCSF or APEB. CAC sessions will last three hours each and will involve guided group discussions that will include members' reactions and feedback to presented research material. Through an iterative development process, the mHealth intervention will be developed and revised based on feedback obtained from these CAC sessions. There will be three CAC sessions convened, and new materials and prototypes modified based on feedback from the last session, will be presented for feedback at a subsequent session. **Each CAC member will receive a $120 cash card at the end of each session, and refreshments will be served at all sessions.**

4.3.2. Mini Pilot and Interview Procedures

Individuals interested in the mini pilot will call a dedicated study phone line to a trained research staff. We will give an overview of the study before conducting a screening over the phone to determine eligibility. Upon determining eligibility, we will obtain informed consent individually using the same procedures in Aim 1. We will instruct the index partner to have his primary partner call the study line so that we can determine his eligibility and to verify partnership status. If the primary partner does not call within 3 days, we will call the index partner back to remind them.

Each participant in the couple's interview will receive $100 cash card as a thank-you; the amount of is higher because it takes greater effort for couple members to coordinate their respective schedules for the same appointment time.

Participant Tracking

Study staff will keep track of site visits and recruitment activities in the recruitment log (excel sheet tab inside of the Study Log, saved in the Box folder "Study Logs and Trackers"). The log will include the names of organizations contacted, contacts at these organizations, dates of contact, updates, and action items. The log will be completed by all staff members completing recruitment activities.

Participants who are interested will call the study line or express interest via the study website. The Recruitment Coordinator and Study Recruiter(s) will check the study website daily and update the phone screen "to call" list. All tracking attempts will be noted in the database.

Eligibility will be determined when individuals contact the study via a dedicated phone line. Upon establishing eligibility, study staff will collect contact information for the participant and his primary partner.

HIV status will be verified at the first in person meeting during the consent visit by a letter of diagnosis, copy of pharmacy ART prescription, or a recent ART pill bottle with the participant's name on it.

Participant IDs (PIDs) will be assigned to **newly** screened participants while completing the phone screen questionnaire. Everyone who completes the phone screen, even if they are not eligible, will receive a PID. PID assignment procedures will be the same as Aim 1 in that the Index will have a suffix of "01" and the partner will have a suffix of "02".

SECTION 5: AIM 3 PROCEDURES

3.1. OVERVIEW OF STUDY DESIGN/PROCEDURES:

This study proposes to develop and refine the LetSync app, protocol, and intervention procedures with 110 couples (n= 220) where at least one partner is living with HIV, a Black/African American cisgender man or a transgender woman. The goal of this pilot RCT is to assess acceptability, feasibility, and preliminary evidence of efficacy to impact ART adherence as measured by ARV concentrations in dried blood spots. We will also explore the acceptability of remote dipstick urinalysis and hair collection in addition to remote DBS. We will iteratively develop the app, revise protocol and procedures based on participant feedback, in a 8-month pilot trial using an RCT design. We will then:

1. Randomly assign 55 couples to the intervention arm and 55 couples to the control arm. Those in the intervention arm will receive *LetSync* v1.0 for 8 months while those in the control arm will not use the app. Participants in both arms will be assessed at baseline (T0 or Month 0).
2. Between T0 (Month 0) and T1 (Month 4), we will check in with participants in both arms. With the Intervention participants, we will troubleshoot any app-related issues and confirm their most up-to-date contact information. With the Control participants, we will confirm their contact information.
3. Participants in both arms will be assessed at T1 (Month 4) and T2 (Month 8).
4. We will collect biosamples every two months from participants (Baseline, Month 2, Month 4, Month 6, Month 8).
    1. We will collect dried blood samples from **all** participants, including those who are HIV negative. Hair and urine will be **optional**.

In preparation for the full-scale RCT, we will also pilot-test the protocol and procedures for data collection. Measures/instruments will be collected via questionnaires and DBS/urine/hair samples at baseline, T1, and T2.

Dried blood spot (DBS) samples will be self-collected by participants at home, mailed to a third-party lab we enter an agreement with, and analyzed at said lab. Dipstick urinalysis will be done by participants at home, in which they will insert a dipstick in their urine that indicates the presence (e.g., positive result) or absence (e.g., negative result) of ARV in their urine. Hair samples will be self-collected by participants at home, mailed to UCSF, and analyzed at UCSF Hair Analysis Lab (HAL) for levels of ARVs indicative of adherence to ART.

If possible to gather samples in person (e.g., if participant lives in Bay Area), we will conduct baseline assessment in person if COVID guidelines and scheduling allow; if it is not possible to conduct baseline assessments in person, we will mail detailed video instructions and materials to the participant.

Consistent with study goals to evaluate feasibility and acceptability as primary outcomes, all participants will be asked to participate in a 45 to 60-minute exit interview at T2 to evaluate their experience in the study and identify areas for improvement. A draft of the interview guide is attached as Appendix.

3.2. RECRUITMENT PROCEDURES.

Recruitment efforts will take place remotely (e.g., via online advertisements). Depending on COVID-19 guidelines, in-person recruitment efforts may or may not resume. We will target the San Francisco Bay Area and other U.S. cities with highest prevalence of HIV among racial/ethnic SGM. These cities will be identified using the latest data from the Centers of Disease Control and Prevention (CDC).

- Online recruitment
    - We will place targeted advertisements on social media platforms (e.g., Facebook, Instagram), dating apps (e.g., Grindr, Jack'd), and/or online newspaper and magazines.
    - Study staff will attend virtual webinars or events hosted by community-based organizations serving racial/ethnic and/or sexual minority communities impacted by HIV/AIDS. We will focus on organizations that serve Black MSM and/or trans women living with HIV.
- In-person recruitment
    - Study staff will contact community-based organizations to schedule a visit date. They will drop off study materials (e.g., flyers) for participants to take. They will also attend community events when appropriate (e.g., LGBTQ health-geared events).
- Other methods
    - We will utilize UCSF Recruitment Letter Services and contact participants of other UCSF studies who gave consent to be contacted.

3.3. SCREENING AND ENROLLMENT.

3.3.1. Screening

We will enroll 55 SGM seroconcordant-positive couples and 55 SGM serodiscordant couples. Individuals interested in the study will call a dedicated study phone line to a trained research staff. The staff member will give an overview of the study before conducting a screening over the phone to determine eligibility. We will screen participants based on the inclusion and exclusion criteria.

We will use customer relationship management (CRM) platforms to communicate with participants and manage participant data. Ripple Science (www.ripplescience.com) will be used to manage participant data. Ripple Science is HIPAA-compliant and has undergone IT Risk Assessment with UCSF.

Targeted online advertisements will link to an online pre-screener hosted by UCSF Qualtrics or Ripple that interested individuals can take to see if they qualify. The pre-screener will be used to identify only those who are potentially eligible to avoid a large backlog of candidates to contact.

> **Update X/X/XXXX:** During Phase 1, the team screened a handful of Black trans women living with HIV that would have been eligible to participate had it not been a requirement to identify as a cisgender Black man. The PI applied for an administrative supplement to include 30 couples in which at least one person identifies as a Black transgender woman living with HIV.
>
> **Update 8/4/2022:** We will do away with the pre-screener and have candidates complete a full screener online/asynchronously. The team noticed it was difficult getting pre-screened candidates to complete the full screener and was playing phone tag trying to make this happen. To simplify the process, we will now link online ads to the FULL screener which candidates can complete online and asynchronously.
>
> Only those who are potentially eligible, based on screener responses, will be contacted by study staff. Ineligible responses will be recorded along with the reasons why someone may be ineligible (e.g., not living with HIV, not in a relationship with a cis-gender man or transgender woman). Participants will be asked to send a photo of state-issued identification, along with proof of HIV status (e.g., letter of diagnosis, pill bottle of their ART) bearing their name, to the UCSF-managed study email
>
> **Update 9/20/2022:** The team has been getting more fraudulent responses. To determine the legitimacy of couples, relationship status will be verified **at screening (as opposed to Enrollment)** using the couple verification screening instrument and protocol (see *Appendices*). Partners' responses to a series of questions (e.g., "What is your employment status? What is your partner's employment status?") will be compared for consistency. Upon establishing eligibility, contact information will be collected for the participant and his primary partner. In person, project staff will explain the study, answer questions, and obtain informed consent from each participant separately.

If candidates decline to participate but are otherwise eligible, we will ask them if they're willing to speak with the Principal Investigator to share why they declined to participate. The Principal Invesitgator will ask participants reasons why they chose to decline.

Unresponsive or potentially fraudlent candidates will be flagged for review by other team members. For candidates who are consistently unresponsive, different staff members should take turns contacting them in case this gets the candidates' attention.

After *every* contact attempt, staff members should create a task in Ripple to contact the candidate in the future. The goal is for no "dead ends" to be present.

Update 7/12/2022: 3.3.1.1. Atypical Couples + Interviews

We have been encountering individuals who are eligible to participate, but otherwise cannot because their partner is not interested in doing the study with them. We've also encountered folks who are not in a formal relationship, but are involved with someone (much like a situationship).

At the same time, we're learning it's been difficult to convince Black gay couples to participate, especially because Black gay couples may define relationships differently from a White lens.

We're finding that queer couples define relationships much differently. Definitions of relationships are different by those communities. We may benefit from more qualitative research to understand how relationships are defined. As such, couples' research is very complicated for LGBTQ+ folks of color. As such, we began exploring the idea of conducting supplemental interviews with these flagged folks that explores this topic further.

If we encounter folks who are not in a formal relationship but say they are involved with someone, staff will begin asking them how involved they are in each others' healthcare. Candidates will be presented to the PI on case by case basis to see if they are deemed eligible to participate. For example, if the "friend"/couple who is living together know about each others' health very well and are sexually involved and have on-going whatever kind of relationship, they can still qualify.

We will also begin conducting individual interviews with these candidates to learn more about how they define relationships and how they are involved in each other's care.

3.3.2. Eligibility

Eligibility criteria will be similar as Aims 1 and 2.

At least one member of the couple must:

- Iidentify as Black/African American
- Identify as cis man OR transgender woman
- Be living with HIV.

As long as at least one member of the couple meets these criteria, the race and HIV status of the partner does not matter.

However, BOTH members of the couple must:

- Be assigned male at birth

- Be 18 years old or over

Update 7/2/2022: Cindy and Sam will serve as second line for flagged participants. If Jovon flags someone, our job is to check flagged people to see how we can resolve them. Figure out how to look for flagged people and how often. If time allows for it, for pre-screeners that seem ineligible (e.g., if someone says they're not in relationship), we will still contact people in case they answered incorrectly.

Update 11/4/2022: The team has experienced difficulties pertaining to the recruitment of romantic couples where at least one partner is Black/African American, living with HIV, AND a cis man or trans woman. To address these challenges to launching the pilot RCT, we will implement the following:

1. App: We aim for the app to go live by December 20th 2022. If this is not achieved and the pilot trial is not launched by January 14th, we will be ready to launch the app outside of the App Store/Google Play environments, i.e., statically, in the same way that we have tested mini beta-versions of the app by January 15th.
2. Recruitment: The LetSync app and trial are focused on supportive dyadic relationships. Thus, we will start engaging dyads where there are dynamics to be targeted by the LetSync app intervention, focusing on Black/African American sexual and gender minority dyads. Based on our current recruitment numbers, we are confident that this expansion will allow us to meet our enrollment target by trial start date. **We will open up eligibility criteria to any non-White person of color cis man, trans woman, or non-binary individual who is living with HIV and in a relationship.**

Update 11/4/2022: Due to feedback from Co-I's around the measures around dyadic coordination and relationship outcomes, we will still limit eligibility to romantic couples.

3.3.3. HIV status verification. At the time of screening, study staff will ask for HIV-status verification by showing a letter of diagnosis or ART pill bottle with their name on it via videoconference (e.g., Zoom). An alternative is sending a digital photo to our UCSF-encrypted email address and server. Digital photos will be destroyed upon verification.

Update 9/20/2022: We will now verify HIV information AT CONSENT/ENROLLMENT. This is due to staff members noticing that couples would visibly balk at this request and becoming hard to reach after requesting this.

Update 12/21/2022: We will re-instate verifying HIV information at SCREENING again. The team, with the help of Co-Investigators, decided on 12/20 that it may be more efficient use of our time doing this at screening instead of waiting at consent/enrollment.

On Ripple, we will document what was used to verify HIV status. Staff should also follow the below guidelines on how to verify HIV status.

- If they are on PrEP:

    - Vial or prescription that has the name TRUVADA (Tenofovir disoproxil fumarate + emb), DESCOVY (tenofovir alefenamide + emb), APRETUDE (cabotegravir)
    - No possibility for letter of dx for someone taking PrEP.
- If they are on HIV medications, ONE of the following:
    - Any antiretroviral medications (need to cross-reference with a list)
        - This CANNOT be JUST Truvada or JUST Descovy. If they show us these, we need to ask for another medication.
    - Letter of dx with name, medication
        - Needs to look official (ex. with letterhead, name of provider, etc.)
    - Lab results with name, "HIV viral load", or "HIV PCR", or "HIV RNA"
- Parya's suggestion
    - Pre-enrollment visit: Ask for HIV, relationship, and age verification via email or text, then send scheduling info once we receive verification, then actually enroll.
- What happens if they fail verification? How many times will we allow re-verification?
    - For participants we might personally know, we will take what we already know about them into consideration

3.3.4. Randomization. We will assign each couple a unique study ID and randomly assign couples into intervention and control arms based on couple serostatus. Randomization will be conducted using an online randomization plan generator (www.randomization.com) that allows for stratification.

> **Update 5/18/2022:** We will use a randomization scheme spreadsheet generated by our statistician, Lance Pollack, to randomize couples according to serostatus and gender composition (ex. MSM, trans woman).
>
> **Update 9/20/2022:** If couples break up AFTER randomization, we will still keep them in the study as long as they want to still participate (intention to treat analysis). Excluding their data after they've been randomized is a HUGE no-no in randomized control trials. We'd be introducing non-randomization here.

3.3.5. Enrollment/Consent.

Pre-Enrollment Visit

Scheduling. We will schedule an enrollment visit over Zoom with each member of the couple SEPARATELY. To minimize phone tag, we will use a scheduling platform (ex. Calendly) to let couples choose from available dates.

We will conduct the enrollment visit over Zoom. Participants will be instructed to join the call from a QUIET space free of distractions (ex. they cannot be in the middle of walking, driving, in a loud place such as the gym, etc.).

Prior to the visit, staff will email a copy of the informed consent via DocuSign, and study handouts such as the activity/incentive schedule. 1 day prior to the visit, we will send reminders with instructions (join call from quiet space if needed, if couples scheduled visit together please join separately)

Staff will also instruct particpants to come prepared with documentation of their HIV status if needed (letter of diagnosis or medication bottle).

During Enrollment Visit

Overview. We will give an overview of the call: HIV status verification, review ICF, inform them of randomization status, administer baseline survey, and walk through study activities (if randomized to Intervention, administer app download and walk through.

Review ICF. We will review the ICF with the participant. Participants will give consent by signing via DocuSign in real time.

We will also obtain contact information of at least three other individuals (ex. friends, family), along with the participant's social media info, to use in case we cannot reach the participant.

We will also confirm their most up-to-date address to send materials to.

Explain activities and incentive. Once the baseline is complete, we will walk through the study activities and incentive schedules.

Baseline survey. Once ICF has been signed, the staff will send the unique Qualtrics baseline survey link to the participant. Staff will stay with them on the call until the survey is complete. If participants cannot stay online for the whole time, then they should contact the staff when they have completed the survey at a later time.

After Enrollment Visit

Send baseline survey and signed ICF. Staff will prepare unique baseline survey links for each participant on Qualtrics and email them to participant, along with copy of signed ICF.

Mail study materials. Staff will mail biomarker collection kits and ClinCard to participants' mailing address. We will mail materials using tracked USPS shipping. Staff must pay attention to expected delivery date and contact the participant when it has arrived.

Randomization. Both members of the couple must finish their baseline survey to be randomized. Staff will use the randomization scheme spreadsheet created by Lance Pollack to determine which group the participant will be randomized to.

Once a participant has completed a survey, we will get an email notification sent to *letsync@ucsf.edu*.

Staff will enter the participant's ID and name IN THE ORDER ASSIGNED to the spreadsheet. Staff will call, text, or email the couple to inform which group they've been assigned to.

Track when biosamples have been finished. DBS sample must be completed by X date (2 weeks from when pt gets kit) for them to get the bonus incentive in addition to the regular incentive. Return package must be postmarked by Y date (4 weeks from when pt gets kit) to get incentive in general.The ABSOLUTE LATEST someone can mail back samples is 6 months.

The following is an overview of the research activities for in-person and remote study visits by intervention and control arms. REFLECTS MOST UP-TO-DATE IRB STUDY APPLICATION.

Update 5/27/2022: We will no longer collect hair samples from participants due to low acceptability and feasibility. This was determined after a meeting with the LetSync Dyadic Advisory Board on 5/27/2022 when we ran by different modalities of biosample collection to get their feedback on. We will collect DBS in lieu of hair after having seen other studies that measure adherence to ARV and PrEP successfully collect these.

Intervention arm (*LetSync* v1.0)

1. At T0 (baseline) – remote OR in-person:
    a. Intervention arm participants will be scheduled to do the study initiation visit remotely or in-person at UCSF Mission Bay. We will offer the option of remote or in-person visits, depending on COVID-19 guidelines.
        1. <u>Remote visit procedures</u>
            1. Prior to the teleconference (e.g., Zoom) study visit, study staff will contact the participant, give an overview of the study, answer any questions, and obtain informed consent.
            2. Participants will be mailed a dried blood spot (DBS) collection kit and be instructed to complete a Baseline questionnaire of psychosocial and clinical self-report measures administered via Qualtrics. The questionnaire will collect demographic information such as age, gender, sexual orientation, highest education level attained, and race/ethnicity; self-reported clinical outcomes of adherence to ART, retention in care, and viral suppression; and psychosocial variables (e.g., stigma, stress, social support, experiences with racism, relationship satisfaction, social identity, minority stress).
            3. Participants will also be mailed a take-home urine test and materials to complete.
            4. Study staff will give participants an overview of the study and answer any questions. They will also give participants an overview of how to collect and mail dried blood spot (DBS) samples, and (if willing) hair and/or urine.
            5. Study staff will walk through how to install an Android or iOS version of *LetSync 1.0* on their mobile Smartphone devices.
            6. Participants' ClinCards will be loaded with $10 for completing the Enrollment visit and another $30 for completing the Baseline assessment.
        2. <u>In-person visit procedures</u>
            1. Prior to the study visit:
                1. Study staff will contact the participant, give an overview of the study, answer any questions, and obtain informed consent.

2. Participants will complete a Baseline questionnaire of psychosocial and clinical self-report measures administered via Qualtrics.

2. During the study visit:
    1. Staff will collect a dried blood spot (DBS) sample from participants.
    2. As part of our new exploratory aim to assess the acceptability of remote dipstick urinalysis and hair collection, participants will be asked if they are willing to provide dipstick urinalysis and/or hair samples.
        1. If participant is willing to provide dipstick urinalysis sample: Staff will provide a cup and dipstick for participants to use. Staff will instruct participants how to use the dipstick. Participants will provide the dipstick to the staff.
        2. If participant is willing to provide hair: Staff will demonstrate how to collect, label, and securely store a small hair sample (30-40 strands) for ARV level analysis.
    3. Study staff will walk through how to install an Android or iOS version of *LetSync 1.0* on their mobile Smartphone devices.
    4. Participants' ClinCards will be loaded with $10 for completing the Enrollment visit and another $30 for completing the Baseline assessment.

2. T1 (Month 2) – remote:
    a. Participants will collect and return a dried blood spot (DBS) sample using the kit delivered to their mailing address with necessary supplies and a prepaid return envelope.
        1. Upon successful receipt of the sample, participants will receive $30. Participants will receive a $10 bonus if the sample is post-marked within 7-10 days of requested due date.
    b. Participant will perform dipstick urinalysis using a kit delivered to their mailing address with necessary supplies. They will send a photo of the results, either by texting or emailing, to the study team. Participants will receive $15 for texting/emailing us a photo of their urine sample.
    c. Study staff will check in with participants via text, call, or email. We will ask participants about their experiences using the app, troubleshoot any issues, and confirm that we have their most up-to-date contact information.
3. At T2 (Month 4) – remote or in person:
    a. Intervention arm participants will continue using *LetSync* v1.0.
        1. <u>Remote visit procedures</u>
            1. Participants will collect and return a dried blood spot (DBS) sample using the kit delivered to their mailing address with necessary supplies and a prepaid return envelope.

1. Upon successful receipt of the sample, participants will receive $30. Participants will receive a $10 bonus if the sample is post-marked within 7-10 days of requested due date.

2. Participant will perform dipstick urinalysis using a kit delivered to their mailing address with necessary supplies. They will send a photo of the results, either by texting or emailing, to the study team. Participants will receive $15 for texting/emailing us a photo of their urine sample.
3. Participants will complete an online questionnaire that will be available during a window of time. After 3 days of non-response to the questionnaire, we will remind participants via an E-mail or call from the research staff.
4. Online questionnaire will include validated usability and acceptability measures in addition to those on the Baseline questionnaire.

2. <u>In-person visit procedures</u>
    1. Staff will collect a dried blood spot (DBS) sample from the participant. Participants will receive $40 for the sample.
    2. Staff will collect a dipstick urinalysis test. Participants will receive $15 for the completed urine test.
    3. Participants will complete an online questionnaire that will be available during a window of time. After 3 days of non-response to the questionnaire, we will remind participants via an E-mail or call from the research staff.
    4. Online questionnaire will include validated usability and acceptability measures in addition to those on the Baseline questionnaire. Participants will receive $40 for completing the survey.

4. At T3 (Month 6) – remote:
    a. Procedures will be similar to those at T1 (Month 2).
5. At T4 (Month 8) – remote or in person:
    a. Intervention arm participants will continue using *LetSync* v1.0. We will conduct an Exit Interview in-person or remotely depending on COVID-19 guidelines. Interviews will be audio-recorded and transcribed for analysis. The digitally recorded audio file will be transferred immediately following the interview onto a password-protected laptop and then uploaded to an encrypted transcription service website prior to being permanently deleted on the audio-recorder and laptop. Any personally identifying information will be redacted from the transcripts.
        1. <u>Remote visit procedures</u>
            1. Procedures for biospecimen collection and online survey completion will be the same as T2 (Month 4).
                1.
            2. Staff will conduct the Exit Interview over teleconference (e.g., Zoom) or phone.
        2. <u>In-person visit procedures</u>
            1. Procedures for biospecimen collection and online survey completion will be the same as T2 (Month 4).

2. Staff will conduct the Exit Interview in person.

b. Participants will receive a $20 cash card for completing the Exit Interview, and an additional $50 as a study completion bonus.

Control arm

1. At T0 (baseline) – remote:
    a. Participants randomized to the control arm will be informed of the study objectives and timeline. They will be informed that they can use the app once the study is over.
    b. Participants will be mailed a dried blood spot (DBS) collection kit and be instructed to complete a Baseline questionnaire of psychosocial and clinical self-report measures administered via Qualtrics. The questionnaire will collect demographic information such as age, gender, sexual orientation, highest education level attained, and race/ethnicity; self-reported clinical outcomes of adherence to ART, retention in care, and viral suppression; and psychosocial variables (e.g., stigma, stress, social support, experiences with racism, relationship satisfaction, social identity, minority stress).
    c. As part of our new exploratory aim to assess the acceptability of remote dipstick urinalysis and hair collection, participants will be asked if they are willing to provide urine and/or samples. If so, participants will be mailed a remote urine and/or hair collection kit at no cost to them. The kit will contain materials and instructions on how to send samples back.
    d. Study staff will give participants an overview of the study and answer any questions. They will also give participants an overview of how to collect and mail dried blood spot (DBS) samples, and (if willing) hair and/or urine.
    e. Study staff will walk through how to install an Android or iOS version of *LetSync 1.0* on their mobile Smartphone devices.
    f. Participants will receive a $66 cash card for completing the Baseline assessment.
2. At T1 (Month 2) – remote:
3. At T2 (Month 4) – remote:
    a. Procedures for T2 will be the same as those for participants in the intervention arm at T2.
4. At T3 (Month 6) – remote:
    a. Procedures for T3 will be the same as those for T2.
5. At T4 (Month 8) – remote:

    a. T2 procedures will be identical in both intervention and control arms. At the T2 visit, we will conduct an in-person or remote exit interview to gather qualitative data for evaluating the acceptability of our methodology, including of the remote dried blood spot (DBS), dipstick urinalysis, and/or hair collection. In the exit interview, we will ask participants about the acceptability of sample collection. Participants will receive a $90 cash card for completing the Exit Interview.

We will interact with participants at Baseline, T1, and T2 via in-person visits, phone calls, postal mail, and E-mails. We will contact study participants to remind them of their scheduled visits, hair sample due dates, and to obtain information on acceptability of app and its use.

Follow-up/retention in study. We will collect at least three methods of personal contact, such as their social media handles and additional phone numbers, at the time of enrollment. We will also obtain contact information to three of the participant's close friends and/or family that we will contact only if we cannot reach the participant (see LetSync Secondary Contact Script, attached). We will also maintain regular contact with participants by sending reminders about virtual check-ins, about sending in hair samples, and asking about any app-related issues. In every contact, we will request information on changes in contact information.

Incentives. Incentives will be given to participants in the form of cash or gift cards.

> **Update 8/15/2022:** To encourage participation in a longitudinal study, the study team and co-investigators, namely Lance Pollack, agreed that we should make the incentive structure *graduated,* i.e. increase over time. We will tie an incentive amount to EACH study activity.
>
> We previously discussed awarding "on-time" bonuses to reward participants who complete activities on time. There was some disagreement with this among the co-investigators, because any unused on-time bonuses could have gone towards increasing incentive amounts for study activities overall and encouraging participation in them.
>
> We will also now pay participants via ClinCard, as the team agreed this is the best alternative to paying participants via apps such as Venmo and CashApp (which the university is not supporting at the moment). Participants have historically requested cash, and due to this being a remote study it will not be possible to pay everyone with cash.
>
> **Update 2/21/2023:** We will re-instate "on-time" bonuses for DBS samples to encourage participants to mail them back on a timely basis, and with all the considerations the staff realized such as time it takes for pts to complete DBS sample, mailing it back, and freezing it to ensure limited degradation. We will try this structure out and re-visit if needed (ex. if we don't see pts mailing back samples).

SECTION 6: PARTICIPANT BREAK-UP PROTOCOL

Participants will be screened and enrolled in the study as an intact couple. Participants will be informed at the time of phone screening and consent that this research is a couple's study. However, in the event that an enrolled couple breaks up, the Participant Break-Up Protocol will be followed based on the time point when the break-up occurred and the randomization status of the couple.

6.1 Breakups during Aim 1

- Between Phone Screening and Consent:
    - Participants will be informed that they are no longer eligible for the study due to not being in a couple, and their scheduled interview will be cancelled.
    - Participants will be informed that if and when participants enter into a new primary relationship and meet eligibility and inclusion criteria, they and their new primary partner may enroll as a new couple in a subsequent study (e.g., the pilot trial).
- Between Consent and Couple Interview (if not scheduled on the same day as the individual interviews):
    - Participants will be informed that they are no longer eligible for the study due to not being in a couple, and their couple interview, if scheduled, will be cancelled.
    - Participants will be informed that if and when participants enter into a new primary relationship and meet eligibility and inclusion criteria, they and their new primary partner may enroll as a new couple in a subsequent study (e.g., the pilot trial).
- Both participants will be offered referrals for support and a list of other UCSF CAPS studies (See Appendix XXX).

6.2 Breakups during Aim 2

- Between Phone Screening and the 3rd CAC Session
    - Participants will be informed that they are no longer eligible for the study due to not being in a couple, and their scheduled session will be cancelled.
    - Participants will be informed that if and when participants enter into a new primary relationship and meets eligibility and inclusion criteria, they and their new primary partner may enrol as a new couple in a subsequent study (e.g., the pilot trial).
- Between Consent and mini-pilot
    - Participants will be informed that they are no longer eligible for the study due to not being in a couple, and their scheduled session will be cancelled.
    - Participants will be informed that if and when participants enter into a new primary relationship and meets eligibility and inclusion criteria, they and their new primary partner may enrol as a new couple in a subsequent study (e.g., the pilot trial).
- Both participants will be offered referrals for support and a list of other UCSF CAPS studies located at **https://prevention.ucsf.edu/join-study**

6.3 Breakups during Aim 3

- Between Consent and Randomization
    - Participants will be informed that they are no longer eligible for the study due to not being in a couple, and their scheduled baseline appointment will be cancelled.
- After Randomization

    - Study staff will contact both participants and explain to them that they may use the app and participate in the T1, T2, T3, and T4 surveys, and hair self-collection (if HIV+) as scheduled throughout the rest of the study.
- Between T1 and T4
    - Study staff will contact both participants and explain to them that they may use the app and participate in the remaining surveys and hair self-collection (if HIV+) as scheduled throughout the rest of the study.
- Throughout the Pilot Trial
    - Participants will be asked whether they are still together with their original partner at each time point.
    - If a couple breaks up, study staff will contact both participants to confirm their current contact information, if changed as a result of the break-up. The Tracking Database will be updated with the correct information to ensure continued contact with each participant.
    - The staff member who identified the break-up will communicate this information to the study coordinator and PI via email.
    - In the event that a couple breaks up and then gets back together, the study staff will meet as a team to discuss the situation and determine **the most appropriate way to proceed.**

SECTION 7: PARTICIPANT CRISES PROTOCOL

7.1 Protection of Participants

Remember: Our utmost concern is protecting the safety and welfare of participants. Given the nature of our research project and population, it's possible that during an interview or study visit a participant may make suicidal comments or indicate that they are experiencing significant distress or depression. We've created the following procedures as a safeguard.

Initial Impressions

As you greet and orient participants, look for indications of distress. Address any concerns you have according to the protocol below. Ones that need extra attention are:

- Suicidal Ideation
- Homicidal Ideation
- Grave disability
- Child, Elder and Dependent Adult Abuse
- Intimate Partner Violence
- Emotional Distress

7.2 Clinician Availability

Clinically trained staff members are always available to interviewers. Be familiar with your team's contact information and list of people who should be contacted in case of an emergency. The Principal Investigator and/or Study Coordinator are generally onsite during interviewing hours. Be aware, on a daily basis, of staff availability for clinical and crisis consultation. As a back-up, there will always be a licensed clinician with a cell phone to contact in emergencies. You should always have easy access to these team members and phone numbers. Judy and the Clinical Supervisor (TBD) are ok with calls or texts.

- Clinical Supervisor, TBD cell: (XXX) XXX-XXXX
- Principal Investigator, Dr. Judy Tan's cell: (917) 838-0698

7.3 Protocol for Suicide Risk

7.3.1 Suicidal Comments Should Always Be Explored

It is a myth that talking about suicide to people increases the chances of them actually doing it. A participant's comments could be direct, (e.g., "I want to die," "I'm thinking of killing myself," or "I don't want to go on any more."). They can also be more indirect, such as "Life isn't worth living alone, without my partner."

If you are concerned that the participant is at risk of harm, and if you are a trained clinician, begin a suicide assessment (see Suicide Risk Protocol below). If you are not a trained clinician, involve an available staff clinician with the participant's consent.

7.3.2 Assess the Imminence

If there is evidence that the participant is significantly distressed and suicide may be imminent, take steps to establish contact between the participant and a referral source. Action is imperative when a person meets the following criteria:

- Has a plan,
- Has the means to carry out the plan (i.e., has the medication or weapon),

- Has intent to complete suicide in immediate or near future,
- Has little that they are planning to do in the future,
- Has attempted to commit suicide in the past (approximately 5% of those who attempt but do not complete suicide, do commit at a later date),
- Has not told others about the plans out of a concern that they will try to intervene, and
- Talks about events and close people as though the suicide has already occurred.
- Has given away valuable and sentimental items.

7.3.3 Look for an Obstacle or Hook

Listen for the participant to mention something that would keep them from committing suicide either immediately or in the future. This is the "hook." It might be an upcoming event that the participant would not want to miss. It might be a promise the participant made to a partner. It might be a spiritual belief or a commitment to friends. Listen for this carefully as you are showing your concern and empathy for the participant. If a "hook" is found, mention it to the participant to see if they responds positively. For example, they might say, "You're right, I really did make a promise and I can't go back on that," or "I'm not going to even think about it until after I go back East for the holidays to see our friends...that's something we were planning for a long time." The presence of a hook can usually be used to extract a commitment from the participant that they will not take any immediate action to hurt himself. This is, in essence, a good sign.

7.3.4 Emergency Actions

Ask the participant direct questions and get answers to criteria 1–8 above. If, based on the answers, you believe that risk of harm is imminent, you must next decide if it is an emergency. If you believe that they may take an action between now and a few days from now, the situation is considered an emergency. If this is the case, do not let the participant leave. Contact the Principal Investigator or the Study Coordinator. If they cannot be contacted, persuade the participant to come with you to talk with someone about the suicide now and take the participant in a cab to a nearby ER or call a 24-Hour Suicide Prevention Hotline and ask them to talk to the participant. Don't leave the participant until the situation is resolved with your having a firm commitment from the participant that they is not going to take any action to hurt himself until after a future date.

What to say

- "This is such an important decision. It's so final. It's really important that you talk with someone about this, and I am not the best person."
- “The fact that you told me about this means that you may want to talk it through first. It's important that you talk with someone about your feelings."

7.3.5 Non-Emergency Actions

If you determine that there is risk, but that it is not imminent (for example, the participant is thinking about suicide but has no plan, or there is a plan but the participant is definite about not wanting to do anything until after an upcoming event), talk to the participant about obtaining counseling and make a referral. You should also seek consultation from a clinically trained person while the participant is still present. The focus during this consultation call is on reviewing the imminence, and then developing a plan for support and referral. Work with the participant to devise a plan for getting in touch with the designated referral source. **Refer to Appendix A for a list of resources.**

7.3.6 Document all actions taken

Write a summary email to the Project Director, print a copy for documentation in the participant's file, briefly summarize in the database, and inform other staff members on a "need to know" basis. Follow up any referrals with a phone call within the next 24-48 hours.

Interview Protocol for Non-Suicidal Distress.

7.3.7 A Delicate Balance

Keep in mind that while participant safety is our primary concern, it's also important to consider balancing your response to the participants' needs with unbiased data collection. Although suicidal comments and indications of distress must *always* be explored, it may be possible to complete the interview before conducting a full risk assessment. This is preferable from a research perspective because the data is collected *before* attempting any type of intervention, which could bias the participant's responses.

Example Situation: If, during informed consent, the participant indicates recent significant depression, then:

- Briefly acknowledge their response in order to determine the severity of depression and suicide risk. Then, if risk of harm does not seem imminent and if the participant seems comfortable, continue with the interview.
- Complete the interview, and then revisit the response by saying, "When I asked earlier how you were feeling, you stated that you felt life is not worth living. Will you please tell me more about that?"

To determine the level of risk gather specific information by asking each of the following probes:

- How are you feeling now?
- Are you receiving any type of counseling?
- (If in counseling): When is your next appointment?
- Have you had any counseling in the past?
- Are you taking any medication to help you handle _____?
- Do you have a friend or family member that you can turn to when you are feeling down like this?
- What do you feel you need now?
- Would you like to talk with someone about _____? (Referral)
- (If possibly suicidal): Have you thought about what you might do?

7.3.8 Useful Phone Numbers

- Suicide Hotline: (415) 781-0500
- Mobile Crisis: (415) 255-3610
- Psychiatric Emergency Services (SFGH) 206-8125

7.4 Protocol for Homicidal Ideation

If a participant makes any comments about wanting to hurt or kill another person, or presents with unusually strong rage towards another person, the interviewer needs to assess for potential risk of harm to other people. If there is

- Intent to harm an identifiable victim, and unable to clearly state they have no intent to act on these thoughts (Tarasoff situation - duty to warn enacted and police and intended victim must be warned)
- Participant feels out of control or unable to manage angry feelings (should be treated the same way as suicidality, with problem solving, contracting and potential referrals to a mental health provider, Mobile Crisis Team or Psychiatric Emergency Services).

In either of these cases a clinically trained staff member should be alerted immediately to help assess the situation and level of risk.

7.4.1 Tips for gathering information

Suggested Interviewer Style: Friendly (compassionate, warm, concerned, supportive, client-centered), Frank (direct, candid, unafraid to ask or talk about risks plainly), and Firm (asking in a confident tone and insisting that this discussion is essential, imperative, and necessary). These help establish therapeutic trust, clear expectations, and relational honesty.

Is there homicidal ideation (Normalize): When someone feels as upset as you do, they may have thoughts about hurting the person who has upset or hurt them.
What thoughts have you had like this?

Is there a Plan (Means)
If you decided to try to hurt _____, how would you do it?
Tell me about the plans you've made.

Is there Access to Means
You mentioned that if you were to hurt _____, you'd probably do it by (describe method). How easy would it be for you to do this?

Are there any protective factors? (Normalize): People often have very mixed feelings about harming other people.
What are some reasons that would stop you or prevent you from trying to hurt _____? What is it that most holds you back from actually doing this?

What about past experiences? (History of violence) What have been your past experiences related to hurting people who have hurt you?

Future Expectations
What are some of the things happening in your life or likely to happen in your life right now that would either make you more or less likely to want to hurt_____?
How do you think people who know you would react if you actually did this?
What would they say, think, or feel?
What would be some of the consequences?

7.4.2 Useful Phone Numbers:

Police Liaison: (415) 255-3727

7.5 Protocol for Grave Disability

Although unlikely, participants may develop a significantly impaired mental state at some point during the intervention, i.e. evident upon arrival for an interview or during the course of an interview. This could be caused by acute psychosis, mania, substance use or withdrawal, or acute or progressive medical illness. If the participant is too disorganized or confused to continue the interview, evaluate whether the participant is going to be able to get home safely. If it appears that the participant is no longer able to care for them self, the interviewer should take the steps listed under **Emergency Actions** and consult with an available supervisor.

7.6 Protocol for Suspected Child and Elder/Dependent Adult Abuse

The LetSync team is required to report any cases of suspected child, elder (65 or older), and dependent adult abuse. If participant mentions knowledge of a current abuse situation, the project is required to notify the appropriate agency within the required time period.

- Children under 18: Call Child Protective Services as soon as possible and follow up with written report within 36 hours
- Adults: Call Adult Protective Services and follow up with written report within 2 working days

If a participant reports past abuse, the interviewer should assess whether or not the perpetrator is still in contact with children. If they are either living with children or being left unsupervised with children, the project is required to file a report with CPS. If clinically appropriate, the participant should be involved in the reporting process.

When in doubt about whether a report is required, staff at CPS/APS are available for consultation. Always remember to get the name of the person you spoke with and document the conversation in the participant's file.

The interviewer should always discuss the situation with a supervisor and decide together whether as report needs to be filed.

7.6.1 Useful Phone Numbers:

Adult Protective Services: 557-5230
Child Protective Services: 558-2650, or 1-800-856-5553

7.7 Protocol for Intimate Partner Violence

LetSync is not mandated to report domestic violence and staff are not allowed to break the participant's confidentiality to report battering unless the victim is over 65 or considered a dependent adult (disabled in a wheel chair, unable to physically care for self, etc.).

If a participant reports that there is physical violence or feels increasingly at risk of violence in a relationship, the counselor will want to help the participant develop a safety plan. This may include referrals to shelters, problem-solving places to go (family, friend's house, hotels), or finding ways for participant to keep themselves safe at home.

7.8 Protocol for Emotional Distress

If a participant is under clear emotional distress (e.g., crying, yelling), take the time to figure out if the participant is in a clear headspace to do the interview. It may also be that the interview questions can be triggering.

Let the participant know that you can tell they are feeling distressed from their words and intonation of voice. Ask if they would like to re-schedule the interview on another day and time, which they can do with no penalty to them. It may also be appropriate to refer them to services they clearly mention need of (e.g., psychological counselling, housing assistance, food banks).

SECTION 8: DATA MANAGEMENT

8.1 Participant ID Assignment

After interested individuals are screened and determined to be eligible, they will be assigned a participant ID number. The number will consist of 4 digits (XXXX). The first three digits will refer to the couple, and the last digit will refer to the individual within the partnership. For example:

- 1011, 1012
- 1021, 1022
- 1031, 1032
- etc.

The index partner in the relationship (the HIV-positive, cis-gendered black man) will always be assigned the individual digit of "1", while the primary partner will receive the individual digit of "2". This is not to be confused with the "Partner 1" and "Partner 2" on the screening form, which only refers to the order in which the partners call to be screened.

8.2 Study Tracking

8.2.1 Recruitment activities

Any study staff conducting recruitment activities (see Section 2.4 Recruitment) will, within 24 hours of the activity, add a row to the "Recruitment Activities" tab in the "Study Log" file within the "Study Logs and Trackers" folder in Box.

8.2.2 Screening form log

The "Screening Form Log" tab of the "Study Log" file will be updated within 24 hours of each participant call-in and phone screener questionnaire completion. The staff member who completes the questionnaire will ideally also enter the information into the Screening Form Log.

Each person who calls in and completes a phone screening questionnaire will be entered into this form, regardless of eligibility.

This will be verified weekly by both a recruiter and the study coordinator.

<u>Updating dropdown lists</u>

If changes to answer choices in each column are needed, they can be edited in the "SFL answer options" tab (currently hidden) in the same excel file. If answer choices need to be added, the team member will need to change the data selection range in the "Screening Form Log" tab. To do this:

1. Highlight the appropriate column in the "Screening Form Log" for which you need to update the drop down list.
2. Choose "Data validation" from the "Data" menu.
3. Choose "List" for the "Allow" section under "Settings".
4. Make sure "In-cell dropdown" is checked.
5. In "Source", choose the cells you would like to be included in the dropdown list. Drag to highlight the cells you want.
6. You can also edit the message you see when you hover over the column, as well as the type of Error Alert here as well.
7. Click OK.

8.2.3 Interview scheduling tracker

Once both partners confirm eligibility and interest and the interview is scheduled, the staff member who scheduled the interview will complete a row for the appropriate participants.

This will be verified weekly by both a recruiter and the study coordinator in conjunction with the PI.

8.2.4 Contact tracking

Whenever a participant is contacted, the study team member who contacts said participant will enter the PID, Date, contact method, and notes regarding the call.

This will be verified weekly by both a recruiter and the study coordinator.

8.3 Qualitative interview data procedures

8.3.1 Post-interview procedures for interviewer

1. After completing the interview, the interviewer will review the audio recording to ensure it was properly recorded.
2. The interviewer will review their field notes for clarity and accuracy and summarize the interview while it is still fresh in their mind.
3. Right after the interview, or within 24 hours, the interviewer will type up his/her field notes onto their laptop and upload them to the Field Note folder in UCSF Box. The notes will be labeled with participant ID number(s) and date of interview. Any identifying information will be removed.

8.3.2 Interview transcription

Interview audio files will be sent to a transcription service (e.g., HomeRow) to be transcribed. The study coordinator or PI will send the audio files to the transcription service within 24 hours of interview completion. Interviews will be transcribed verbatim. The interviews are expected to be transcribed within 7 business days of the transcription service receiving them.

When the transcriptions are received from the transcription service, the study coordinator will upload the transcriptions to the UCSF Box Interview Transcription folder and label them with Participant ID number(s) and interview date.

The interviewer will then be told that the transcript is available, and they will need to access the file and ensure that the written version is accurate. The interviewer will listen to the audio recording and make necessary corrections and will remove identifying information. The clean version will be saved as "0101.clean, 0102.clean, etc." These clean files will be loaded into the analytic program to be coded.

The study coordinator will also upload the transcription into DeDoose in the file folder for LetSync (may still need to be set up).

The study coordinator will update the PI about uploaded transcripts on a weekly basis and will track of the status of interview completion and transcription under the Interview Tab in the LetSync Study Log.

8.3.3 Qualitative Coding and Analysis

The team will use DeDoose to code and analyze the interviews.

Couples' Interview Transcripts

The team, trained by Drs. Arnold and Tan, will conduct couple-level analysis of the individual interview transcripts first, using both a deductive and inductive approach. The team will read all individual transcripts and develop a codebook based on the interview guides, the theoretical framework, and emergent themes. Taking a subset of interviews, the team will read and re-read the transcripts to gain familiarity with the major themes within the data. They will then develop a preliminary codebook, which will contain parent and child codes designed to capture and describe the data. Using the preliminary codebook, the team will then collaboratively code 2-3 transcripts, openly discussing the rationale behind code application and chunking particular segments of data. Once the team has reached a shared understanding for code application, they will separately code 1-2 transcripts, with Dr. Arnold measuring the level of coding agreement between different coders and providing training and feedback to the team members until all coders reach a coder agreement threshold of 90 percent. Once coder agreement has been achieved, the team will be assigned transcripts to code in Dedoose and will convene on a weekly basis to discuss analysis and particular narratives, patterns, and emergent findings.

The team will compare and contrast each transcript from individual interview with that of the partner to discover overlaps between narratives and to identify points of corroboration and contradiction. With the couple as the unit of analysis, we will cross-analyze significant statements, formulating themes based on both partners' perspectives on their relationship, resiliency, dyadic coordination around health and care engagement, and respective roles in their own and each other's healthcare. Comparing both partners' perspectives will allow triangulation to derive a fuller, more contextualized understanding of the nature of dyadic processes in HIV care engagement in the context of social and structural challenges and barriers to care.

Individual Interview Transcripts

After dyadic analysis, we will conduct individual-level analyses. We will develop the codebook by reading all transcripts and iteratively generating and revising codes based on discussions of major themes that are linked to our theoretical framework and that emerge from our data. After several sessions of simultaneously applying codes to 3 transcripts (2 individual and 1 couple interview) as a team and discussing the coding system, we will use 1 couple's individual and couple interview transcripts to verify consistency in code application between coders. We will revise the codebook and repeat this process until reaching 90% agreement. Thereafter, we will independently code and create analytic memos based on our conceptual framework and emergent findings.

8.4 Data Storage/Maintaining confidentiality

All electronic data will be stored via password-protected laptops in UCSF Box, Qualtrics, or DeDoose.

All hard copies of forms with data (e.g., consent forms, etc.) will be stored in a locked file cabinet in the UCSF Mission Hall office. Only the study coordinator and PI will have access to the cabinet, and other team members may request access when needed.

Any hard copies of forms that are scanned and uploaded to Box will be deidentified and labeled with Participant ID.

If confidential data must be sent from one UCSF entity to another, the email will be labeled "SECURE" in accordance with UCSF IT policy to ensure confidentiality of information.

SECTION 9: QUALITY ASSURANCE

9.1 Staff Training and Certifications

9.1.1 Interview Training

Study staff will be trained in interviewing by the PIs (Judy Tan and Emily Arnold). This will include:

- Practice interviewing with UCSF staff
- PI review of and feedback on transcripts

Each interviewer must review the separate protocols for emergency reporting procedures and intimate partner violence procedures.

9.1.2 Staff Certification

The Study Coordinator will ensure that all study staff are up-to-date on CITI training requirements and upload the certificates to the appropriate study folder.

The Study Coordinator will ensure that the petty cash handler and any other study staff needing petty cash certification for any reason maintain certification. The Study coordinator will upload the certificate to the appropriate study folder.

9.2 Qualitative Data Quality Assurance

The investigators will regularly review the interview transcripts to ensure that all topic areas are being discussed with participants and data are collected. They will also review summaries as they become available. In instances where topics are not investigated, training will be offered to interviewers to ensure that study data are collected appropriately across the entire sample.

PI Judy Tan (917-838-0698) and Co-I Emily Arnold (personal cell phone number: TBD) will be available for calls from staff (interviewers) or participants around difficult issues in experienced in the field.

SECTION 10: OFFICE PROCEDURES

10.1 Petty Cash

Project staff requesting petty cash will meet with the petty cash custodian on a weekly basis to log receipts and petty cash requests.

The petty cash custodian is in charge of the petty cash lockbox, tracking, and reporting as per UCSF requirements.

10.1.1 Tracking Petty Cash Flow

Using the "LetSync Petty Cash Tracking" file located within the "Admin" > "Petty Cash"folder in Box, the petty cash custodian will fill in a new row for any petty cash transation that s/he initiates. This includes collection of receipts.

- When giving petty cash to interviewers, the petty cash custodian will note this amount in the "Amount Given to Staff" column. The petty cash custodian will note this amount in the petty cash tracking log immediately after giving petty cash to study team members.
- When receiving receipts for participant transactions from interviewers, the petty cash custodian will note this amount in the "Receipts Received from Staff in Current Transaction" column.
- The "Cumulative Total of Receipts" column will automatically add the receipts of all transactions. DO not edit this.

All petty cash receipts will be stored in a designated folder in a locked file cabinet at the petty cash custodian's desk.

Once per month, the petty cash custodian will meet with the PI to verify that petty cash transactions add up.

Update 2/7/2022: Twice a year, the petty cash custodian will meet with the department head to verify amount of petty cash in hand.

10.2 Storage of participant forms

Forms with participant information on them will be kept in participant-designated file folders in a locked cabinet of the study coordinator.

10.2 Printing of study documents

The study coordinator, with help from team members, will keep track of the number of forms that are available as hard copies (e.g., consent forms, questionnaires, interview guides, etc.) and print new copies when needed.

10.3 Project Management File

The study coordinator will keep the Project Management excel file (found in the "Admin" folder) updated. This includes:

- Login credentials for any study-related websites or other apps
- Study phone information
- Required reporting dates

- Other pieces as necessary

10.3 Reporting requirements

10.3.1 Research Performance Progress Report (RPPR)

The study coordinator will keep track of the variables needed to be included in the RPPR forms sent to the NIH at the end of each project year. The study coordinator will assist the PI in completing the RPPR to be submitted.

The study coordinator will make sure that the necessary reporting items are being tracked in the study logs, which are the following:

- Age (in years)
- Race
- Ethnicity
- Gender

10.3.2 Recruitment Milestone Reporting (RMR)

The study coordinator will keep track of the recruitment numbers needed to be included in the RMR forms sent to the NIH. The study coordinator will send this to the PI so she can submit to the NIH.

The study coordinator will make sure that the necessary reporting items are being tracked in the study logs.

SECTION 11: HUMAN SUBJECTS

11.1. Potential Risks to Subjects

A risk posed to participants will be loss of confidentiality. Mini-pilot participants risk losing confidentiality over unsecured transmission of private data. Another risk is the psychological discomfort due to unpleasant memories that the survey or interview questions may elicit. Although highly unlikely, there is a low risk of interpersonal disagreements during couple's interviews that pose unpleasant interactions. Intimate partner violence (IPV) is common among same-sex gay couples. In any couples-based research, in order to protect against the risks of IPV resulting from research participation of couples, researchers should inquire about IPV. The proposed research does not directly study IPV and thus will not involve content related to IPV. However, because we will be inquiring about IPV at screening, there is a risk of distress while revealing IPV experiences to investigators/research staff, fear of reprisal, and actual reprisal.

11.2 Adequacy of Protection against Risks

11.2.1 Informed consent and assent

Written informed consent will be obtained from each subject at entry into the study. Informed consent is obtained by the following process:

1. The subject will be asked to review the study consent form and will be given ample time to do so. The consent form will be at a 6th grade reading level.
2. A member of the research team will meet with the subject to review the form, to confirm the subject's understanding of the study, and to answer any questions the subject might have. Potential participants will be informed that their participation in the study is voluntary and that they may decline to participate for any reason without any negative consequences. We will inform individuals that they may refuse to answer any question, and that any information they provide will be strictly confidential. We will also inform individuals that the study is being conducted by our team at the University of California, San Francisco, and that its purpose is to examine issues of importance to BMSM living with HIV, including relationships, engagement in care and adherence to treatment, general health outcomes, and thoughts on HIV prevention programs.
3. Once the subject demonstrates understanding of the study and agrees to participate in the study, the consent will be signed in the presence of the member of the research team.

11.2.2 Protections Against Risk

All study procedures will be submitted for approval at the Institutional Review Board (IRB) at UCSF. Protecting the identity and confidentiality of the participants will be a top concern for all involved in the project. To accomplish this, a number of steps will be taken:

- All participants will be assigned a unique identification (ID) number. We will assign ID numbers to each survey record, so names will not be associated with individuals' answers to the questions. All private identifiable information collected from participants will be stored separately from the participants' research data, e.g., transcripts, hair samples, and questionnaire using a password-protected and encrypted laptop per UCSF minimum security standards. The key linking personally identifiable information to study ID will be stored separately under passcode.
- We will regularly obtain up-to-date human subjects and ethics training certifications indicating that all investigators and key personnel have fulfilled all requirements for performing research involving human subjects, thereby meeting NIH policy. Research staff will receive regular "refresher" training on handling confidential information from participants. Staff who takes

notes on paper (e.g., at a CAC session) will document only the necessary information, will never list identifying information, and will destroy the notes by placing them in a secure shredder bin once they are transferred onto the study laptop. Any physical copy of study-related information will be handled in this way.

- All data will be accessed and stored on UCSF-managed and serviced laptops and iPads and only on these devices. All data files containing participant information—even de-identified information—will be password-protected. All research laptops and iPads are password-protected and secured with Duo two-factor authentication process and have installed on them Pulse Secure Virtual Private Network (VPN), which secures a user's transactions. Any transmission of data will be encrypted across public networks as if it were directly connected to the UCSF network. UCSF provides a secure environment for all computing by protecting all computers and servers with anti-virus, anti-spyware, intrusion prevention, proactive threat scanning, and personal firewall for Windows computers. On OS X and Linux computers, UCSF provides anti-virus and anti-spyware.
- UCSF's Qualtrics software will be used to administer and store all self-administered surveys. Qualtrics is a web-based HIPAA-compliant and secure electronic data capture and storage for research studies. All Qualtrics web connections are secured with authentication and data logging.
- Digital recording devices will be erased subsequent to interview transcription. Transmission of data will be done using via UCSF's secure VPN. The qualitative interview transcriptionist service will transmit files over military grade 128-bit Secure Socket Layer (SSL) encryption security in transit and 256-bit AES encryption at rest.
- All interviews, CAC sessions, and in-person visits will be conducted in a private space at CAPS or APEB, a HIPAA-compliant community-based primary care clinic. Audio files and transcripts will be labeled according to the unique ID number and the file will be password-protected.
- We will supply all participants with a study phone number and email address where they can contact us for any questions or concerns.
- Participants will be instructed to use the app on their private mobile phones in locations where their privacy is ensured, and will be informed about ways to help protect their privacy. Data collected via the study app will be securely captured and monitored using data confidentiality and authentication protocols, including a data encryption solution for mHealth (DE4MHA). Past research has shown that DE4MHA allows users to safely obtain and exchange health information with the data being transferred securely and managed internally using systems set up by the UCSF Information Technology Services. All tracking information will be destroyed after the completion of the study.

To protect against the <u>risk of interpersonal disagreements between couples or psychological discomfort</u>:

- We will emphasize that the participant may stop or terminate his participation at any time without negative consequences.
- The interviewer will be trained by the PI to mitigate potential disagreements and psychological discomfort from occurring and to handle them if and when they do occur. In the event that the interviewer or staff observes the participant(s) experiencing psychological discomfort or having disagreements, the interviewer will pause and ask if participant(s) would like to continue. If the disagreements still continue, then the interviewer will end the interview. A protocol will be in place for reporting these as minor adverse events to the PI.

To protect against the <u>risk of IPV or related reprisal due to research participation</u>:

- Exclusion criteria include participant reporting fear of IPV resulting from participation. We will evaluate fear of reprisal prior to enrollment in the study via a Yes/No question, "Are you fearful or in danger from your partner as a result of your participation in the study?" To maintain privacy, participants will be screened privately and separately from their partner. Suspected IPV will not be specifically listed as a reason for exclusion to the participant or his partner.
- We will use the following IPV-research guidelines set forth by the World Health Organization (WHO) for ensuring participants', including:
    - The safety of respondents and the research team is paramount and should infuse all project decisions.
    - Protecting confidentiality is essential to ensure both safety and data quality.
    - All research team members should be carefully selected and receive specialized training and ongoing support.
    - The study design must include a number of actions aimed at reducing any possible distress caused to the participants by the research.
    - Field workers should be trained to refer women requesting assistance to available sources of support. Where few resources exist, it may be necessary for the study to create short-term support mechanisms.
    - Researchers and donors have an ethical obligation to help ensure that their findings are properly interpreted and used to advance policy and intervention development.
    - Violence questions should be incorporated into surveys designed for other purposes only when ethical and methodological requirements can be met.
- We will give all participants a detailed referral list that includes local counseling centers, community-based resources and services, and emergency shelters that will have been vetted and regularly updated. Study staff will call regularly to confirm that local hotlines provided on study information cards are still connected.
- The PI, Dr. Tan, will meet with Bay Area community-based organizations and nonprofit advocacy groups that specifically serve the population to build rapport to help ensure that these supportive services will be prepared for any increase in help seeking that the study may generate.
- If a participant becomes agitated or threatens violence while at the study offices, Dr. Hoff, a study consultant and Clinical Psychologist, will be called on her emergency phone line to intervene and prescribe follow-up procedures.

11.2 Potential benefits of the proposed research to participants and others

There are no direct benefits to individual participants in the study. Participants may gain knowledge and awareness from the incidental exposure to information about treatment information and referrals. They may derive satisfaction from contributing to research and advancing scientific knowledge for improving the health of their community. Finally, they may enjoy using the app individually and with their partner.

11.3 Adverse Event Reporting

An internal (on-site) adverse event that PI determines to be (1) definitely, probably or possibly related AND (2) serious or unexpected, will be reported to the UCSF IRB within 5 working days of UCSF PI awareness.

Internal, related deaths and life-threatening events will be reported to the UCSF IRB immediately.

An external (off-site) adverse event that the PI determines (1) changes the study risks or benefits, OR (2) necessitates modification to the IRB-approved consent document(s), and/or the IRB-approved application/protocol, will be reported to the UCSF IRB within 10 working days of UCSF PI awareness.

SECTION 12: SURVEY

On page 1 is ACEs. We changed the response format from yes/no to what you see because some of the investigators wanted to try and differentiate early childhood trauma from later trauma.

On page 2 is an experience discrimination instrument. Perhaps this could be adapted to be a "stuff been through" instrument…"Have any of the following happened to either of you since you became a couple?" (excluding the 3rd item about being rejected by a partner). There is also a single item about break-ups that might be useful.

On pages 3-6 are the substance use items they used. The primary sources were NIDA Assist and the AUDIT-C. The "window" was changed to 60 days for the purposes of the MP+ study (since they assessed sexual risk using a 60-day window). I would use the time windows suggested in the original instruments (probably 30 days).

From page 7 onward is the mental health section from the actual survey. That section asked the full CES-D. There is a short form we could replace it with, but I lobbied for the full CES-D in MP+ because past research had shown that the positive and negative affect scores differentially impacted health care uptake. It is followed by the General Anxiety Disorder scale, and then questions about medications. So, the medication questions were "set up" by the fact that they ask about depression symptoms and anxiety symptoms first. In Philadelphia ACE they ask about depression in a single item. I adapted that to create an anxiety item as well using language from the GAD. For the purposes of this study single questions might be sufficient.

SECTION 13: CHANGE HISTORY

Version	Date	Description of Change	Other Documents Affected
1.0	10/1/2019	New Document	--
1.1	8/18/2020	Revised Interview procedures for in-person and remotely Added Protocol for Participants under Emotional Distress (Section 7.8)	
1.2	10/6/2020	Outlined procedures for Aim 2	
1.3	2/17/2021	Added which information is necessary for RPPR in Section 10.3 Added Appendix B on write-out of methods for various procedures	
1.4	4/17/2021	Added information about secondary coding and process of writing memos in Appendix B	
1.5	5/12/2021	Added rationale and procedures for cognitive interviewing in Appendix B	
1.6	6/15/2021	Expanded on cognitive interviewing procedures in Appendix B as well as data analysis, assigning ratings to each item	
1.7	9/9/2021	Expanded on cognitive interviewing procedures in Appendix B, namely the second and third rounds of interviews	
1.8	10/6/2021	Expanded on Phase 1 recruitment methods in Appendix B	
1.9	2/7/2022	Expanded on Phase 2 and 3 methods in Appendix B	
2.0	6/23/2022	Revised study timeline and biosample collection modalities	
2.1	8/15/2022	Amended incentive structure to make it increase over time (i.e., follow a graduated schedule)	
2.2	11/4/2022	Amended Phase 3 eligibility criteria to expand it to DYADS of Black/African American sexual and gender minority folks living with HIV	
2.3	2/27/2023	Amended incentive structure, procedures for Intervention and Control to remove any mention of hair	LetSync Study Activity Handout (changed from v3 → v4 with revised incentive structure)