It Takes Two (T2): A couples-based approach to HIV prevention for transgender women and their partners

NCT04067661

September 12, 2022

Study Application (Version 1.17)

1.0 General Information

***Enter the full title of your study:**

It Takes Two: A couples-based approach to HIV prevention for transgender women and their partners

***Enter the study alias:**

T2
* This field allows you to enter an abbreviated version of the Study Title to quickly identify this study.

2.0 Add departments

2.1 and Specify Research Location:

Is Primary?	Department Name
◉	**UCSF** - *138342* - M_MED-CORE-DPSC
○	**UCSF** - *123012* - M_ObGyn-Bixby-ZSFG

3.0 List the key study personnel: (Note: external and affiliated collaborators who are not in the UCSF directory can be identified later in the Qualifications of Key Study Personnel section at the end of the form)

3.1 *Please add a Principal Investigator for the study:

Johnson, Mallory PhD

Select if applicable

☐ Department Chair ☐ Resident

☐ Fellow

If the Principal Investigator is a Fellow, the name of the Faculty Advisor must be supplied below.

3.2 If applicable, please select the Research Staff personnel

A) Additional Investigators

Gamarel, Kristine E
Co-Principal Investigator
Neilands, Torsten PhD
Other Investigator
Sevelius, Jeanne PhD
Other Investigator

B) Research Support Staff

Johnson, Jack
Research Assistant
Stein, Ellen S
Study Coordinator

3.3 *Please add a Study Contact

Johnson, Mallory PhD
Sevelius, Jeanne PhD
Stein, Ellen S

The Study Contact(s) will receive all important system notifications along with the Principal Investigator. (e.g. The project contact(s) are typically either the Study Coordinator or the Principal Investigator themselves).

3.4 If applicable, please add a Faculty Advisor/Mentor:

3.5 If applicable, please select the Designated Department Approval(s)

Add the name of the individual authorized to approve and sign off on this protocol from your Department (e.g. the Department Chair or Dean).

4.0 Initial Screening Questions

Updated January 2019 - Revised Common Rule (January 2018) Compliant - v92

4.1 * PROJECT SUMMARY: (REQUIRED) Give a brief overview of this project (250 words or less). Tell us what this study is about, who is being studied, and what it aims to achieve. If you have an NIH Abstract, paste it here (Click on the orange question mark to the right for more detailed instructions):

Transgender women (i.e., individuals with a feminine and/or female gender identity who were assigned
male at birth) are disproportionately affected by HIV and transmission risk, which has been attributed, in
part, to primary partnerships.

The overarching goal of the study is to test the efficacy of a promising couples-focused HIV prevention intervention to reduce HIV transmission risk among transgender women and their primary
partners by integrating biomedical and behavioral risk reduction strategies to help couples choose the most
appropriate HIV prevention plan for their relationship.

4.2 * HUD DEVICE: (REQUIRED) Does this application involve a Humanitarian Use Device (HUD):

- (•) No
- ( ) Yes, and it includes a research component
- ( ) Yes, and it involves clinical care ONLY

4.3 * TYPE OF RESEARCH: (REQUIRED) Select the option that best fits your project (Click the orange question mark to the right for definitions and guidance):

- ○ Biomedical research (including medical records review, biospecimen collection and/or use, other healthcare or health outcomes related activities, research database, biospecimen bank, or recruitment registry)
- ○ Social, behavioral, educational, and/or public policy research
- ◉ Hybrid - includes aspects of BOTH types of research (check this option if your research is mainly social/behavioral but also involves specimen collection or blood draws to look at biological measures)

4.4 * SUBJECT CONTACT: (REQUIRED) Does this study involve ANY contact or interactions with participants:

- ◉ Yes (including phone, email or web contact)
- ○ No (limited to medical records review, biological specimen analysis, and/or data analysis)

4.5 * RISK LEVEL: (REQUIRED) What is your estimation of the risk level, including all screening procedures and study activities:

- ◉ Minimal risk
- ○ Greater than minimal risk

4.6 * REVIEW LEVEL: (REQUIRED) Requested review level (Click on the orange question mark to the right for definitions and guidance):

- ○ Full Committee
- ◉ Expedited
- ○ Exempt

4.7 * EXPEDITED REVIEW CATEGORIES: (REQUIRED) If you think this study qualifies for expedited review, select the regulatory categories that the research falls under: (check all that apply)

- ☐ Category 1: A very limited number of studies of approved drugs and devices
- ☑ Category 2: Blood sampling
- ☑ Category 3: Noninvasive specimen collection (e.g. buccal swabs, urine, hair and nail clippings, etc.)
- ☐ Category 4: Noninvasive clinical procedures (e.g. physical sensors such as pulse oximeters, MRI, EKG, EEG, ultrasound, moderate exercise testing, etc.)
- ☐ Category 5: Research involving materials (data, documents, records, or specimens) that were previously collected for either nonresearch or research purposes
- ☑ Category 6: Use of recordings (voice, video, digital or image)
- ☐ Category 7: Low risk behavioral research or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies

* Does the collection of blood samples meet requirements outlined by HHS Office for Human Research Protections for **Expedited Review Research Category 2**: **(REQUIRED)**

- For healthy, nonpregnant adults who weigh at least 110 pounds the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week;
- From other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected, the

amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week

(•) Yes ( ) No

4.9 * DATA/SPECIMEN ANALYSIS ONLY: (REQUIRED) Does this study ONLY involve records review and /or biospecimen analysis (do not check 'Yes' if this is a registry, research or recruitment database, or biospecimen repository):

( ) Yes (•) No

4.10 * CLINICAL TRIAL: (REQUIRED)
Is this a clinical trial:

According to The World Health Organization (WHO) and the International Committee of Medical Journal Editors (ICMJE) a clinical trial is:

- Any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes.

ICMJE requires registration of a clinical trial in a public database (such as ClinicalTrials.gov) prior to enrollment, for eventual publication of results in member biomedical journals.
Guidance: Public Law 110-85 requires that all investigators who perform an *applicable clinical trial* must ensure that the trial is registered on a government web site called **ClinicalTrials.gov**.

The FDA requires registration for 'applicable clinical trials,' defined as follows:

- For any trials of drugs and biologics: controlled clinical investigations, other than Phase 1 investigations, of a product subject to FDA regulation.
- For trials of biomedical devices: controlled trials with health outcomes of devices subject to FDA regulation, other than small feasibility studies, and pediatric post-market surveillance.

For additional information on the **ClinicalTrials.gov** registration process at UCSF and the definition of a clinical trial for purposes of registration, visit the **ClinicalTrials.gov section of the UCSF Clinical Research Resource HUB**.

(•) Yes ( ) No

Clinical Trial Registration - 'NCT' number for this trial:

NCT04067661

4.11 * CLINICAL TRIAL PHASE: (REQUIRED) Check the applicable phase(s):

- [ ] Phase 0
- [ ] Phase 1
- [ ] Phase 1/2
- [ ] Phase 2
- [ ] Phase 2/3
- [ ] Phase 3
- [ ] Phase 4
- [x] Not Applicable

4.12 * INVESTIGATOR-INITIATED: (REQUIRED) Is this an investigator-initiated study:

- (•) Yes ( ) No

The UCSF IRB recommends use of the Virtual Regulatory Binder to manage your study.

4.13 * CANCER: (REQUIRED) Does this study involve cancer (e.g., the study involves patients with cancer or at risk for cancer, including behavioral research, epidemiological research, public policy research, specimen analysis, and chart reviews):

- ( ) Yes (•) No

4.14 * RADIATION EXPOSURE: (REQUIRED) Does your protocol involve any radiation exposure to patients /subjects EITHER from standard care OR for research purposes (e.g., x-rays, CT-scans, DEXA, CT-guided biopsy, radiation therapy, or nuclear medicine including PET, MUGA or bone scans):

- ( ) Yes (•) No

4.15 SCIENTIFIC REVIEW: If this study has undergone scientific or scholarly review, please indicate which entity performed the review (check all that apply):

- [ ] Cancer Center Protocol Review Committee (PRC) (Full approval is required prior to final IRB approval for cancer-related protocols.)
- [ ] CTSI Clinical Research Services (CRS) Advisory Committee
- [ ] CTSI Consultation Services
- [ ] Departmental scientific review
- [ ] Other:

4.16 * STEM CELLS: (REQUIRED) Does this study involve human stem cells (including iPS cells and adult stem cells), gametes or embryos:

- (•) No
- ( ) Yes, and requires IRB and GESCR review
- ( ) Yes, and requires GESCR review, but NOT IRB review

4.17 * FINANCIAL INTERESTS: (REQUIRED) Do you or any other responsible personnel (or the spouse, registered domestic partner and/or dependent children thereof) have financial interests related to this study:

- ( ) Yes (•) No

5.0 Funding

5.1 * FEDERAL FUNDING: (REQUIRED) Is this study currently supported in whole or in part by Federal funding, *even by a subcontract*, OR has it received ANY Federal funding in the past:

(●) Yes ( ) No

5.2 * DoD INVOLVEMENT: Is this project linked in any way to the Department of Defense (DoD): (REQUIRED)

( ) Yes (●) No

5.3 SPONSORS: Identify all sponsors and provide the funding details. If funding comes from a Subcontract, please list only the Prime Sponsor:

External Sponsors:

View Details	Sponsor Name	Sponsor Type	Awardee Institution:	Contract Type:	Project Number	UCSF RAS System Award Number ("A" + 6 digits)
⊟	NIH Natl Institute of Mental Health	01	UCSF	Subcontract	P0527903	

Sponsor Name:	NIH Natl Institute of Mental Health
Sponsor Type:	01
Sponsor Role:	Funding
CFDA Number:	
Grant/Contract Number:	1R01MH115765
Awardee Institution::	UCSF
Is Institution the Primary Grant Holder:	No
if No, then who is the Primary Grantee?	University of Michigan
Contract Type:	Subcontract
Project Number:	P0527903
UCSF RAS System Award Number ("A" + 6 digits):	
Grant Number for Studies Not Funded thru UCSF:	
Grant Title:	A couples-based approach to HIV prevention for transgender women and their partners
PI Name: (If PI is not the same as identified on the study.)	Gamarel, K. (University of Michigan MPI)
Explain Any Significant Discrepancy:	

Other Funding Sources and Unfunded Research - Gift, Program, Departmental or other Internal Funding (check all that apply):

☐ Funded by gift (specify source below)

- [ ] Funded by UCSF or UC-wide program (specify source below)
- [ ] Specific departmental funding (specify source below)
- [ ] Unfunded (miscellaneous departmental funding)
- [ ] Unfunded student project

6.0 Sites, Programs, Resources, and External IRB Review

6.1 UCSF AND AFFILIATED SITES (check all that apply):

- [ ] UCSF Benioff Children's Hospital Oakland (BCHO)
- [x] UCSF China Basin clinics and facilities
- [ ] UCSF Helen Diller Family Comprehensive Cancer Center
- [x] UCSF Langley Porter Psychiatric Institute (LPPI)
- [x] UCSF Medical Center at Mission Bay (Benioff Children's Hospital, the Betty Irene Moore Women's Hospital, Bakar Cancer Hospital, or outpatient clinics)
- [ ] UCSF Mount Zion
- [x] UCSF Parnassus (Moffitt-Long hospital, dental clinics or other outpatient clinics)
- [x] UCSF Other Sites (including Laurel Heights and all the other sites outside the main hospitals)
- [ ] Zuckerberg San Francisco General (ZSFG)
- [ ] SF VA Medical Center (SF VAMC)
- [ ] Fresno - UCSF Fresno OR Community Medical Center (CMC)
- [ ] Gladstone
- [ ] Institute on Aging (IOA)
- [ ] Jewish Home
- [ ] SF Dept of Public Health (DPH)
- [ ] Vitalant (formerly Blood Centers of the Pacific and Blood Systems Research Institute)

6.2 LOCATIONS: At what locations will study visits and activities occur:

We intend to conduct study visits, activities, and procedures at the UCSF Alliance Health Project (AHP) offices located at 1930 Market Street, San Francisco, CA. 94102.

When on-site work is limited as a result of local county health department, California State, or Federal directives, or for participants residing outside of the immediate SF Bay Area, procedures and participant visits will be conducted remotely.

CTSI will oversee an EHR Recruitment Letter service for UCSF Health patients who identify as transgender females.

6.3 OFF-SITE PROCEDURES: Will any study procedures or tests be conducted off-site by non-UCSF personnel:

- ( ) Yes
- (•) No

6.4 RESEARCH PROGRAMS: Check any UCSF research programs this study is associated with:

- [ ] Cancer Center
- [x] Center for AIDS Prevention Sciences (CAPS)
- [ ] Global Health Sciences
- [ ] Immune Tolerance Network (ITN)
- [ ] Neurosciences Clinical Research Unit (NCRU)
- [ ] Osher Center
- [ ] Positive Health Program

6.5 * CTSI CRS SERVICES: (REQUIRED) Will this study be carried out at one of the UCSF Clinical Research

Services (CRS) units or utilize CRS services:

◉ Yes ○ No

The CRS budget request form can be found at: http://accelerate.ucsf.edu/files/crs/BudgetRequest.docx. Follow the instructions on the form to submit.

6.6 * MULTI-CENTER TRIAL: (REQUIRED) Is this a multi-center or multi-site research trial:

By '**multi-center trial**' we mean a study where the protocol is developed by an lead investigator, an industry sponsor, consortium, a disease-group, etc.,and multiple sites across the nation or in different countries participate in the trial. The local sites do not have any control over the design of the protocol.

○ Yes ◉ No

6.8 OTHER SITE TYPES: Check all the other types of sites not affiliated with UCSF with which you are cooperating or collaborating on this project:

Do NOT check any boxes below if this is a multi-center clinical trial, UCSF is just one of the sites, and neither UCSF nor one of its faculty-linked affiliates (SF VAMC, Gladstone, ZSFG) are the coordinating center.

☐ Other UC Campus

☑ Other institution

☐ Other community-based site

☐ Foreign Country

☐ Sovereign Native American nation (e.g. Navajo Nation, Oglala Sioux Tribe, Havasupai, etc.)

6.11 * OUTSIDE RELIANCES: (REQUIRED) Are any of the collaborating sites requesting to rely on UCSF's IRB:

◉ Yes ○ No

* List the sites that are requesting to rely (more details will be requested in the Outside Sites section): **(REQUIRED)**

University of Michigan is requesting to rely on / defer to UCSF IRB.

6.14 * RELYING ON AN EXTERNAL IRB: (REQUIRED) Does this application include a request to rely on an external IRB (a central IRB (other than the NCI CIRB) or an external IRB (other UC campus, commercial, or institutional):

○ Yes ◉ No

7.0 Outside Site Information

7.1 Outside Site Information

If you have more than 10 sites to add, list the outside sites in the Outside Sites List document and upload it in the Other Study Documents section of the Initial Review Submission Packet form. Any sites requesting to rely on UCSF's IRB must be listed below.

Click "Add a new row" to enter information for a site. Click it again to add a second site again to add a third site, a fourth site, etc.

Outside Site Information

Non-UCSF affiliated site information:

Site name:

University of Michigan

Contact name:

Kristi Gamarel

Email:

kgamarel@umich.edu

Phone:

(734) 647-3178

For Federally-funded studies only, corresponding FWA#:

*** The research at this site will be reviewed by:**

- ○ The non-affiliated site's IRB or a private IRB
- ◉ The non-affiliated site is requesting UCSF to be the IRB of record for this study
- ○ The non-affiliated site is not engaged in the human subjects research and has provided a letter of support

If the other site's IRB approval letter is available now, attach it to the application. If the IRB approval letter is not yet available, submit it once you receive it.

Or, if the other site is **not engaged** in human subjects research, attach the letter of support to your application.

Request for UCSF to Serve As the IRB of Record

The non-affiliated site has reviewed UCSF's guidance "When UCSF Can Serve as IRB of Record" and made an initial determination that UCSF's IRB can serve as the IRB of record:

(●) Yes ( ) No

If **not**, do NOT submit your application until after the other site has completed this step.

List the collaborators and describe the scope of work that will be carried out at the non-affiliated site:

Kristi Gamarel, PhD - Multi- Principal Investigator - University of Michigan. Data
analysis of de-identified data only.

A letter from the non-affiliated site deferring IRB approval to the UCSF IRB is attached:

(●) Yes ( ) No

Note: your application cannot be processed without this letter.

Collaborators' training certificates for Human Subjects Training Course are attached:

(●) Yes ( ) No

Note: your application cannot be processed without the training certificates.

Outside Site Information

Non-UCSF affiliated site information:

Site name:

Columbia University, Research Foundation for Mental Hygiene

Contact name:

Jae Sevelius, PhD.

Email:

js6254@columbia.edu

Phone:

(646) 774-6931

For Federally-funded studies only, corresponding FWA#:

FWA00006105

*** The research at this site will be reviewed by:**

- (●) The non-affiliated site's IRB or a private IRB
- ( ) The non-affiliated site is requesting UCSF to be the IRB of record for this study
- ( ) The non-affiliated site is not engaged in the human subjects research and has provided a letter of support

If the other site's IRB approval letter is available now, attach it to the application. If the IRB approval letter is not yet available, submit it once you receive it.

Or, if the other site is **not engaged** in human subjects research, attach the letter of support to your application.

8.0 Research Plan and Procedures

8.1 HYPOTHESIS: Describe the hypothesis or what the study hopes to prove:

We hypothesize that couples in the intervention condition will have lower Composite Risk for HIV (CR-HIV) at 12-month follow-up compared to couples in the control condition.

8.2 AIMS: List the specific aims:

The primary specific aim is to:
1. Evaluate the efficacy of the T2 couples HIV counseling intervention on Composite Risk for HIV (CR-HIV) compared to an enhanced standard of care (SOC) control condition.
The secondary aims are to:
1. Assess the effects of the T2 couples HIV counseling intervention on theory-based mediators (i. e. couples' self-efficacy, communication and joint problem-solving skills, coping with gender-based minority stress and social oppression).
2. Explore partner gender, couple HIV status (seroconcordant negative/seroconcordant positive /serodiscordant) as moderators of the effect of the intervention on CR-HIV.

8.3 DESIGN: Briefly describe the study design (e.g., observational, interventional, randomized, placebo-controlled, blinded, cross-over, cross-sectional, longitudinal, pharmacokinetic, etc.):

Using a two-arm randomized controlled trial (RCT) design, we will examine intervention effects on Composite Risk for HIV (CR-HIV) at 12-month follow-up comparing couples randomized to the intervention versus an enhanced standard of care (SOC). To achieve these aims, we will recruit and randomize 54 couples (108 participants) to test a theory-based couples-focused intervention that addresses within-couple and extra-dyadic sexual risk, structural factors related to risk, routine testing for HIV and other sexual transmitted infections (STI), preexposure prophylaxis (PrEP) uptake and adherence, and antiretroviral therapy (ART) adherence (for couples in which one partner is HIV-positive).

After completing baseline surveys, couples are randomized (stratified by couple serostatus at enrollment) to the intervention or enhanced standard of care using a computerized secure and fraud-resistant procedure employed in our teams prior studies. UCF has used this method in several RCTs; our experience with over 700 participants indicates that it is sucessful in achieving balance across demographic, mediating, and outcome variables.

Couples are followed quarterly over 12 months. Behavioral data and HIV viral load tests for HIV-positive participants are collected and analyzed using state-of-the-science dyadic analyses. If the intervention demonstrates efficacy compared to enhanced standard of care control condition, there will be methodologically rigorous support for implementing this approach within HIV prevention and care settings in order to reduce disparities in HIV transmission and acquisition among some of the highest priority HIV prevention populations in the United States.

8.4 BACKGROUND AND SIGNIFICANCE: Briefly provide the background and significance of this study (e.g. why is this study needed) (space limit: one half page):

If this is a first in humans study, please summarize the safety data from the animal studies. For pediatric drug or device studies, please identify if this is the first study in pediatric populations.

Relationship dynamics influence seeking HIV prevention and care and reducing sexual risk behaviors among partnerships with trans women (TW). There is a robust body of literature documenting the role of well-functioning primary relationships in supporting preventative health behaviors and in buffering partners against stress. Our team's study of 191 TW-male couples in San Francisco found that male partners who reported being highly motivated to strengthen their relationship also had lower odds of engaging in CAS with outside partners. By contrast, male partners who reported more individual appetitive motives (e.g., to have a satisfying and adventurous sex life) had greater odds of condomless anal sex (CAS) with outside partners. Additional evidence from our team illustrates that greater relationship commitment buffers TW from the negative effects of discrimination on health outcomes. However, our qualitative work with TW-couples also revealed complex interactions between relationship dynamics and HIV prevention behaviors, such that many TW fear having explicit conversations about HIV and prevention planning with their partners, due in part to anxiety about power differentials and the risk that their male partner will reject them. Thus, couples-based HIV prevention is a promising and urgently needed HIV intervention modality for couples. Despite acceptability of couples-based prevention interventions for heterosexual and MSM partnerships, to our knowledge, only our pilot Couples-focused HIV Intervention Program (CHIP) has been developed to meet the unique prevention needs of TW couples (R34MH093232). Those results demonstrated that the CHIP intervention was feasible and promising in reducing HIV risk (i.e., sexual risk behavior) among TW couples. However, assessing the efficacy of this intervention is needed. The original design of the CHIP protocol predated the published results showing the protective effects of PrEP and viral suppression against HIV transmission, and thus CHIP lacked content related to biomedical HIV prevention strategies for TW couples. Although the CDC recently supported CHIP as the first "good" evidence-based intervention for reducing HIV risk among transgender people, the intervention needs to incorporate biomedical prevention strategies with longer follow-ups in order to be considered a "best" evidence-based intervention and to be relevant to current priorities in biobehavioral HIV prevention.

8.5 PRELIMINARY STUDIES: Briefly summarize any preliminary studies relevant to your proposed research (space limit: one half page):

This RCT builds upon our previous qualitative study at UCSF: Study #18-25144. The previous qualitative study informed decisions about target populations, recruitment, retention, and intervention.

Development and pilot test of the Couples HIV Intervention Program (CHIP) for TW-male couples
Our team recently completed a pilot RCT of CHIP, an HIV prevention program for TW couples. CHIP was adapted from Project Connect, a CDC-endorsed "high impact" HIV intervention for couples that focuses on relationship quality/functioning, communication, and shared commitment. The design of CHIP involved iterative rounds of quantitative and qualitative research with TW-male couples to identify intervention targets and gender-sensitive delivery processes for HIV prevention for racially/ethnically diverse TW-male partners across different age groups. Over a 13-month outreach and recruitment period, the study team recruited 56 TW-male partners (n=112 participants) and examined the acceptability, feasibility, and 3-month outcomes on sexual risk behavior (45.5 % Black, 14.3 % Hispanic, 24.1 Other, and 16.1 % White). Couples randomized to the control arm received basic HIV information. Couples in the intervention arm (CHIP) received three sessions designed to improve relationship and couples' communication skills to promote HIV risk reduction. They received two couples-focused sessions in which the couple met with a counselor to promote positive relationship dynamics, communication skills, and to identify HIV risk reduction goals; each partner also had 1 individual session with the counselor to describe their personal HIV prevention concerns in the context of their relationship and with outside partners. At 3-month followup, participants in the intervention arm had lower odds of CAS with primary partners (OR=0.5, 95%CI: 0.3-1.0), reduced odds of engaging in sex with any casual partner (OR=0.3, 95%CI: 0.1-1.0), and reductions in overall number of casual partners (B=-1.45, SE=0.4) compared with the control arm. In exit interviews, TW and male intervention participants commented favorably on focusing on strengthening relationships, communication around HIV, and coping with gender minority stressors, and described interest in further couples-focused programs with more than three sessions. These results provide support for the feasibility and acceptability of CHIP, and demonstrate the team's ability to recruit and implement a couples-focused intervention for TW and their primary partners.

8.6 * TREATMENT PROTOCOL: Is this a treatment study, i.e. does this study intend to provide treatment to individuals with a medical or psychological condition: (REQUIRED)

- ○ Yes
- ◉ No

8.7 * BILLABLE PROCEDURES: Does this study involve any procedures, lab tests or imaging studies that have a CPT code and could be billable to patients, their insurance, Medi-Cal, Medicare, or any other entity (answer 'Yes' even if the study is going to pay for all the procedures): (REQUIRED)

- ○ Yes
- ◉ No

If you are not sure if your study involves billable procedures, send an email to the UCSF Office of Clinical Research (OCR) for help answering this question.

8.8 * COMMON RESEARCH ACTIVITIES: Types of research activities that will be carried out. Check all that apply and describe in more detail in the 'Procedures / Methods' section: (REQUIRED)

- ☑ Interviews, questionnaires, surveys
- ☐ Educational or cognitive tests
- ☐ Focus groups
- ☐ Social media-based research activities
- ☐ Observation
- ☐ Fitness tests or other exertion activities
- ☐ Use of mobile health apps or other apps
- ☐ Collection of data from wearable tech such as Fitbit, Apple Watch, Garmin, motion actigraphs, etc.)
- ☐ Non-invasive imaging or testing (MRI, EEG, pulse oximetry, etc.)
- ☐ Imaging procedures or treatment procedures that involve radiation (x-rays, CT scans, CT-guided biopsies, DEXA scans, MUGA or PET scan)
- ☐ Administration of contrast agent
- ☑ Randomization to one intervention versus another
- ☐ Use of placebo
- ☐ Biopsy conducted solely for research purposes
- ☐ Sham surgical procedure
- ☐ None of the above

8.9 * PROCEDURES / METHODS: (REQUIRED)

Describe the research methods and study activities taking place at each site (e.g. what will participants be asked to do and what will members of the study team do?). If there will be multiple participant groups or study sites, explain what will happen with each group or study sites.

If some of the activities would occur even if the person were not in the study, as in the case of treatment or tests performed for diagnostic purposes, **clearly differentiate between those activities that will be done solely for research purposes and those that are happening as part of routine care.**

Please call our office at 415-476-1814 and ask to speak to someone on the Expedited Review team if you need help differentiating between what parts are research and what parts aren't.

Recruitment: Participants are recruited by a team that is experienced in conducting transgender research, using a multi-pronged approach including recontacting potentially eligible participants from prior studies who gave permission for future contact; street, agency, and event-based outreach; posting and distribution of Recruitment Flyers; internet-based advertising on Facebook and Grynder.

Additionally, w*e are collaborating with the CTSI Consultation Service to provide cohort identification and direct mail for recruitment. The Dear Patient letter (attached) will be sent to UCSF patients identified from the APeX record systems via a data extraction by Academic Research Systems (ARS) of patients with a diagnosis of [XXX]. These patients [are/are not] known to or under the care of the researcher team. The CTSI Consultation Service will coordinate the mailing on behalf of the study. Interested subjects will contact the study staff as described in the letter. The data extract will be delivered to the CTSI Consultation Service's MyResearch account in order to facilitate the direct mail activities while ensuring privacy and confidentiality of the patients identified. Protected data elements included in the data pull and delivered to the honest broker may include MRN, name, mailing address, and diagnosis or encounter date. Additional non-PHI data elements may also be collected to facilitate the mailing.*

Pre-Screening: Potential participants are pre-screened by Research Assistants (RA) by telephone or in-person at the Alliance Health Project (AHP) site. RAs describe basic study eligibility criteria (>18 years of age, gender, in a relationship, English speaking). For those who provisionally qualify, Partner 1 is pre-screened using a Screening Form in REDCap that includes questions on recent HIV risk, and the name and contact information of the partner. Study RA contacts Partner 2 within one week to pre-screen using a REDCap Screening Form. If the couple is provisionally eligibile AND both partners wish to enroll, they are scheduled for an Eligibility Visit at AHP to verifiy HIV status. If HIV-positive, they are asked to bring documentation of their status.

Eligibility Visit:
1. Visits occur at the AHP site. Both partners attend the Eligibility Visit together at AHP, and RAs conduct Oral Informed Consent with each partner in separate rooms.
2. RA completes an Eligibility Visit Form in REDCap for each partner, and confidentially verifies HIV status by:
   a. Review recent (last 30 days) HIV Letter of Diagnosis, HIV medication bottles, or medication prescription;
   b. Confirm prior participation in the Healthy Divas Study for HIV positive trans women;
   c. Conduct basic HIV pre-test counseling, OraQuick point-of-care HIV antibody test with saliva from participants' mouth, and disclose result along with post-test counseling*.
3. Enter HIV status of the partners in REDCap, which is programmed to inform the RA if the couple may enroll in the study based on their HIV status and responses to eligibility questions. If a potential participant indicates that study participation may pose safety risks to them, a 'flag' is generated in REDCap, and the RAs tell the couple that they are not eligible for the study at this time, but may rescreen in 6 months either together or with a new partner should they break up.
4. Study enrollment requires the participation of both partners, as a couple. If both agree, schedule Enrollment Visit at AHP or remotely. The Enrollment visit can immediately follow the eligibility Visit.
5. RA provides each partner with a visit incentive, Resource List, condoms, and lubricant.

* If a potential participant has a **new** positive HIV-antibody test result at the Eligibility Visit, the RA provides supportive counseling and provides a Referral List to clinics where HIV confirmatory testing can be obtained. They offer to help set up that appointment and/or accompany them. Care is taken to ensure there is no disclosure to the other partner and the couple is told that they are not eligible for the study at this time, but may rescreen in 6 months either together, or with a new partner should they break up.

Enrollment Visit:
1. Visits occur at the AHP site or remotely. RAs obtain signed Informed Consent from both partners.
2. RAs obtain signed Release of Information Forms to contact HIV medical provider for positive participants, should they be needed for future lab results.
3. RAs collect contact locator information from each partner.
4. For HIV positive participants, a trained phlebotomist draws 20 ml venous blood for viral load testing or the participant is asked to have blood drawn at a Quest Laboratory Service Center.
5. For HIV negative participants who have taken HIV pre-exposure prophyaxis (PrEP) medication in the last 3 months, dried blood spot (DBS) fingerstick procedures are conducted by the phlebotomist or a hair sample is collected for remotely conducted visits.

6. Each partner completes an audio computer assisted self-interviewing (ACASI) survey in REDCap on a tablet, or for remote visits, the survey is interviewer-administered.
7. REDCap provides the RAs with the randomization arm for the couple, who are informed of the assignment. Couples are randomized (stratified by couple serostatus at enrollment) to either the study intervention* or Standard of Care (SOC) using a computerized, secure, and fraud-resistant procedure. UCSF has used this method in several RCTs and our experience with over 700 participants indicates that it is successful in acheiving balance across demographic, mediating, and outcome variables.
8. Couples assigned to the SOC controlarm watch a ~13 minute video set that reviews HIV Prevention; PrEP & PEP; Condom Use; and U equals U concepts.
9. RAs schedule their 3, 6, 9, and 12-month quarterly follow-up visits and provide appointment information, visit incentives, a Resource List, condoms, and lubricant.
10. Couples who are assigned to the study intervention arm* are introduced to the Health Counselor, who leads Intervention Session 1 (20 minutes). When completed, the Health Counselor schedules Intervention Sessions 2 /3 /4 and provides appointment cards, visit incentives, a Resource List, condoms, and lubricant.

The Couples Study Intervention* includes four weekly counseling sessions with both members of the dyad. Sessions last 20-45 minutes, and focus on providing information about HIV risk reduction strategies, communication and joint problem solving in the relationship, identifying gender minority stressors and social oppression, supporting each other's health, and the development of an HIV prevention plan. Couples learn different HIV prevention strategies, discuss their unique HIV prevention needs and how relationship dynamics impact their risk. Sessions are designed to help couples identify how gender minority stressors (e.g., discrimination) and social-structural oppression (e.g., poverty, unemployment) impact relationship functioning and interactions with healthcare settings to work towards empowering couples to communicate about these stressors. Through counseling facilitation, couples identify stressors specific and structural factors that are most relevant to their relationship dynamics. Partners learn and practice communication and conflict resolution skills, and practice problem-solving as a couple. The last session helps couples problem-solve barriers to effective communication, use those skills to develop an HIV prevention plan that meets both partners' needs, and identify existing and potential sources of support. Importantly, The intervention program focuses on the future: partners will not be asked to reveal recent risk behaviors/exposures to each other. Instead the focus is on the couple building a prevention plan that reflects their relationship goals, risk behaviors, and serostatus. Foundational to the intervention is helping couples transform their motivations to protect their relationship and their partner, while building couples' self-efficacy, communication, joint problem-solving skills, and effective coping with gender minority stressors and social-structural oppression so that couples can develop and adhere to an HIV prevention plan.

Intervention Session 1 (20 minutes) called '*Glad You Came*'. In this first session, the couples receive an overview of the intervention, work with the facilitator to develop session boundaries, identify relationship strengths, set one relationship goal and amplify a positive moment in the relationship.
Intervention Session 2 (45 minutes) is called '*In the Heat of the Moment*'. In this session, couples discuss their communication styles and where differences come up, learn and practice communication techniques, develop a plan for taking time outs, set one relationship goal and amplify a positive moment in the relationship.
Intervention Session 3 (45 minutes) is called '*Let's Talk About (Safer) Sex*'. In this session, couples learn about sexual health and prevention strategies, identify their current strategies, learn about relationship agreements, set one relationship goal and amplify a positive moment in the relationship.
Intervention Session 4 (45 minutes) is called '*It Takes Two*'. In this final session, couples review the sexual health and safer sex goals; identify ways to support each other in these strategies;
and plan for the future. The counselor also provides couples with linkage to services as needed.

All intervention sessions are audio-recorded for Quality Assurance and trainiing purposes, unless participants wish to opt out, which they may do during the informed consent process.

Quarterly Follow-up visits: Couples complete quarterly follow-up visits at 3-, 6-, 9-, and 12-months post-enrollment. The quarterly follow-up survey largely repeats questions from the baseline survey. Static information is not repeated, intimate partner violence (IPV) is assessed only at baseline, the 3-month assessment include measures of satisfaction with the intervention (for those randomized to it). When a relationship dissolution is reported at a follow-up visit, the survey will assses if the dissolution was linked to the intervention or to other factors.

1. RAs update contact information for each partner.
2. For HIV positive participants, viral load testing is conducted.
3. Each partner completes an audio computer assisted self-interviewing (ACASI) or interviewer-administered survey.
4. RA provides each partner with a visit incentive, Resource List, condoms, lubricant, and reminds the of the next visit date.

Retention Procedures: In our prior trials we developed procedures to maintain at minimum 80-90% follow-up rates. A computerized scheduling system tracks due dates and completion status of follow-ups. Calls are made to participants who have not been scheduled or missed an appointment. The RA will call participants 1 week, and 1 day before a follow-up is due to confirm the appointment. Couples come to visits together if break up has not occurred, but complete all assessment activities separately. Couples are followed individually in case of relationship break-ups.

SARS-CoV-2 Safety Considerations:

1. Study visits will take place at the Alliance Health Project (AHP) Offices. AHP is a division of the Department of Psychiatry and Behavioral Sciences with a Services Center located at 1930 Market Street. At AHP, the following practices are in place to prevent transmission of COVID-19 for staff, clients, and research participants in accordance with guidance from UCSF and the San Francisco Department of Public Health (SFDPH):

- On-site staffing is limited to a minimum number of staff necessary to provide essential services, with no more than 15 staff on-site at the same time and most staff reporting on-site one day per week. An On-Site Supervisor is present for all shifts. All staff have completed the mandatory COVID-19 and Working Onsite at UCSF training. Visits are provided by appointment with a limited number of staggered slots to facilitate a maximum of six clients in the building at the same time and a maximum of 24 clients in the building per day.
- All staff are required to complete the UCSF Daily Health Screen before entering AHP. The On-Site Supervisor and Project Director will monitor compliance with this requirement. The doors to AHP remain locked at all times, and clients and other visitors (i.e., delivery personnel or other service vendors) to the building are asked the same health screening questions by staff through the closed door or via intercom system before entering. These questions, along with other entry instructions, are posted on the front doors.
- Building signage provided by UCSF Facilities Services is deployed throughout the building to inform and remind staff, clients, and other visitors of COVID prevention measures. This includes signage at building entrances about health screening and masking requirements, handwashing reminders in restrooms and other sinks, instructions to use a paper towel to open refrigeration and microwave doors, and signs indicating the maximum number of occupants allowed in each room. Floor markers have also been placed outside the main entrance and in the lobby to indicate where clients should stand to maintain physical distancing.
- All staff, clients, study participants and other visitors are expected to maintain a physical distance of at least six feet from other people at all times while on-site. Occupancy in all rooms has been limited to allow for at least 60 square feet per person. In the lobby, other common areas, and spaces where clients are seen for services, furniture has been removed and rearranged to maintain physical distance. In addition, clear plastic barriers have been added.
- All staff working at AHP are required to wash hands thoroughly with soap and water for 20 seconds or longer upon entering, and frequently while on-site. Reminder signage provided by UCSF Facilities is posted in all restrooms and at other sinks. Hand sanitizer is available in the lobby and other common spaces.
- All staff, clients, study participants and other visitors to the building are required to wear surgical masks provided to them. Staff are required to wear a personal face covering upon entering and once inside to wash their hands, then put on surgical face masks provided to them. Staff are required to wear these surgical face masks at all times while on-site and may be reused as long as they remain clean and dry. Phlebotomy staff must wear N95 masks, gloves, and face shields when collecting blood or handling other biohazardous materials in accordance with the UCSF Supplemental Laboratory Safety Procedures to Reduce COVID-19 Transmission and the SFDPH Preferred and Alternative PPE Use by Behavioral Health Clinical Scenario.
- AHP follows guidelines for cleaning shared work areas in the UCSF Protocol for Working Onsite. Using disinfecting wipes or other EPA-approved disinfectants, staff clean frequently touched surfaces in the lobby, other common areas, and spaces accessed by clients. Caddies containing cleaning supplies and instructions are provided in each area that requires daily disinfection. Rooms in which clients are seen for services are left vacant for at least 30 minutes after cleaning and before they can be used again for another client

appointment. A janitorial service provides additional daily cleaning of kitchen, lab, and restrooms.
- AHP continuously assesses and revises COVID prevention policies and procedures based on direction from UCSF. The Medical Director and Operations Manager shares responsibility for reviewing new guidance, revising workplans accordingly, and notifies staff, clients, and other visitors as well as other UCSF entities (e.g., Emergency Operations Center, Environmental Health & Safety, Facilities) as needed.

2. In the event that in-person contact due to the SARS CoV-2 pandemic is restricted by UCSF, SFDPH, or any other entity, the following modifications will be made to conduct visits remotely:

Remote Pre-Screening: Procedures will take place exclusively by telephone or using an approved teleconference platform (Zoom, Facebook Messenger video chat, Apple FaceTime, Google G Suite Hangouts video or Skype for business).

Remote Eligibility Visit: RAs send the verbal ICF to the partners by email, surface mail, or DocuSign and schedule a time to review the ICF with each. Using their copy, each partner will follow along during the informed consent discussion which will occur by phone or on an approved videoconferencing platform (Zoom, Facebook Messenger video chat, Apple FaceTime, Google G Suite Hangouts video or Skype for business). RAs verify HIV status of each partner to determine couple eligibility by:

a. Participant can text a photo of a recent (last 30 days) HIV Letter of Diagnosis, HIV medication bottle, or medication prescription if HIV-positive;

b. Participant may text a photo of a recent (last 30 days) PrEP medication bottle or prescription if HIV-negative and on PrEP;

c. HIV-positive status can be verified for formerly participants of the Healthy Divas study for HIV-positive trans women;

d. Participants self-administer an OraQuick HIV antibody test that is mailed to them with instructions, and text back a photo of the test result (**See T2 Participant OraQuick Instructions)**;

e. Participants self-administer an OraQuick HIV antibody test that is mailed to them while a trained HIV Pre/Post-test counselor provides step-by-step guidance by phone or using an approved video-conference platform.

f. RA enters HIV status of partners into REDCap, which infroms the RA if the couple can enroll based on their HIV status and responses to eligibility questions. Study enrollment requires participation of each partner, as a couple. If both agree, an Enrollment Visit is scheduled. Each partner is emailed a Resource List. Visit incentives are provided in the form of an Amazon gift code emailed to participant, cash mailed to a secure address with the understanding that if lost by USPO it cannot be replaced, or sent via CashAp.

Remote Enrollment Visit:
1. Each partner is sent the study ICF and a Release of Information for their care provider if HIV-positive, via email, surface mail, or DocuSign. After reviewing the ICF and answering questions, RAs help participant to sign and return the ICF and ROI. If P1 and/or P2 are unable to use DocuSign, two paper copies of the ICF (and appropriate ROI form) are mailed along with a stamped, self-addressed envelope. When received, RA sets up a videoconference or phone call to review ICF (and ROI) and answer questions. Participants sign one copy to return in the stamped-self-addressed envelope and retain the second copy.

2. RAs collect Contact Locator Information from each partner on the phone or via an approved videoconference platform (Zoom, Facebook Messenger video chat, Apple FaceTime, Google G Suite Hangouts video or Skype for business).

3. RAs complete REDCap Enrollment Visit Forms and conduct Baseline Survey separately with P1 & P2 by phone, zoom, or on an approved video-conferencing platform.

4. RAs determine the correct labs to collect from P1 and P2.

- If participant is **HIV-negative and not taking PrEP**, no labs are required**.**
- If participant is **HIV-positive**, the participant is asked to go to a **QUEST Patient Service Center** to have their blood drawn for HIV viral load test processing. See **Attachment T2 Participant Instructions for Quest Blood Collection**.
- If the participant cannot or will not agree to any of these methods, they may send us a recent (last 30 days) HIV viral load lab result OR using a ROI, we will request an HIV viral load result from within the last 30 days from the medical provider.

5. REDCap provides the RAs with the couples' randomization arm and the RAs inform them of the assignment.

6. Couples assigned to the control condition are emailed the HIV-risk reduction videoset to watch, and RAs schedule the 3, 6, 9, and 12-month follow-up visits for the couple.
7. Couples assigned to the intervention arm are contacted by a Health Counselor, who schedules and conducts the four weekly intervention sessions on an approved videoconference platform, ensuring the couple has adequate privacy.
8. Each partner is emailed a Resource List. Visit incentives are provided in the form of an Amazon gift code emailed to participant, cash mailed to a secure address with the understanding that if lost by USPO it cannot be replaced, or sent via CashAp.

Remote Quarterly Follow-up visits

1. RAs collect Contact Locator Information from each partner on the phone or via an approved videoconference platform (Zoom, Facebook Messenger video chat, Apple FaceTime, Google G Suite Hangouts video or Skype for business).
2. Follow-up surveys are interviewer-administered on the phone or an approved teleconference platform.
3. RAs determine the correct labs to collect from P1 and P2.

- If participant is **HIV-negative and not taking PrEP**, no labs are required**.**
- If participant is **HIV-positive**, the participant is asked to go to a **QUEST Patient Service Center** to have their blood drawn for HIV viral load test processing. See **Attachment T2 Participant Instructions for Quest Blood Collection**.
- If the participant cannot or will not agree to any of these methods, they may send us a recent (last 30 days) HIV viral load lab result OR using a ROI, we will request an HIV viral load result from within the last 30 days from the medical provider.

4. Each partner is emailed a Resource List. Visit incentives are provided in the form of an Amazon gift code emailed to participant, cash mailed to a secure address with the understanding that if lost by USPO it cannot be replaced, or sent via CashAp.

8.11 INSTRUMENTS: List all questionnaires, surveys, interview, or focus group guides that will be used for this study:

If the instruments are not complete or not available because they will be developed as part of this study, describe the basic content or include an outline and submit the final versions to the IRB with a modification for approval prior to use.

Assessments focus on: (1) predisposing factors related to our mechanisms and the CR-HIV outcome; (3) measures of feasibility/acceptability; (4) primary and secondary outcomes; (5) theory-based mechanisms of action.
1. Predisposing Factors. Stigma, oppression, and relationship functioning are extra-individual predisposing factors which may influence our hypothesized mechanisms of change and CR-HIV. Participants will complete measures of relationship functioning, which include the Dyadic Adjustment scale, Commitment scale, and the Power and Attitudes in Relationships scale. We will assess everyday experiences of transgender discrimination, including discrimination experienced by male partners due to being in a relationship with a TW, as well as our validated measure of relationship stigma. We will also assess upstream structural factors that may be associated with CR-HIV (e.g., poverty, employment status).
2. Mechanism of Change. Participants will complete the Couples Efficacy to Reduce HIV Threat

scale which assesses each partner's confidence in their ability to engage in joint effort, communication, and planning and decision making together to reduce HIV. Participants will complete the Communication Patterns Questionnaire, as well as an indicator of Joint problem-solving skills, which will be assessed with the adherence problem solving / readiness scale. We will use the Dyadic Coping Inventory which assesses the extent to which couples work together, engage in mutual decision making, and engage in open communication to alleviate a stressor (e. g., minority stress and social oppression).
3. Feasibility and Acceptability of Intervention. In regards to acceptability, participants will complete the Client Satisfaction Survey at their 3-month assessment, which is an 8-item measure assessing satisfaction with the intervention. Additionally, we will track session attendance.
4. CR-HIV (primary outcome) is a couple-level binary indicator of any HIV risk (e.g., yes=1 vs. no=0), which is an algorithm based on whether one or both partners report condomless anal or vaginal sex with a HIV serodiscordant or status-unknown primary or other partner in the past 3 months. Couples are coded as 0 if neither partner reports condomless anal or vaginal sex. If one or both partners in the dyad report condomless sex with a serodiscordant or status-unknown primary or other partner, then the couple is coded as 1 if (i) the HIV-negative participant is not adherent to PrEP and/or (ii) the HIV-positive participant is not virally suppressed. Sexual risk behavior will be measured using the assessment that we have used in our previous studies to explore the number of occasions of different sexual acts (vaginal, anal; receptive, insertive) with three different types of partners (primary partner, casual partner, paying partner), use of condoms during the past 3 months, and knowledge about partners' HIV status. Assessments ascertain sexual behaviors with non-trans male, non-trans female, and transgender partners, and will be asked at each follow-up. At-risk sex will be defined as any vaginal or anal intercourse without condoms that occurs with a person of known positive or unknown serostatus during the follow-up period. Of the participants who report condomless sex with a serodiscordant or unknown serostatus partner, we will attempt to assess PrEP use using dried blood spot (DBS) procedures for biological measurement of adherence from tenofovir diphosphate concentrations in blood plasma. We will use dosing categories for quantification similar to those used in past drug-level studies of PrEP adherence, allowing us to estimate the number of tablets participant are taking per week (e.g., 700-1249 fmol for 4-6x per week and > 1250 for daily dosing). HIV-positive participants will have their blood drawn at each follow-up visit to determine viral suppression. Viral suppression is indicated by an undetectable HIV-1 level on the COBAS® AmpliPrep/COBAS® TaqMan® HIV test kit (Roche Molecular Systems, Inc.), which has a threshold for undetectability = < 20 copies/mL and is conducted at each follow-up assessment visit. Our secondary outcomes include self-report HIV and STI testing over the 12 months of follow-up.
5. Theory-based mechanisms of action. Covariates will include sociodemographic variables such as age, education and income level, employment, race/ethnicity, living situation, which have been previously found to be structural drivers of HIV risk. While the intervention does not target mental health or substance use, we will assess depressive symptoms using the Center for Epidemiologic Studies Depression Scale (CES-D), and anxiety symptoms will be measured with the Beck Anxiety Inventory. We will also assess alcohol use and other drugs with the AUDIT as well as the Alcohol, Smoking, and Substance Involvement Test (ASSIST) given their associations with HIV outcomes. We will also assess history/current health care engagement (i.e., HIV prevention, primary care, mental health).

Attach any unpublished instruments in the 'Other Study Documents' section of the Initial Review Submission Packet form after completing the study application. Published instruments should NOT be attached.

8.12 * BIOSPECIMEN COLLECTION: Are you drawing any blood or collecting other biosamples (e.g. tissue, buccal swabs, urine, saliva, hair, etc.) for analysis under this protocol and/or storage for future research: (REQUIRED)

(•) Yes ( ) No

* Could this study generate genetic data that may be broadly shared (e.g., submitted to NIH in compliance with **Genomic Data Sharing (GDS)/Genome-Wide Association Studies (GWAS)** requirements): **(REQUIRED)**

( ) Yes (•) No

Please check the Resource Sharing Plan section of your funding notice. You will not be able to share the data as required by your

funding agency if the consent form doesn't include the required language.

8.13 STATISTICAL METHODS: Briefly summarize the methods and types of analyses that will be performed:

Preliminary analyses and missing data. Frequency tables for all variables and measures of central tendency and variability for continuous variables will characterize the sample and will be stratified by study arm to check for imbalances. If the intervention and control groups differ significantly at baseline on one or more covariates, we will use methods based on the Rubin causal model (e.g., propensity scores, double-robust estimation) to obtain the desired marginal effect estimates under the counterfactual assumption of balanced groups.81-85 We will address incomplete data with multiple imputation (MI)86 because MI makes the relatively mild assumption that incomplete data arise from a conditionally missing-at-random (MAR) mechanism. 87
Auxiliary variables will be included to help meet the MAR assumption;88, 89 sensitivity analyses will be conducted with weighted MI to assess the MAR assumption's robustness90 using SAS91 and Mplus.
Primary analyses to address Primary Specific Aim 1. If the CHIP intervention is successful, a lower proportion of intervention participants will engage in CR-HIV relative to control group participants following intervention exposure. Therefore, to address Specific Aim 1 we hypothesize that the odds of CR-HIV will be lower for CHIP participants than for control participants (Hypothesis 1). Our primary interest is to estimate the marginal or population-average effects of CHIP exposure on CR-HIV rather than the effect for a hypothetical average subject or couple.92 Moreover, within-subject and within-couple CR-HIV correlations are nuisance parameters rather than quantities of interest to be modeled explicitly. Finally, the statistical literature indicates the superior performance of generalized estimating equations (GEE) relative to generalized linear mixed models (GLMMs) for the analysis of dyadic data with categorical outcomes such as CR-HIV. 93 Accordingly, we will use GEE for the proposed primary analysis to test Hypothesis 1 by a planned time-averaged comparison of post-baseline measurements of CR-HIV from the intervention group with the post-baseline measures of CRHIV from the control group. Alpha (α) will be set at .05 for this planned comparison. Any additional post-hoc comparisons (e.g., paired comparisons of groups at each time point) will maintain nominal alpha of .05 through the use of simulation-based stepdown multiple comparison methods.94 The alternating logistic regression (ALR) approach implemented in SAS PROC GENMOD will be used to address the 3-level clustering of observations within participants and participants within dyads. Though GEE estimates are consistent even if the correlation structure is misspecified, GEE's statistical efficiency improves as the working correlation structure more closely approximates the actual correlation structure;95 therefore, various correlation structures suitable for the study's design will be considered (e.g., exchangeable; nested-1).96 The QIC statistic will be used to select the final correlation structure. 97 Couple serostatus will be included as a covariate as required by the stratified randomized design.98 Additional relevant covariates such as relationship length, as well as intersectionality criteria and structural drivers (e.g., age, race/ethnicity, poverty, unemployment) will be included if they improve QIC. We will use Robust Huber-White "sandwich" standard errors to obtain correct inferences even if the chosen correlation structure remains slightly misspecified.
Secondary analyses to address Secondary Specific Aims 1 and 2: Exploring mediation and moderation. To explore the effect of CHIP on hypothesized mechanisms of change, secondary analyses will explore whether participants assigned to CHIP report higher mean scores on theory-based constructs such as couple selfefficacy, communication and joint problem-solving strategies, and dyadic coping with gender minority stressors following the intervention. These analyses will also investigate whether these constructs at 3, 6 and 9 months mediate the relationship between intervention group assignment and CR-HIV at 6, 9 and 12 months, respectively, and whether couple HIV-serostatus and (in line with NIH guidelines to consider sex as a biological variable) whether gender moderate these associations. Mediation and moderation will be assessed using the causal inference-based approach of Valeri and VanderWeele, which yields optimal estimates of indirect effects in the presence of moderators and non-continuous outcomes and mediators .99 Mplus will be used to fit causal mediation-moderation models because it adjusts standard errors for clustering of participants within couples.
Secondary analyses to address moderation and subgroup differences in intersectional variables. As noted above in C.1 Preliminary Studies, the intervention is designed to be equally efficacious across intersectional subgroups of participants, so we do not anticipate differential intervention effects by subgroup. However, we will conduct additional exploratory sensitivity analyses to evaluate the moderating effects of age, HIV status, race/ethnicity, poverty, and unemployment to explore whether these intersectionality criteria and structural drivers enhance or dampen the intervention's effects on CR-HIV and the theory-based mediators listed above. Where cell sizes permit, subgroup analyses will be performed, stratifying on race/ethnicity, age, and poverty. While our study is not formally powered to examine subgroup differences and it would be

infeasible to recruit sufficiently large numbers of participants in each intersectional category to formally test for differences, these
analyses may illuminate trends in group differences, which can inform future studies of specific subpopulations if trends are detected. Moderation and subgroup analyses will be performed using the same GEE and causal inference approaches described above to test for moderation and moderated mediation, respectively.
Secondary exploratory dyadic analyses. Intact dyads enable analyses that explore how predisposing factors, such as relationship functioning and gender minority stressors affect behavior change in partnerships. We will extend the analyses described above to include actor and partner effects for covariates and mediators. Actor effects describe the influence that one's standing on independent or mediating variables (e.g., the trans woman's communication) has on one's own dependent variables (e.g., self CR-HIV) whereas partner effects describe the influence that one's standing on independent variables has on the dependent variables of one's partner (e. g., the trans woman's effect on her partner's CR-HIV). This technique illuminates the effects that partners in intimate relationships can have on both their own and their partner's behaviors. Actor and partner effects can be evaluated in models with either continuous101 (e.g., problem solving) or categorical dependent variables (e.g., CR-HIV).100 A closely related approach uses sums and differences of continuous covariates and mediators to quantify within-couple and between-couple effects. For continuous dependent variables, within-couple hypotheses will be tested with a GEE model in which couple-level difference scores on the outcome variable (e.g., communication) will be regressed onto both the couple-level difference and sum scores for the predictor variable (e.g., self-efficacy).102 Computing sums and differences for categorical outcomes is not feasible, but it is still possible to investigate the effects of sums and differences of individuals'
continuous covariates and mediators on individual-level categorical responses (e.g., CR-HIV) to tease apart the separate influences of between-couple and within-couple effects of mediators on individuals' categorical outcomes.

8.14 REFERENCES: List only the 5-10 most relevant references (a separate bibliography can be attached for reference purposes if this study involves novel approaches, agents, or an emerging technology that the IRB may not be familiar with):

1. Baral SD, Poteat T, Stromdahl S, et al. Worldwide burden of HIV in transgender women: a systematic
review and meta-analysis. Lancet Infect Dis. 2013;13(3):214-222.
2. Operario D, Nemoto T, Iwamoto M, et al. Unprotected sexual behavior and HIV risk in the context of
primary partnerships for transgender women. AIDS Behav. 2011;15(3):674-682. PMC3049202
3. El-Bassel N, Gilbert L, Witte SS, et al. Couples-based HIV prevention in the United States: Advantages,
gaps, and future directions. J Acquir Immune Def Syndr. 2011;55:S98-101.
4. Sevelius JM, Keatley J, Calma N, et al. 'I am not a man': Trans-specific barriers and facilitators to PrEP
acceptability among transgender women. Glob Public Health. 2016; 11(7-8): 1060-75 26963756
5. Operario D, Nemoto T, Iwamoto M, et al. Risk for HIV and unprotected sexual behavior in male primary
partners of transgender women. Arch Sex Behav. 2011;40(6):1255-1261. PMID: 21604064
6. Gamarel KE, Reisner SL, Laurenceau J-P, et al. Gender minority stress, mental health, and relationship
quality: A dyadic investigator of transgender women and their cisgender male partners. J Fam Psychol.
2014;28(4):437-447. PMC4122619
7. Gamarel KE, Reisner SL, Darbes LA, et al. Dyadic dynamics of HIV risk among transgender women
and their primary male partners: The role of sexual agreement types and motivations. AIDS Care.
2015;28(1):104-111. PMC4713318
8. Operario D, Gamarel KE, Iwamoto M, et al. Couples-focused prevention program to reduce HIV risk
among transgender women and their primary male partners: Feasibility and promise of the Couples HIV
Intervention Program. AIDS Behav. 2017; 21(8): 2452-2463. PMC5179320
9. Reisner SL, Gamarel KE, Nemoto T, et al. Dyadic effects of gender minority stressors in substance
behaviors among transgender women and their non-transgender male partners. Psychology of Sexual
Orientation and Gender Diversity. 2014;1(1):63-71. PMC4311402
10. Deutsch M, Glidden D, Sevelius J, et al. Preexposure chemoprophylaxis for HIV prevention in transgender women: A subgroup analysis of the iPrEx trial. Lancet HIV. 2015;2(12):e512-519. PMC5111857

9.0 Biospecimen Collection and/or Bank Administration

9.1 * TYPE OF SPECIMENS (check all that apply): (REQUIRED)

- [x] Blood (provide amount below)
- [ ] Tissue (describe below)
- [x] Other type of biospecimen, such as sputum, cerebrospinal fluid, buccal swabs, etc. (describe below)
- [ ] Existing/archival materials (name source below)

Briefly describe the types of biospecimens that will be collected. Provide the amount of blood, if applicable. For leftover/existing/archival material, identify the source:

1. Oral swab for HIV-antibody testing conducted at the Eligibilty Visit
2. Fingerstick blood (3-5 drops) for DBS card to assess PrEP adherence at in-person Enrollment and Follow-up visits when not operating remotely.
3. Venous Blood (20 ml) approximately 4 teaspoons for HIV RNA Viral Load at in-person Enrollment and Follow-up visits when not operating remotely.

ONLY FOR REMOTE VISITS: Quest Lab-collected blood sample for HIV RNA Viral Load at remote Enrollment and Follow-up visits (remunerated an additional $40.00).

This protocol is modified to clarify that hair sample analysis will not be pursued by the investigators due to futility.

9.2 * SPECIMENS ARE: (check all that apply): (REQUIRED)

- [ ] Leftover specimens from a clinical diagnostic or therapeutic procedure
- [x] Specimens collected for research purposes only (including extra samples taken during a clinical procedure)
- [ ] Other

9.3 * FUTURE SPECIMEN USE: Will any specimens or portions of specimens be retained after the study is over for possible use in future research studies: (REQUIRED)

- ( ) Yes
- (•) No

9.5 * SPECIMEN DESTINATION: Indicate where specimens will ultimately be stored: (REQUIRED)

Outside Entities: Indicate where specimens will be sent if they will not remain at UCSF (choose at least one; check all that apply):

- [ ] Cooperative group bank
- [ ] NIH
- [x] Other university or collaborator
- [ ] Industry sponsor
- [x] Other

☐ N/A - all specimens will remain at UCSF

Specify to what institution, cooperative group, or company specimens will be transferred:

1. DBS cards will be analyzed at a specialty lab at the University of Colorado
2. HIV viral loads will be processed by Quest (commercial laboratory)

Internal Storage: If specimens will remain at UCSF, in what kind of facility will they reside (choose at least one; check all that apply):

☐ UCSF repository/bank being established under this protocol
☐ Existing UCSF specimen repository/bank with IRB approval
☐ National cooperative group bank housed at UCSF
☐ Other location at UCSF (please describe)
☑ N/A - no specimens will be retained at UCSF facilities

9.6 SPECIMENS SENT OUTSIDE UCSF - IDENTIFIABILITY: Will direct identifiers be associated with specimens or shared with other researchers and/or outside entities:

○ Yes
◉ No
○ N/A - Specimens will not be shared with others

10.0 Drugs and Devices

10.1 * DRUGS AND/OR BIOLOGICS: Are you STUDYING any drugs and/or biologics that are either approved or unapproved: (REQUIRED)

○ Yes ◉ No

Note: This question is frequently answered incorrectly. If any drugs or biologics, approved or unapproved, are being administered under this protocol, you should check 'Yes' unless you are *absolutely* sure that NONE of the drugs are part of the research protocol. Tip: Ask the PI or the sponsor if you are not sure how to answer this question.

10.3 * MEDICAL DEVICES: Are you STUDYING any medical devices, in vitro diagnostics, or assays that are either approved or unapproved:(REQUIRED)

○ Yes ◉ No

11.0 Sample Size and Eligibility Criteria

11.1 ENROLLMENT TARGET: How many people will you enroll:

108

If there are multiple participant groups, indicate how many people will be in each group:

Control condition: 54 participants / 27 dyads

Intervention condition: 54 participants / 27 dyads

11.3 SAMPLE SIZE JUSTIFICATION: Explain how and why the number of people was chosen. For multi-site studies, this is referring to the number that will be enrolled across all sites:

Power analyses were generated using the two-group repeated proportions module in NCSS PASS 15104 to compute minimum detectable effect sizes for the primary analysis to address Hypothesis 1. Our pilot study found standardized effect sizes ranging from .38 to .42,16 so we powered our study to detect similarly-sized effects in worst-case scenarios where within-participant clustering of outcomes are substantial. The study will begin with 200 participants from 100 couples evenly assigned to the intervention and control groups. Assuming 20% attrition, data from 160 participants from 80 couples will be available for analysis at all time points. Due to the clustered nature of the dyadic data, observations from participants who belong to the same couple will be correlated. In m-PI Operario's previous study of 190 TW and their male partners, for instance, the average within-couple correlation of sexual risk measurements was r=. 07. Accordingly, we lowered the effective sample size (ESS) input for the power analyses to be ESS= N/DEFF, where DEFF is the design effect or variance inflation attributable to using correlated data. DEFF is computed as 1+(M-1)*r, where M is the number of participants per dyad (i.e., two). Therefore DEFF=1+(2-1)*.07=1.07, so ESS=160/1.07=149. Assuming, α=.05, power=.80, and ESS=149, we computed the minimum detectable odds ratio (OR), proportion difference (pdiff), and standardized proportion difference (h) for the proposed time-averaged comparisons, assuming four post-baseline measurements and a wide range of CR-HIV base rates P0 for levels of risk for TW and their partners seen in the literature.4,5,20 Since the within-subject correlation ρ for repeated measures is unknown, we varied it across a wide range from .20 to .80 (see Table 2). The obtained minimum detectable effect size estimates are similar to or smaller than those detected in our pilot study, suggesting that our study is sufficiently powered to test primary Hypothesis 1.

Original Power Calculations. Originally, our sample size of 100 couples would allow us the statistical power to engage in meaningful comparisons between the two intervention arms. We assumed the 200 participants from 100 couples will be evenly assigned to the intervention arms: 50 couples in intervention and 50 couples in control. Assuming 20% attrition, data from 160 participants (80 couples) would have been available for analysis at all time points (i.e., 3-, 6-, 9, 12-month follow up). Using NCSS PASS, we conducted as series of power calculations to determine the maximum sample size requested to address the primary study aims. We computed the minimum detectable odds ratio (OR), proportion difference (pdiff), and standardized proportion difference (h) across our two study arms for the proposed time-averaged comparisons, assuming four post-baseline measurements and a wide range of base proportions for levels of risk for TW and their partners seen in the literature (i.e., 10%-50%). Since the within-subject correlation ρ for repeated measures is unknown, we varied it across a wide range from .20 to .80. Under these conditions, ORs ranged from 0.17 to 0.56, raw proportion differences ranged from 6.6% to 20.5%, and standardized proportion differences (h) ranged from .27 to .42. Revised Power Calculations. We repeated the power analysis approach utilized in our proposal submission. The revised power analysis again assumes alpha=0.05, power=0.80, 4 post-baseline measurements, and baseline reference proportions ranging from 0.10 to 0.50. The within-subject correlation for repeated measures was allowed to vary from 0.20 to 0.80. The N of participants was varied from 100 to 200 to illustrate the potential impact of various sample size reductions on the ranges of minimum detectable effect sizes. Conventional benchmarks for effect size are h=0. 20 for a small effect size, h=0.50 for a medium effect size, and h=0.80 for a large effect size. Assuming we reach at least 50% of our goal of recruiting 100 couples, under most circumstances we will still be able to detect a small-to-medium effect size. Even under the least advantageous combination of circumstances (recruiting only 50 couples, baseline reference proportions closer to 10%, and very high correlations between repeated measures), a medium-to-large effect size is still detectable.

Our Data Safety Monitoring Board (DSMB) reviewed and approved this request on February 14, 2022, and our NIMH sponsor approved the request on July 26, 2022.

11.4 * PARTICIPANT AGE RANGE: Eligible age ranges: (REQUIRED)

- [ ] 0-6 years
- [ ] 7-12 years
- [ ] 13-17 years
- [x] 18-64 years
- [ ] 65+

11.5 * STUDY POPULATIONS: Data will be collected from or about the following types of people (check all that apply): (REQUIRED)

- [ ] Inpatients
- [x] Outpatients
- [ ] Family members or caregivers
- [ ] Providers
- [ ] People who have a condition but who are not being seen as patients
- [x] Healthy volunteers
- [ ] Students
- [ ] Staff of UCSF or affiliated institutions
- [ ] None of the above

11.6 * SPECIAL SUBJECT GROUPS: Check the populations that may be enrolled: (REQUIRED)

- [ ] Children / Minors
- [ ] Adult subjects unable to consent for themselves
- [ ] Adult subjects unable to consent for themselves (emergency setting)
- [ ] Subjects with diminished capacity to consent
- [ ] Subjects unable to read, speak or understand English
- [ ] Pregnant women
- [ ] Fetuses
- [ ] Neonates
- [ ] Prisoners
- [ ] Economically or educationally disadvantaged persons
- [x] None of the above

11.7 INCLUSION CRITERIA: Briefly describe the population(s) that will be involved in this study. Include anyone that data will be collected from or about (e.g. patients, healthy controls, caregivers, providers, administrators, students, parents, family members, etc.):

Inclusion criteria:

1. Age 18 or older;
2. Self-reported primary partnership for at least 3 months;
3. Have had sex with primary partner in the last 6 months;
4. Either partner has had condomless sex with any partner in last 6 months;
5. At least one partner must be a trans woman;
6. Able to provide informed consent;
7. English speaking; and
8. Couples may be HIV-negative concordant, HIV-positive concordant, or HIV serodiscordant.

11.8 EXCLUSION CRITERIA: List any exclusion criteria (e.g. reasons why someone would not be included in the study):

Exclusion criteria:

1. Appears to be psychotic, or otherwise unable to complete Informed Consent procedures.
2. Participation would be unsafe.

11.9 * RESEARCH CONDUCTED ON PATIENT CARE WARDS: Do any study activities take place on any patient care units including inpatient wards, peri- or post-operative care units, operating rooms, or in the Emergency Department at UCSF Health medical facilities: (REQUIRED)

- ( ) Yes
- (•) No

11.11 * EMERGENCY DEPARTMENT: Does your protocol or study involve any of the following patient related activities in the emergency department (e.g. subject identification, recruitment, consent, blood draws, specimen retrieval, involvement of ED staff (nursing, tech, and/or physician), or any other ED based procedures): (REQUIRED)

○ Yes ◉ No

12.0 Recruitment and Consent

12.1 * COMPETITIVE ENROLLMENT: Is this a competitive enrollment clinical trial? By competitive enrollment, we mean that sites who do not enroll participants early may not get to participate at all: (REQUIRED)

○ Yes ◉ No

12.2 * SUBJECT IDENTIFICATION METHODS: What kinds of methods will be used to identify potential participants for recruitment (check all that apply): (REQUIRED)

- ☑ Review of patients' conditions, history, test results, etc. (includes patients seen in clinic, scheduled for surgery, a procedure, imaging, or tests, or seen in the Emergency Department as well as searching through medical record data for possible cohort identification)
- ☐ Already approved recruitment registry
- ☑ Re-contact of participants from the investigators' previous studies
- ☐ Referrals from colleagues (attach the 'Dear Colleague' letter or other recruitment materials you will provide to colleagues)
- ☑ Referrals from the community / word of mouth
- ☑ Advertisements (flyers, brochures, radio or t.v. ads, posting on clinical research sites or social media, presentation of the study at community events/media, etc.)
- ☐ Online recruiting tool (describe below)
- ☑ CTSI Recruitment Services unit
- ☐ Posting on UCSF Clinical Trials, ClinicalTrials.gov or other publicly available clinical trial website
- ☐ Other method (describe below)

Attach your recruitment materials (e.g., flyers, ads, recruitment letter templates, email text, etc.) in the Other Study Documents section of the Initial Review Submission Packet Form.

* Provide details about the subject identification methods: **(REQUIRED)**

A multi-pronged approach to recruitment will take place including:
1. Flyering at trans friendly venues;
2. Outreach to agencies, clinics, single-room occupancy hotels;
3. Word-of-mouth referrals;
4. Participants from the previously conducted Healthy Divas study of HIV-positive trans women who have given permission to be
   contacted will ne informed about the T2 Study and invited to screen.
5. CTSI recruitment service.

* Did all the participants of previous studies provide permission to be contacted for future studies: **(REQUIRED)**

◉ Yes ○ No

12.3 * SEARCHING OF MEDICAL RECORDS: (REQUIRED)

Whose patients are they:

- [ ] Investigators' own patients or patients seen within the same practice
- [x] Patients not under the care of the investigators

How and by whom will records be accessed and searched (check all that apply):

- [ ] Self-search in APeX or other medical records source
- [ ] Self-search using UCSF's Research Cohort Selection Tool
- [x] CTSI Consultation Service Recruitment Services
- [ ] UCSF Academic Research Services (ARS)
- [ ] University of California Research Exchange (UC ReX)
- [ ] Other method (describe below)

12.4 DETERMINATION OF ELIGIBILITY: How, when, and by whom will eligibility for recruitment be determined:

Potential participants call the study recruitment line or come in person to our community site during drop-in hours. Trained Research Assistants (RAs) will describe the basic study eligiblity criteria and complete the Partner 1 Screening Form. If Partner 1 is provisionally eligible, Partner 2 information is collected. Partner 2 is screened within one week by the RAs, using the Partner 2 Screening Form. Both forms are in REDCap, which will inform the RAs if the couple can be scheduled for an Eligibility Visit. At the Eligiblity Visit, oral informed consent to be screened is obtained, a brief eligibility survey is administered, and HIV status is verified.

12.5 * INITIATION OF CONTACT: Who initiates contact (check all that apply): (REQUIRED)

- [x] Investigators/study team
- [ ] UCSF recruitment unit (e.g. CTSI Consultation Services)
- [x] Potential participant
- [ ] Other (explain below)

12.6 * HOW IS CONTACT INITIATED: (check all that apply): (REQUIRED)

- [x] In person
- [x] Phone
- [ ] Letter / email
- [ ] Website or app
- [ ] Other (explain below)

Attach the telephone recruitment script in the Other Study Documents section of the Initial Review Submission Packet Form. If potential participants will initiate contact, attach the telephone screening script that will be used to provide more information about the study and determine if callers are eligible to participate.

12.7 RECRUITMENT PLAN: Based on the checkboxes you chose above, please provide a narrative describing your recruitment plan. We want to know:

- **Who is conducting the search for potential participants, and how?**
- **How are potential subjects being approached for recruitment? By whom, and when?**

If there will be more than one participant group (e.g. patients, healthy controls, caregivers, family members, providers, etc.), provide details about the recruitment plans for each group. (Recommended length - 100-250 words)

Consistent with our prior work, we will take a multifaceted approach to recruitment by using flyering in targeted venues, and outreach to agencies, clinics, bars, and CBOs. These

connections, along with input from Dr. Sevelius' community advisory boards (CAB) and strong working relationships with local agencies that serve TW, will be used in recruitment efforts to meet the proposed timeline. Those who are interested in the study may call the study recruitment line. Trained study Research Assistants (RA) will screen potential partners for eligibility. If partner 1 of the couple is provisionally eligible, the name and contact information for partner 2 is collected. Partner 2 is contacted and screened within one week and if the partners are deemed preliminary eligible to participate as a couple AND both wish to pursue the study, the couple completes an Eligibility Visit.

Additionally, we *are collaborating with the CTSI Consultation Service to provide cohort identification and direct mail for recruitment. The Dear Patient letter (attached) will be sent to UCSF patients identified from the APeX record systems via a data extraction by Academic Research Systems (ARS) of patients who identify as transgender females. These patients are not known to or under the care of the researcher team. The CTSI Consultation Service will coordinate the mailing on behalf of the study. Interested subjects will contact the study staff as described in the letter. The data extract will be delivered to the CTSI Consultation Service's MyResearch account in order to facilitate the direct mail activities while ensuring privacy and confidentiality of the patients identified. Protected data elements included in the data pull and delivered to the honest broker may include MRN, name, mailing address, and diagnosis or encounter date. Additional non-PHI data elements may also be collected to facilitate the mailing.*

12.8 * CONSENT METHODS: How will permission to participate (i.e., informed consent) be obtained from each potential participant. If there will be multiple groups and different plans for consenting each, check all that apply. See the orange Help bubble to the right for more detailed guidance. Participants will (check all that apply): (REQUIRED)

- [x] Sign a consent form at the end of the consent discussion (signed consent)
- [x] Provide online 'eConsent' using an E-Signature system
- [ ] Click through a link in a survey or email after reading about the study and then complete the study online (electronic consent)
- [x] Be told about the study and be given a handout/information sheet and be asked if they agree to participate (verbal consent)
- [ ] Complete the study activities and turn in materials, as in the case of a completed survey that is placed in a drop box or mailed to the study team (implied consent)
- [ ] Not be able to provide consent and will have a family member consent for them, as in the case of a critically ill or unconscious patient (surrogate consent)
- [ ] Not be able to provide consent (emergency waiver of consent - allowed for minimal risk research or greater than minimal risk research with an approved community consultation plan)
- [ ] Not know about the study, as in the case of chart reviews or observations of public behavior (waiver of consent)
- [ ] Other method (describe below)

Attach your consent form, information sheet, or electronic consent text in the Informed Consent Documents section of the Initial Review Submission Packet Form.

12.9 * CONSENT PROCESS: Describe the process for obtaining informed consent, including details such as who will have the consent discussion and when participants will be asked to sign the consent form in relation to finding out about the study: (REQUIRED) We encourage researchers to review our guidance on obtaining and documenting informed consent.

- **If there are multiple groups being consented differently, provide details about the consent process for each group.**
- **If you are relying on verbal or implied consent, provide details about how that will happen.**
- **For studies using online recruitment and consent or consent via mail, provide details here.**

Two consent processes will take place: (1) Verbal Informed Consent will be conducted for the Eligibility Visit and
(2) Signed Informed Consent will be conducted at the Baseline Enrollment Visit.

1. Verbal Informed Consent for the Eligibility Visit: After partner 1 and partner 2 have been screened and each express interest in participating in ther study as a couple, they complete an

Eligibility Visit. If the visit is in-person, a trained Research Assistant (RA) reads the Verbal Informed Consent to each partner separately. If eligible and interested in participating as a couple, they are scheduled for the Baseline Enrollment Visit. Because this is a couples study, both partners in the couple must be eligible and interested in participating. If the visit must take place remotely, this occurs as described in Section 8.9 Procedures and Methods.

2. Signed Informed Consent for T2 study enrollment:

- **If the visit is in-person:** a trained RA meets with each partner to review the ICF in detail. The ICF can be read by the participant or read aloud to the participant by the RA, who confirms that the potential participant understands the risks, benefits, and procedures of the study, and all questions are answered. If both members of the couple wish to consent, they each sign the witnessed ICF and are enrolled together as a couple. Participants are informed that in the event of a break up after the enrollment visit, the individual partners should still complete all quarterly follow-up assessment visits at 3, 6, 9, and 12-months post-enrollment.
- **If the visit is remote**: a trained RA will send P1 and P2 the study ICF and ROI through DocuSign and schedule a videoconference call to review, answer any questions, and help participant sign the ICF and ROI via DocuSign. If P1 and/or P2 are unable to use DocuSign, mail two paper copies of the ICFand ROI with a stamped-self-addressed envelope. When these are received by the participant, a videoconference or phone call is set up to review ICF and ROI and answer any questions. Participant signs one copy and returns in the stamped-self-addressed envelope, retaining the second copy.

* It is important that the people obtaining consent are qualified to do so. Briefly describe the training and experience these individuals have in obtaining informed consent: **(REQUIRED)**

All indiviauls obtaining informed consent have completed the CITI training in Human Subjects Research and received study-specific training on obtaining voluntary informed consent.

12.10 * CONSENT COMPREHENSION: Indicate how the study team will assess and enhance the subjects' understanding of study procedures, risks, and benefits prior to signing the consent form (check all that apply): (REQUIRED) Tip: Review the Consent Comprehension - Learning Notes in the Help bubble at the right for specific questions that can be asked to assess comprehension, consider using the UCSF Decision-Making Capacity Assesment Tool, and review our guidance on obtaining written or verbal informed consent for more detail on how to conduct the assessment.

- [x] The study team will engage the potential participant in a dialogue, using open-ended questions about the nature of the study or the experimental treatment, the risks and benefits of participating, and the voluntary nature of participation
- [x] Potential participants will be asked or shown a series of questions to assess their understanding of the study purpose, procedures, risks and benefits, as well as the voluntary nature of participation (especially appropriate when the consent process happens online or through a mobile health app)
- [ ] Other method (describe below):

Provide details of the other approaches that will be used, if using another method to assess comprehension:

All participants will give informed consent to participate in the project. Research Assistants (RA) will read, review, and discuss the consent forms with all potential participants prior to asking them to sign. If the potential participant appears confused or indicates he/she doesn't understand the consent, the RA will attempt to identify the misunderstanding and to explain the consent again. If the potential participant still does not comprehend the consent, he/she will be excluded from the study. We will confirm that potential participants understand the material covered in the consent procedure by asking questions prior to asking the person sign the consent form. These will include openended (e.g., "Could you tell me what's going to happen if you enroll in the study?") and closed questions (e.g., Will you get free medications as part of this research study?"). Responses that suggest confusion or inaccuracies that staff cannot successfully clarify will result in exclusion from the study and direction to appropriate outside referrals. Interviewers will witness and date the consent after the participant signs.

12.11 * DECEPTION: Does this study rely on some deception or misinformation about what the

researchers are observing to get valid data? (REQUIRED)

○ Yes ◉ No

12.13 * WAIVER OF DOCUMENTATION OF SIGNED CONSENT: Select the regulatory category under which the IRB may waive the requirement to obtain *signed* consent for this study:

○ The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether they want documentation linking them with the research. 46.117(c)(1)

◉ The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context. 46.117(c) (2)

12.14 TIME: What is the estimated time commitment for participants (per visit and in total):

The total estimted time commitment from participants will range from **480 - 755 minutes (8 hours - 12.5 hours)** dependant on HIV and medications staus and randomization assignment. The estimated time per visit is:

Pre-Screening (**15 minutes):** Completion of P1 or P2 Screening Form

Eligibility Visit (40-65 minutes): Oral Informed Consent (15 minutes); eligibility survey (5 minutes); confirmation of HIV status (5-30 minutes) depending if verification is done via HIV Letter of Diagnosis/medication bottles, prior known HIV positive study participant, or HIV oral antibody test with pre- & post-test counseling (30 min); enter test results to REDCap (5 min); Schedule Baseline Enrollment Visit (5 min), Provide incentive (5 min).

Baseline Enrollment Visit (**125-160 minutes):** Written Informed Consent (30 minutes); collect contact locator information (10 minutes); collect appropriate laboratory specimen (0-20 minutes) depending on HIV status and PrEP medication - DBS collection if HIV negative and has taken PrEP in last 3 months or venous blood draw for HIV viral load testing if HIV positive, or no testing if HIV-negative and not taking PrEP; complete survey (60 min); obtain randomization arm and inform couple (5 min); observe control arm videos (10 min) or Intervention Counseling Session 1 (20 min); Schedule next visits (5 min); Provide incentive (5 min).

Intervention Sessions 2-4 (45 minutes each = 135 minutes)

Quarterly Follow-up Visits (75-95 minutes x 4): Update contact information (5 minutes); Complete survey (60 min); collect appropriate laboratory specimen (0-20 minutes) depending on HIV status and PrEP medication - DBS collection if HIV negative and has taken PrEP in last 3 months or venous blood draw for HIV viral load testing if HIV positive, or no specimen if HIV negative and not on PrEP; schedule next visit (5 min), provide incentive (5 min).

IMPORTANT TIP: Ensure this information is consistent with the information provided in the consent form.

12.17 OTHER ALTERNATIVES: Describe other alternatives to study participation, if any, that are available to prospective subjects:

Individuals are free to decline participation. Regardless of decision to participate, a list of community resources will be made available.

13.0

Waiver of Consent/Authorization for Recruitment Purposes

This section is required when medical records may be reviewed to determine eligibility for recruitment.

13.1 * PRACTICABILITY OF OBTAINING CONSENT PRIOR TO ACCESS: Study personnel need to access protected health information (PHI) during the recruitment process and it is not practicable to obtain informed consent until potential subjects have been identified: (REQUIRED)

- (•) Yes

If **no**, a waiver of consent/authorization is NOT needed.

13.2 * RISK TO PRIVACY: A waiver for screening of health records to identify potential subjects poses no more than minimal risk to privacy for participants:

- (•) Yes

If **no**, a waiver of authorization can NOT be granted.

13.3 * RIGHTS/WELFARE: Screening health records prior to obtaining consent will not adversely affect subjects' rights and welfare:

- (•) Yes

If **no**, a waiver of authorization can NOT be granted.

13.4 * IDENTIFIERS: Check all the identifiers that will be collected prior to obtaining informed consent:

- [x] Names
- [x] Dates
- [x] Postal addresses
- [x] Phone numbers
- [ ] Fax numbers
- [x] Email addresses
- [x] Social Security Numbers*
- [x] Medical record numbers
- [ ] Health plan numbers
- [ ] Account numbers
- [ ] License or certificate numbers
- [ ] Vehicle ID numbers
- [ ] Device identifiers or serial numbers
- [ ] Web URLs
- [ ] IP address numbers
- [ ] Biometric identifiers
- [ ] Facial photos or other identifiable images
- [x] Any other unique identifier
- [ ] None

Note: HIPAA rules require that you collect the minimum necessary.

13.5 * HEALTH INFORMATION: Describe any health information that will be collected prior to obtaining informed consent:

We are collaborating with the CTSI Consultation Service to provide cohort identification and direct mail for recruitment. The Dear Patient letter (attached) will be sent to UCSF patients identified from the APeX record systems via a data extraction by Academic Research Systems (ARS) of patients of female transgender. These patients are not known to or under the care of the researcher team. The CTSI Consultation Service will coordinate the mailing on behalf of the study. Interested subjects will contact the study staff as described in the letter. The data extract will be delivered to the CTSI Consultation Service's MyResearch account in order to facilitate the direct mail activities while ensuring privacy and confidentiality of the patients identified. Protected data elements included in the data pull and delivered to the honest broker may include MRN, name, mailing address, and diagnosis or encounter date. Additional non-PHI data elements may also be collected to facilitate the mailing.

Note: HIPAA requires that you collect the minimum necessary.

13.6 * DATA RETENTION/DESTRUCTION PLAN: Describe your plan to destroy any identifiable data collected to determine eligibility for recruitment. This should be done at the earliest opportunity. If you plan to retain identifiable recruitment data, provide the justification for doing so:

This information will be reviewed only by the study Principal Investigator and Project Director. It will be destroyed within 6 months of receipt and issuance of letters to potentially eligible participants.

14.0 Risks and Benefits

14.1 RESEARCH-RELATED RISKS: Check if your study involves any of these specific research-related risks to participants that may need to be disclosed in the consent form:

- [x] Physical discomforts or pain
- [x] Risks to employment, or social or legal standing
- [ ] Risk that the study team may observe possible evidence of child abuse, elder abuse, or a threat to self or others that they are required to report

* For any boxes checked above, describe how you will minimize these risks and discomforts, e.g., adding or increasing the frequency of monitoring, additional screening to identify and exclude people with diminished kidney or liver function, or modification of procedures such as changing imaging studies to avoid giving contrast agent to people who are more likely to suffer side effects from it, etc.: **(REQUIRED)**

Potential risks could include: 1) embarrassment and sensitivity related to questioning about HIV status, personal coping, and sexual behavior; 2) release of confidential information about the participant; 3) risks due to venipuncture.

The risks associated with gathering information from participants by properly trained and supervised research staff are low and include risks of loss of privacy and distress or discomfort. We have conducted previous large intervention and assessment protocols that involve vulnerable subjects and highly confidential or sensitive personal information. As a result, we have a staff of experienced interviewers, intervention facilitators, and supervisors, and have established protocols for quality assurance, emergency procedures, crisis intervention and referral, and initial and on-going staff training. Interviewers and intervention facilitators on staff have experience working with participants of low socioeconomic status and racial/ethnic minorities. We will have predominantly female interviewers and facilitators, and many of our research staff members self-identify as racial or ethnic minorities and/or transgender. Typically, interviewers and intervention facilitators spend 40 hours in initial training sessions and observed practice. Training includes reading and discussing intervention protocols and selected articles about interviewing, tracking, and locating participants and attending lecture sessions regarding emergency procedures, mandatory reporting, confidentiality, and research ethics. All interviews and intervention sessions will be audio recorded; 20% of the recordings will be selected at random for review for quality assurance and training. We have developed assessment and intervention quality assurance protocols for several other projects. Assessment and intervention staff will attend separate ongoing bi-

monthly supervision meetings where quality assurance and problem-solving topics will be discussed.
In addition, we collect oral swabs for HIV testing and blood samples for viral load and PrEP adherence assement. Staff members who are state certified as HIV test counselors will conduct pre- and post-test counseling. The viral load assays and PrEP adherence testing will be for the primary outcome analysis. We have established protocols for quality assurance, emergency procedures, crisis intervention and referral, and initial and on-going staff training.
Phlebotomists will be certified by the State of California, and will complete the UCSF Bloodborne Pathogens training upon hire and annually thereafter. We will strictly adhere to all UCSF safety policies and procedures regarding the collection and processing of biological substances. Although venipuncture (3 above) might cause minor physical pain at the site, this risk is no more than what individuals would experience at a routine healthcare appointment.
Safety monitoring procedures. All safety-related risks will be monitored routinely at all points of participant contact. The security of confidential information will be monitored regularly. Research interviewers will be trained in asking questions about sensitive topics in a caring and nonthreatening manner and will stop questioning at the first sign of discomfort or on request (1 above). Privacy, confidentiality, and disclosure comfort will be emphasized in every session. All participants will be reminded that they are not required to disclose their HIV status (or any other personal information) to anyone at any time. Participants will be informed that assessment responses will be kept confidential and will not be used against them in any manner, including for reasons of legal action or medical treatment. Research interviewers will be trained to identify a participant who reports distress. For participants who report distress or suicidality (4 above), a protocol will facilitate staff action, including steps to assess the level of distress, to obtain emergency contact information for clinical supervisors, and to obtain up-to-date phone numbers for crisis centers, hotlines, and referral agencies.
Safety-related risk reporting and action plan. Research interviewers and intervention staff will report breach of confidentiality risks incurred by participants to the Project Director, who will in turn inform the PI. Any participant in need of treatment due to distress will be referred for appropriate services after staff follow the participant distress protocol and inform the Project Director and PI. Finally, the PI will be responsible for informing the DSMB chair, IRB through the IRB adverse event reporting procedure and the Project Officer through immediate e-mail of any life-threatening incidents and through annual reports of other incidents. The PI will take appropriate action to stop the study, release a participant from the study, or modify procedures to reduce and/or eliminate the abovementioned risks if they occur at an unacceptable level.

14.2 * RISKS: Describe any anticipated risks and discomforts not listed above: (REQUIRED)

COVID-19 related issues: Due to the COVID-19 public health crisis, thereis a chance we may be required to conduct research visits remotely. Approved videoconference platforms include Zoom, Facebook Messenger video chat, Google G Suite Hangouts video or Skype for business. However, use of these platforms may present some security risks and therefore may present additional risk to privacy and confidentiality for participants.

14.3
MINIMIZING RISKS: Describe the steps you have taken to minimize the risks/discomforts to subjects. Examples include:

- **designing the study to make use of procedures involving less risk when appropriate**
- **minimizing study procedures by taking advantage of clinical procedures conducted on the study participants**
- **mitigating risks by planning special monitoring or conducting supportive interventions for the study**
- **having a plan for evaluation and possible referral of subjects who report suicidal ideation**

Please see above.

14.5 * BENEFITS: (REQUIRED) Note: These are the benefits that the IRB will consider during their review. They are not necessarily appropriate to include in the consent form.

Possible immediate and/or direct benefits to participants and society at large (check all that apply):

- [ ] Positive health outcome (e.g. improvement of condition, relief of pain, increased mobility, etc.)
- [ ] Closer follow-up than standard care may lead to improved outcomes or patient engagement
- [ ] Health and lifestyle changes may occur as a result of participation
- [x] Knowledge may be gained about their health and health conditions
- [ ] Feeling of contribution to knowledge in the health or social sciences field
- [ ] The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children
- [ ] Other benefit (describe below)
- [ ] None

14.6 RISK TO BENEFIT RATIO: Explain why the risks to subjects are reasonable in relation to anticipated benefits, if any, to the participant or society:

There may be no direct benefit to participants in this research. However, they may learn new skills for interpersonal communication and HIV prevention. The larger public health community, as well as transgender women and their partners, may benefit if the intervention demonstrates efficacy. The minimal risks of this behavioral intervention are outweighed by the potential benefits of the research.

14.7 * DATA AND SAFETY MONITORING: Do you have a Data and Safety Monitoring Plan (DSMP) for this study (A DSMP is required for Greater than Minimal Risk research): (Click the Help link for guidance on risk determination) (REQUIRED)

(•) Yes ( ) No

This is not required for minimal risk research but the UCSF IRB strongly recommends one to ensure the data collected are adequate to meet the research aims:

15.0 Data and Safety Monitoring Plan

15.1 * DATA AND SAFETY MONITORING PLAN (DSMP): (REQUIRED) Provide a summary of the DSMP:

All greater than minimal risk studies are required to provide a plan. Lack of an adequate plan is one of the most common reasons why IRB approval is delayed.

Instructions:

Describe the plan for monitoring data quality and participant safety. Key areas that should be included in the plan are:

- An explanation of the plan to monitor data collection, study progress, and safety
- A description of who will perform the monitoring and at what frequency (e.g., the PI only, a contract research organization, a Data and Safety Monitoring Board or Data Monitoring Committee, etc.)
- The type of data and events that will be reviewed (e.g., adverse events, breaches of confidentiality, unanticipated problems involving risk to participants or others, unblinded efficacy data, etc.)
- Procedures and timeline for communicating monitoring results to the UCSF IRB, the study sponsor, and other appropriate entities

As appropriate:

- A plan for conducting and reporting interim analysis
- Clearly defined stopping rules
- Clearly defined rules for withdrawing participants from study interventions

ADVERSE EVENTS
An internal (on-site) adverse event that the investigators determine to be:
1. Definitely, probably, or possibly related AND
2. Serious or unexpected will be reported within 5 working days of awareness. Internal, related deaths and life-threatening events will be reported immediately. These reports will be made using the iRIS Adverse Event Reporting Form.

An external (off-site) adverse event that the investigators determine: changes study risks / benefits, OR necessitates modification to the IRB-approved consent document(s), and/or the IRB-approved application/protocol will be reported within 10 working days of UCSF PI awareness. These reports will be made using the iRIS Adverse Event Reporting Form.

OTHER TYPES of EVENTS or SAFETY INFORMATION
Audit or Monitoring Report with significant findings, DSMB/DMC Report, Hold on Study Activities due to unexpected risk or required by any oversight entity (e.g. UCSF, FDA, OHRP), and Updated Investigator Brochure will be reported within 10 working days of awareness using the iRIS Reporting Form. Other Safety Information or Publication and Pharmacy Packet Inserts for change to risk language will be reported within 10 working days of awareness using the iRIS Reporting Form. If there is no change to risk language, reporting is not required.

PROTOCOL VIOLATIONS and RESEARCH-RELATED INCIDENTS
Major violation including, but not limited to incorrect intervention given, enrollment of ineligible participant, key safety procedure/lab not done or done outside window will be reported within 10 working days of awareness using the iRIS Protocol Violation/Incident Report Form. Immediate Protocol Change to Protect Participant Safety will be reported within 10 working days of occurance using the iRIS Protocol Violation/Incident Report Form. Major incident, including but not limited to problem with consent or recruitment process, significant complaint or concern, lapse in study approval, loss of adequate resources will be reported within 10 working days of awareness using the iRIS Protocol Violation/Incident Report Form. Potential breaches of privacy or confidentiality will be reported within 48 hours of awareness using the iRIS Protocol Violation/Incident Report Form.

In addition to adhering to the above UCSF IRB reporting requirements, we will implement the following:
Data risks and monitoring
Data-related risks. Data-related risks to participants could consist of circumstances where an insufficient amount of data was collected to answer the research questions or high/systematic attrition in the trial or intervention participation (insufficient dosing).
Data monitoring procedures. Overall recruitment goals will be monitored monthly, as will missing data and follow-up failures. Torsten Neilands, Ph.D. will serve as the study's biostatistician and will provide ongoing monitoring of study progress.
Attrition reduction plan (i.e., retention plan). We will carefully monitor attrition in the trial. Retention is facilitated by a "user-friendly" centrally located storefront walk-in site with flexible hours. Extensive contact information is collected at baseline to facilitate tracking, including the names of one to three contacts who may know the whereabouts of a participant if lost to follow-up. With the participant's consent, upon enrollment these contacts are notified by a tracking specialist who introduces him or herself and lets them know that the participant is enrolled in a "Health Study." The tracking specialist also indicates that individuals may be contacted later if we lose contact with the participant. Additional contact information includes addresses of sites that the participant frequents, such as needle exchanges, free food lines, shelters, bars, probation /parole offices, and community-based organizations. Reminder messages are sent prior to each visit. Mobile outreach is used for participants more than 30 days late for scheduled appointments. Participants receive a business-sized card with the next scheduled interview, session, or assesment date.
Holiday and birthday cards are sent to each participant to help maintain participant morale and interest in the study. Finally, we will provide a welcoming environment with healthy snacks and a community resource board at the community site, and provide special gifts with the project logo (e.g. t-shirts, tote bags, sports bottles) at strategic follow-up points to foster a positive attachment with the study. In Dr. Johnson's Balance Project with HIV-positive adults experiencing high ART side effects, we retained 93% of 249 randomized participants for 18 months.95 In another study using similar retention methods, we retained 92% for 6 months.96 In our PATH project with the urban poor living with HIV, we have retained 91% of 219 randomized

participants for 12 months, despite high levels of incarceration, housing instability, substance use, and mental illness,97 which likely most closely approaches the life circumstances of the transgender women we propose to recruit for the trial.
Data-related risk reporting and action plan. Research interviewers and recruitment staff will be responsible for compiling numbers of participants recruited, completing required assessments, maintaining databases, and identifying missing data and missing follow-up assessments. The data manager will prepare recruitment and missing data reports for weekly review by the Project Director, Statistician, Co-Is, and PI. All data are de-identified and stored on a firewall-protected server. Upon recognition of unacceptable recruitment or follow-up rates, or of missing data, the PI will intervene with strategies to remedy the shortcomings. Completion rates of the intervention will be monitored in a similar fashion.
Safety-related risks. Safety-related risks could include:
Potential risks could include: 1) embarrassment and sensitivity related to questioning about HIV status, personal coping, and sexual behavior; 2) release of confidential information about the participant; 3) risks due to venipuncture; and 4) recognition of the need for treatment for psychological distress/suicidality.
Safety monitoring procedures. All safety-related risks will be monitored routinely at the time of the assessment or intervention session. The security of confidential information will be monitored regularly. Research interviewers will be trained in asking questions about sensitive topics in a caring and nonthreatening manner and will stop questioning at the first sign of discomfort or on request. Privacy, confidentiality, and disclosure comfort will be emphasized in every session. All participants will be reminded that they are not required to disclose their HIV status (or any other personal information) to anyone at any time. Participants will be informed that assessment responses will be kept confidential and will not be used against them in any manner, including for reasons of legal action or medical treatment. Research interviewers will be trained to identify a participant who reports distress. For participants who report distress or suicidality, a protocol will facilitate staff action, including steps to assess the level of distress, to obtain emergency contact information for clinical supervisors, and to obtain up-to-date phone numbers for crisis centers, hotlines, and referral agencies.
Safety-related risk reporting and action plan. Research interviewers and intervention staff will report breach of confidentiality risks incurred by participants to the Project Director, who will in turn inform the PI. Any participant in need of treatment due to distress will be referred for appropriate services after staff follow the participant distress protocol and inform the Project Director and PI. Finally, the PI will be responsible for informing the DSMB chair, IRB through the IRB adverse event reporting procedure and the Project Officer through immediate e-mail of any life-threatening incidents and through annual reports of other incidents. The PI will take appropriate action to stop the study, release a participant from the study, or modify procedures to reduce and/or eliminate the abovementioned risks if they occur at an unacceptable level.
Adverse events. Adverse events will be tracked and follow-through will be conducted via referrals and follow-up. An adverse event form will be developed detailing the incident, actions taken, supervisor notes, and follow-up steps. The form, supplemented by regular session notes, will be sent immediately to appropriate agencies, including the DSMB chair, IRB and NIH. Any action recommended by the DSMB or IRB will be conveyed to the NIH. The DSMB will be responsible for the monitoring and reporting of any adverse events.
The UCSF Institutional Review Board (IRB). All problems related to participant safety will be reported to the IRB by the PI within 10 working days. Specifically, we will report in writing: 1) all serious
adverse events associated with study procedures, and 2) any incidents or problems involving the conduct of the study or patient participation, including problems with the recruitment or consent processes. The PI will provide a discussion of any side effects or problems noticed in the course of the study to the IRB on an annual basis.

15.2 * DATA AND SAFETY MONITORING BOARD (DSMB): (REQUIRED) Will a Data and Safety Monitoring Board (DSMB) be established:

- (•) Yes
- ( ) No

15.3 DSMB DETAILS: Provide details about the DSMB, including meeting frequency, and the affiliations and qualifications of members: Attach the DSMB charter to the Other Study Documents section. If the DSMB has not yet been established, submit details and the charter to us as soon as they become available.

Data and Safety Monitoring Board (DSMB). With consultation from NIH, we have identied three people to serve as members of the DSMB. These members have expertise in behavioral clinical trials and research with transgender women. The DSMB members have met one time to date via

teleconference, and will reconvene six months after the study launch, and annually thereafter to monitor study progress throughout the course of the trial.

16.0 Confidentiality, Privacy, and Data Security

16.1 PROTECTING PRIVACY: Indicate how subject privacy will be protected:

- [x] Conduct conversations about the research in a private room
- [x] Ask the subject how they wish to be communicated with – what phone numbers can be called, can messages be left, can they receive mail about the study at home, etc.
- [x] Take special measures to ensure that data collected about sensitive issues do not get added to their medical records or shared with others without the subject's permission
- [x] Other methods (describe below)

Describe the other methods for protecting privacy:

The following privacy protection steps will be taken: 1) interviewers and other staff will participate in initial training, follow-up training, and ongoing monitoring and supervision to ensure understanding of the ethical issues involved in this research; 2) only the trained staff will know the name, identification (ID) number, and contact information of participants. The list that links the participant's name with the ID number will be kept in a locked file cabinet accessible only by the PI, the PD, and the interviewers; 3) consent forms will be kept in locked files; 4) any personal identifiers linked to data will be removed and replaced by code numbers in all records. Electronic copies of the data will be stored on a secure server and paper copies will be destroyed at the end of the study.

16.2 SENSITIVE DATA: Do any of the instruments ask about illegal or stigmatized behavior:

(•) Yes ( ) No

IMPORTANT NOTE: Indicate in the consent form what kinds of sensitive information will be collected.

16.3 SIGNIFICANT CONSEQUENCES OF A LOSS OF PRIVACY OR CONFIDENTIALITY: Could a breach of privacy or confidentiality result in any significant consequences to participants, such as criminal or civil liability, loss of state or federal benefits, or be damaging to the participant's financial standing, employability, or reputation:

(•) Yes ( ) No

Check all that apply:

- [x] Embarrassment
- [ ] Criminal or civil liability
- [ ] Loss of state or federal benefits
- [x] Damaging to the participant's financial standing, employability, or reputation
- [ ] Potential risks to insurability (health, disability, or life insurance)

Describe the potential consequences:

Transgender or HIV status could be revealed.

16.4 EXTRA CONFIDENTIALITY MEASURES: Explain any extra steps that will be taken to assure confidentiality and protect identifiable information from improper use and disclosure, if any:

We have conducted previous large intervention and assessment protocols that involve vulnerable subjects and highly confidential or sensitive personal information. As a result, we have a staff of experienced interviewers, intervention facilitators, and supervisors, and we have established protocols for quality assurance, emergency procedures, crisis intervention and referral, and initial and on-going staff training. Typically, interviewers and intervention facilitators spend 40 hours in initial training sessions and observed practice. Training includes reading and discussing intervention protocols and selected articles about interviewing, tracking, and locating participants and attending lecture sessions regarding emergency procedures, mandatory reporting, confidentiality, and research ethics. All intervention sessions will be audio recorded. We have developed assessment and intervention quality assurance protocols for several other projects. Assessment and intervention staff will attend separate ongoing bi-monthly supervision meetings where quality assurance and problem-solving topics will be discussed. Privacy, confidentiality, and disclosure comfort will be emphasized in every session. Research interviewers and intervention staff will report breach of confidentiality risks incurred by participants to the Project Director, who will in turn inform the PI. While couples will come for site visits together, all participants will undergo assessments and testing separately/individually.

16.5 * REPORTABILITY: Do you anticipate that this study may collect information that State or Federal law requires to be reported to other officials, such as elder abuse, child abuse, or threat to self or others: (REQUIRED)

○ Yes ◉ No

16.6 CERTIFICATE OF CONFIDENTIALITY: Will this study obain a Certificate of Confidentiality:

◉ Yes ○ No

Please include the recommended Certificate of Confidentiality language in the consent form.

16.7 SHARING OF RESEARCH RESULTS: Will there be any sharing of EXPERIMENTAL research test results with subjects or their care providers:

○ Yes ◉ No

16.9 * HIPAA APPLICABILITY: Study data will be: (REQUIRED)

- ☑ Derived from a medical record (e.g. APeX, OnCore, etc. Identify source below)
- ☐ Added to the hospital or clinical medical record
- ☐ Created or collected as part of health care
- ☐ Used to make health care decisions
- ☑ Obtained from the subject, including interviews, questionnaires
- ☐ Obtained ONLY from a foreign country or countries
- ☐ Obtained ONLY from records open to the public
- ☐ Obtained from existing research records
- ☐ None of the above
- ☐ Derived from the Integrated Data Repository (IDR) or The Health Record Data Service (THREDS) at SFGH

In addition to signing a consent form, each subject will have to sign the UCSF Research Subject Authorization Form (HIPAA Form). Upload the HIPAA Authorization Form in the Other Study Documents section of the Initial Review Submission Packet Form. Failure to have patients sign the HIPAA Authorization is one of the most common findings from QIU Routine Site Visits. Please call the IRB office at 415-476-1814 if you have questions about HIPAA research requirements.

If derived from a medical record, identify source:

SFDPH Carelink EMR; APEX

16.10 * IDENTIFIERS: Check all identifiers that will be collected and included in the research records, even temporarily: (REQUIRED)

- [x] Names
- [x] Dates
- [x] Postal addresses
- [x] Phone numbers
- [ ] Fax numbers
- [x] Email addresses
- [ ] Social Security Numbers*
- [ ] Medical record numbers
- [ ] Health plan numbers
- [ ] Account numbers
- [ ] License or certificate numbers
- [ ] Vehicle ID numbers
- [ ] Device identifiers or serial numbers
- [ ] Web URLs
- [ ] IP address numbers
- [ ] Biometric identifiers
- [ ] Facial photos or other identifiable images
- [x] Any other unique identifier
- [ ] None

* Could study records include *ANY* photos or images (even 'unidentifiable' ones): **(REQUIRED)**

○ Yes ◉ No

16.11 * PATIENT RECORDS: Will health information or other clinical data be accessed from UCSF Health, Benioff Children's Hospital Oakland, or Zuckerberg San Francisco General (ZSFG): (REQUIRED)

◉ Yes ○ No

16.14 * HIPAA - PERMISSION TO ACCESS SENSITIVE DATA: Does the research require access to any of the following types of health information from the medical record: (check all that apply) (REQUIRED)

- [ ] Drug or alcohol abuse, diagnosis or treatment
- [x] HIV/AIDS testing information
- [ ] Genetic testing information
- [ ] Mental health diagnosis or treatment
- [ ] None of the above

Important note: Ensure that participants initial the corresponding line(s) in Section C of the HIPAA authorization form during the consent process.

16.18 * DATA COLLECTION AND STORAGE: (check all that apply): (REQUIRED)

Collection methods:

- [ ] Electronic case report form systems (eCRFs), such as OnCore or sponsor-provided clinical trial management portal
- [x] UCSF ITS approved Web-based online survey tools: Qualtrics or RedCap
- [ ] Other web-based online surveys or computer-assisted interview tool
- [ ] Mobile applications (mobile or tablet-based)
- [ ] Text Messaging
- [ ] Wearable devices
- [ ] Audio/video recordings
- [ ] Photographs
- [x] Paper-based (surveys, logs, diaries, etc.)
- [ ] Other:

* What online survey or computer assisted interview tool will you use: **(REQUIRED)**

- [ ] Qualtrics (Recommended)
- [x] RedCAP (Recommended)
- [ ] Survey Monkey (NOT recommended and may require UCSF ITS Security review)
- [ ] Other

* Data will be collected/stored in systems owned by (check all that apply): **(REQUIRED)**

- [ ] Study sponsor
- [x] UCSF data center (including OnCore, RedCap, Qualtrics, and MyResearch)
- [ ] UCSF encrypted server, workstation, or laptop residing outside of UCSF data center
- [ ] Personal devices, such as laptops or tablets that are not owned or managed by UCSF
- [ ] SF VAMC
- [ ] Zuckerberg San Francisco General Hospital
- [ ] Benioff Children's Hospital Oakland
- [ ] Langley Porter Psychiatric Institution
- [ ] Other UCSF affiliate clinic or location (specify below)
- [ ] Cloud vendor such as Amazon Web Services (AWS), Salesforce, etc. (specify below)
- [ ] Other academic institution
- [ ] 3rd party vendor (business entity)
- [ ] Other (explain below)

16.19 * ADDITION OF RECORDS TO A REGISTRY: Will patient records reviewed under this approval be added to a research database, repository, or registry (either already existing or established under this protocol): (REQUIRED)

- (•) Yes
- ( ) No

This activity generally requires patient consent and HIPAA Authorization. A Waiver of Consent/Authorization may be granted for patients who are deceased or lost to follow up, but ongoing patients should be consented at their next clinic visit prior to accessing their health records or they may provide consent and HIPAA authorization for research use of their health information by mail or through a certified E-Signature system such as DocuSign. You may be asked to revise your consent plans.

16.20 * DATA SHARING: During the lifecycle of data collection, transmission, and storage, will identifiable information be shared with or be accessible to anyone outside of UCSF: (REQUIRED)

○ Yes ◉ No

17.0 Financial Considerations

17.1 * PAYMENT: Will subjects be paid for participation, reimbursed for time or expenses, or receive any other kind of compensation: (REQUIRED)

◉ Yes ○ No

17.2 PAYMENT METHODS: Subjects payment or compensation method (check all that apply):

Payments will be (check all that apply):

- ☑ Cash
- ☐ Check
- ☑ Gift card
- ☐ Debit card
- ☐ UCSF Research Subject Payment Card
- ☐ Reimbursement for parking and other expenses
- ☐ Other:

17.3 PAYMENT SCHEDULE: Describe the schedule and amounts of payments, including the total subjects can receive for completing the study:

- **If there are multiple visits over time, explain how payments will be prorated for partial completion**
- **If deviating from recommendations in Subject Payment Guidelines, include specific justification below**

Payment schedule

- $0 for Pre-Screening
- $20 per person for Eligibility Visit
- $100 per person for In-Person Enrollment Visit; **HIV-positive participants who complete Remote Enrollment visits with blood drawn at a Quest Service Center receive an additional $40USD ($140.00 total).**
- $20 per person per intervention session (x 3 sessions)
- $50 per person per In-person Follow-up assessment visits (x 4 follow-ups); **HIV-positive participants who complete Remote Follow-up visits with blood drawn at a Quest Service Center receive an additional $40USD ($90 total).**

Effective approximately September 8, 2023, currently enrolled participants who self-report use of Pre-Exposure Prophylaxis medications (PrEP) will no longer be asked to provide a self-collected hair sample and will be advised that any previously collected samples will not be analyzed by the investigators.

Effective approximately March 15, 2023, currently enrolled participants will be informed that if they complete all outstanding quarterly follow-up visits, they will receive an additional $50 bonus payable at completion of their 12-month visit.

Requested approval in February 2023 to add a one-time bonus payment of $50 for currently enrolled participants who complete all outstanding quarterly follow-up visits, to be provided at the final 12-month follow-up visit.

Total for participants assigned to control condition (including eligibility visit): $320 (if eligible for bonus payment, $370)

Total for participants assigned to intervention (including the eligibility visit): $380 (if eligible for bonus payment, $430)

17.4 COSTS TO SUBJECTS: Will subjects or their insurance be charged for any study activities:

○ Yes ◉ No

18.0 Other Approvals and Registrations

18.4 OTHER APPROVALS: Indicate if this study involves other regulated materials and requires approval and/or authorization from the following regulatory committees:

☐ Institutional Biological Safety Committee (IBC)

Specify BUA #:

☐ Institutional Animal Care and Use Committee (IACUC)

Specify IACUC #:

☐ Controlled Substances

19.0 Qualifications of Key Study Personnel and Affiliated Personnel

NEW: January 2019 - Affiliated personnel who do not need access to iRIS no longer need to get a UCSF ID. Instead, add them below in the Affiliated Personnel table below.

19.1 Qualifications of Key Study Personnel:

Instructions:

For UCSF Key Study Personnel (KSP)* listed in **Section 3.0,** select the KSP from the drop down list and add a description of their study responsibilities, qualifications and training. In study responsibilities, identify every individual who will be involved in the consent process. Under qualifications, please include:

- Academic Title
- Institutional Affiliation (UCSF, SFGH, VAMC, etc.)
- Department
- Certifications

NOTE: This information is required and your application will be considered incomplete without it. If this study involves invasive or risky procedures, or procedures requiring special training or certification, please identify who will be conducting these procedures and provide details about their qualifications and training. Click the orange question mark for more information and examples.

Training Requirements:
The IRB requires that all Key Study Personnel complete Human Subjects Protection Training through **CITI** prior to approval of a new study, or a modification in which KSP are being added. More information on the CITI training requirement can be found on our **website.**

* **Definition of Key Study Personnel and CITI Training Requirements (Nov, 2015):** UCSF Key Study Personnel include the Principal Investigator, other investigators and research personnel who are directly involved in conducting research with study participants or who are directly involved in using study participants' identifiable private information during the course of the research. Key Personnel also include faculty mentors /advisors who provide direct oversight to Postdoctoral Fellows, Residents and Clinical Fellows serving as PI on the IRB application.

KSP Name	Description of Study Responsibilities - Briefly describe what will each person be doing on the study. If there are procedures requiring special expertise or certification, identify who will be carrying these out. Also identify who will be obtaining informed consent.	Qualifications, Licensure, and Training
Dr. Sevelius, Jeanne PhD	Jeanne ("Jae") Sevelius, PhD is a study Co-Investigator. She will participate in scientific oversight of study activities including protocol development, assessment and intervention development, quality control, and manuscript preparation.	Dr. Sevelius has a PhD in clinical psychology, is a licensed clinical psychologist with a specialization in gender studies. She has a faculty appointment without salary in the Department of Medicine at UCSF and is faculty at the Columbia University, Research Foundation for Mental Hygiene.
Gamarel, Kristine E	Kristine Gamarel, PhD serves as a Principal Investigator (MPI) of the study. She provides scientific oversight for study decision-making, lead assessment development and data analysis, and contribute expertise on HIV prevention at the couple level.	Dr. Gamarel has a PhD in social psychology and is an Assistant Professor in Health Behavior and Health Education at the University of Michigan. As a social psychologist with expertise in health psychology and public health, the major focus of her work seeks to eliminate health inequities in partnership with sexual and gender minority communities. Her research includes cohort studies and couples-based and m-health/e-health approaches to address HIV prevention and treatment, alcohol reduction, and tobacco control and prevention.

Stein, Ellen S	Ellen Stein serves as Project Director for the study. She will maintain close communication with the study investigators and statistical staff; supervise field research staff; oversee the collection of high-quality data and fidelity to the study protocol; act as the primary liaison between the study and the UCSF IRB; and participate in management of study finances.	Ms. Stein has more than 20 years experience leading longitudinal research research studies domestically and internationally.
Johnson, Jack	Jack Johnson is a study Research Assistant who is responsible for recruitment, Informed Consent, and enrollment of eligible couples to the study.	Mr. Johnson has a background in HIV prevention work and advocacy in Sacramento and the Bay Area.
Dr. Johnson, Mallory PhD	Dr. Mallory Johnson is the UCSF study PI of record with respect to administrative management of the It Takes Two study grant award from NIH. He works in close collaboration with Drs. Gamarel and Sevelius.	Dr. Johnson, Professor in the UCSF Department of Medicine, is Co-Director of the NIH-funded Center for AIDS Prevention Studies (CAPS) and Director the the CAPS Developmental Core.

19.2 Affiliated Personnel:

Instructions:

This section is for personnel who are not listed in **Section 3.0: Grant Key Personnel Access to the Study** because their names were not found in the User Directory when both the iRIS Database and MyAccess directories were searched. Add any study personnel who fit ALL of the following criteria in the table below:

- They meet the definition of Key Study Personnel (see above), **and**
- They are associated with a UCSF-affiliated institution (e.g., VAMC, Gladstone, Institute on Aging, Vitalant, NCIRE, SFDPH, or ZSFG), **and**
- They do not have a UCSF ID, **and**
- They do not need access to the study application and other study materials in iRIS.

Note: Attach a **CITI Certificate** for all persons listed below in the **Other Study Documents** section of the **Initial Review Submission Packet Form** after completing the **Study Application**.

Click the orange question mark icon to the right for more information on who to include and who not to include in this section.

Do not list personnel from outside sites/non-UCSF-affiliated institutions. Contacts for those sites (i.e. other institution, community-based site, foreign country, or Sovereign Native American nation) should be listed in the **Outside Sites** section of the application.

If there are no personnel on your study that meet the above criteria, leave this section blank.

Name	Institution	Telephone	E-mail	Role
No External Personnel has been added to this IRB Study				

Please describe the study responsibilities and qualifications of each affiliated person listed above:

20.0 End of Study Application

End of Study Application Form

To continue working on the Study Application:
Click on the section you need to edit in the left-hand menu. Remember to save through the entire Study Application after making changes.

If you are done working on the Study Application:
Important: Before proceeding, please go back to Section 4.0 Initial Screening Questions and **Save and Continue** through the form to make sure all the relevant sections and questions have been included. If you've changed any answers since you started, the branching may have changed. Your application will be incomplete and it will have to be returned for corrections.

Once you are sure the form is complete, click **Save and Continue**. If this is a new study, you will automatically enter the **Initial Review Submission Packet Form**, where you can attach **consent forms** or other **study documents**. Review the **Initial Review Submission Checklist** for a list of required attachments.

Answer all questions and attach all required documents to speed up your approval.

The UCSF IRB welcomes feedback about the IRB Study Application Form. Please click the link to answer a **survey** about the application form.