STUDY PROTOCOL DRAFT: 2/10/2023

Formative and Pilot Intervention Research for Prevention and Treatment of HIV/AIDS (R34 Clinical Trial Option):

HIV Risk Reduction Intervention for Transwomen with Intimate Partner Victimization

Investigators:

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Sponsor:

National Institute of Health

1. Background

- Transgender women (TW) are among the populations most heavily affected by HIV in the United States (US), with nearly 1 in 5 TW living with HIV.
- IPV is a pervasive public health problem for transgender people. Results of the 2015 US Transgender Survey (USTS) indicated that over half (54%) of TW experience lifetime IPV, and comparative research shows elevated IPV rates among transgender people compared with their cisgender counterparts.
- IPV is associated with increased HIV risk due to greater likelihood of condomless sex, sex with high-risk partners (e.g., who are HIV-positive or who inject drugs), and compromised condom negotiation skills, as well as high rates of posttraumatic stress disorder (PTSD) and substance use disorder (SUD) which are also associated with HIV risk behaviors. Despite the dual and interconnected risks of HIV and IPV among TW, there are few empirically based HIV prevention interventions that target TW, and none that target HIV risks related to IPV in this population.
- To address syndemics of HIV and IPV, multicomponent interventions that target relevant risk factors and that consider population-specific vulnerabilities are needed.

2. Study Objective

The purpose of this treatment development research is to develop a brief intervention that concurrently targets HIV and IPV risk, as well as addresses inter-related risks of HIV and IPV (e.g., substance use and PTSD) for TW – referred to as Supporting Transwomen Affirmation, Relationships and Sex (STARS). STARS will:

- Be based on the Gender Affirmation Framework, which emphasizes interpersonal processes to positively affirm the identities and unique needs of TW.
- Integrate a trauma-informed empowerment approach.
- Include gender-affirming and empowering HIV prevention counseling that addresses HIV risk within the context of IPV and related risk factors (e.g., substance use and PTSD), and a range of HIV risk reduction options.
- Provide TW with behavioral skills and resources for addressing IPV and maximizing personal safety.

3. Study Aims

The aims of this treatment development research are to:

(1) Develop a behavioral intervention manual that addresses the specific and unique HIV prevention needs of TW with IPV, and that uses a gender-affirmative, empowering, and trauma-informed approach

(2) Evaluate the feasibility, acceptability, safety, and initial effects of STARS through three phases of intervention development.

We are primarily interested in exploring the pattern of results for any evidence of support for the intervention's influence on our primary and secondary outcomes.

Long-term aim: The findings from this R34 intervention development study will provide the groundwork to examine the efficacy of STARS in a future, large-scale clinical trial, which can be readily implemented in real-world settings.

4. Description of Study Design, Materials and Methods

4.1 Study Design

Phase 1, Initial Development: Employ qualitative methods to strengthen our understanding of the dynamics between HIV risk and IPV among TW, and use those findings to develop a STARS manual, interventionist training protocol, and fidelity scales.

Phase 2, Open Trial: Conduct an open pilot of the STARS protocol and use cognitive interviewing techniques to refine the STARS manual, interventionist training protocol, and fidelity scales, based on participant feedback.

Phase 3, Pilot RCT: Conduct a pilot test of the STARS protocol using a two-arm trial comparing effects of the STARS intervention vs Relaxation Training (a validated time and attention matched control) over 6-months of follow up with respect to our primary and secondary outcomes.

4.2 Study Procedures

Phase 1 (*Year 1 & 2, April 2021 – June 2022)*

General Overview

- Formative phase
- Development of STARS
- Focus group and informant interviews
- Feedback on STARS
- Fidelity
- Interventions training and fidelity

Participants/eligibility

- Individuals will be eligible if they are:
  (1) 18+ years old;
  (2) Assigned male at birth but identify as female, transgender, or transfeminine;
  (3) Endorse at least one IPV incident during the previous 12 months based on the Conflict Tactic Scales-Revised (CTS-2; Straus, 2017) or the trans-specific IPV Scale (T-IPV Scale; Peitzmeier et al, in press);
  (4) Report at least one instance of condomless anal sex in the last 3 months.
- Individuals will be considered ineligible if they:
  (1) Have been diagnosed with HIV or test positive for HIV.
- Individuals expressing interest in the research will undergo brief screening by telephone and then complete a more detailed in-person eligibility assessment prior to enrollment.
- All participants will provide informed consent prior to initiating the study protocol.

Recruitment & Retention

- All research activities will take place in Providence, Rhode Island metropolitan area
- Participant reimbursement:
  - Focus group participants will receive $30 reimbursement and a brochure with a list of TW-sensitive HIV testing sites and other social/health services upon completing the study.
  - Key informants will receive $30 upon completing the study.

- Multifaceted recruitment approach: online advertisements in social media for TW audiences, placing fliers in targeted venues, and conducting in-person outreach to agencies, clinics, bars and community events.
- Retention strategies: close communication and collaboration with CBOs that serve local TW and hiring an outreach specialist from within the local trans community.

Procedures
- Develop/design a preliminary manual for STARS and control (relaxation training; RT).
- Conduct focus groups and individual interviews (if applicable) with TW with HIV risk and IPV (n = 18) to understand ways of increasing acceptability and efficacy of STARS and acceptability of RT for this population.
- Designate specific benchmarks to determine if additional focus groups are needed to further develop STARS.
- Solicit feedback on STARS from participants, and community experts/key informants that provide services for TW.
- Solicit feedback from participants regarding barriers to attending sessions and brainstorm methods to address barriers and maximize attendance.
- Assess the acceptability and feasibility of booster sessions, including their number, length, timing, and setting (i.e., phone-calls vs. in person).
- Make changes to STARS based on feedback
- Develop STARS and RT interventionist training protocol and fidelity scales.

Analysis
- Focus groups and interviews (if applicable) will be audio-recorded, transcribed and coded using qualitative analysis.
- A descriptive summary will be developed to represent key content of the focus group.

Phase 2 (*Year 2, June – February 2023)*

General Overview
- Refinement phase: gain experience with the screening, assessment and intervention to inform subsequent refinement of protocol and procedures
- Cognitive interviewing and open pilot (nonrandomized)

Participants/eligibility
- Individuals will be eligible if they are:
  (1) 18+ years old;
  (2) Assigned male at birth but identify as female, transgender, or transfeminine;
  (3) Endorse at least one IPV incident during the previous 12 months based on the Conflict Tactic Scales-Revised (CTS-2; Straus, 2017) or the trans-specific IPV Scale (T-IPV Scale; Peitzmeier et al, in press);
  (4) Report at least one instance of condomless anal sex in the last 3 months.
- Individuals will be considered ineligible if they:
  (1) Have been diagnosed with HIV or test positive for HIV.
- Individuals expressing interest in the research will undergo brief screening online or by telephone and then complete a more detailed in-person eligibility assessment prior to enrollment.
- All participants will provide informed consent prior to initiating the study protocol.

Recruitment & Retention
- All research activities will take place online via Zoom and/or in Providence, Rhode Island metropolitan area

- Participant reimbursement: Participants will receive $75 for their first assessment and $50 for their second and third assessments as reimbursement ($175 total), as well as a brochure with a list of TW-sensitive HIV testing sites and other social/health services. All transportation required for the study will also be covered using study funds.
- Multifaceted recruitment approach: online advertisements in social media for TW audiences, placing fliers in targeted venues, and conducting in-person outreach to agencies, clinics, bars and community events.
- Retention strategies: close communication and collaboration with CBOs that serve local TW and hiring an outreach specialist from within the local trans community.

Procedures

- Pilot STARS among TW (*n*=5-8) with elevated HIV risk and IPV.
- Elicit feedback via exit interviews (structured informant interview and evaluation surveys) to finalize STARS protocol and research procedures.
- Refine and finalize STARS manual, interventionist training protocol, and fidelity scales using participant feedback and acceptability and feasibility metrics.

Analysis

- Detailed notes of IDI exit interviews will be analyzed (consider recording) to review feedback and make final adjustments
- At the end of phase 2, compute descriptive data on all target outcomes in Table 1 and discuss how actual outcomes compare to target outcomes.
- Discrepancies will result in: 1) investigation of the reason for failure to meet this outcome, and 2) discussion among the research team.

Table 1. Target Outcomes

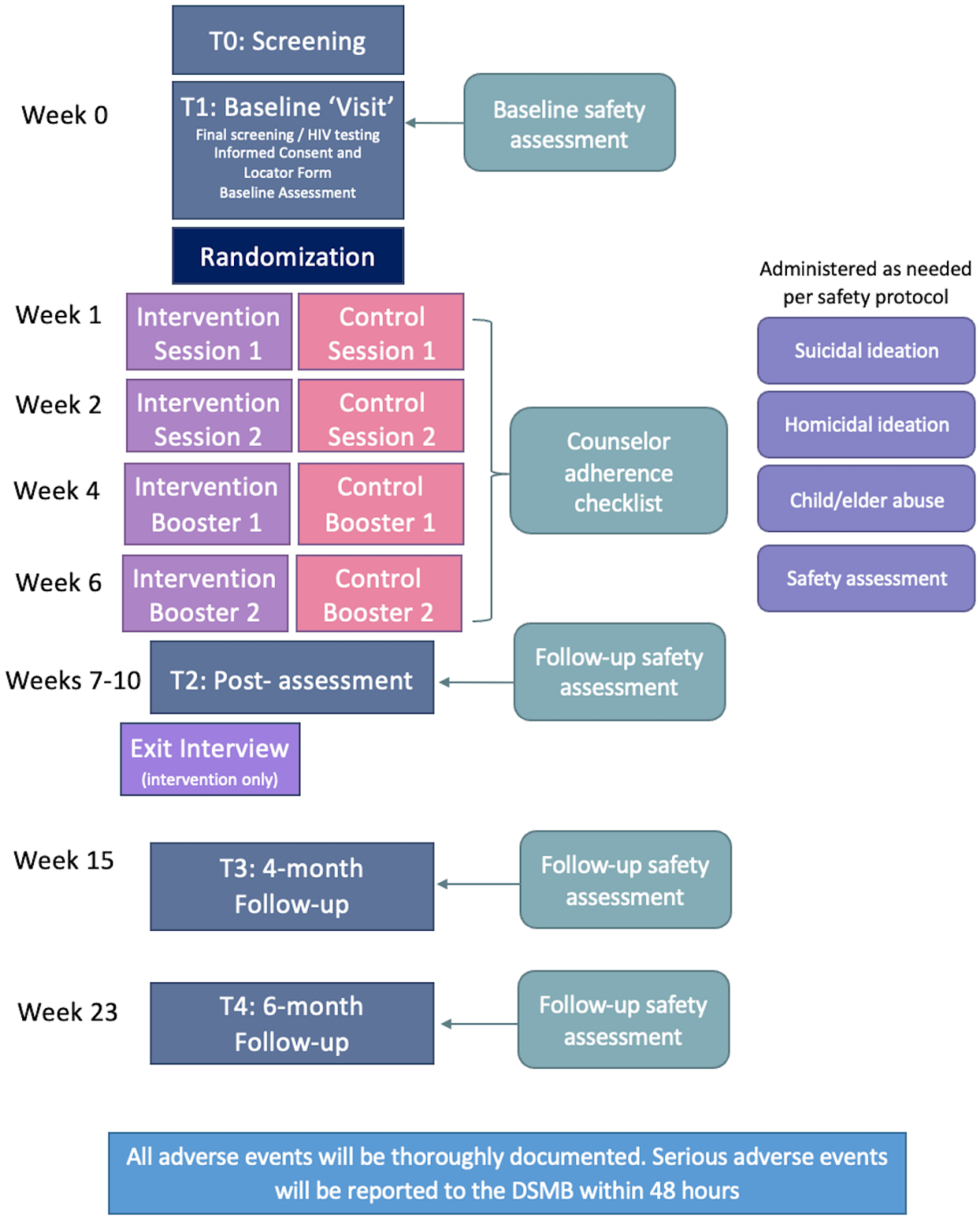
Description (Assessment method)	Target
Feasibility and Acceptability-- SAS, RT	
Acceptability (End of Intervention Survey; see C10.3)	Endorsing an average score of 3 or more (out of 5) for each rated intervention component).
Satisfaction (Client Satisfaction Questionnaire-8; see C10.3)	Average > 24 (or a mean score of 3 on each of the 8 items)
Intervention attendance	70% of all participants complete at the initial session and at least 2 of 3 booster sessions
Intervention Fidelity (see C8.4)	SAS and RT interventions achieve at least 80% adherence on a random subset of sessions
Safety	
Adverse events	No serious adverse events or injuries that are possibly, probably, or definitely related to study participation.
Feasibility and Acceptability—Research Procedures	
Recruitment rate	Average of 3-4 enrolled per month
STI testing procedures	80% of participants complete STI testing procedures at baseline and 70% at 6-month follow-up
Timeliness of assessments	80% of follow-up assessments occur within 3-weeks of due date
Completeness of self-report instruments and interviews	Self-report instruments have 80% of items completed and interviews 90% of items completed in 90% of cases
Retention rate	80% complete 3-mo and 70% complete 6-mo f/u assessments
Participant burden	Qualitative responses from exit interviews do not suggest undue burden of intervention or research procedures

Phase 3 *(Years 1-4, October 2021 – July 2024)*

General Overview

- Pilot RCT phase: two-arm, randomized, controlled design with up to 50 TW.
- Participants will be followed for up to 6-months post enrollment with assessments taking place at T1: Baseline; T2: Post-intervention; T3: 4-months follow up; and T4: 6-months follow up.
- Refer to Figure 1 below for the study flow
- The control group will be given an attention and time-matched control condition focused on relaxation and stress reduction.
- Both the STARS intervention and the control protocol consist of two one-hour sessions held one week apart and two brief 20-30 minute booster sessions held two- and four-weeks after the 2nd hour long session.
- Both interventions are designed to be delivered by peer counselors. Requirements for peer counselors include identifying as trans women or trans feminine and having leadership roles in the trans community.

Figure 1. STARS - Phase 3: Randomized Controlled Trial (RCT) Study Flow Chart



Participants/eligibility

- Individuals will be eligible if they are:

  (1) 18+ years old;

  (2) Assigned male at birth but identify as female, transgender, or transfeminine;

(3) Endorse at least one IPV incident during the previous 12 months based on the Conflict Tactic Scales-Revised (CTS-2; Straus, 2017) or the trans-specific IPV Scale (T-IPV Scale; Peitzmeier et al, in press);

(4) Report at least one instance of condomless anal sex in the last 6-months.

- Individuals will be considered ineligible if they:

  (1) Have been diagnosed with HIV or test positive for HIV.

- Individuals expressing interest in the research will undergo brief screening online or by telephone and then complete a more detailed in-person eligibility assessment prior to enrollment.
- All participants will provide informed consent prior to initiating the study protocol.

Recruitment

- All research activities will take place online via Zoom and/or in Providence, Rhode Island metropolitan area
- Multifaceted recruitment approach: online advertisements in social media for TW audiences, placing fliers in targeted venues, and conducting in-person outreach to agencies, clinics, bars and community events.
- Retention strategies: close communication and collaboration with CBOs that serve local TW and hiring an outreach specialist from within the local trans community.

Compensation

- Participant reimbursement: Participants will have an opportunity to earn up to $250 in total – they will receive $50 for completing the T1: baseline assessment; $50 for the T2: post-intervention assessment, $25 for the exit interview; $50 for the T3: 4-month follow up; $50 for the T4: 6-month assessment; and a $25 bonus if they complete all four assessments (T1-T4).
- Participants will be given the option to receive their compensation in the form of an Amazon gift card or on a VISA clincard.

Procedures

- Conduct a randomized pilot trial of STARS in 50 TW with elevated HIV risk and IPV to demonstrate the (a) feasibility, (b) acceptability, and (c) safety of the intervention.
- Examine preliminary evidence that relative to an attention and time matched control, STARS will result in improvements in our:
  - Primary outcomes;
  - Secondary outcomes; and
  - Mechanisms of change consistent with the theoretical foundations of the intervention, including greater perceived gender affirmation, and increases in empowerment and self-efficacy.
- Test, diagnose and (if positive) treat baseline STIs (and HIV) prior to initiating the STARS program. The research staff will work with participants to find gender-affirming health care clinics in their area that provide free or low-cost STI and HIV testing. Participants will be encouraged to

get tested for STIs as part of the research study; however, STI testing is not a requirement for participation.

- Complete a baseline behavioral and psychosocial baseline survey assessments administered via ACASI. Refer to the Phase 3 RCT Measures document for the complete list of standardized measures administered at baseline and at follow up.
- Upon completion of the baseline assessment, participants will be randomized to either the Intervention (STARS) condition or to a time-attention matched control (see details below).
    - **STARS Intervention** *(the final version of STARS was developed though an iterative process and refined/finalized by findings from Phases 1 and 2)*
        - Participants randomized to STARS will participate in a brief intervention immediately following the baseline (BL) assessment consisting of two one-hour sessions held one week apart and two brief 20-30 minute booster sessions held two- and four-weeks after the 2nd hour long session.
        - Participants will develop personalized risk reduction plan (RRP), which will include participants identifying "next steps" for reducing their HIV and IPV related risks.
        - Booster sessions will include a review of the RRP, identification and reinforcement of accomplishments, as well as identification of and problem solving around any social barriers to the RRP.
        - The RRP will be revised based on identified accomplishments and social barriers at each booster session.
    - **Control Intervention**
        - Participants randomized to the time-attention matched control condition will participate in a relaxation and stress reduction intervention that also consists of two one-hour sessions held one week apart and two brief 20-30 minute booster sessions held two- and four-weeks after the 2nd hour long session.
        - Content will serve to keep the RA blind to participant condition and will include a series of guided relaxations (e.g., breathing meditation, visual imagery).
        - During booster sessions, the interventionist will review participants' success with their relaxation plan and identify further strategies to integrate relaxation into daily lives.

<u>Analysis</u>

- At 2-time points during phase 3, compute descriptive data on all target outcomes in Table 1 and discuss how actual outcomes compare to target outcomes.

  Discrepancies will result in: 1) investigation of the reason for failure to meet this outcome, and 2) discussion among the research team.

4.3 Measures *(Phases 2 & 3)* -- For the complete list of standardized measures administered at baseline and at follow up time points, refer to the Phase 3 RCT Measures document.

Acceptability:

- 8-item Client Satisfaction Questionnaire-Revised (CSQ-8-R) (Attkisson & Zwick, 1982) will be used to assess satisfaction with the intervention.
- An End of Intervention Questionnaire (EIQ) will be developed that will assess the perceived helpfulness of intervention components.
- These scales will be administered to both conditions after the initial 90-min intervention (PI), as well as after each booster session.
- Exit interviews will be conducted with participants randomized to the STARS intervention.

Primary Outcomes:

(1) **Composite Risk for HIV (CR-HIV)** is a binary indicator of any HIV risk (e.g., yes=1 vs. no=0), which is an algorithm based on whether the participant:

- report condomless anal sex with a HIV serodiscordant or status-unknown primary or other partner in the past 3 months;
- is using PrEP;
- is in a monogamous partnership with an HIV-uninfected partner or an ;
- is in a monogamous partnership with an HIV-infected partner who is virally suppressed.
- If participants are not certain about the latter two indicators, they are coded as having HIV risk according to this algorithm.

(2) **IPV frequency** will be assessed with:

- The Composite Abuse Scale revised short form (CASr-SF).and
- A trans-specific IPV Scale (T-IPV Scale; Peitzmeier et al, in press) that assesses IPV unique to TW (e.g., being forced not pursuing aspects of gender transition that you wanted).

(3) **IPV safety** will be assessed with the:

- Measure Of Victim Empowerment Related to Safety (MOVERS; Goodman et al., 2015), which is a 13-item scale that measures IPV survivors' safety-related psychosocial skills and efficacy and expectations of support, as well as the extent to which survivors feel that their efforts to achieve safety might create new difficulties.

Secondary Outcomes:

- **Biologically determined STI diagnoses, including HIV** - The research staff will work with participants to find gender-affirming health care clinics in their area that provide free or low-cost STI and HIV testing. Participants will be encouraged to get tested for STIs as part of the research

study; however, STI testing is not a requirement for participation. HIV self-test kits will be mailed to willing participants and the research staff will walk participants through testing procedures as well as post-test result counseling (as needed) over Zoom or in-person.

- Self-reported discrete **behavioral risk indicators**: CAS, multiple and concurrent partnerships, partners' HIV status, monogamy and sexual agreements, substance use including injection drug use, HIV testing behaviors (including self-testing) and knowledge, intentions to use PrEP, PrEP uptake, use of any HIV prevention services, and use of any additional IPV-related services/resources.

Exploratory Tertiary Outcome/Potential Mediators: Refer to the Phase 3 RCT Measures document for the complete list of standardized measures administered at baseline and at follow up time points.

5. Dissemination

- Throughout the study, we will disseminate process reports and descriptive summaries of the findings to colleagues at social service and medical/health agencies with whom we established MOUs.
- As data are evaluated, we will prepare brief reports describing the major findings from the study which we will share with our community partners, HIV prevention and IPV scientists, and TW health and advocacy organizations through publications and presentations at professional conferences.