PRS Project Efficacy Criteria for Structural (SI) Evidence-Based Interventions (EBIs)

Intervention Description

- Clear description of key aspects of the intervention

Quality of Study Design*

- Prospective study design
- Appropriate and concurrent comparison arm (provided it is similar to intervention arm with respect to population, setting, and time frame, and identical with respect to follow-up interval, recall period, and outcome measures; or adjusted analysis)
- Random, minimally biased, or moderately biased allocation of participants to study arms, allowing for selection bias unrelated to the intervention or HIV risk. Assignment may be based on pre-established groups or selection into something other than the intervention, provided neither is directly related to HIV risk.
    - For a study that grouped units of assignment (e.g., individual, couple, personal network) into larger groups for delivery of the intervention, analysis should be adjusted for the potential cluster effect or intraclass correlation (ICC) among participants receiving the intervention together, unless there are only two groups, or studies report that the ICC was small enough (estimated to be <0.10) that adjustment was unnecessary.

Quality of Study Implementation and Data Analysis

- Follow-up assessment ≥ 3-months post completion of intervention for each study arm with recall not referring to pre-intervention period
    - Note: This criterion is not applicable for engagement in, linkage to, retention in, and re-engagement in care outcomes, HIV testing, antiretroviral treatment (ART) uptake, Pre-exposure prophylaxis (PrEP)-related outcomes, AIDS mortality
- Comparison between intervention arm and an appropriate comparison arm
- Analysis of participants in study arms as originally allocated regardless of contamination or logistic/implementation issues
    - Note: Data from contaminated participants may be excluded if numbers are small, but participants may not be re-assigned for analytic purposes
- Analysis of participants regardless of the level of intervention exposure
    - Note: Participants exposed to < 50% of the entire intended intervention may be excluded
- Use of appropriate cluster-level analyses if assigned to study arms by cluster or group
- Analysis must be based on post-intervention levels or on pre-post changes in measures between groups
    - Note: If pre-post changes are used in analysis, measures must be identical, including identical recall period
- Analysis is based on an $\alpha = .05$ (or more stringent) and a 2-sided test
- With nonrandomized assignment, either no statistical differences in baseline levels of the outcome exist or baseline differences are statistically controlled for in the analysis
    - If moderately biased assignment was used, differences in baseline demographics must be controlled for in the analysis.
- Analytic sample ≥ 40 participants per study arm

- Note: Studies that meet all evidence-based criteria with the exception of sample size (i.e., n ≥ 40 per arm), and have at least 25 participants per study arm will be considered as evidence-informed (see Structural Evidence-Informed [EI] criteria).

Strength of Evidence

Demonstrated Significant Positive Intervention Effects

- Positive and statistically significant ($p < .05$) intervention effect for ≥1 relevant outcome measure
- A positive intervention effect is defined as:
  - a greater reduction (or lower increase) in HIV/STD incidence, risk behaviors or HIV-related stigma;
  - a greater increase in HIV protective behaviors (including HIV testing, PrEP-related behaviors);
  - greater improvement in, or higher level of, a medication adherence-related behavioral or biologic outcome (including viral suppression);
  - a greater increase in ART or PrEP prescriptions by providers; or
  - greater improvement in engagement in, linkage to, retention in, engagement or re-engagement in HIV medical care in the intervention arm relative to the comparison arm
- A relevant outcome is defined as:
  - Sex risk behaviors (e.g., abstinence, mutual monogamy, number of sex partners, consistent condom use with anal/vaginal sex, condomless anal/vaginal sex, proportion of anal/vaginal sex acts protected, refusal to have unsafe sex) directly impacting HIV risk
  - Drug injection behaviors (e.g., frequency of injection drug use, needle sharing)
  - PrEP-related:
    - Screening for PrEP eligibility and referring to PrEP services: assessed HIV risk behavior to identify participants as eligible PrEP candidates and referred them to PrEP services (e.g., scheduled the first PrEP service appointment)
    - Linkage to PrEP care: a participant completed a healthcare visit that includes being prescribed PrEP
    - PrEP initiation/uptake: initiation of PrEP among PrEP-naïve participants or those who were not PrEP users as defined by study authors via self-report or medical or pharmacy records (e.g., filled a prescription for PrEP, started PrEP)
    - PrEP use: on PrEP (including lifetime, current use) based on self-report or medical or pharmacy records
    - PrEP medication adherence or persistence: taking PrEP on a regularly agreed to schedule (e.g., daily dose, on demand) measured by electronic data monitoring (e.g., Medication Event Monitoring System [MEMS] caps), pill count, pharmacy refill, self-reported adherence, or medical record
    - PrEP drug levels: based on assays that assess PrEP drug or drug metabolite levels in plasma, urine, hair, or dried blood spots
    - Retention in PrEP care: completed PrEP medical visit(s) over a period of time (e.g., attended one visit every 3 months for at least 6 months) that is self-reported or documented in medical records
    - PrEP at the system or community level (e.g., number of people on PrEP assessed at the healthcare system or community level)
  - ART or PrEP prescriptions (as outcomes of provider interventions only; self-reported by provider or documented in medical or pharmacy records)
  - HIV-related stigma
  - HIV testing (e.g., utilization of HIV C&T services, repeat testing, self-testing)
    - Note: HIV testing is a relevant outcome only if the study reports new HIV infections

- a medication adherence outcome measure that may include electronic data monitoring (e.g., MEMs caps), pill count, pharmacy refill, or self-reported adherence
- a biologic measure indicating HIV or STD (e.g., prevalence or incidence measures of hepatitis, HIV, or other STDs)
  - Note: Biologic measures of STD infections are relevant outcomes only as a proxy for HIV behavior
- HIV morbidity or AIDS mortality (includes biologic measures of HIV viral suppression or CD4 count)
- HIV medical care visit – measures of a completed outpatient primary HIV medical care visit or HIV viral load and/or CD4 count when used as proxies for a HIV medical care visit
  - For *engagement in care*, a relevant outcome is having one completed HIV medical visit
  - For *linkage to care*, a relevant outcome is the completed first HIV medical visit for newly diagnosed HIV-positive persons
  - For *retention in care*, a relevant outcome is having completed multiple HIV medical visits over a period of time
  - For *re-engagement in care*, a relevant outcome is the completed HIV medical visit for persons who were lost to or inconsistent in care
    - Note: Completed HIV medical visits must be documented in medical records, administrative or agency records, or surveillance reports
    - Note: Self-reports of completed medical visits validated by medical records; administrative or agency records are also acceptable

- In summary, the effect must be:
  - reported at the required follow-up
  - based on the quality of the study design
  - based on the study implementation and analysis

No Demonstrated Significant Negative Intervention Effects

- No negative and statistically significant ($p < .05$) intervention effect for any relevant outcome
  - A negative intervention effect is defined as:
    - a greater increase in HIV/STD incidence, risk behaviors or HIV-related stigma;
    - a greater decrease in HIV protective behaviors (including HIV testing, PrEP-related behaviors);
    - greater reduction in, or lower level of, a medication adherence-related behavioral or biologic outcome;
    - greater decrease in ART or PrEP prescriptions by providers; or
    - lower level of engagement in, linkage to, retention in, or re-engagement in HIV medical care in the intervention arm relative to the comparison arm

Additional Limitations to Evaluate

- No evidence that additional limitations resulted in a fatal flaw:
  - A fatal flaw has occurred when the overall evaluation of limitations indicates they resulted in considerable bias, thus substantially reducing the confidence of the findings.
  - Examples of item limitations to check for possible fatal flaw:
    - Effects only found within potentially biased subset analyses
    - Substantial missing data. Missing data plus loss to attrition exceeds acceptable limits for retention alone (≥ 40%)
      - Note: This criterion is not applicable for engagement in, linkage to, retention in, and re-engagement in care outcomes, HIV testing, antiretroviral treatment (ART) uptake, linkage

to PrEP care, retention in PrEP care, PrEP prescribing behavior, PrEP utilization, or AIDS mortality

- Study arm non-equivalence: statistically significant differences between arms in important baseline demographics or risk factors
- Differential retention: (1) significant difference between study arms in characteristics among retained or attrited participants; OR (2) more than minimal rate of differential retention (>10%)
    - Note: This criterion is not applicable for engagement in, linkage to, retention in, and re-engagement in care outcomes, HIV testing, ART uptake, linkage to PrEP care, retention in PrEP care, PrEP prescribing behavior, PrEP utilization, or AIDS mortality
- Intervention activities did not match with the intervention concepts or guiding theories intended to produce the desired outcomes
- Report does not clearly describe issues related to generalizability
- Too many post hoc analyses (even with Bonferroni corrections)
- Inconsistent findings between effects

*Additional study designs (e.g., before/after study design) will be evaluated as Structural Evidence-Informed Interventions (EIs).

All criteria must be satisfied for an intervention to be considered a Structural EBI.

Adapted from: Lyles et al., (2006), Lyles et al., (2007), Higa et al., (2016), Sipe et al., (2017).