PRS Efficacy Criteria for Pre-Exposure Prophylaxis (PrEP) Evidence-Based Interventions (EBIs)

Intervention Description

- Clear description of key aspects of the intervention

Quality of Study Design*

- 2 or more study arms
- 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 reports adjusted analysis)
- Random allocation or the use of methods that allocate participants to study arms and do not cause substantial concern. These methods allow 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 arranged 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 larger 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 initiation of intervention for each study arm for patient-level study
    - at least one post intervention follow-up assessment (no specific follow-up or recall period) for healthcare provider-level or system-level study
- At least a 60% retention rate at a single follow-up assessment in each study arm for screening for PrEP eligibility and referring to PrEP services, PrEP initiation/uptake, PrEP use, PrEP medication adherence or persistence, PrEP drug levels, or HIV incidence
- Comparison between an intervention arm(s) and an appropriate comparison arm(s)
- Analysis of participants in study arms as originally allocated (i.e., participants may not be re-assigned for analytic purposes)
- Data from contamination of participants (e.g., control participants receive intervention) may be excluded if these numbers are small
- Analysis of participants regardless of the level of intervention exposure

  Note: Participants exposed to < 50% of the entire intended intervention may be excluded.
- If participants are excluded due to contamination or low exposure to the intervention, retention rate must acknowledge the exclusion of these participants at each assessment
- Use of appropriate cluster-level analyses if assigned to study arms by cluster or group

- Analysis must be based on follow-up levels or on pre-post changes in measures between study arms
  Note: If pre-post changes are used in analysis, measures must be identical, including identical recall period.
- Analysis is based on a p-value of < 0.05 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
- Baseline 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 at baseline will be considered as evidence-informed interventions (see PrEP Evidence-Informed criteria)

Strength of Evidence

Demonstrated Significant Positive Intervention Effects

- Statistically significant (p < 0.05) positive intervention effect for ≥ 1 relevant outcome measure in the intervention arm relative to the comparison arm
  - A positive intervention effect is defined as an improvement in relevant PrEP-related behavioral or biologic outcomes in an intervention arm relative to a comparison arm
  - Relevant PrEP-related behavioral or biological outcomes include:

PrEP Patient-Level

- Screening for PrEP eligibility and referring to PrEP services: assessed HIV risk behavior to identify a participant as an eligible PrEP candidate and referred them to PrEP services (e.g., scheduled the first PrEP service appointment)
- Linkage to PrEP care: a participant completed 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 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
- HIV incidence: HIV infections that are self-reported or documented in medical records

PrEP Healthcare Provider- or System-Level

- PrEP prescribing behavior: self-reported by provider or documented in medical or pharmacy records

        - PrEP utilization among health care systems and communities: number of people on PrEP assessed at the healthcare system or community level

No Demonstrated Significant Negative Intervention Effects

- No negative and statistically significant ($p < 0.05$) intervention effects for any PrEP-relevant outcome in the intervention arm relative to the comparison arm.
    - A negative intervention effect is defined as the intervention arm showing:
        - Greater reduction in, or lower level of, PrEP initiation/uptake, PrEP use, PrEP medication adherence or persistence or PrEP drug levels
        - Lower level of screening for PrEP and referring to PrEP services, linkage to PrEP care, retention in PrEP care
        - Greater increase in HIV incidence
        - Lower proportion of PrEP prescribing behavior
        - Lower proportion of people on PrEP assessed at the healthcare system or community level

Additional Limitations to Evaluate

- No evidence that additional limitations resulted in considerable bias that reduces the confidence of the findings
    - Examples of limitations:
        - Too many post-hoc analyses
        - Inconsistent evidence between effects
        - Inappropriate subset analyses
        - Not accounting for various reasons why participants were not included in the PrEP outcome
        - Not adjusting for cluster effects for studies that allocated individuals to a group-level intervention
        - Not accounting for factors that may influence findings (e.g., historical events)
        - Other notable biases threatening internal or external validity

*Additional study designs (e.g., before/after study design) will be evaluated with evidence-informed criteria for PrEP.

All criteria must be satisfied for an intervention to be considered a PrEP Evidence-Based Intervention (EBI).