THE OPENS TRIAL OFFERING WOMEN PREP WITH EDUCATION, SHARED DECISION-MAKING, AND TRAUMA-INFORMED CARE

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Statistical Analysis Plan

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Offering Women PrEP with Education and Shared Decision-making

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LIST OF ABBREVIATIONS

Abbreviations	**Definitions**
AE	Adverse Events
DCS	Decisional Conflict Scale
DST	Decisional Support Tool
EMR	Electronic medical record
HIV	Human Immunodeficiency Virus
ITT	Intention-to-treat
MRN	Medical record number
PP	Per protocol
PrEP	Pre-exposure prophylaxis

1. Study overview

To address the significant barriers to PrEP implementation for those who were assigned female at birth and self-identify as a woman and address racial inequities in HIV prevention in the United States (US), a novel approach that accounts for multilevel influences is necessary. This study is one part of a multi-component project and involves a patient-level intervention in one public health family planning clinic in Duval County Florida, where the majority of patients are women of color. The area has one of the highest HIV incidence rates among women in the US. The investigators developed a tablet-based decision support tool that helps users learn about HIV vulnerabilities and HIV prevention strategies to inform how they consider options for reducing their likelihood of acquiring HIV. Participants will be randomized to use the HIV decision support tool before their visit or standard counseling (without the use of the tool) and will be surveyed about the use of the tool, experiences with HIV prevention counseling, and intentions about the use of HIV prevention. A subset of participants, all individuals who self-identify as a woman and as Black or Latina, will also complete a post-clinic visit interview. The investigators will follow-up with participants at three months following their initial visit to see if they have initiated the HIV prevention method(s) they chose at their visit. The main outcomes will include a quantitative and qualitative assessment of PrEP or other HIV prevention use, decisional certainty, and satisfaction with information about HIV prevention options.

1.1 Study objectives

Aim 1a: Women who use the HIV prevention decision support tool will be more likely to have initiated PrEP within 3 months compared to women who received standard counseling at the time of their initial appointment.

Aim 1b: The HIV prevention decision support tool will increase women's knowledge of PrEP and other HIV prevention methods compared to women who received standard counseling at the time of their initial appointment.

Aim 1c: The HIV prevention decision support tool will increase participants' decisional certainty in their choice of an HIV prevention method compared to women who received standard counseling at the time of their initial appointment.

1.2 Study Design and Randomization

The study is a parallel-group Randomized Control Trial with up to 384 participants recruited from family planning sites in Duval County, Florida and randomized 1:1 into two groups (192 in intervention group, 192 in control). Study duration: 3 months.

Treatment: Participants in this arm will receive the HIV prevention DST intervention and will receive the intervention immediately before their provider visit.

Control: Participants in this arm will receive usual care.

Randomization procedures: Randomization will be implemented using randomly permuted blocks of randomly selected size 2 and 4, stratified by clinic and race. All randomization will occur by research staff with the use of a REDCap randomization instrument.

1.3 Study Population

Inclusion Criteria:

- Identify as a woman
- Age 18 years old to 45
- Not known to be living with HIV
- Not known to be taking PrEP
- English speaking
- Interested in participating in the study

Exclusion Criteria:

- Unable to consent
- Currently using PrEP
- Cisgender men
- Unwilling to be contacted in 3 months
- Already participated in the study

1.4 Intervention

HIV Prevention Decision Support Tool (DST): The tool is founded on principles of decision-science and developed in a systematic manner including pilot testing. The tool will present HIV prevention information through a tablet in the clinical setting. The decision support tool will address barriers to PrEP delivery, including 1) limited client knowledge about PrEP, 2) limited time to educate patients in busy clinics, 3) women's lack of knowledge of their own HIV vulnerability, and 4) hesitancy of women to initiate discussions about PrEP with providers due to judgmental attitudes and stigma. Also, the tool emphasizes the highly variable and individual nature of baseline risk.

1.5 Sample size calculation

Using standard methods, we estimate that a sample of 320 women will provide 80% power in two-sided tests with alpha of 0.05 to detect a between-group difference of 10 percentage points in PrEP uptake, from 5% among controls to 15% in the intervention arm. This estimate is conservative, for two reasons. First, in addition to multiple imputation, which will capture some information from women with missing 3-month outcomes, we will enroll 384 women to protect against a loss to follow-up of up to 20%. Second, because women rather than providers will be randomized, any within-provider clustering of outcomes will increase precision in the proposed mixed models including random effects for provider.

1.6 Study Procedures

Both groups will complete surveys at three measurement timelines: baseline (t_0), immediately post-appointment (t_1), and at 3-months (t_2). Data collection will occur via electronic survey hosted on RedCAP. Neither the participants nor the study team will be blinded.

Research assistants will approach eligible patients in the clinic waiting room prior to their appointments. They will assess eligible and complete consent procedures in private location on site. Participants will then complete a baseline questionnaire on a tablet. After completion of initial questionnaire, participant will be randomized to a treatment using a randomization module in RedCAP. Participants randomized to the intervention group will then immediately receive access to the DST via a tablet provided by the research assistant to review in advance of their clinical visit.

After the participant's visit with the provider, they will be asked to complete a post-visit survey about their clinic visit and counseling, risk perception, decision making, sexual history, and their experience with the decision support tool if they are in the intervention arm.

Three months post-visit, research staff will follow-up with participants by phone, email, or SMS to administer a short survey and ask participants about their chosen HIV prevention method, and if they initiated PrEP.

Upon completion of the study, research staff will extract data from the medical record pertaining to participants' PrEP prescriptions, history of sexually transmitted infections, zip code, and insurance status.

2. Population of analysis

We will conduct an intention to teat (ITT) analysis as well as a per protocol (PP) analysis. ITT will serve as our primary analysis. For PP analyses, individuals in the intervention group will be considered members of the control group if they did not receive or did not interact with the DST for even one minute.

2.1 VARIABLES

2.1.1 Background and demographic characteristics

Demography and baseline characteristics will be statistically summarized by treatment group.

Demographic variables include age, gender, race and ethnicity, income, parental income, educational attainment, housing status and language spoken at home.

Baseline behavioral variables include variables related to potential HIV exposure, including: sexual and drug use behaviors, past diagnoses of sexually-transmitted-infections, as well as reproductive behaviors including: pregnancy status and desire, contraceptive use.

2.1.2 Outcomes

2.1.2.1 Primary outcome variables

- **PrEP prescriptions:** The number of participants who received a PrEP prescription and date of prescription, obtained by chart extraction from the medical record.

2.1.2.2 Secondary variables

- **Number of Patients Reporting PrEP use:** Participants will be contacted at follow-up and asked if took PrEP in the past 3 months regardless of where it was obtained.

- **Patient-Perceived HIV risk:** Participants will be asked about how worried they are about getting HIV in the next 6 months.
- **Knowledge of PrEP:** Participants will be asked a series of questions about PrEP to assess PrEP knowledge.
- **Decisional Conflict:** Participants will be asked questions derived from the Decisional Conflict Scale to provide a measure of decision quality about their HIV prevention decision immediately following their visit.
- **Interpersonal Quality of HIV Prevention Care:** A scale for patient-centered HIV prevention counseling focusing on patient preferences and reflecting satisfaction and confidence in the counseling session, derived from the Interpersonal Quality of Family Planning Care Scale developed by the PI.
- **Intention to Use Any HIV Prevention Method:** Participants will be asked if they plan to use any HIV prevention method after the initial visit.
- **Satisfaction with Information Received about HIV Prevention:** Participants will be asked about their satisfaction with HIV prevention counseling.
- Confidence in decision to use an HIV prevention method. A one-time, one-item measure of certainty of plan to use HIV prevention after the initial visit. Participants can select from 4 options: 1 ("completely unsure"), 2 ("mostly unsure"), 3 ("mostly sure, but not 100%"), or 4 ("100% sure").
- **Perceived Quality of Information Received about HIV Prevention:** Participants will also be asked questions about the perceived quality of the HIV prevention information they received during their health care visit.
- **Acceptability of HIV Prevention Methods:** Participants will be asked to rate their preference for a method (even if they never used it). Participants can select from condoms, PrEP, PEP, treatment as prevention, regular partner testing, or other method.
- **Acceptability of the Decision Support Tool:** Participants in the experimental arm are asked four questions about their experiences using the DST.
- Perception of the Decision Support Tool: Participants in the experimental arm will be asked about the degree to which they liked/disliked the tool. Response options vary: "I did not like it at all", "I somewhat disliked it", "I somewhat liked it", "I really liked it".
- Willingness to Use the Decision Support Tool at Future Visits: Participants in the experimental arm will be asked about whether they would use the tool again if they returned to the clinic. Response options are "yes", "no", "unsure".
- Recommend the Decision Support Tool: Participants in the experimental arm will be asked whether they would recommend the tool a friend. Response options are "yes", "no", "unsure".
- Satisfaction with the Decision Support Tool: Participants in the experimental arm will be asked about the degree to which they were satisfied with the information in the tool. Response options vary from 1-5: "very unsatisfied" to "very satisfied".
- HIV Prevention Method Use (any method – planned or new method): A self-reported measure of HIV prevention method use, including those who reported discontinuing the initial HIV prevention method(s) that were reported post-clinic visit. A response of "yes" to any of the following questions: since your [baseline] visit, have you used….for HIV prevention – abstinence, condoms, PEP, PrEP, regular HIV testing, treatment as prevention, regular sexually transmitted disease (STD) testing, other method. The outcome will be dichotomized to those who responded affirmatively vs other responses ("no"/"unsure").
- **HIV Prevention Method Continuation:** A self-reported measure of HIV prevention method continuation.

- **HIV Prevention Method Use:** A self-reported measure of HIV prevention method use, including those who reported discontinuing the initial HIV prevention method(s) that were reported post-clinic visit.

2.1.3 Other metrics

- Percentage of missing answers in questionnaires
- Response times per questionnaire

2.2 Hypotheses

1. The intervention will result in significantly higher number of PrEP prescriptions compared to the control group.
2. The intervention will result in significantly higher number of individuals reporting PrEP initiation compared to the control group.
3. The intervention will result in significantly higher level of patient-perceived HIV risk post-visit compared to the control group.
4. The intervention group will report significantly higher PrEP knowledge compared to the control group.
5. The intervention group will report significantly higher quality of HIV care compared to the control group.
6. The intervention group will report significantly higher intention to initiate any HIV prevention method compared to the control group.
7. The intervention group will report significantly higher satisfaction with information received about HIV prevention compared to the control group.
8. The intervention group will report significantly higher confidence in decision to use an HIV prevention method compared to the control group.
9. The intervention group will report significantly higher acceptability of HIV prevention methods compared to the control group.
10. The intervention group will report significantly lower decisional conflict, as documented by the full scale and subscales, compared to the control group.
11. The intervention will result in significantly higher number of individuals reporting ongoing PrEP use at 3 months post-visit compared to the control group.
12. A significantly higher proportion of the intervention group will report use of any HIV prevention method at 3 months-post study initiation compared to the control group.
13. A significantly higher proportion of the intervention group will report significantly higher continuation of any HIV prevention method at 3 months-post study initiation compared to the control group.
14. The intervention group will report high acceptability of the DST.
15. A high proportion of the intervention group will report positive impression of the DST.
16. A high proportion of the intervention group will report willingness to use the DST at a future visit.
17. A high proportion of the intervention group will report willingness to recommend to a friend.
18. The intervention group will report high satisfaction with the DST.

1. STATISTICAL METHODOLGY

3.1 General methodology

All outcomes will be presented using descriptive statistics; normally distributed data by the mean and standard deviation (SD) and skewed distributions by the median and interquartile range (IQR). Demography and baseline characteristics will be statistically summarized by treatment group. For binary or categorical items, counts and proportions will be calculated and reported. For continuous outcomes, we will use t-tests for independent samples and for categorical outcome we will employ χ 2 or Fisher's exact-tests to examine baseline differences between training and control group in demographic data or measured variables. Categorical variables will be assessed and collapsed in cases of small cell sizes for increased power. Scale items of questionnaires (e.g., Decisional Conflict Scale) will be recoded (where applicable) and a scale mean or sum score will be calculated and reported. Composite scale variables will be assessed for skewness through histograms and normal Q-Q plots. Where the normality assumption is not met, median and IQR will be reported. Sign tests will be used to detect differences between groups. Further, in instances where a strong skew is detected, scales will be transformed into binary variables and analyzed as binary data.

3.2 Subject disposition

The number and proportion of screened, randomized, treated and analyzed subjects will be provided. Where necessary, the CONSORT flow chart will be presented to describe the subject disposition in the statistical analysis report.

3.3 Primary and secondary data analyses

In primary and secondary data analyses, all stated hypotheses will be tested. In all analyses an error probability of α = .05 will be set a priori for descriptive statistics calculations. In addition to statistical significance, effect sizes (e.g., Cohen's d) will be reported. Publication of results will follow CONSORT guidelines for transparent reporting of randomized trials.

3.3.1 Primary analysis (H1)

PrEP prescriptions within 3 months of primary study visit will be extracted from participants' electronic medical records (EMRs). Data will be matched to survey data using participant medical record numbers (MRNs). Summary statistics will be presented by treatment group. Differences in PrEP prescriptions between groups will be examined by χ 2 or Fisher's exact-tests as appropriate. Effect size will be calculated.

3.3.2 Secondary data analyses

The analysis plan for H2-H9 is as follows:

Summary statistics will be presented by treatment group. Differences between study groups at t_1 will be assessed through $\chi 2$ or Fisher's exact tests as appropriate. Cohen's d will be calculated as measure for effect size.

The analysis plan for H10 is as follows:

Full scale and subscales will scored as instructed in the Decisional Conflict Scale manual. Summary statistics will be presented by treatment group for the full scale and by subscale. To assess differences in scale score distribution between groups, we will perform t-tests or sign tests as appropriate. In case of high positive skew (as common in the literature) we will create binary variables demarcating no conflict versus any conflict and perform $\chi 2$ tests. Cohen's d will be calculated as measure for effect size.

The analysis plan for H11-H13 is as follows:

Summary statistics will be presented by treatment group. Differences between study groups at t_2 will be assessed through $\chi 2$ or Fisher's exact tests as appropriate. Cohen's d will be calculated as measure for effect size.

The analysis plan for H14-H18 is as follows:

Summary statistics will be presented for the intervention group.

3.4 Safety analysis

3.4.1 Analysis of adverse events (AEs)

The number and percentage of subjects who had at least one serious adverse event, classification of serious adverse event, adverse events of special interest and classification of adverse events of special interest from study will be provided.

4. DATA PROCESSING CONVENTIONS

4.1 Definition of baseline

In this study, baseline values are defined as those data collected before intervention (screening visit).

4.2 Missing data

We will report proportions of missing values for all collected variables where needed. Baseline characteristics missing data will be imputed by multiple imputation with chained equations (MICE) procedures as appropriate.

4.3 Statistical analysis software

All statistical analysis and summary will be carried out using Stata version 16.1 or higher.