COVER PAGE

Official Study Title: Feasibility of Positive Links for Youth Care Engagement Intervention

NCT number: NCT05689515

IRB Approval Date: 01.03.2024

Unique Protocol ID: HSC20220752H

Form CT
UTHSA Clinical Trial Description

This form is not mandatory. Other documents are acceptable if equivalent information is provided.

UTHSCSA Tracking Number *(internal use only)*	22-752H	**1. Original Version Date**	06MAY2019
		1.1. Revision Date(s) *add rows as needed*	03JAN2024

Title: Feasibility of Positive Links for Youth Care Engagement Intervention

2. Background

Briefly discuss the important literature relevant to the trial and that provides background for the trial. Include the importance of the trial and any relevant treatment issues or controversies.

Innovative interventions are needed to increase care engagement and virologic suppression in youth and emerging adults living with HIV (YLWH). Youth living with HIV are less likely to engage in care than any other age group, and have specific developmental needs and face unique socio/structural challenges. Among youth who were diagnosed with HIV in 2012 or earlier, only 55% were retained in HIV care, and 44% had a suppressed viral load. Virologic suppression in YLWH was 17% in 2018 the South Texas Ryan White Program, and as low as 6% in some cohorts. Data also show that, though YLWH may achieve virologic suppression in sites with optimal support for this population, sustained virologic suppression is uncommon. Clearly, current strategies to achieve care engagement for YLWH are insufficient and ineffective. Surveillance data for Texas shows that 20–29-year-olds have the highest rates of new diagnoses and Latinx individuals are both the majority of new diagnoses (43%) and new AIDS diagnoses (40%) demonstrating an overwhelming burden of disease. Intervention is urgently needed to increase engagement in care in young MSM, particularly minority MSM in the South. Mobile health interventions offer novel opportunities for engagement of YLWH, but knowledge gaps prevent effective deployment.

3. Objectives and Endpoints *All data points collected in the study should support an objective or have a regulatory purpose.*
Complete the table – add rows as needed.

3.1. Objective(s) *Clearly and concisely define the primary and secondary outcomes.*	**3.2. Endpoint** *Clearly define the endpoints. (endpoints are the basis for concluding that the objective has been met).*	**3.3. Justification for Endpoint** *Briefly explain why the endpoint(s) were chosen.*
Assess feasibility and usability of mHealth intervention, Positive Links for Youth (PL4Y) in 18-29yos living with HIV in South Texas.	Survey of feasibility and usability of the PL4Y intervention at 12 months (final endpoint). As this is a pilot study, we are concerned with the feasibility of usage of the mHealth intervention. This objective will be met if at least 35 of the 40 intervention arm participants complete the survey.	As this is a pilot study, our primary goal is to assess feasibility and usability of this new intervention. With these data, we can modify the intervention in preparation for a scale up to a larger RCT.
Assess the impact of an adapted version of an existing mHealth intervention for care engagement, Positive Links for Youth (PL4Y) among YLWH receiving care in South Texas.	We will assess HIV-1 plasma RNA viral load for all participants at 12 months. The primary outcome of the study is virologic suppression to <200 copies/mL at 12 months. This will give us an adequate amount of data to see medium scale differences in the study arms.	Virologic suppression is the primary goal of HIV treatment. Virologic failure is defined as a measurement over 200 copies per mL by the Department of Health and Human Services, and is the primary determinant of successful HIV control.

4. Rationale

Briefly state the reason for conducting the clinical trial.

In observational studies, Positive Links (PL) has shown success in increasing engagement in care and virologic suppression at 12 months in the adult population of a moderately sized publicly-funded HIV clinic. PL's impact has not been studied when compared with usual care, and its appropriateness for YLWH or majority Latinx populations is unknown. YLWH have unique developmental needs as they navigate shifting roles with family and peers and adopt adult roles and responsibilities. and face social and structural challenges. However, youth are uniquely receptive to mHealth interventions and often prefer online or text-based messaging to in person discussions or phone calls. To successfully conduct a fully powered randomized controlled trial of PL4Y in YLWH, a pilot study must address preliminary feasibility and efficacy of the intervention and the logistical aspects of implementing an mHealth study in this setting. A pilot RCT will focus on optimization of the environment for a larger RCT, including adapting recruitment strategies to focus YWLH, putting PL4Y into operation, and integrating study processes into existing clinic practice. Despite compelling qualitative and observational data on the impact of PL on HIV outcomes in adults in Virginia, PL has not been studied in youth or in an RCT.

5. Study Design

5.1. Number of Groups/Arms	2	**Group name(s)**	Intervention, Control

5.2. Overall Design
Select all applicable

☒	**Randomization**	☐	**Cluster Randomized**				
☐	**Group-Sequential**	☐	**Adaptive Design**				
☐	**Parallel Design**	☐	**Placebo-Controlled**				
☐	**Superiority**	☐	**Equivalence**	☐	**Non-inferiority**		
Device	☐ Pilot	☐	Pivotal	☐	Post-Approval		
Drug/Biologic	☐ Phase 1	☐ Phase 1/2	☐ Phase 2	☐ Phase 2/3	☐ Phase 3	☐ Phase 4	
☐	**Dose escalation**	*If yes, details →*					
☐	**Dose ranging**	*If yes, details →*					
☐	**Sub-studies**	*If yes, details →*					

5.3. Other Design Details:
Participants will be randomized in a 2:1 ratio to intervention (PL4Y use) or standard of care. Follow up is 12 months.

6. Study Population

6.1. Study Population(s) Label/Name *To add more populations – select a row, copy & paste*	**6.2. Identify the criteria for inclusion** *The criteria that every potential participant must satisfy, to qualify for study entry.* All individuals in this study population must meet all of the inclusion criteria in order to be eligible to participate in the study	**6.3. Identify the criteria for exclusion** *The characteristics that make an individual ineligible for study participation.* All individuals in this study population meeting any of the exclusion criteria at baseline will be excluded from study participation.
YLWH – Youth Living with HIV	To enroll, individuals must (a) have confirmed HIV infection; (b) be 18-29 years old; (c) have a recent diagnosis of HIV (within past 6 months) or be virologically unsuppressed (>1000 copies/ml) or disengaged from HIV care (<2 visits/last 12 months >90 days apart).	Participants meet exclusion criteria if they (a) cannot consent; (b) are unwilling to come to visits; or (c) are unwilling to be in San Antonio for a year.
Study subpopulation- exit interview participants (App/intervention arm only)	6-10 participants in the App arm will be selected using stratified sampling for demographic and app engagement diversity. These individuals must be 1) in the App/intervention group and 2) willing to	Same as above.

	participate in an additional 30–60-minute interview.	

6.4. Will screen failures be allowed to re-screen at a later date?	☐	**No**	☒	**Yes**	*If yes, describe criteria below ↓*
A participant may be allowed to re-screen at a later date if there are changes in their living situation and they decide to stay in San Antonio, changes in their mental status, or other circumstances which would otherwise alter the original decision to fall under exclusion criteria.					

7. Study Intervention(s) being tested or evaluated

This can include prevention, diagnostic or therapeutic interventions (e.g., drug or device) or educational, health services or basic science interventions (e.g., educational program, health care delivery model, or examining basic physiology)

Mobile health app to increase rates of engagement in HIV care in YLWH.

8. Protocol-Directed procedures, items, services or tests

List all procedures directed by the study plan - including items or services provided as part of routine or conventional care and those needed to diagnosis or treat research related complications.

Important Note – The protocol directed procedures listed must match those in the Schedule of Activities (attachment)

8.1. Drugs *(trade and generic, dosage, route of administration)*

N/A

8.2. Devices

N/A

8.3. Biologics

8.4. Laboratory Tests

HIV Viral Load testing (only if not already available in past 60 days as a part of routine care)

8.5. Imaging Procedures

N/A

8.6. Other Research Procedures *(e.g., other safety and efficacy assessments.)*

Questionnaires at study visits, monitoring engagement with the App, exit interview (only for a subset of participants in intervention arm) etc

A four-question survey will be administered to all participants at the end of the study through a REDCap survey. This will allow our participants to share their thoughts about the study.

8.7 Attach a Schedule of Activities (SOA) Excel File [Download the Template here: *Schedule of Activities]*	*Check to indicate that the SOA Excel File is attached →* ☒

9.	**Preparation/Handling/ Storage/Accountability of Investigational Drug, Biologic, or Device**
☒	*N/A - This study does not include any investigational products (e.g. drugs, devices or biologics)*
☐	*N/A - An Investigator Brochure is attached*
☐	*N/A - A Drug/Device Manual is attached*

9.1. Acquisition and accountability

State how the study intervention and control product will be provided to the investigator. Describe plans about how and by whom the study intervention will be distributed, including participation of a drug repository or pharmacy, and plans for disposal of expired or return of unused product.

9.2. Formulation, Appearance, Packaging, and Labeling

Describe the formulation, appearance, packaging, and labeling of the study intervention and control product, as supplied. Information in this section can usually be obtained from the IB or the package insert, or device labeling. This section should include the name of the manufacturer of the study intervention and control product.

9.3. Product Storage and Stability

Describe storage and stability requirements (e.g., protection from light, temperature, humidity) for the study intervention and control product. For studies in which multi-dose vials are utilized, provide additional information regarding stability and expiration time after initial use (e.g., the seal is broken).

9.4. Preparation

Describe the preparation of the study intervention and control product, including any preparation required by study staff and/or study participants. Include thawing, diluting, mixing, and reconstitution/preparation instructions in this section. For devices, include any relevant assembly or use instructions.

10. Study Intervention Additional Details

10.1. Measures to Minimize Bias: Randomization and Blinding

This section should contain a description of randomization and blinding procedures (if applicable to the study design). It should include a description or a table that describes how study participants will be assigned to study groups, without being so specific that blinding or randomization might be compromised. Plans for the maintenance of trial randomization codes and appropriate blinding for the study should be discussed. The timing and procedures for planned and unplanned breaking of randomization codes should be included. Include a statement regarding when unblinding may occur and who may unblind. Provide the criteria for breaking the study blind or participant code. Discuss the circumstances in which the blind would be broken for an individual or for all participants (e.g., for serious adverse evets (SAEs)). Indicate to whom the intentional and unintentional breaking of the blind should be reported.

After completing enrollment and informed consent, participants will be randomly assigned to PL4Y in a 2:1 fashion (intervention: control) with a target enrollment of 40 receiving the intervention and 20 in the control arm for a total of 60 participants. There is no blinding in this study protocol.

10.2. Study Intervention Compliance

Define how adherence to the protocol (e.g., administration of study intervention, use of device,) will be assessed, and verified (if applicable, e.g., plasma assays, electronic monitoring devices, daily diaries).

PL4Y App paradata will be used to assess engagement with the intervention for the intervention arm.

10.3. Permitted Concomitant Therapy

This section should be consistent with the medication restrictions in the inclusion/exclusion criteria previously listed. Describe how allowed concomitant therapy might affect the outcome (e.g., drug-drug interaction, direct effects on the study endpoints).

N/A, no exclusions for concomitant therapy

10.4. Rescue Medicine

List all medications, treatments, and/or procedures that may be provided during the study for "rescue therapy" and relevant instructions.

☒ *N/A, no rescue medicine, this is a behavioral intervention*

11. Study Intervention Discontinuation

11.1. Discontinuation of Study Intervention

Describe the criteria for discontinuing the study intervention (e.g., halting rules), including any monitoring test(s) and associated clinical decision point(s). Include reasons for temporary discontinuation of the study intervention (e.g., type and quantity of adverse events), clearly stating the length of time, if applicable, and describe the data to be collected at the time of study intervention discontinuation and approaches for restarting administration of or re-challenging with study intervention.

If any participant ceases to make use of the App, the study team would still like to follow them and have them come in for visits. We will reach out to the participant by phone or email to ensure that there are no issues with access. A participant may be eligible for disenrollment based on the judgment of the PI.

11.2. Continued Follow-up Discontinuation of Study Intervention

Describe efforts that will be made to continue follow-up of participants who discontinue the study intervention, but remain in the study for follow-up, especially for safety and efficacy study endpoints (if applicable). Reasonable efforts must be made to undertake protocol-specified safety follow-up procedures to capture adverse events (AE), serious adverse events (SAE), and unanticipated problems involving risks to subjects or others (UPIRSOs).

For any participant who ceases to use the App, we will continue with the study visits and check in on their usage of the App and obtain their thoughts on how beneficial or user friendly it is. This will allow us to obtain information on participant progress and viral load.

12. Statistical Considerations

12.1. Statistical Hypotheses

State the formal and testable null and alternative hypotheses for primary and key secondary endpoints, specifying the type of comparison (e.g., superiority, equivalence or non-inferiority, dose response) and time period for which each endpoint will be analyzed.

N/A – This is a pilot study with a small sample size to assess feasibility and acceptability. There are no formal null or alternative statistical hypotheses.

12.2. Sample Size Determination

Include number of participants to recruit, screen, and enroll to have adequate power to test the key hypotheses for the study. Provide all information needed to validate your calculations and judge the feasibility of enrolling and following the necessary number of participants.

As this is a small pilot in a new population where effect sizes of the intervention are unknown, sample size calculations were not attempted. However, this sample size (60) should be sufficient to detect small to medium-sized effects in a pilot. The total population of YLWH meeting eligibility criteria is estimated at 243, so this enrollment should be achievable. We will screen up to 180 potential participants to meet the required sample size of 60.

12.3. Populations for Analyses

Clearly identify and describe the analysis datasets (e.g., which participants will be included in each).

Analyses will be conducted between the two randomized study groups, the intervention group and the control (standard of care) group.

12.4. Statistical Analyses

Include analysis of primary efficacy endpoints, secondary endpoints, safety analyses, and any planned interim analyses

Virologic suppression between the two randomized groups at 12 months will be analyzed using a Chi-square test or Fisher's exact test if appropriate with a statistical significance cutoff of $p<0.05$. Additional comparisons will be made for virologic suppression at 6 months and engagement in care at 6 and 12 months. Analyses will be conducted in IBM SPSS Statistics v25. These data may be able to be used to estimate effect sizes for the future RCT.