STUDY00002534: Project Engage: A Wrist Biosensor-based mHealth Suite to Support Alcohol Intervention in Young People Living With HIV

NCT05431855

Study Protocol

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PROTOCOL TITLE:

A wrist biosensor-based mHealth suite to support alcohol intervention in young people living with HIV

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VERSION NUMBER/DATE: 6.0 / 10/15/2023
REVISION HISTORY

Revision #	Version Date	Summary of Changes	Consent Change?
2.1	5.13.2022	**Section 6**: Updated Engage measures to remove measures that were previously submitted in error and additional details regarding the recruitment and enrollment process per IRB reviewer feedback. **Section 7**: Details were provided on how data from both the Skyn biosensor and the mEMA app will be deidentified from the study participant as well as how the data will be stored and managed securely and language pertaining to the manufacturer not using study data to support adoption/change indication for the device. **Section 8**: Provided explanation as to why alcohol levels measured by the Skyn biosensor will not be provided to the subjects **Section 10**: Added the inclusion criteria of being diagnosed as HIV+ **Section 13**: Additional details regarding recruitment to be conducted by the CEC **Section 18**: Addition of DSMB members and qualifications	Yes

		Section 22: Contact information for participants who have questions throughout the study was provided **Section 26**: Additional description of core and site activities as they pertain the SHARE Program overall and the Engage project.	
2.2	6.29.2022	**Section 6:** Other related studies are now included (e.g. inclusion of STUDY00002535, SHARE P01: DEFINE)**;** Confirmation that the zoom meetings will not be recorded**;** Updated language surrounding the viral load test results, including information related to email encryption. Participants will not be emailing their viral load results. Rather, if participants opt to provide their viral load results as an attachment, that attachment will be uploaded to the secure REDCap platform and will not be sent by the participant via email; Removed language related to reasons for refusal as these are not currently programmed into REDCap. Should we add this back, we will do so with an IRB modification. **Section 8:** Language added that only encrypted email communications will be used to convey VL results. We will not provide VL results via telephone. Instructions for encryption are built into the study personnel's standard operating procedure. **Section 11:** Removed language related to minimal risk **Section 17:** Updated language to state that zoom meetings will not be recorded. **Section 18:** Updated the description related to the DSMB to include that only aggregate data will be shared. No personally identifiable information will be shared or connected to the aggregate data discussed in the meeting. **Section 20:** Removed language related to minimal risk **Section 22:** Removed language related to reasons for refusal as these are not currently programmed into REDCap. Should we add this back, we will do so with an IRB modification.	Yes
2.3	07.08.2022	**Section 6:** The SHARE screening process has been updated to include language relevant to the three options for eligible participants to enroll, description of process to retain screener information for enrollment purposes only, clarification of the triage process (randomization) for Define or Engage, and redirection to the SIU Connect repository.	

		Section 10: Inclusion and exclusion criteria is consistent related to pregnancy **Section 15**: We have removed the language related to violation of confidentiality is considered minimal	
2.4	10.05.2022	**Section 6**: We have added details about prorating participants' compensation for the EMA assessments if they respond to less than 80% of the assessments. Info about the tutorial videos for the EMA and Skyn apps was included. **Section 22**: We have added information regarding a video that will accompany the informed consent form	Yes
3.0	02.01.2023	**We have modified the following protocol sections:** **Section 1.0**: study sample size from 222 to 160 **Section 3.0**: study sample size from 222 to 160, with 15% attrition anticipated **Section 6.0**: participant incentive schedule to reflect reduced sample size. **Section 9.0**: Study timeline to reflect new sample size **Section 12**: Total sample size **Section 13**: Total sample size We have also updated the consent form to include the sample size change.	Yes
4.0	06.06.2023	**Section 13:** We have modified Section 13 of the protocol to include information related to the use of the BuildClinical platform for social media recruitment. Attached to this modification please find the accompanying materials for IRB review (advertisements, study landing page, pre-screener form, ad copy).	No
5.0	08.25.2023	**Section 6:** We have updated the measures table to include the addition of the Sexual Sensation Seeking Scale	No
6.0	10.15.2023	**Section 1:** Added information on the inclusion of the eWrapper app **Section 5:** Added the eWrapper app **Section 6:** Details on the eWrapper app intervention were added. Information regarding how incentives are delivered following completion of baseline and follow up surveys was added. The incentive structure was adjusted to accommodate for the inclusion of the eWrapper app **Section 19:** Details concerning the security of the eWrapper app were added	Yes

		Section 22: Added that an agreement to send back study materials will be included in the consent process	
7.0	04.29.2024	**Section 6**: We have updated the incentives for EMA assessments to increase retention and to prevent device loss.	Yes
8.0	10.21.2024	**Section 18:** • Modified language to include the addition of the University of South Florida as the primary Data Science Core site due to Dr. Sam Wu's transition from UF to USF. **Section 19:** • Added additional language related to the transfer to FDOH data to include USF. **Section 24:** • Modified language to include USF Data Science Core activities. **Section 26:** • We have added the Northeastern University and the University of South Florida as they are new sites to the SHARE program and removed Nova Southeastern University.	No

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1.0 Study Summary

Study Title	**A wrist biosensor-based mHealth suite to support alcohol intervention in young people living with HIV**
Study Design	Overview: Young people living with HIV (YPLWH) will be asked to wear a wrist alcohol biosensor (BACtrack Skyn) for 30 days and report their alcohol use using daily ecological momentary assessment (EMA). Data from the 30-day period will be used to develop and validate the algorithm for alcohol detection based on Skyn data. We will also collect alcohol biomarker (i.e., PEth) at 1-month follow up.
Primary Objective	Health Services Research: to develop a mHealth suite based on the Skyn biosensor to help self-management of alcohol use among YPLWH.
Secondary Objective(s)	N/A
Research Intervention(s)/ Investigational Agent(s)	Behavioral Intervention: Single Group, Randomized **eWrapper-Engagement strategies to facilitate alcohol biosensor wearing** We will conduct a 30-day micro-randomized trial (MRT)--a clinical trial design for developing and optimizing mHealth interventions to test which engagement strategy works better, for who, and under what condition. Participants will be micro-randomized in the morning and in the evening, to either a prompt delivering non-contingent small reward (reciprocity); or a prompt containing feedback on self-monitoring progress based on dynamic self-regulation theories (personalized feedback); or no prompt. Up to 60 Engage participants will engage with the eWrapper application.
IND/IDE #	
Study Population	This study will only recruit participants who are 18 to 29 years of age due to focus on YPLWH. Targeted enrollment of women and minorities is summarized in the accompanying Planned Enrollment Table. The distribution by gender and ethnicity is expected to be similar to that of the people living with HIV (PLWH) in the state of Florida, given that we will be recruiting across the state.
Sample Size	N = 160
Study Duration for individual participants	Approximately 2 calendar months
Study Specific Abbreviations/ Definitions	**ART:** Antiretroviral Therapy **ARV(S):** Antiretroviral **ASSIST:** Alcohol, Smoking and Substance Involvement Screening Test **CITI**: Collaborative IRB Training Initiative

	CoM: College of Medicine **DBS**: Dried Blood Spot **DSC:** Data Science Core **eHARS:** Enhanced HIV/AIDS Reporting System **EHR**: Electronic Health Record **EMA**: Ecological momentary analysis **FDOH:** Florida Department of Health **FDOH HSP**: Florida Department of Health HIV/AIDS Surveillance Program **GLMM:** Generalized Linear Mixed Model **GUID:** Globally Unique IDentifier **HIV**: Human Immunodeficiency Virus **NIAAA**: National Institute on Alcohol Abuse and Alcoholism **$NIAAA_{DA}$**: National Institute on Alcohol Abuse and Alcoholism Data Archive **NLP:** Natural Language Processing **REDCap®:** Research Electronic Data Capture **RERAC**: Recruitment, Engagement, Retention, and Assessment Center **SHARC:** Southern HIV and Alcohol Research Consortium **SHARE: S**elf-management of **H**IV and **A**lcohol **R**eaching **E**merging adults **SEM:** Structural Equation Models **SMC**: Study Monitoring Committee **TLFB:** Timeline Follow-back **USF**: University of South Florida **VL**: Viral Load **YAC:** Youth Advisory Council **YPLWH**: Young People Living with HIV

2.0 Objectives*

This project aims to (1) develop and validate machine learning algorithm for proximal and distal drinking detection based on biosensor-derived transdermal alcohol concentration (TAC) data. (a) Drinking reported in the EMA (proximal drinking) will be used to develop and optimize machine learning algorithm for detecting drinking episodes based on TAC. (b) PEth level at 1 month (distal drinking) will be used to further validate the algorithm; (2) explore whether wearing the biosensor (thus self-monitoring) for 30 days is associated with reduced alcohol use; and (3) pilot test the feasibility of using the eWrapper app as engagement strategies to increase Skyn sensor wearing time.

3.0 Background*

Despite the high prevalence of alcohol use and its detrimental consequences in YPLWH, developmentally-tailored intervention targeting alcohol use in YPLWH is rare.

In Dr. Wang's current R21 project (data collection still ongoing), we collected data from 28 adult drinkers (21 HIV-, 7 HIV+, 61% male, Mean age=32.8, SD=15.2) to test feasibility, acceptability and preliminary validity of the Skyn biosensor in both laboratory and field settings. During two lab sessions, participants wore the sensor while they consumed 3 standard drinks (15min for each) in succession with a break (15min) in between. Breathalyzer was used to obtain breath alcohol concentration (BrAC) readings at set intervals (30min during drinking and 15min after drinking period). The correlation between peak TAC and BrAC was r =.23 (N=22) for session 1, and r =.60 (N=16) for session 2. It should be noted that TAC and BrAC are not linearly translatable. The correlations here are similar or higher than what was reported in prior research using the same lab administration paradigm for SCRAM biosensor (r =.24), which is considered gold standard for TAC.127 Also, we speculate the lower correlation for session 1 were due to less stable data quality at earlier stage (2019) where we used an early production version of Skyn. The current version of Skyn is more stable (updated hardware and software), so we expect TAC and BrAC readings in the proposed study will be closely related like that for session 2. Participants also wore the wrist sensor for 2 weeks in their daily lives at all times besides bathing/showering/swimming and when charging the device. Participants were incentivized to wear the biosensor at least 80% of the time and to complete at least 80% EMA. Participants have had good adherence, wearing it 87% of the time on average, and completing 76% of EMAs. The Skyn TAC readings showed a visible drinking curve (coded by two independent coders) for 99 out of 114 drinking episodes (86.8%) reported in the EMA from 27 participants who completed the two-week field test. The episodes that were not detected by the Skyn were mostly 1-2 drinks (80%). The spearman correlation between peak

TAC and self-reported number of drinks was .63, indicating good agreement. At the end of 2 weeks, participants completed a usability/acceptability survey, where they rated Skyn as easy to learn (M=4.22, SD=0.95) and easy to use (M=3.96, SD=1.29) on a scale from 1 = "strongly disagree" to 5 = "strongly agree".

Despite the overall decline in new HIV infections in U.S., adolescents and emerging adults aged 13 to 29 remain disproportionately affected by HIV who account for 37% of all new HIV diagnoses. Alcohol use is more common among YPLWH than other age groups, creating a significant barrier for mitigating transmission, achieving viral suppression, and reducing comorbidities. Despite the high prevalence of alcohol use and its detrimental consequences in this population, developmentally-tailored intervention targeting alcohol use in YPLWH is rare. Self-management emerged as an important strategy in the context of medical adherence and chronic disease management, with self-monitoring and personalized feedback being two key elements to improve health outcomes including alcohol use. Recent development of wrist alcohol sensors provides a promising tool for self-monitoring and feedback based on objective data. Our current R21 project (N=28) showed acceptability and initial validity of a wrist-worn biosensor (BACtrack Skyn) in both laboratory and field settings. However, without existing analysis software, accurate detection of alcohol use (e.g., start time, consumption level) based wrist sensor data remains a significant barrier. Some literature also suggests that HIV may impact blood alcohol concentration, so a detection algorithm specific to this population is needed.

To address these challenges and achieve the overall P01 goal to improve self-management of alcohol use and HIV care among YPLWH, we propose to develop the first wrist biosensor-based mHealth suite for alcohol self-monitoring with validated alcohol detection algorithm tailored for YPLWH. YPLWH (N = 160, 136 after 15% attrition,18-29 years) will wear the Skyn biosensor for 30 days and report alcohol use via smartphone-based ecological momentary assessment (EMA). Data from the 30-day period will be used to (a) develop and validate machine learning algorithm for alcohol detection in YPLWH based on Skyn data. We will collect alcohol biomarker (i.e., PEth) at 1-month follow up to explore whether wearing the sensor for 30 days impacts alcohol use.

4.0 Study Endpoints*

By the end of this study, we will develop a mHealth suite based on the Skyn biosensor to help self-management of alcohol use among YPLWH.

5.0 Study Intervention/Investigational Agent

eWrapper-Engagement strategies to facilitate alcohol biosensor wearing: We will conduct a 30-day micro-randomized trial (MRT)--a clinical trial design for developing and optimizing mHealth interventions

to test which engagement strategy works better, for who, and under what condition among a subset of participants (up to 60). Participants will be micro-randomized in the morning and in the evening, to either a prompt delivering non-contingent small reward (reciprocity); or a prompt containing feedback on self-monitoring progress based on dynamic self-regulation theories (personalized feedback); or no prompt. The eWrapper app will also collect paradata about participants' usage of the app (e.g., how often message notifications were clicked, how often the application was opened). Additionally, information on how long participants wore the Skyn biosensor will be calculated based on downloaded Skyn sensor data from its web portal using an algorithm based on motion and temperature. None of these data will involve any personal identifier. The eWrapper app security has been evaluated by the University of Florida IT risk assessment and deemed acceptable if only used on the study iPhones.

6.0 Procedures Involved*

The SHARE Program's Community Engagement Core (CEC), Administrative Core (AC), and Data Science Core (DSC) are charged with the identification of participants for the SHARE Program's studies (inclusive of Engage).

Recruitment materials will include different electronic and printed materials (e.g. insta-stories; flyers, brochures, and palm-cards) and be distributed via social media sites, smartphone applications, email, as well as at community venues, clinics, and agencies as recommended by the Youth Advisory Committee (YAC) and stakeholders. Promotional materials (both virtual and physical) will include a brief description of the study and a rapid way to access the screening questionnaire – a hyperlink or QR code. In the unlikely event that we do not accrue participants at the rate proposed with these time-tested procedures, we will pivot to more traditional venue and clinic-based recruitment approaches while adhering to COVID-19 safety recommendations. Participants will be self-identified through contact with (electronic or printed) recruitment materials.

After completing the eligibility screener, those deemed eligible will be asked if they are interested in participating in the SHARE Program. **If they are not eligible**, they will be routed to a page with a link to the SIU Connect repository (IRB approved STUDY00002871), which gives them the option to complete the consent and enrollment process for SIU Connect if they meet the eligibility criteria. This is a separate and independent process from the SHARE Program.

If they are eligible, participants will be notified that should they choose to participate, they will be invited to enroll in either DEFINE or ENGAGE, and which they are invited to is by chance. They will then be given three options (*please refer to the SHARE Program Screening Forms attachment*):

- **Option 1 - Yes**: The participant will be automatically triaged by the DSC to the DEFINE (STUDY00002535) or ENGAGE studies where they will complete the consent and enrollment process.

- **Option 2 – No but want to join later**: If this option is selected, participants will be directed to provide their email address and click submit. As indicated on the REDCap form, by clicking "submit" they are giving permission for the SHARE DSC to retain their information to follow-up via email that will include a link to return to this page and select "Yes" to complete the enrollment process, and they are informed that this data retained will not be linked with any data collected as part of their potential enrollment in any of the SHARE studies. The participant will receive up to 3 emails to prompt them to complete the enrollment process. If they ignore all prompts, they will no longer be contacted and will be deemed ineligible, and their email address will be removed from our database.

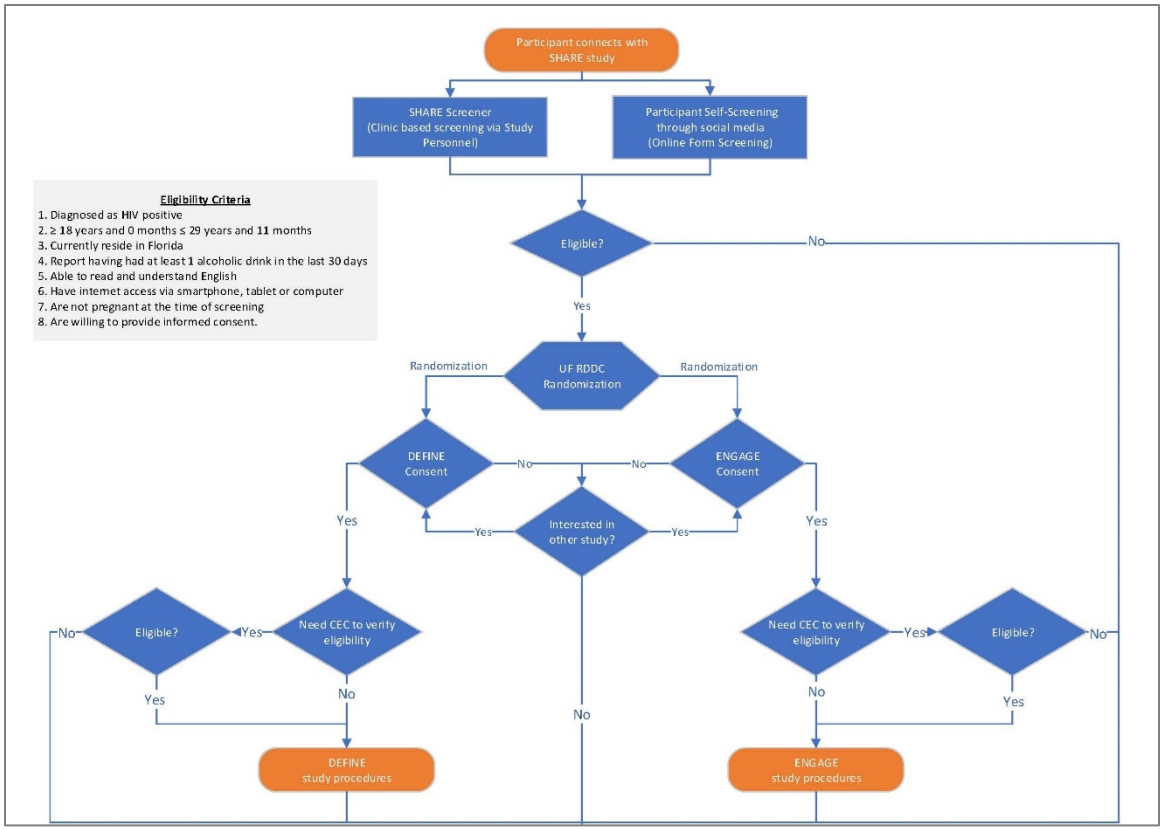
- **Option 3 – Not interested**: If individuals are eligible but not interested, they will be directed to a page in REDCap where a link to the SIU Connect repository where they can choose to navigate to the repository screening page.

  Participants will not enroll in SHARE as an overarching protocol, rather, they will enroll in a specific study that is within the umbrella of the overall SHARE program. Screening data will not be linked to any enrolled participants in any of the SHARE Studies and the screening data is not capturing any identifiable data unless participants selection option 2 and provide their email address and phone number (where we have inserted an additional statement to this effect).

  Once a participant consents and is enrolled, a member of the CEC will contact participants to confirm their HIV and Florida residency status, giving the participants the option to upload documents to the secure REDCap platform or schedule a virtual conference via HIPAA compliant zoom with CEC relationships specialists. These zoom sessions will not be recorded, they will simply be conducted to confirm HIV status for eligibility purposes, if the zoom session is the preference of the participant. If the preference of the participant is to upload proof of HIV status, these documents will not be stored in the DSC participant database; rather, their participant record will be verified by the CEC coordinator and documentation will be removed unless the documentation also serves as the participants viral load as required for study enrollment. Once verification of HIV status, age, and Florida residency is complete, the CEC will confirm the participants method for providing HIV viral load results if not already provided (DBS test kit, release of information, or document upload), and confirm the selection and information in the DSC participant database and notify the AC of any DBS test kits that must be shipped to participants. Only authorized CEC staff and research assistants will directly interact with participants throughout the study.

  Engagement and retention efforts: We will maintain regular contact with participants through the contact information provided by them at the time of consent. Reminders will be sent to participants before each assessment.

  SHARE Recruitment and Enrollment process:



Study Procedures: Once enrolled, participants will be asked to wear a wrist alcohol biosensor (BACtrack Skyn) for 30 days, report their alcohol use using daily ecological momentary assessment (EMA), and use the eWrapper app where randomized messages will be delivered to the participant. We will also collect alcohol biomarker (i.e., PEth) at 1-month follow up.

Materials:

1. Online survey including questions on demographic characteristics, alcohol use (including Timeline follow back) and substance use, mental health symptoms, ART adherence, and acceptability & usability of the wrist worn biosensor.
2. An alcohol biomarker Phosphatidylethanol (PEth) will be collected from participants after they complete the 30-day period.
3. Transdermal alcohol concentration readings collected by the Skyn wrist biosensor. Data will be downloaded regularly by the Data Science core to secure UF drives.
4. Self-reported alcohol use and related factors assessed by ecological momentary assessment App (mEMA). Data will be

uploaded to a secure encrypted cloud storage which researcher can have real time access and will be downloaded regularly by the Data Science core to secure UF drives.

5. The eWrapper app, developed by our team and the Florida Center for Interactive Media (FCIM). The app is an animal raising game which includes engagement strategies to promote engagement in terms of wearing the Skyn biosensor. Data will be downloaded regularly by the Data Science core to secure UF drives.
6. Viral load abstracted from participants' health record or via dried blood spots (DBS) test.

Baseline/follow up assessments: Online survey (baseline and follow up): At baseline and 1-month follow up, participants will be asked to complete online surveys programmed in REDCap; completion will take about 30 minutes. Baseline survey will include questions such as demographics (e.g., age, race/ethnicity, biological sex, sexual/gender identity, mode of transmission), alcohol (AUDIT) and other substance use (ASSIST), mental health symptoms (DSM-5 Self-rated Level 1 cross-cutting symptom measure - adult), ART adherence (Visual Analogue Scale), and sexual risk behaviors. The same survey questions minus demographics will be used at follow up. Additionally, we will assess usability and acceptability of the biosensor at follow up using established measures such as System Usability Scale and the Mobile App Rating Scale, with some open-ended questions about user-desired features. Survey links will be sent to each participant at each assessment point and can be completed at his/her convenience. Completion of the baseline survey will result in a $25 compensation for the participant, which will be provided to the participant once the 30-day study trial begins. Completion of the follow up survey will result in a $35 compensation for the participant, which will be provided to the participant after they have returned their study materials.

Timeline follow back (TLFB) (baseline and follow up): We will use an online version of TLFB provided by the University of Washington, which has shown comparable validity to the in-person interview-based TLFB, and is more amiable for remote data collection. Participants will receive $25 for complete the baseline online assessments (survey and TLFB), and $35 for the follow up online assessments to increase retention.

Phosphatidylethanol (PEth) (follow up only): We will collect dried blood spots (DBS) to test for PEth level at 1-month follow up. Research staff will mail the DBS collection kit and an illustrated instruction sheet to participant's preferrable address, with a prepaid pre-addressed envelope for participants to return the sample. The DBS collection kit will be provided by the United States Drug Testing Laboratories (USDTL Inc.), which is a reputable lab for PEth test. The collection kit includes DBS collection supplies (e.g., sterile safety lancet, collection card with five circles for blood drops) and a drying box. Participants will be encouraged

to watch a video on YouTube produced by USDTL which walks through the DBS collection process to make sure they perform each step properly. After collection is complete, participants will mail back the DBS sample to our research team. The DBS is stable for at least 9 months at ambient temperature. After receiving kits, research staff will store samples to be sent to USDTL for testing PEth in batches. Participants will receive $10 for providing PEth biomarker.

Viral load (follow up only): As a common measure across projects, HIV viral load will be abstracted from the Florida Department of Health (FDOH) surveillance data at follow up (detail see Data Science Core). Participants have several options for how they would like this data submitted. VL measurements collected during follow-up or after may be used, as long as they are collected no later than 1 month from the follow-up survey date (exceptions to this must be approved by the REC). Participants may submit VL test results from their standard care providers as long as they were measured using a level of detection of within the required window period. Clinical care VL measurements can be used as long as they were measured using a level of detection of <200 copies/mL or below. VL measurements using a level of detection ≥200mL will not be accepted. If participants decide to obtain a copy of their standard care VL test results, they may take a picture of their newly obtained standard care VL test result using their personal cell phone and submit the picture through a secure REDCap online submission form as a file attachment.

Participants who cannot or do not wish to visit a medical provider may be referred to their local health department for free VL testing or they may request HemaSpot™ Blood Sampling Kit. The participant will indicate this as the preferred option for providing VL upon enrollment/baseline and the Data Science Core will communicate the information to the Admin Core, who will mail the Spot*On Sciences HemaSpot™ blood sampling kit to the address provided by the participant. This kit includes the HemaSpot™ device, 2 lancets, 2 alcohol pads, 2 sterile gauze pads, and 2 adhesive bandages. The kit also contains printed instructions, as well as a link to an instructional video, from the manufacturer on how to collect and handle your blood with the items provided. The kit requires about 2-3 drops of blood and takes less than 5 minutes to complete. The participant will then mail the completed kit to Florida State University, Center for Translational Behavioral Sciences, 2010 Levy Avenue, Suite B0266, Tallahassee, FL 32310. The research team will provide the participants with a mailing kit and pay for the postage. Participants will complete this process only once for ENGAGE by the 30-day follow-up; however, participants may be requested to resubmit another kit in the event there was an error in the collection, handling, and/or mailing of the original kit. Upon receipt of the specimen, Admin Core personnel will ensure the specimen is properly and securely stored at the Center for Translational Behavioral Science until the next scheduled specimen batch will be shipped to the analyzing laboratory. Specimens are anticipated to be stored

on site for no more than 90 days prior to shipping for analysis. The Admin Core personnel are responsible for ensuring that all specimens are de-identified and tracked only by the participant's GUID. Specimens will be destroyed by the analyzing laboratory upon completion of viral load analysis and transmittal of viral load results to the Data Science Core. Participants will receive $10 for providing VL data.

Alcohol biosensor and EMA: After participants are enrolled, we will mail the Skyn biosensor to their preferred address along with the instructions for each study related app. We will also mail a study iPhone with data plan to the participant to facilitate data collection if they don't own one, because the Skyn app is currently only compatible with iOS system. Research staff will instruct participants on downloading the apps on their own smartphone (if they use the study iPhone, all apps will be preinstalled), and train participants on how to use the Skyn biosensor and its associated app (Skyn app) and the EMA app (mEMA) remotely via videoconferencing, until participants demonstrate efficiency with using these technologies. The research staff will send tutorial videos corresponding to the Skyn app and the EMA app, allowing for the participants to have a point of reference if they have questions about the materials for the study. Likewise, research staff will also be available to help the participants with troubleshooting if any issues occur during the 30-day period.

Biosensor: Participants will be asked to wear the Skyn biosensor at all times during the 30-day period. They will be allowed to take it off for bath, swimming, charging the device, or when their activities may cause damage to the biosensor. Since the biosensor also has motion and temperature sensors, it's possible to determine whether participants take it off. At the end of the 30-day trial, participants will mail back the Skyn biosensor (and the study iPhone if applicable) using a pre-paid and pre-labeled box back to us in order to get their compensation. Participants will not be compensated for the study activities during the 30-day period and follow-up if they do not return the study devices or the device/s get lost. Returning the study devices late (not within two weeks after the 30-day study period is completed) or damage of the biosensor/iPhone will result in deduction ($100) in compensation to encourage careful handling of the device/s. **EMA**: Participants will be instructed to enter information on their drinking behaviors using an EMA app called mEMA (ilumivu, Inc.). This app is developed for mobile-based EMA to collect real-time data in daily life. Participants will be asked to initiate an on-demand survey in the app whenever they start a drinking episode. This survey will include questions on the drinking episode such as the starting and ending times of their drinking, type and number of drinks, and food intake. To capture any potentially missed self-initiated entry at the time of drinking, the EMA app will also prompt questions at a fixed schedule every morning to ask about alcohol consumption in the past 24 hours. The morning prompts will also

include reminders to check the battery life of the biosensor and report issues they had with the sensor. Once a survey is completed, the app automatically pushes data into its cloud-based data portal and researchers can access data in real time. Troubleshooting and noncompliance procedures: We will contact participants via phone call if we notice any issues (e.g., missing daily prompt, reported biosensor malfunction) so that these issues can be resolved in time. Drinking data will be obtained via phone call if both daily and self-initiated surveys are missing. Participants will receive $60 for completing the EMA assessments over the whole 30-day period, if they respond to more than 80% of the EMA assessments. If the participant's response rate is lower than 80%, then the $60 compensation will be prorated as follows: 60-79% EMA assessment response rate = $50, 50-59% EMA assessment response rate = $40, 40-49% EMA assessment response rate = $30, 20-39% EMA assessment response rate = $20, 0-20% EMA assessment response rate = $10. There will be bonus for participants to complete 80% or more EMA assessments. Bonus will increase each week and accumulate to up to $100 total if they complete 80% or more each week on a continuous basis (Week 1: $10, Week 2: $20, Week 3: $30, Week 4: $40). If their completion rate falls below 80%, they will not get bonus that week, and the bonus amount resets at $10 again. Participants will be notified by the study RA during the middle of the 30-day period if their response rate is below the targeted 80%, encouraging them to increase their response rate to be over 80%. For those who also use eWrapper as part of their 30-day trial, they will be expected to receive $10 from playing the eWrapper game, so their EMA compensation will be reduced by $10 from the original EMA payment scheme.

eWrapper: The eWrapper app was developed by our team and the Florida Center for Interactive Media (FCIM). The app is an animal raising game which includes engagement strategies to promote engagement in terms of wearing the Skyn biosensor. Engagement will be reinforced via a point system and a virtual environment, which starts with a giraffe, but allows the user to unlock new environments, animals, and accessories for their animals. The more the participant wears the Skyn sensor, the more points they will receive as a reward. Also, participants will be micro-randomized in the morning and in the evening, to either a prompt delivering non-contingent small reward (either $1 cash reward or free points for the game); or a prompt containing feedback on self-monitoring progress based on dynamic self-regulation theories (personalized feedback); or no prompt. During the 30-day period, the number of times the participant will receive these $1 reciprocity messages will total around 10, accounting for $10 of their compensation. The eWrapper app will collect paradata as participants use it. Specifically, the following information will be recorded:

- App Usage: when the app is opened and game scenes are loaded

- Skyn Data Source Connections: whenever the eWrapper succeeds or fails to connect to the Skyn wearing time summary database (a Json file).

- Gameplay Interactions: whenever the player purchases from the shop, completes the tutorial, interacts with any of the popups or animals, daily reward collections, etc.

Additionally, information on how long participants wore the Skyn biosensor will be calculated based on downloaded Skyn sensor data from its web portal using an algorithm based on motion and temperature. None of these data will involve any personal identifier.

Measures (Short Name)	Required common measure	ENGAGE**	
		T^1	T^2
Screening		√	
Consent		√	
HIPAA Authorization		√	
Demographics(survey)	√	√	
HIV Viral Load Submission		√	
ART Adherence	√	√	√
Sex Risk	√	√	√
DSM-5 Self-Rated Level 1 Cross-Cutting Symptom Measure—Adult	√	√	√
Alcohol-Smoking-Substance Screening Test (ASSIST)	√	√	√
Timeline Followback	√	√	√
Berger's Scale Revised for Adolescents (HIV Stigma)		√	√
Sexual Sensation Seeking Scale		√	√
Perceived Stress Scale (PSS)		√	√
Pittsburgh Sleep Quality Index (PSQI)		√	√
Usability Acceptability Survey			√
Biosensor Wearing Status		√ (not in REDCap)	
Ecological Momentary Assessment Questionnaire (EMA)		√ (not in REDCap)	
Eligibility Verification		√	

The participant incentive schedule is as follows:

Timepoint	Year 1	Year 2	TOTAL Participants
Baseline	70 participants x $25 per participant	90 participants x $25 per participant	160
PEth Analysis	70 participants x $10 per participant	90 participants x $10 per participant	160
Viral Load	70 participants x $10 per participant	90 participants x $10 per participant	160
EMA and eWrapper if applicable	70 participants x $160	90 participants x $160	160
1-month follow up	60 participants x $35 per participant	100 participants x $35 per participant	160

7.0 Data and Specimen Banking*

Data Banking: We will link information collected from this study with information abstracted from electronic medical records (EMR) and state surveillance including the Enhanced HIV/AIDS Reporting System (eHARS). These data will be updated first at baseline, from 1 year prior to study enrollment until 2 years after the 1-month follow-up. We have already established this procedure of data linkage and management with eHARS in our previous studies approved by the University of Florida IRB. To link the data, a single research team member, who does not have access to research data, will generate a list of individuals with their identifying information who have enrolled in the study. This list, together with the SHARE_ID number, will be sent securely to a single contact at the FDOH in Tallahassee. There, the DOH contacts will use the identifying information to obtain the latest HIV surveillance data for that individual, add the SHARE_ID number to the surveillance data, remove all other identifying information, and send the data back securely to our Research Data Manager. Our team has used this process multiple times over the past 4 years, and we have never had any type of data security issue.

Biological samples collected for the purposes of this study will not be used to conduct any future research. They will be destroyed after analysis is completed. The utilization of at-home Dried Blood Spot (DBS) test kits with study participants will be centralized within the administrative and community engagement cores. This centralization will allow for identifiable participant data to be properly secured and accessible only by those key personnel identified in the approved IRB protocol within the Admin Core at the contact site and will minimize the risk of breach of participant confidentiality. All biological samples collected will be securely stored upon receipt from the participants in the Center for Translational Behavioral Science, accessed only by authorized study personnel, before sending to the vendor for analysis. The Admin Core will oversee all aspects of at home test kits by facilitating transport from the vendor to the Admin Core, shipment of test kits to study participants, receipt of collected samples, de-identification of samples and preparation of samples for transport to the vendor laboratory for analysis and maintain secure access to the vendor's web-based portal for sample analysis results. Participants will be provided with unidentifiable shipping materials in order to confidentially return specimens to the study team. Only participant ID number and date may be associated with DBS specimens. Specimens obtained will be de-identified and sent securely via postal mail to the processing laboratory on a monthly basis. All results will be communicated to the study team via HIPAA compliant email or fax communication. The processing laboratory will destroy the specimens upon completion of analysis and transmittal of results to the project team.

Data collected during the research study from the Skyn biosensor and the EMA app (mEMA) will not contain any personal identifier. To use the app needed for data collection with the Skyn biosensor, the participants will receive a premade study email address and password to log into the app. Therefore, no personal information will be collected via the app. The mEMA app will use a unique eight-digit code for each participant, so there will also be no personal identifier with the data collected from the app. All data collected from the Skyn biosensor and mEMA app will first go to a secure cloud storage hosted by the respective company. The researchers will then have a secure download (password protected login for the research account) to access the participant's data. All downloaded data will be stored on a secure UF drive managed by the data science core team. The device manufacturer will not use study data to support adoption/change indication for the device.

Survey data will be available to the research team and authorized staff. Data collected during this research study may be used for future research purposes. The data stored will be de-identified. Data that cannot be linked to participants (i.e., de-identified data) will be kept indefinitely; these data will be saved for future use and may be shared with other researchers. At the end of the study data collected will be made available, in accordance with the NIH Data Sharing Policy (http://grants.nih.gov/grants/policy/data_sharing). These data will be saved for future use and may be shared with other researchers. By participating in this study, participants are agreeing to allow us to save and share their data anonymously. Publications and/or presentations that result from this study will not include any identifying data.

8.0 Sharing of Results with Subjects*

Results from the self-report surveys will not be shared with subjects or others.

Results of HIV viral load DBS will be made available to participants upon request. The research team will not share these results with any other individuals. Participants who request their results will receive their results via encrypted email only. The protocol team will develop email templates for sharing both detectable and undetectable VL results. The templates will include a brief introduction of the research staff delivering the results followed by either detectable or undetectable VL results and the meaning of those results, as well as information regarding available resources. For those who had undetectable VL, no further step is needed. For those who had detectable VL, any necessary referrals will be provided. Participants will also be recommended to follow up with health care provider.

Data measured by the Skyn biosensor pertaining to the participant's alcohol level will not be provided to the participant. The app associated with the Skyn biosensor does not display active alcohol levels on its interface and the Skyn biosensor has not been FDA-approved to give up-to-date readings for current alcohol levels.

9.0 Study Timelines*

The table below lays out the planned research tasks and the corresponding timeline. The first 6 months will be preparatory to the recruitment, such as staff hiring/training, IRB approval, manual of procedures, and database development. Once recruitment is started (planned N = 160), we anticipate on average recruiting 10 participants per month into this project. This means we can finish recruitment at the beginning of Month 30. We will start data analysis at Month 24 when we have at least 70% of the data collected on the Skyn biosensor for machine learning models and continue to analyze data and writing papers through the study period.

Study Timeline

Research tasks	Y1				Y2				Y3				Y4				Y5	
IRB, staff hiring/training, protocol/database building																		
Recruitment and assessments, data monitoring																		
Data merge/analysis and result dissemination																		
Integrate biosensor and/or app into Project Sustain																		

10.0 Inclusion and Exclusion Criteria*

Inclusion Criteria: To be considered eligible for the study an individual must meet the following criteria: 1) be 18 years and 0 months to 29 years and 11 months; 2) currently reside in Florida; 3) report having had at least 1 alcoholic drink in the last 30 days; 4) able to read and understand English; 5) have internet access via smartphone, tablet or computer; 6) be diagnosed as HIV+ and 7) willing to provide informed consent; 8) Are not pregnant at the time of enrollment.

The population specifically targeted are YPLWH between the ages of 18 and 29 who are currently living in Florida. Given that only 0.4% of YPLWH in Florida are between 13 to 18, we elected not to include those younger than 18. Those who report being pregnant at time of screening will be excluded from the study.

The following categories will be excluded from eligibility for participation:

- Adults unable to consent
- Individuals who are not yet adults

- Individuals who are not diagnosed as HIV+
- Incidental recruitment of pregnant women may occur, but pregnancy is not part of the study's exclusion criteria
- Prisoners
- Pregnant women

11.0 Vulnerable Populations*:

2019 HIV prevalence data for Florida revealed that approximately 75% of persons living with HIV in that state belong to racial/ethnic minority populations (38% Black, 36% Hispanic/Latinx, and 2% American Indian, Asian, and mixed race) compared to 24% White. Seventy-three percent identify as male, 26% as female, and less than 1% as transgender (male to female and female to male). We anticipate that young people who enroll in Project Engage will reflect the gender and race/ethnicity characteristics of the broader Florida population of individuals with HIV.

- Minority Group(s)/Non-English Speakers – This project will include individuals who meet the inclusion criteria, regardless of race or ethnicity. - Subjects will be English speakers.
- Elderly (65+) – This project will not include those over age 29.
- Gender imbalance – It is expected that there will be more male than female individuals who participate.
- Pregnant women – Participants who report to be pregnant will be excluded from the study.
- Minors – No minors will be directly recruited for the purposes of this project.

12.0 Local Number of Subjects

160 total participants will be recruited across the state of Florida.

13.0 Recruitment Methods

The goal is to recruit 160 young people living with HIV (YPLWH) (N = 136 after 15% attrition, 18-29 years of age, estimated to include 73% male, 26% female, 1% transgender, 70% racial and ethnic minorities) into the study.

Recruitment for the study will be conducted by the CEC. Recruitment materials will include different electronic and printed materials (e.g. insta-stories; flyers, brochures, and palm-cards) and be distributed via social media sites, smartphone applications, email, as well as at community venues, clinics, and agencies as recommended by the Youth Advisory Committee (YAC) and stakeholders. Promotional materials (both virtual and physical) will include a brief description of the study and a rapid way to access the screening questionnaire – a hyperlink or QR code.

In the unlikely event that we do not accrue participants at the rate proposed with these time-tested procedures, we will pivot to more traditional venue and clinic-based recruitment approaches while adhering to COVID-19 safety recommendations. Participants will be self-identified through contact with (electronic or printed) recruitment materials. Additionally, we plan to utilize BuildClinical for an online recruitment campaign. The addition of BuildClinical is intended to address recruitment challenges for the study. BuildClinical is a data-driven platform that helps academic researchers recruit participants for research studies more efficiently using social media, software, and machine learning. BuildClinical has a long-standing history of working IRBs in the US to ensure they adhere to all the appropriate guidelines and procedures. BuildClinical utilizes study-specific advertisements to engage participants on digital platforms such as Facebook, Google, WebMD, etc. and redirect them to a study-specific landing page should they click it. On the landing page, the person can complete an online pre-screen questionnaire that gets routed into BuildClinical's platform. BuildClinical's Secure Socket Layer (SSL) software encrypts all inputted information and keeps information private and HIPAA compliant. The BuildClinical backend servers are stored in the United States at some of the most secure data centers in the world. All data collected from the BuildClinical screener is intended to inform the machine learning approach to tailoring the recruitment campaign and allows members of the CEC team to contact interested participants, who may then be directed to the SHARE study screener in REDCap. **No data collected in the BuildClinical screener will be linked to any study data** and the CEC will request that BuildClinical delete of all data collected as part of the pre-screener process upon conclusion of the campaign.

14.0 Withdrawal of Subjects*

A participant meets the criteria for “premature discontinuation” if they withdraw from the study before completion. Completion represents completing all interviews and surveys (pre and post). Participants meeting the criteria for premature discontinuation will be reported to the study team. Participants may choose to leave the study at any point. Participants may be removed from the study based on changes in eligibility and/or safety concerns after careful review and consideration by the study team as appropriate.

Participants will not be tracked after they withdraw and all data collection will be stopped at that time; however, the research team will keep track of which participants have withdrawn and the timepoint at which they were withdrawn from the study. If a participant withdraws before the completion of the study activities, the participant’s responses will remain a part of the study data corpus. Participant data will be included, unless a participant requests that their data is removed. In such cases, the participant’s data will be deleted. Participants will be informed of the ability to request their data is removed in the consent process.

15.0 Risks to Subjects*

Every effort will be made to ensure that study participants are protected from risks. The risks are as follows: 1) breach of confidentiality, 2) emotional discomfort when completing surveys and/or while using the mobile app, 3) medical complications from PEth biomarker collection or viral load test, and 4) concerns about data security associated with apps. The protection against each risk is described in detail below.

Breach of Confidentiality: A potential risk to participants is violation of confidentiality.. We will take the utmost caution to protect the confidentiality of all participant responses. We will minimize this risk by maintaining confidentiality and discretion in all study activities. Study data files will not have any identifying information about the study participants and will be tracked through a unique numerical identifier (study ID). This research specifically targets a vulnerable population, YPLWH. We will take every step to minimize the risk of identifying/linking data being successfully subpoenaed, stolen, or inadvertently released. The study will safeguard against the risk of the linking information being stolen by keeping such information in an encrypted, password protected file on FSU's secure server to which only the MPI (Naar) and study Project Coordinator have access. These individuals will have completed CITI certification for human subject's research ethics training (http://citiprogram.org). Furthermore, a certificate of confidentiality (CoC) will be in place.

Emotional discomfort: It is possible that participants may experience emotional discomfort when completing surveys and/or while using the mobile app. The study may precipitate discomfort and/or an emotional response when YPLWH provide information about their lives and HIV status. Further, participants may feel embarrassed about discussing sensitive issues. To minimize harm, participants are not required to answer any questions or provide any information that they do not wish to provide. They are also not required to use any features of the app that they do not wish to use, and they will have the freedom to uninstall the app from their phone at any time. All participants will be told during the informed consent/assent process that their participation is voluntary and that they can chose to stop participating at any time without any consequences.

Medical complications/discomfort from finger prick for PEth biomarker: The measurements that are involved in this study require finger prick to collect blood samples. This procedure may cause local discomfort, bleeding, or bruising; rarely infection can occur at the blood draw site. This measurement should not be considered greater than minimal risk in and of itself given its routine use in general health care delivery.

Medical complications/discomfort from VL DBS collection: The measurements that are involved in this study require dried blood spot (DBS) samples. The HemaSpot® sampling kit will be used for DBS collection. A disposable lancet provided in the kit will be used to prick

the finger for the collection of 2-3 drops of blood. This procedure may cause local discomfort, bleeding, or bruising; rarely small clot or infection can occur at the blood site. This measurement should not be considered greater than minimal risk in and of itself given its routine use in general health care delivery.

Concerns about app data security: Participants may be concerned about the security of their data, particularly since it is collected and stored electronically. Our study team has significant experience developing security protocols for Internet-based studies, and we will take a variety of steps to ensure participant security, including using a dedicated server behind a firewall, encryption of data, separation of identifiers from responses, and password-protected access to data. Therefore, we believe that this risk will be minimal.

Crisis Mitigation: Some of the measures we are using contain sensitive information and may be triggering to some participants. As we have done in previous studies, we have put in place procedures to protect participants' safety and well-being. During the programming of our assessments, sensitive questions such as suicide attempts, trauma experiences, and sexual abuse will be flagged. When responses reach a predetermined critical level, the system will send an automated notification to the Project Director who will initiate our crisis management and safety protocols directed by clinical psychologists, Drs. Ennis and Naar. Remote interviewers (e.g. guiding participants through the assisted survey) will also be given the ability to activate this system during Zoom meetings with participants. The clinician on call will contact the participant to initiate a crisis intervention counseling session using a HIPAA compliant telehealth platform. In the case of bandwidth or technology failure, the clinician will make standard telephone call. During the session, the clinician will assess the specific nature of the participant's situation and develop a plan to connect the participant needed community resources. In cases of acute emergencies, the clinician will call 911 and follow-up with wellness checks. Standard case notes will be used to document all crisis intervention sessions.

No information about the study's actual purpose with be withheld from study subjects. We do not anticipate unforeseeable risks.

16.0 Potential Benefits to Subjects*

The risk to individual participants is small and the potential benefit to society is substantial. There are no direct benefits to participants, although some persons enjoy participating in studies that can provide information to help others.

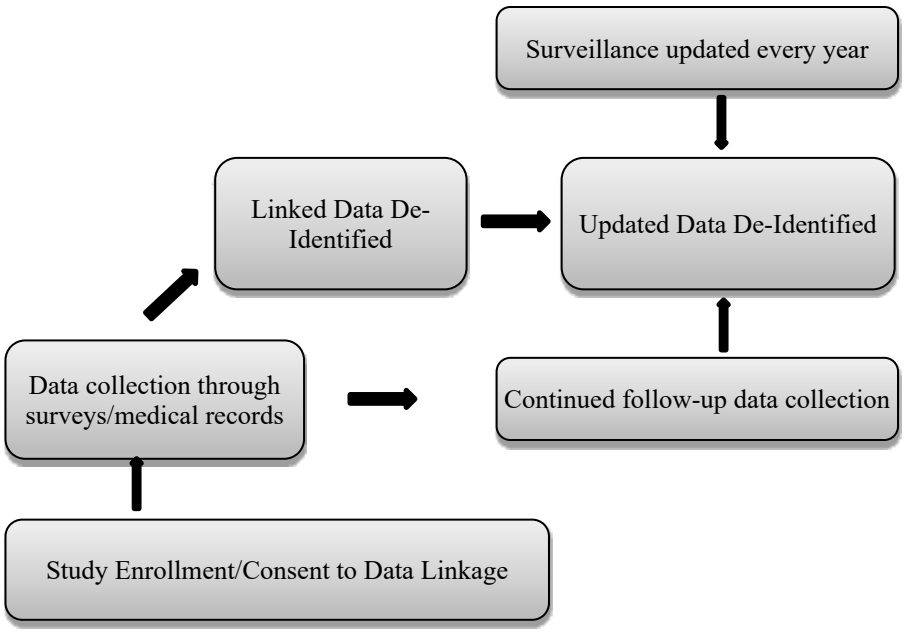
17.0 Data Management* and Confidentiality

Confidentiality: Prior to involvement, all study personnel will complete the required web-based Collaborative IRB Training Initiative (CITI)

course. All study personnel facilitating enrollment will adhere to the study protocols for obtaining informed consent from participants. Further, confidentiality will be protected through the use of unique participant identifiers, and all study data (quantitative, qualitative, recordings, etc.) will be securely stored at the Center for Translational Behavioral Science under lock and key, or on Florida State University password-protected secure servers, with access granted only to authorized study personnel. To further protect the privacy of the study participants, the study will obtain a Certificate of Confidentiality from the U.S. Department of Health and Human (DHHS). With this Certificate in place, researchers cannot be forced to turn over identifying information about a study participant in any Federal, State, or local criminal, administrative, legislative, or other proceedings. This Certificate does not prevent a study participant from volunteering to turn over their research information, nor does it prevent researchers from providing research-related information to others when requested by the study participant.

Data Management: All study data will be kept confidential in accordance with Florida state laws and Federal law. When study activities with participants are conducted virtually, the Zoom HIPAA compliant platform will be utilized to ensure participant confidentiality. Zoom meetings will not be recorded. Participants will be assigned a unique ID and all other identifiable participant data will be redacted from study records.

Information collected from this study will be linked with information abstracted from electronic medical records (EMR) and state surveillance including the Enhanced HIV/AIDS Reporting System (eHARS). We will obtain your data 1 year prior to your baseline assessment and 2 years post your follow-up assessment. DSC has already established this procedure of data linkage and management with eHARS in previous IRB-approved



studies. We will use the NIH Global Unique ID (GUID) to conduct data linkage. Specifically, we will collect each participant's legal name at birth, date of birth, sex, and city/municipality of birth. A single research team member supervised by Dr. Wu, and who does not have access to research data, will access GUID tool to perform bulk GUID generation for participants enrolled in the study. The GUID list will be sent securely to a single contact at the Florida Department of Health (FDOH) in Tallahassee. There, the contact will use the GUID list to obtain the latest HIV, and mental health and substance use surveillance data for these individuals, remove all other identifying information, and send the data back securely to our data science core. For this specific study, the data linkage process will also be approved by the FDOH IRB and accompanied by a Data Sharing Agreement between the research team and FDOH. For subjects reported no clinical visit, viral load will be collected using DBS procedure to supplement FDOH data. This process has been used multiple times over the past 4 years, and no data security issues have occurred.

To enable linkage of subjects who have incomplete Personally Identifiable Information (PII) to generate GUID, we will employ a second cryptographic hash function that is based on less PII to generate SHARE_ID. In other words, we will send GUID and SHARE_ID lists to FDOH. Because cryptographic hash is a one-way function, it is practically impossible to recover PHI from the GUID or SHARE_ID. The requested disclosure of PHI is the minimum necessary for research purposes.

In addition, the Data Science Core will utilize clinical natural language processing methods for extracting social determinants of health and behavioral determinants of health behaviors (e.g., smoking, substance abuse, alcohol use) utilizing the Florida Department of Health, HIV/AIDS Surveillance Program (FDOH HSP), the OneFlorida Data Trust, and the University of South Florida Policy and Services Research Data Center (USF PSRDC).

Brief summary of the assessment schedule for data that will eventually be shared with the $NIAAA_{DA}$ (via executed DUA00000137):

The core staff will link information collected from this study with public health surveillance data including the Enhanced HIV/AIDS Reporting System (eHARS). We will use the NIH GUID to conduct data linkage, which should be an improved procedure of data linkage and management with eHARS in our previous Florida Cohort study approved by the UF IRB (IRB #201500849). Specifically, we will collect each participant's legal name at birth, date of birth, sex, and city/municipality of birth. A single research team member supervised by Dr. Wu, and who does not have access to research data, will access GUID tool to perform bulk GUID generation for participants enrolled in the study. The GUID list will be sent securely to a single contact at the Florida Department of Health (FDOH) in Tallahassee. There, the contact will use the GUID list to obtain the latest HIV,

and mental health and substance use surveillance data for these individuals, remove all other identifying information, and send the data back securely to our data science core. For this specific study, the data linkage process will also be approved by the FDOH IRB and accompanied by a Data Sharing Agreement between the research team and FDOH. For subjects reported no clinical visit, viral load will be collected using DBS procedure to supplement FDOH data.

In addition to active participant data, the SHARE P01 Data Science Core will utilize clinical natural language processing (NLP) methods for extracting social determinants of health (SDOH) and behavioral determinants of health behaviors (BDOH, e.g., smoking, substance abuse, alcohol use) utilizing the Florida Department of Health, HIV/AIDS Surveillance Program (FDOH HSP), the OneFlorida Data Trust, the University of South Florida Policy and Services Research Data Center (USF PSRDC) (see Data Science Core Research Strategy for full list of available databases). The data integration activities will be performed during the first three years of this project.

Listing of proposed data collection instruments (assessments) that do not currently exist in the NDA (if applicable):

All measures have been previously utilized by the MPIs in preliminary studies and across the NIH Adolescent Trials Network for HIV/AIDS Interventions or are accepted in the literature. For further synergy, all three projects will test age, ethnicity, biological sex and gender, other substance use and mental health as moderators.

18.0 Provisions to Monitor the Data to Ensure the Safety of Subjects*

Data Storage and Sharing: Participant data will be de-identified and stored in a centralized location within the Data Science Core at the University Florida. Additionally, Data Science Core personnel at the University of South Florida will access data stored at the University of Florida and Florida State University in line with the DSC aims and associated tasks. Only approved study personnel will have the ability to access identifiable data, which will be stored and disposed of according to applicable federal and state statutes and institutional rules/regulations. The associated project core leads at the contact institution will utilize the confidential and secure transfer and acquisition of relevant study between the Data Science Core and research projects as described in the approved IRB protocol and associated agreements.

Monitoring Data Quality: The Admin Core will provide regulatory support and monitoring for the study team. This will include the development of protocols, Standard Operating Procedures (SOPs), and will assist the project leads with the finalization of measures. Quantitative study data will be entered into RedCap by the Data Science Core PI and study personnel as applicable, for all study timepoints within each

project. All Electronic Health Record (EHR) data utilized from respective study sites will be securely submitted every six months or upon data download as applicable. The MPIs and project leads will be responsible for continual monitoring of the database, data structure, and data quality and report these efforts at bi-annual SMC meetings.

Data Safety and Monitoring Board: In order to comply with the NIH policy related to a single institutional review board, it is the recommendation of the study team to utilize an independent study monitoring committee (SMC). Members selected as part of the SMC will possess the relevant expertise (e.g., HIV-related research and prevention, adolescent health and medicine, and adolescent and emerging adult sexual health and substance use). A committee of individuals, coordinated by the contact MPI and project manager, will at minimum participate in bi-annual tele-conference meetings to:

1. Review the study's ongoing compliance with data safety standards, required IRB monitoring and approvals, recruitment, accrual and retention, risks vs. benefits, protocol and timeline changes, and study progress toward the achieving the overall study aims.
2. Review unanticipated study problems and all adverse events, and report concerns to the appropriate governing bodies should a risk to participant safety require such reporting.
3. Assess participating sites and provide feedback and/or make ethical recommendations for necessity of external site participation in the achievement of study aims.

Members of the Monitoring Board will be required to:

1. Have no direct contact with study MPIs and key personnel outside of relevant study monitoring activities.
2. Sign a Conflict-of-Interest statement, and disclose all relationships and affiliations related to the study and/or associated interests relevant to the aims and objectives of the study that could present or be perceived as a conflict of interest.

SMC Meeting Format: The format for all SMC meetings will be an open and closed session, followed open session (if needed) where the MPIs will be informed of recommendations of the SMC. The open sessions will include the MPIs and applicable study personnel (project manager, project coordinators), wherein issues will be discussed related to study conduct and progress of the study, including accrual, compliance with overall study design, compliance with regulatory functions and oversight, adverse

events, and will review aggregate study data. No personally identifiable information will be shared or connected to the aggregate data discussed in the meeting. The closed session will allow for SMC members to participate in confidential and independent discussion related to study recommendations. Any suggestions related to early termination of a study component will require a vote of the SMC members.

NAME	ROLE	EXPERTISE
Marvin Belzer, MD Director, Division of Adolescent and Young Adult Medicine; Attending Physician, Children's Hospital of Los Angeles Professor of Pediatrics and Medicine, Keck School of Medicine of USC mbelzer@chla.usc.edu 323.361.2153		Adolescent and Young Adult Medicine & Behavioral Health, HIV
Larry Brown, MD Director of the Division of Child and Adolescent Psychiatry Vice Chair of the Department of Psychiatry and Human Behavior, Brown University larry_brown@brown.edu 401.444.8539		HIV and risk behaviors among adolescents and young adults, HIV biobehavioral clinical trial research, substance use and depression among PLWH, mHealth
Ken Resnicow, PhD Professor of Health Behavior and Health Education University of Michigan, School of Public Health kresnic@umich.edu 734.647.0212		Health behavior, e-Health technology, Health messaging, Substance Use, Minority and Health Disparity Research
Samantha Chahin, MPH SHARE Study Coordinator Florida State University Samantha.chahin@med.fsu.edu	*Designee*	

19.0 Provisions to Protect the Privacy Interests of Subjects

Privacy Interests – Interactions. In order to protect the privacy interests of study participants, recruitment, consent, enrollment, and retention activities will be centralized to the greatest extent possible.

Privacy Interests – Data. All data transferred from FDOH to the study team will transferred through the secure FSU Dropbox portal or FDOH

MoveIT data transfer system, as a password protected and/or encrypted file accessed through login/password. The study team will then store the received data as an encrypted file on the secure FSU Network server and the USF Health Informatics Data Management System. Data will be stored and disposed of per prevailing record retention regulations and sponsor requirements where applicable. The requested disclosure of PHI is the minimum necessary for research purposes.

Privacy Interests – Access. Only those members included on this study protocol as engaged personnel will have access to study data. Prior to upload to any shared file storage/management system, all participant data will be fully de-identified and stored as encrypted, password protected files to ensure data security and fidelity.

Breach of Confidentiality: We will take every precaution to minimize risks to study participants. All research staff members are required to complete ethical clearance certification regarding protection of human subjects. We also have a strong data and safety monitoring plan in place to protect participants. Adverse events will be reported to FSU using the Adverse Event Reporting Forms as well as to the NIH. Reports will be sent within 24 hours of notification by the MPIs. Annual updates on enrollment and retention will also be sent to the FSU IRB and reported to the NIH.

All NIH-funded studies collecting sensitive data are now considered to be granted a Certificate of confidentiality. This certificate will protect the confidentiality of all research records generated by this study. Individually identifiable health information will be protected in accordance with the Health Insurance Portability and Accountability Act of 1996. All research personnel will be trained on human subjects' protection and HIPAA procedures.

Alcohol monitoring using wrist biosensor: The risk for breach of confidentiality associated with the biosensor is very low. Participants will be given a study account for them to use to log into the Skyn app, so no personal information (e.g., email address) will be collected from the Skyn sensor or app. The data will be uploaded to its encrypted cloud-based storage and will be downloaded to secure drives managed by the Data Science core. Only study ID will be used to link the data. Login to the data portal for data downloading is password protected. Only the study PI and key personnel will have the login information for downloading the data. The Skyn biosensor and its associated app and database have been evaluated by the University of Florida IT Risk Assessment team and deemed low risk.

Ecological momentary assessment (EMA) of self-reported drinking: The risk for breach of confidentiality associated with the EMA app is very low because of its encrypted cloud-based storage. Additionally, the App will use an 8-digit code generated by its system for participants to use as

the unique identifier to collect data, so no personal information (e.g., phone number) will be collected. Login to the data portal for data downloading is password protected. Only the study PI and key personnel will have the login information for downloading the data. The EMA app and its database have been evaluated by the University of Florida Risk Assessment team and deemed low risk.

eWrapper app specific security: We have included numerous features to ensure app security and privacy. All relevant app communications (e.g., those between users or between users and study staff) will be secured via industry standard encrypted Secure Socket Layer (SSL) communications links. These connections will ensure that all communications are inaccessible to unauthorized third parties. Furthermore, the app can be updated regularly to address any unforeseen security updates to the software libraries underlying the secured communication links. Beyond encrypting communication, the app itself requires users to set up a password as part of their onboarding procedures. This adds a layer of security to protect privacy and confidentiality and allows the user to share their phone generally with others without granting access to the app. The app is designed to be non-stigmatizing and un-interpretable by anyone seeing the app on a participant's phone. Additionally, the app icon and reminders are discrete and do not utilize HIV-related language or imagery. Moreover, mobile phone screens themselves are also constructed to prevent surreptitious observation. Within the app, participants set up a profile and choose a username. Participants are required to choose a username that is different from any names they may use as part of their personal email address or social media accounts. Consent documents will also encourage participants to activate their phone's native locking feature for a further layer of security. These software security solutions will provide the layers of both communications' security and physical access security to ensure that only authorized users have access to the information stored on the phone as well as the information being shared over communications links. Finally, the app platform is engineered to keep PHI safe and secure and is HIPAA compliant.

20.0 Compensation for Research-Related Injury

Due to the nature of the study, no research-related injury is expected, and no funds are available for research-related injury

21.0 Economic Burden to Subjects

The research does not anticipate any costs that subjects may be responsible for because of participation in the research.

22.0 Consent Process

Informed consent will be automated. The consent process will provide an interactive multimedia experience that will enable potential participants to make informed decisions using a point-and-click interface and allows

the research team to assess whether the potential participant has fully understood the parameters for participation via a series of interactive questions and answers. Those who click on the "yes" button will be redirected to a secure database to read and provide informed consent. For those who would like, there will be an additional consent video that will provide an overview of the information in the informed consent. Participants who watch this video will be directed to the written copy of the informed consent following the video's completion. Those who provide consent will receive a link to complete the baseline assessment and instructed that a research team member will contact them to schedule a session to complete an assisted survey. With guidance from our YAC and stakeholders, we will use an electronic consent platform such as REDCap's Cloud's flexible eConsent solution to develop an engaging informed consent for each study. As part of this process, participants will be asked if they are willing to enroll or are already enrolled in a mobile payment service such as CashApp for distribution of the incentive. We will send e-gift cards for incentives to participants who chose not to enroll in the mobile payment service. Upon approval of the HIPAA Authorization form contents from the Florida Department of Health (FDOH), participants will be asked to complete the HIPAA authorization form to authorize accessing viral load information from their electronic health records or from the FDOH database. Recruitment of study subjects will not occur until FDOH approves the HIPAA authorization, as the covered entity. Moreover, the participant will be asked to sign an agreement in which they agree to send back study materials to the ENGAGE study team in Gainesville, Florida. After providing this information, the participant will be redirected via secure hyperlink to a separate database to complete the baseline assessment.

The risk of potential coercion will be minimized by following standard procedures for obtaining informed consent from participants. During the e-consent process, study procedures, risks, benefits, and alternatives to participate will be explained to participants. Participants will be told that they do not have to answer any questions if they do not wish to and can drop out of the study at any time without affecting their medical care or the cost of their care. They will be told that they may not benefit directly from the study, and that all information will be kept strictly confidential, except as required by law. Participants will also be reminded that study participation is voluntary and that refusing to participate or withdrawing from the study at any time will not result in any negative consequences.

Any participants who have questions or concerns that arise during the consent process can contact the SHARE Program's Community Engagement Core personnel at SHARE.CEC@med.fsu.edu and/or Dr. Sylvie Naar and/or Dr. Yan Wang at sylvie.naar@med.fsu.edu and/or ywang48@phhp.ufl.edu.

23.0 Process to Document Consent in Writing

The study team will obtain consent via REDCap enrollment form. Clicking on "Yes" and providing their electronic signature on the REDCap form will be considered consent to participate.

24.0 Setting

All data will be gathered and analyzed by IRB approved personnel within the Data Science Core at the University of Florida, the University of South Florida, at the University of Michigan, and at Florida State University's Center for Translational Behavioral Science. This is a virtual study, which means that all study assessments and activities will take place online or virtually. There will be no face-to-face interactions with participants for this study.

25.0 Resources Available

Feasibility of Recruitment and Study Completion. Dr. Sylvie Naar (SHARE Program MPI) has spent two years developing active partnerships with state and community level stakeholders in Florida, toward the goals of the federal End the HIV Epidemic initiative. These collaborations have been developed through her ongoing projects within her Scale It Up – Florida research program that houses the NIH funded Scale It Up project, the FDOH funded FLEX Peer Navigation service program, as well as her iREP community needs assessment, all of which focus on adolescents and young adults living with or at-risk for HIV. The effort to establish community-based connections with individuals and organizations to that end has facilitated a far-reaching state-wide network of engaged stakeholders within community-based organizations, HIV treatment clinics, testing service providers, and members of the target population. Further, these connections have created a large state-wide participant recruitment audience who are members of the study's target population. Additionally, the support of NIH funding toward the success of this project will allow for adequate personnel, supplies, infrastructure, technology, and other necessary means to be utilized to ensure study completion.

A summary of the recruitment and assessment activities the entire SHARE program is found in Table 1. Our projected yearly accrual rate is reasonable given that there are 8,000 YPLWH in Florida in our target age group. Furthermore, in 2019, 8% of the 4,584 newly diagnosed HIV cases in the state were between 18 and 29. The RERAC will manage the distribution and processing of the biomarker self-assessment kits and all of the participant engagement, tracking and retention functions.

Table 1: RERAC Schedule of Recruitment and Assessments

Activity	Year 1	Year 2	Year 3	Year 4	Year 5

Screen	1,152	2,304	2,304	384	
Recruitment	144	288	288	48	13
Baseline	144	288	288	48	13
Follow-ups	72	500	900	611	118

Resources available. As mentioned above, the Scale It Up Florida program has developed program specific services and resources to aid individuals within the target population of this study. The FLEX Peer Navigation program is designed specifically to address the needs of YPLWH by providing a peer-level navigation resource providing information and referrals to resources that are specific to the unique needs of YPLWH through the use of a need's assessment, partnership with Ryan White case managers in all 67 Florida counties.

Facilities. The Center for Translational Behavioral Science (CTBScience) is a university center, affiliated with the FSU College of Medicine. This facility provides 6 faculty offices, 4 research core offices, a program manager office, two shared postdoc offices, offices for a research coordinator and research assistants, and a shared space for students and staff working with faculty. The center also houses 4 multifunctional participant spaces, 2 of which can function as working sleep laboratories equipped with state-of-the-art sleep diagnostic equipment, video monitoring / recording capability and 2 of which have the ability to be used as both assessment rooms and therapy rooms. Further, the center houses a conference room with video conferencing capabilities and a community space that functions as a group meeting room and/or classroom. Within its three cores (Management Core, Methods Core, and Community Engagement), the Center has a dedicated clinical trials coordinator, administrative coordinator, grants contracts administrator, data manager, biostatisticians, and a communications expert as well as access to FSU's IT, library, and other administrative resources. CTBScience also hosts the Adolescent Trials Network (ATN) Scale It Up Center's Analytic Core, Implementation Science Core, and Management Core, with dedicated faculty members assisting with protocol development, recruitment and retention, sustainment, study management, data management and analysis, and dissemination. There is a Youth Community Advisory Board (YCAB) nationwide for the ATN, and an ATN Bioethics Working Group, which is made up of a team of national ethics experts. The Management core, along with the study team will maintain responsibility for the overall conduct and implementation of the study. The study team is responsible for data management, analysis and reporting. The Protocol Leads are responsible for scientific leadership and dissemination.

Required CITI Training. All study team members will be adequately trained in the responsible conduct of research, and the study team will continue weekly meetings to discuss project status, address concerns, and ensure protocol compliance. Study participants will be fully informed of the study team members roles and functions, and provided information

related to reporting of concerns. If serious or unexpected adverse events occur during the study, the PI will report these occurrences within the specified time frames to the IRB.

26.0 Multi-Site Research*

All information included in this section is relevant to SHARE Program as a whole. Those below specific to the Engage study are identified as such (see tables).

Selection of the sIRB

The Florida State University (FSU) has been selected to serve as the single IRB of record (sIRB) for the proposed study. All participating domestic institutions engaged in human subjects research have agreed to rely on the FSU IRB, and any domestic sites added after the award will be required to complete a reliance agreement unless they meet exclusion criteria related to engagement in human subjects research.

Exceptions: *There are no sites meeting the criteria for an exception to the single IRB requirement.*

FSU IRB Compliance and Qualifications

The FSU IRB currently oversees a multitude of human subjects research studies including behavioral clinical trials. Further, the FSU IRB currently oversees Dr. Naar's multi-site project (Scale It Up, U19), and maintains oversight of each study component and collaborates with 20 external domestic sites.

FSU's IRB operates in compliance with all relevant federal and local regulations and is registered with FDA and OHRP. FSU maintains an active Federal Wide Assurance (FWA) with the Office for Human Research Protections (FWA00000168).

The FSU IRB has appropriate membership, including the professional competence necessary to review the proposed research, and is supported by the FSU Office for Human Subjects Protection (OHSP)..

Reliance Agreements

Before initiating any engaged study activities, each participating site will fully execute a reliance agreement with the sIRB. This agreement will clarify the roles and responsibilities of both the sIRB and each participating site. Further, FSU is a signatory to the SMART IRB Agreement and will facilitate the SMART IRB agreement with all applicable external domestic sites.

Communication Plan

The FSU IRB utilizes an online protocol submission system that is accessible by FSU faculty and staff members, with the ability to allow external access as requested for external site investigators collaborating on multi-site projects. All protocol materials will be submitted to the sIRB through the online system and all external domestic sites will provide the necessary assurances to the FSU Admin Core team overseeing the regulatory components of the project. The FSU Admin Core team will provide each site with the necessary materials applicable to their sites as required and will communicate directly with each participating site's IRBs and/or Human Research Protection Program offices/personnel. When necessary, the FSU OHSP in support of the sIRB will communicate directly with participating site Human Research Protection Program offices.

The Admin Core, under the supervision of the contact MPI and core/project leads, will provide coordination services by:

1. Coordinating communication with all external domestic sites
2. Request and receive information and required documentation for all participating sites
3. Develop template materials for review by the sIRB and assist external participating sites with modifications as necessary
4. Compile, review, and submit all protocol materials to the sIRB online system related to initial approvals, study modifications, continuing reviews, etc.
5. Provide all necessary documentation to all participating sites

Participating sites will follow local procedures in order to coordinate, collect, verify, and disseminate information for:

1. Local context
2. Site variations and/or necessary modifications related to recruiting, informed consent, HIPAA, and study populations
3. Conflict of interest and disclosure management
4. Completion of ancillary reviews
5. Ensuring proper CITI training of all engaged study personnel and provide certifications to the Admin Core at FSU.
6. Complying with requirements of all Continuing Reviews or study closures
7. Monitoring and reporting adverse events All modifications have been communicated to sites and approved (including approval by the site's IRB of record) before the modification is implemented.

A study query system will be developed by the SHARE Program AC and will allow for investigators and study personnel to submit queries related to study activities to the centralized study email address. This query system will be monitored by the SHARE Program AC and will

have automatic triage functions built into the query system to alert necessary study personnel based on responses entered.

In line the proposal, the SHARE Program will utilize Microsoft Teams, housed on the Florida State University network, to conduct study team meetings, share de-identified study specific information and regulatory. In line with the existing agreement FSU Information Technology Services has with Microsoft, the study team will abide by the privacies and security set forth, wherein no identifiable participant data will be stored on Microsoft OneDrive unless encrypted and password protected.

All direct recruitment activities for Define, Engage, and Sustain will be within the SHARE Program Cores as follows:

Core	Function
FSU - Admin Core	- Will order, distribute, and track PEth and DBS test kits and facilitate shipment of returned kits to laboratory for Define, Engage, and Sustain - Will track, disburse, and reconcile participant incentives for Define, Engage, and Sustain - Will oversee regulatory components of recruitment (e.g., social media marketing campaign development and oversight) for Define, Engage, and Sustain
FSU - Community Engagement Core	- Will facilitate field-based recruitment efforts including organizational stakeholder and participant engagement, provide study related recruitment materials, and facilitate consent and enrollment for Define, Engage, and Sustain - Will manage social media and other digital recruitment activities, and facilitate Scientific and Youth Advisory Councils for Define, Engage, and Sustain
UF, USF & FSU– Data Science Core	- Will develop and manage REDCap consent and survey tools/instruments for Define, Engage, and Sustain - Will manage all identifiable participant data and survey responses for Define, Engage, and Sustain - Will facilitate and manage FDOH Data for Define, Engage, and Sustain - Will integrate and oversee Data Sharing Plan requirements

The following external to FSU sites are involved in the SHARE Program and are considered engaged in human subject activities and will participate in the activities as described above.

Site	Core/Project	Name/Role
University of Florida	ENGAGE Project Admin Core	**Yan Wang**, PhD; Project PI **Bob Cooke**, PhD; Co-I

University of Central Florida	DEFINE Project	**Karina Villalba**, PhD; Site PI
University of Michigan	Data Science Core SUSTAIN Project	**Inbal Nahum-Shani**, PhD; Site PI
University of California, San Diego	DEFINE Project	**Sharon Nichols**, PhD; Site PI
University of South Florida	Data Science Core	**Samuel Wu, PhD; Site PI, DSC Lead**
Northeastern University	SUSTAIN Project	**Robert Leeman, PhD; Co-I**