Title: Laboratory and field validation of a wrist-worn alcohol monitor

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Protocol

1. Project Title

Laboratory and field validation of a wrist-worn alcohol monitor

2. Investigator(s):

Yan Wang, PhD (Principal Investigator)
Robert Cook, MD, MPH (Co-Investigator)
Eric Porges, PhD (Co-Investigator)

3. Abstract:

Alcohol use among persons living with HIV remains a significant barrier for ending the HIV epidemic. The newest generation of wrist-worn alcohol monitor provides an unprecedented opportunity for improving alcohol intervention among this population. The proposed project will be the first study to validate the BACtrack Skyn wrist-worn alcohol monitor (Fig.1) in HIV+ drinkers with HIV- drinkers as comparison and evaluate its utility for research/clinical application.

4. Background:

As HIV infection becomes a chronic condition with antiretroviral treatment, alcohol use remains a significant barrier for mitigating transmission,[1] achieving viral suppression,[2,3] and reducing comorbidities and all-cause mortality.[4-9] In general, there are few effective alcohol interventions for persons living with HIV (PLWH).[3,10] Traditional interventions also tend to have limited long-term benefit, partly due to the lack of individualized feedback and the absence of continuing care outside of the clinical setting.[11] More cost-effective interventions (e.g., mHealth intervention) that can be individualized and implemented in daily life to sustain behavior change are urgently needed for PLWH.[10,12]

Mobile technologies (e.g., smartphone applications) are rapidly changing the landscape of medical care and interventions,[13-17] including for PLWH.[18] Currently, smartphone-based intervention has shown some evidence of efficacy for alcohol use among PLWH.[12,19] However, accurately monitoring alcohol consumption remains a significant challenge.[20,21] According to the Integrated Theory of Health Behavior Change, self-monitoring is a key element of self-management to improve health outcomes.[22] Recent developments in wearable alcohol monitors provide a potential powerful tool to monitor alcohol use in real-time with minimal participant burden.[20,23-28]

Transdermal alcohol monitors can provide noninvasive, continuous monitoring of alcohol use by detecting ethanol diffused through the skin.[27,31] Secure Continuous Remote Alcohol Monitor (SCRAM) anklet (Alcohol Monitoring Systems, Inc.) is the most widely used transdermal monitor but is designed to be used for law enforcement purposes.[32] However, wider application of SCRAM anklet in clinical and intervention settings is limited by its shortcomings including its large size, high cost, and social stigma.[20,25,29] The newest generation of wrist-worn alcohol monitor (BACtrack Skyn) is designed for consumer use and

addresses these limitations. The device looks like a fitness tracker, is inexpensive, samples up to every second, and transmits and shows data in real-time via a smartphone app. These advantages make this wrist-worn alcohol monitor a potentially ideal tool to be incorporated into smartphone-based intervention for alcohol use. However, prior to its application in research, thorough validation investigations of the monitor are needed. In this project, we will validate the Skyn monitor among 20 HIV+ drinkers and 20 HIV- drinkers (as comparison group) in both laboratory and field settings.

Fig.1. BACtrack Skyn Alcohol Monitor

5. Specific Aims:

Aim 1: Assess the validity and reliability of the Skyn monitor through comparison with laboratory grade breathalyzer in two fixed-dose lab alcohol administration sessions (Sec. 4.3, 4.5)

Hypothesis 1a: The monitor will be able to detect alcohol use at a low threshold (e.g., one drink).

Hypothesis 1b: The parameters of transdermal alcohol concentration (TAC) (e.g., peak, time-to-peak, area under the curve) will be correlated with number of drinks and breath alcohol concentration (BrAC).

Hypothesis 1c: The TAC readings in two lab sessions will show high correlation (test-retest reliability).

Aim 2: Validate Skyn monitor in daily life using a 2-week ecological momentary assessment (EMA), and evaluate its acceptability and usability for daily alcohol monitoring (Sec.4.4)

Hypothesis 2a: The monitor detected drinking episodes will correspond with self-reports in EMA.

Hypothesis 2b: The TAC readings will correlate with number of drinks in each drinking episode.

Exploratory Aim: Explore factors (e.g., gender, HIV status) that may be associated with individual differences in monitor readings (e.g., peak, time-to-peak, correlation with consumption level).

6. Research Plan:

Overview

This study will include two parts: laboratory and field validation of the Skyn monitor(Fig. 2). We will need complete data from 20 HIV+ drinkers (~50% male) and 20 HIV- drinkers (~50% male), but we will screen to 160 participants to account for potential screen failure and drop out. Participants will be invited to complete all components of the study or only the field test portion given the COVID pandemic. The PI will decide who will complete all components and who will complete only the field testing. Participants will first complete an alcohol administration session (Lab Session 1) at the simulated bar lab, where they will consume 3 standard drinks (i.e., 3 12oz beers) at a determined consumption rate (30min). The transdermal alcohol concentration (TAC) readings collected from the Skyn monitor will be compared with breath alcohol concentration (BrAC) and may be compared with the Secure Continuous Remote Alcohol Monitor (SCRAM; Alcohol Monitoring Systems, Inc.) anklet. After completing Lab Session 1, during a two-week field test, participants will use the Skyn monitor and record drinking episodes using an EMA app. After the field test, participants will return to the bar lab to complete a second alcohol administration session using the same procedures as in Lab Session 1 to obtain test-retest reliability of the monitor. They will also complete a questionnaire on the acceptability and usability based on their experience with the Skyn monitor and its smartphone app.

Of note, BACtrack Skyn monitor has been approved in our previous study (IRB201700455 for laboratory alcohol administration study where participants wear the monitor while they self-administer alcohol in the bar lab).

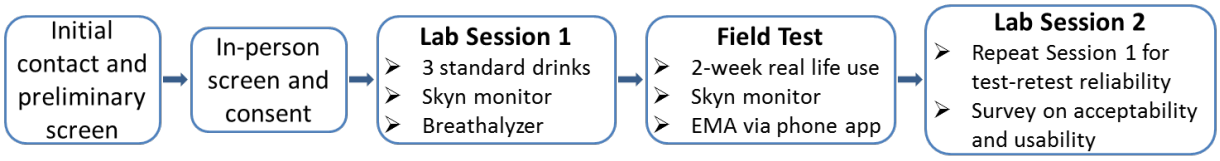

Figure 2. Study Procedures

Participants

Participants will be HIV+ and HIV- drinkers aged 21 - 64. HIV+ drinkers will be primarily recruited from the existing Florida Cohort registry managed by SHARC (Director: Dr. Cook). We will recruit from those who live in North-Central Florida area (n = 237, 60% male, 70% drank alcohol in past year) within 90 miles of the data collection site (not applicable to field only participants). We will also recruit participants from HealthStreet and Consent2Share through their referral service(s), the Center for Cognitive Aging and Memory (CAM) Registry, self-referrals from patients who see our flyers or social media advertising, and/or referrals from other UF HIV/alcohol studies (e.g., IRB201901192, IRB201702564). For referrals, research coordinators for the other studies will introduce this study to their participants at the end of their study procedures. Interested participants can choose to be screened onsite (if they are in another alcohol administration study like IRB201901192 and we have available study staff to do so), call us for further information, or leave their contact

information using the Contact Authorization Form. We will also send research staff to recruit from local community, such as local events (e.g., free HIV testing events) and clinics/organizations (e.g., Department of Health, Infectious Disease clinic within the UF Medical Plaza). For in-person recruitment, physicians at the clinic (e.g., Dr. Jennifer Janelle at UF infectious disease) will introduce our research staff after they meet with the patients for their appointment. If the patients agree, the physician will ask our research staff to go and talk with the patients in a private room (e.g., the exam room) about the study. They will either perform the preliminary screen on site for those who express interest and want to be screened right away, or use Contact Authorization Form to collect information from those who prefer to receive a phone call about the study later for preliminary screening. When our research staff are not present in the clinics, patients can also use the Contact Authorization Form to leave their contact information for the clinical staff to send the information to us. Our research staff will contact the patients and follow the same procedures.

We will encourage each HIV+ drinker to refer up to 3 other drinkers, including persons that they suspect are HIV-, to participate. This will provide a comparison sample of HIV- drinkers who are likely to be of similar age and socio-economic status as the HIV+ participants. Additional inclusion criteria include self-reported ≥5 days with at least 1 alcoholic drink, and ≥1days with at least 3 drinks (the level of alcohol consumption in lab sessions) in the past 30 days. Exclusion criteria include recent addiction treatment or treatment seeking; urine positive for illegal drugs except THC (not applicable to those who are only invited to do field test); past & current alcohol withdrawal; severe alcohol use disorder (DSM-5); meeting criteria for current nicotine dependence(not applicable to field only participants) or current substance use disorder(excluding mild cannabis use disorder and mild/moderate alcohol use disorder) ; medical conditions (other than HIV) contraindicating alcohol; pregnancy/breastfeeding in women; psychosis or other severe psychiatric conditions. Current use of antidepressant medication will not be an exclusion criteria for participants who are only completing the field test portion of the study.

Screening

Potential participants will be contacted via phone call using their contact information in the Florida Cohort Registry, or they will contact our research staff if they are referred by others (i.e., HealthStreet, already enrolled participants) or self-referred (i.e., see our flyers in local HIV clinics). A trained research assistant (RA) will introduce the study and ask a few screening questions if the participant expresses interest. If the participant meets preliminary eligibility, the RA will schedule an in-person screen. For those who are asked to complete the field test only, portions of the in-person screening can be done remotely via phone call or password-protected UF zoom .If participants do not meet the preliminary eligibility, their data will be destroyed once their study status becomes clear. The in-person screen will include informed consent (can be signed in-person or as eICF through REDCap which will be sent via email), breath alcohol test (not applicable to field only participants), HIV test (only conducted on persons of unknown status to confirm HIV- status for the comparison group), drug and pregnancy test (women) (not applicable to field only participants), vital sign, height and weight collection, timeline followback (TLFB)[49] for past 30-day alcohol use, and diagnostic interview for substance use disorder/withdrawal. The measures used at this step include the “Clinical interview measures” and “Timeline followback”. The CIWA (which is included in the “clinical interview measures”) may be waived for HIV+ participants who complete the screening remotely. The SCID-V will also be conducted at this time, to assess

for current and past substance use disorders. The screen will take approximately 2 hours, and participants will receive $20 for completing it. Participants who come to their in-person screen as originally scheduled will be provided an additional $10 payment. If screening is done remotely participants will receive $10 as compensation for using their phone minutes and $10 for completing the first set of questionnaires. They will receive $10 for coming in to pick up the skyn device and completing the second half of the in-person screen plus an extra $10 if they keep their originally scheduled appointment. HIV+ participants who complete the entire screening remotely will have the option of having the skyn device and other study materials mailed to them to their preferred address. For participants who are HIV+, we will ask them to bring in medical records of their most recent HIV lab values (CD4/Viral load) at any in-person appointment and will provide $20 compensation for doing so. If the participant shows up for the in-person screening but the appointment needs to be rescheduled due to reasons on our end (e.g., logistic issues), then they will still receive the $20 for this appointment. Those eligible will be scheduled for two drinking sessions. For those who screen out at the in-person screen, their data collected up to the point will be retained in the same way as those who are deemed eligible, because they sign the consent form before going through the in-person screen. However, like other participants they have the right to revoke authorization to use their data in writing. Screening documents will be assessed by Dr. Wang to confirm eligibility, a signature will be provided only if the participant is eligible.

Participants will be given the option to receive an e-gift card, or receive the gift card via mail, if they do not want travel to UF campus to pick up a gift card.

For those who are deemed eligible for the study after the in-person screen, they will also complete the baseline survey (can be sent via email), where they will answer questions on demographics, drinking history, alcohol use disorder, alcohol effects, drinking motives, other substance use, and HIV treatment/adherence (for HIV+ participants only). Information obtained from these questions will be used to explore factors contributing to interpersonal variations in transdermal alcohol concentration and how they impact participant compliance in the field test (as some preliminary findings for building a larger project on this exploratory R21).

Lab Session 1. Participants will be asked not to eat for 3 hours pre-arrival, and arrive with a non-positive BrAC reading (.00%) detected by a laboratory degree breathalyzer (Alco-Sensor VXL, Intoximeters). In the event that an individual registers a positive breath alcohol level, there will be two possibilities. If the individual's breath alcohol level is likely to decline to 0.00% in a reasonable amount of time (i.e., 0.02% or lower), they will be offered the chance to remain at the research facility to be re-tested and take part in the appointment when their breath alcohol level reaches 0.00%. If it is not feasible for the participant to wait, they will be offered one opportunity to reschedule this appointment. Instruction/practice of the EMA app, Skyn monitor and its app will take place prior to the drinking session when participants are sober. The RA will help participants download the EMA app (Sec.4.4) on their smartphone, enter an 8-digit unique ID code for each participant, and show them how to enter a drinking session and answer the prompted questions. The RA will also help download the Skyn app and show participants how to pair the app with the monitor. The recording of data should automatically begin once the Skyn monitor is paired with the app. Instructions and demonstration of how to charge and operate the Skyn monitor will also be given. Procedures for the two-week field test will be explained. Participants will have time to

practice with the apps and monitor until they feel efficient with all. Further, participants may also be asked to wear the Secure Continuous Remote Alcohol Monitor (SCRAM; Alcohol Monitoring Systems, Inc.) anklet for the duration of the drinking session. The SCRAM anklet is similar to the Skyn device although it is worn around the ankle rather than the wrist. The SCRAM anklet will be used to evaluate whether transdermal alcohol concentration (TAC) readings obtained from each device converge, given that the SCRAM anklet is a validated TAC monitor. The SCRAM anklet has been approved and risk assessed in our previous study (IRB201700623).

Once practice with apps and monitor is completed, vital signs (including blood pressure, pulse, height and weight) will be collected, urine drug and pregnancy screening will occur, and participants will be provided a light snack (150-200 calories). Next, participants will be asked to complete some questionnaires (e.g., Alcohol Urge Questionnaire (AUQ); Positive and Negative Affect Scale (PANAS); Alcohol Purchase Task (APT); real time impaired control scale (ICRT); and a single-item question asking how much one wants alcohol currently).

Next, the drinking session will begin. We will provide several common beer brands with similar calorie (125-150) and alcohol level (~4.5% ABV) for the participants to choose from. Participants will be instructed to wear the Skyn monitor and SCRAM anklet and drink 3 beers by completing each beer in 15 minutes[50] with a 15-minute break in between (30min in total for each beer). During this time, the participant's BrAC will be measured every 30 minutes. Following the end of each beer during the 15-minute rest period, participants will also complete a brief packet of questionnaires very similar to the one they completed before drinking, plus the Biphasic Alcohol Effects Scale (BAES) and a single-item question asking how much one likes the effects of alcohol. Alcohol administration will be conducted per NIAAA guidelines[51].

At the end of the 90-minute drinking period, participants will give breath alcohol readings approximately every 15 minutes for the remainder of the session. Every hour participants will also complete the same brief packet of questionnaires they completed earlier in the session. At the end of the evening participants will remove the SCRAM anklet. All participants are required to remain in the simulated lab or research office for two hours after drinking and until the participant's breath alcohol drops to the safe level of 0.00%. During this time, participants will be provided free Wi-Fi, TV, magazines, snacks and nonalcoholic beverages (e.g., water, juice).

Once the participant's breath alcohol level falls to a BrAC of 0.00%, they will be provided transportation back home. This transportation can only be taken directly home. Transportation will be by car unless the participant resides within a half mile of the research facility, in which case there will be an option for them to walk, along with a member of the study staff. For the participant's safety, it will not be possible for them to drive themselves home or for them to have a friend or family member pick them up.

The whole lab session is expected to last about 5-6 hours, and participants will receive $15/hour. Payment for drinking session is capped at $90 as we expect most people will reach .00% by then. Participants who come to their lab session as originally scheduled will be provided an additional $10 payment.

Field Test. After Lab Session 1 or when "field test only" participants come to the lab to pick up the device, participants will be instructed to wear the Skyn monitor in their daily life for a 2-week period. They can see the readings from the Skyn app on their phone if they want, but not required for this study. They will be allowed to take it off for shower or bath, swimming, charging the device, or when their activities may cause damage to the monitor (e.g., exposure in the rain). Since the monitor also has a temperature sensor, it's possible to determine whether participants take it off. We will ask participants to check the battery status every other day and charge it if needed. The RA will be available to answer questions over the phone to help troubleshoot remotely, or have the participant bring in the Skyn monitor if they really need in-person assistance with the device itself or the app.

Due to the fact that the Skyn app is only compatible with iOS system, participants who do not own an iPhone will be provided with one to complete the two-week field test. The iPhone is to be used for research purposes only. Any personal use is not allowed except participants need to reach out to us about the study (e.g., they need help with the Skyn device). The iPhone must be returned intact at the end of this period, otherwise $200 will be deducted from participant payment.

At the end of the 2-week period the RA will schedule a time with the participants who are doing the field test only to drop off the skyn device and study iPhone (if we loan them a phone). At this visit they will also complete a survey on the acceptability and usability of Skyn and its app as well as the TLFB. Payment for the 2-week period will occur after they complete these measures. If the participant is unable to return to the lab, we will conduct the usability/acceptability survey and the TLFB remotely. The participant will also have the option of mailing the study devices back to the lab. If mailing the devices, the study team will send a prepaid box or envelope to the participant's preferred address.

Of note, the procedures for field alcohol monitoring using transdermal alcohol monitor and EMA have been approved by IRB in our previous study (IRB201700623, where HIV+ and HIV- participants are asked to wear a transdermal alcohol monitor and use the EMA app described below for two weeks).

EMA: Participants will be instructed to enter information on each drinking session using an EMA app called mEMA (ilumivu, Inc.). This app is developed for mobile-based ecological momentary assessment to collect real-time data in daily life (Fig. 4). Researchers can create questions and set up the prompt type for each question (e.g., scheduled, or on-demand). In this study, participants will be asked to initiate an on-demand survey in the app whenever they start a drinking episode. This survey include questions regarding the drinking episode such as the starting and ending times of each drink, types of drinks, drinking amount, 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 monitor and to upload EMA data, and report issues they had with the Skyn monitor. The app uses cloud storage and researchers can access data in real time once uploaded by the participants. We will contact participants via phone call if we notice any issues (e.g., missing daily prompt, reported monitor malfunction) so that these issues can be resolved in time. Participants will receive $70 ($5/day) and a bonus of $70 if they complete ≥80% of the EMA questions, wear the monitor ≥80% of the time, and return it to the lab.[52]

Lab Session 2. For those who are asked to complete all study components, after completing the two-week field test, participants will return to the lab for a second drinking session. The procedures will be the same as in Lab Session 1 with only one exception: Instead of training/practice with the monitor and app, participants will be asked to complete a survey on the acceptability and usability of Skyn and its app. The survey will include questions adapted from established instruments such as the System Usability Scale[53] and the Mobile App Rating Scale[54], with some open-ended questions about user-desired features. Before dismissal, the RA will help uninstall the apps on the participant's phone. Payment structure is the same as in Lab Session 1.

Data sources and management. In the lab sessions, we will record information about the drinking episode (start and end times of each beer) and the BrAC data (time, reading). TAC readings from Skyn monitor and SCRAM anklet will later be downloaded from their respective web porter as a csv/Excel file and stored on a secured server at UF. In the field test, EMA data is cloud-based and will be downloaded to a secured server at UF on a daily basis when active data collection is in process. All data will be linked using the 8-digit ID code assigned to the participant.

Analysis plan for Aim 1: *Assess the validity and reliability of the Skyn monitor through comparison with laboratory grade breathalyzer in two fixed-dose lab alcohol administration sessions*. *H1a. Threshold of detection.* We define the threshold of detection as the consumption level with a 60% or higher detection rate. Rate of successful detection at the end of 1 beer, 2 beers, and 3 beers will be calculated respectively. This will be done by observing the data series and curves from the monitor readings.[45,48] Successful detection of consumed alcohol is defined by a TAC peak (e.g., ≥.02g/dL) with a reasonably visible elevation slope for absorption (i.e., TAC curve goes up at a reasonable pace) and a declination slope for elimination (i.e., TAC curve goes down at the reasonable pace). *H1b1. Relationship between TAC and number of drinks.* The means of peak TAC readings and the areas under the curve will be calculated for 1, 2, and 3 drinks respectively. We expect a linear increase of peak TAC and area under the curve as number of drinks increase from 1 to 3. *H1b2. Relationship between TAC and BrAC.* We will examine the relationship between TAC and BrAC in three ways. First, a simple correlation will be calculated between recorded peak TAC and peak BrAC. A scatter plot will be produced to illustrate the bivariate correlation between these two readings. Second, the Bland-Altman method[55,56] will be used to examine the magnitude of peak differences between TAC and BrAC. The average of paired TAC and BrAC peak values are plotted on x-axis, and the difference between them on y-axis. Stable TAC results across all BrAC levels will line up with a zero slope, which will suggest there is no systematic bias in estimating BrAC. Third, we will calculate the time-to-peak based on recorded TAC and BrAC readings. Their differences will be calculated to determine time delays in BrAC to TAC peaks. All these analyses will be conducted for TAC and BrAC readings obtained after each beer respectively. *H1c: Two*-week test-retest reliability. Pearson correlational coefficients will be calculated to indicate test-retest reliability using TAC peak /time-to-peak for each participant in two lab sessions. A correlation ≥ .7 indicates good test-retest reliability.

Analysis plan for Aim 2. *Validate Skyn monitor in daily life using a 2-week ecological momentary assessment (EMA), and evaluate its acceptability and usability for daily use*. H2a. Agreement between monitor and self-reports in EMA. Using the same definition of a successful detection and procedure of determining drinking episode in monitor data as in

H1a, we will calculate the detection rates by self-reported number of drinks. A receiver operating characteristic (ROC) curve will be plotted. H2b: Relationship between TAC and number of drinks. First, simple correlations will be calculated to examine the association between TAC (peak, AUC) and self-reported number of drinks using all drinking episodes. Second, a multilevel analysis will be used to examine the association between TAC (peak, and AUC) and number of drinks accounting for nested data within person. Acceptability and Usability. Ratings of the Skyn monitor will be summarized on aspects such as wearability, ease to operate, satisfaction with the product, and willingness to wear.

Analysis plan for Exploratory Aim. *Explore factors that may be associated with individual differences in monitor readings*. *T*-tests or Chi-square will be used to examine group differences (e.g., male vs. female, HIV+ vs. HIV-) in TAC parameters (i.e., peak, time-to-peak) and their relationships with # of drinks and BrAC.

Sample size and power. This is for how many participants need to complete the study. For Aim 1, the sample size was based on prior laboratory validation studies of transdermal alcohol monitors.[36,45,57] Also, power analysis shows that a sample size of 40 will give us 80% power to detect a correlation ≥.60. For Aim 2, power analysis shows that n = 40 will give us 90% power (α = .05) to detect an effect size ≥.13 in a multilevel analysis with r = .60 between measures.[58,59] For Exploratory Aim, n = 20 in each group can give us 80% power to detect a large difference (d ≥ .80).

7. Possible Discomforts and Risks:

Potential risks in this study include:

1. Breach *of confidentiality*: Our study will collect data on alcohol use from persons living with HIV. HIV infection is a very sensitive health condition. Breach of confidentiality could occur via communications with participants, loss of research data, and transfer of data. Consequently, procedures have been established to ensure the protection of this information, described in the Adequacy of Protection against Risks section.

2. Alcohol consumption: Potential risks in this study were identified in accordance with the recommended guidelines on ethyl alcohol administration in human experimentation put forth by the National Advisory Council on Alcohol Abuse and Alcoholism (2005). Steps taken to minimize these risks were also developed in accordance with these documents.

A number of medical conditions could potentially be worsened by acute alcohol administration (e.g., liver disease, cardiac abnormality, pancreatitis, diabetes, neurological problems, and gastrointestinal disorders). As a result, participants with such medical problems or who currently take medications contraindicating alcohol consumption at the level in this study will be excluded.

Alcohol self-administration in a research study by individuals who are severely alcohol dependent as evidenced by current withdrawal, a history of withdrawal or diagnosis of current severe alcohol use disorder may pose a risk to their health and safety. Alcohol self-administration in a research study by individuals who are seeking treatment for alcohol dependence or who have recently engaged in intensive treatment for alcohol dependence may compromise their efforts to reach or to maintain abstinence or moderate levels of alcohol use.

Alcohol may cause nausea in high doses, however, nausea is not expected at the doses that will be consumed in this sample of frequent heavy drinkers. Only current drinkers who had at least 1 drinking day with 3 or more drinks in the past month are selected for the study, thus ensuring that any amount of alcohol consumed during an alcohol administration session is less than or equal to an amount of alcohol they consume on their own.

Another area of potential risk to participants under the influence of alcohol involves their safety during the experimental procedures. Although impairment of gross motor coordination in drinkers is rare at the alcohol doses to be consumed in this study, all participants will be under the close supervision of the experimenters to prevent possible accidents such as falls. Alcohol is a reinforcing agent, which may cause changes in behavior including repetitive or excessive alcohol consumption.

3. Breath screening, urine tests and HIV oral swabs testing: Breath screening and urine collections are performed primarily as safeguards and should add no risks other than those normally associated with these procedures. Oral swab is noninvasive and performed only to obtain HIV status of the participant (mainly for confirming HIV- status for the comparison group). It is possible that persons may receive a test result that was unexpected (e.g. a positive pregnancy test, a positive HIV test), and this could result in emotional distress. Our staff will be trained to assist as described in Adequacy of Protection against Risks section.

4. Questionnaires and interview: The assessments used in this study deal with some sensitive issues including participants' alcohol-related problems and other psychiatric conditions. The major disadvantages of these assessments are the time taken to complete them and possible breach of confidentiality. Our past experience with these measures indicates that they are acceptable to participants.

5. Alcohol monitoring using wrist and ankle monitor: The wristband and ankle monitors are noninvasive and adjustable for different wrist and ankle sizes, respectively. It's very unlikely to cause any discomfort based on our experience.

6. *Ecological momentary assessment (EMA) of self-reported drinking*: The EMA involves minimal risk as it only collects self-reported drinking data and issues related to the monitor. The major disadvantage of this assessment is the time taken to complete daily reports. The possibility of confidentiality breach is very low, because the data collected from the mobile app will be encrypted and pushed to the cloud-based storage database. No data are ever stored on the server's file server but always in the database. Access to the database is gated so entry is only permitted to users entering through the approved route (i.e. you can't hack your way into the database by guessing at the url).

Protection against Risks

Recruitment: The HIV+ drinkers will be recruited from the existing Florida Cohort registry (a database of PLWH who are consented to be contacted for research) managed by the Southern HIV and Alcohol Research Consortium and from the Consent2Share registry. We will focus on recruiting participants living in North Florida (n = 237, 60% male, 70% drank alcohol in past year) within 50 miles of the data collection site. The racial distribution of these participants is 40% white, 53% black, 3% Latino, and 4% other (primarily mixed race). We expect to get a similar distribution in our sample. We expect similar racial distribution of the HIV- drinkers, and some additional HIV-positive drinkers, as we will use participant referrals to recruit HIV- drinkers. They are likely to come from similar demographic background.

Screening: Potential participants will be contacted via phone call using their contact information in the registry or call our research staff if referred by other participants. A trained research assistant (RA) will introduce the study and ask a few screening questions (e.g., past 30 day use of alcohol) if the participant expresses interest. If the participant meets preliminary eligibility, the RA will schedule an in-person screen. At the outset of the in-person screening appointment, picture identification (i.e., passport, driver's license or state-issued identification card) is examined in order to verify the participant's identity and to ensure that they are 21 years or older. This ensures that no alcohol consumption on the part of individuals under age 21 will take place in this study. The in-person screen will include breath alcohol test, drug and pregnancy test (women), HIV test if HIV status unknown, timeline follow back (TLFB) for past 30-day alcohol use, medical history, and diagnostic interview for substance use disorder/withdrawal. The screen will take approximately 2 hour, and participants will receive $20 for completing the screen. Participants who come to their in-person screen as originally scheduled will be provided an additional $10 payment. For participants who are HIV+, we will ask them to bring in medical records of their most recent HIV lab values (CD4/Viral load) at any in-person appointment and will provide $20 compensation for doing so.

Informed consent: At the in-person screen appointment, the entire consent form will be reviewed in detail with the participant in a private, one-on-one setting at one of our research offices. If using eICF, the RA will go over the consent form with the participant over the phone and have them sign electronically. Participants will be told that the purpose of this study is to evaluate a new wrist worn alcohol monitor in lab alcohol drinking sessions and 2-week field use. Potential risks will be described. Any questions the participant may have will be addressed. If the participant wishes, he/she may take the consent form home and consider it further before signing. They may also request to speak to anyone on the research team about questions they have. Once the participant has signed the consent, they may withdraw consent at any time. This informed consent form will serve as documentation of the major aspects of the consent process. The informed consent form will be signed and dated by the participant, and countersigned and dated by the staff member obtaining consent. A copy of the signed informed consent form will be given to the participant. Informed consent will be obtained prior to performance of any protocol specified procedures at the in-person screening with the exception of initial breath alcohol screening, which will take place at the outset. Determination must be made that participants' breath alcohol concentration = 0.00% so that they can provide informed consent to participate.

1. Breach of confidentiality. Precautions are taken to ensure that all research materials are inaccessible to anyone other than the investigators. Whenever possible, research participants will be referred to by study-assigned ID numbers rather than by their name or other personal information. Accordingly, results of interviews and questionnaires, breath alcohol concentration, and urine drug/pregnancy screening are recorded by staff members on paper forms using study IDs only. Urine testing and HIV test will take place only at our research offices. Urine samples will be used for the purposes of this testing only and will be discarded after tests are completed. HIV test will be conducted by research staff who has HIV 500/501 certification, which is a certification required for anyone who will perform HIV oral test, granted by the Florida Department of Health. Standard procedure outlined by the DOH will be followed if anyone is tested positive in the oral test.

Some private identifiable information about individuals will be collected to enroll and contact participants. This information will be collected primarily via paper forms, which will be stored in locked filing cabinets at the research facility and only be accessible by study staff and other authorized individuals (e.g., members of the University of Florida Institutional Review Board). This includes a master list connecting participant study identification numbers to participant names.

Research data will be entered and stored on a secure server at the University of Florida, with no identifying information. Lab data (including monitor readings, breathalyzer readings, and information related to drinking such as timing and number of beer) and field data (including monitor readings and self-reports using EMA) will be linked using study ID. None of the study documents or communications with participants will directly identify the study as related to HIV. HIV status will be coded with the code key stored separately in a protected file on UF server. The code key will be destroyed after the study conclusion. No results will be published in a personally identifiable manner.

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.

Florida law requires reporting of newly discovered HIV cases. If participants test positive for HIV, we will do the following:

- Refer each participant to the Alachua county Health Department for another confirmatory test.
- Provide information on medical and support services available to the participant; and
- Discuss information on the importance of notifying previous and current sexual partners that they may have been exposed to HIV and how to prevent HIV transmission.

2. Alcohol consumption: Participants will only be enrolled in the study if they self-report consuming the requisite level of alcohol use. This minimum level of alcohol consumption greatly decreases the likelihood that any individual in this study will consume alcohol at a level greater than to which they are accustomed. Participants will also be excluded should they self-report any condition that contraindicates alcohol consumption (e.g., a history of clinically significant withdrawal detected at the in-person screening). Females will be screened for pregnancy at the in-person screening, as well as during the pre-session appointment on the day of the alcohol drinking session. Also, considering the health consequences of alcohol use on persons living with HIV, we only administered 3 beers to remain below the binge drinking limit.

Alcohol drinking sessions will be conducted by research staff who are experienced with these methods and have been carefully trained. As described above, all participants will be under supervision to prevent possible accidents. Several steps will be taken to ensure that alcohol consumption in this study occurs in a safe manner, in accordance with the

recommended guidelines on ethyl alcohol administration in human experimentation, set forth by the National Advisory Council on Alcohol Abuse and Alcoholism (2005).

Participants will not be permitted to drive themselves to alcohol drinking sessions, which will decrease the likelihood that individuals will attempt to drive after consuming alcohol as part of this study. Participants will not leave the laboratory facility on the University of Florida campus where the study will be taking place during the self-administration procedure. Given that smoking is not allowed on the University of Florida campus, this necessitates exclusion of individuals who are currently nicotine dependent as we will not be able to allow them smoking breaks during the alcohol drinking period and nicotine deprivation may present a confound to the results of this study. Participants will be asked to remain at the research facility until their breath alcohol concentration drops to the safe level of 0.00%. When it is time for dismissal, participants will be provided transportation (either university shuttle, Uber, or Taxi service) directly home by the study.

Several protocol features diminish the chance that study participants will leave the bar lab before dismissal by study staff and we have plans in place in case this occurs. As part of the informed consent process, we advise all participants of study requirements, including the requirement to stay until their BrAC falls to a safe level. We reiterate these requirements verbally before the alcohol drinking session. Thus, participants are made aware multiple times of the requirement to remain in the facility for at least two hours after the end of the alcohol drinking period and until they reach a safe BrAC. The pay structure of the study also discourages early departure. We pay participants $15/hour for the alcohol drinking session, so participants will receive only a prorated portion of the payment should they end the session early.

Administration of alcohol to individuals in treatment for addictive behaviors could potentially impede the progress of their recovery. As a result, we will not enroll individuals who have taken part in inpatient or intensive outpatient treatment for alcohol use or other addictive behaviors in the past 12 months. Further, we will not enroll individuals with a lifetime history of clinically significant withdrawal from alcohol; a lifetime history of medical intervention for withdrawal or who currently present in a manner suggestive of withdrawal, based on the Clinical Institute Withdrawal Assessment for Alcohol (CIWA-Ar). These steps regarding withdrawal will also have the benefit of excluding individuals who are severely dependent on alcohol, for whom alcohol consumption in this study may not be safe.

3. Breath screening, urine tests and HIV oral swabs testing: All these noninvasive tests were performed as safeguards or for confirming eligibility, so there is minimal risk. If participants become emotionally distressed by the test results (e.g. unexpected positive result for pregnancy or HIV), our staff will receive basic training to help calm them down but will refer them to a clinical psychologist at UF (e.g., Dr. Nicole Ennis who is also part of the SHARC team) if necessary. Persons become newly aware of their HIV+ status will also be referred for care linkage at the Department of Health or UF Infectious Disease department.

4. *Questionnaires and interview*: The major risk of the assessments is potential loss of confidentiality, which we have addressed above. To minimize any discomfort associated with reporting sensitive behaviors, participants will be informed that they may refuse to respond to questions that they are not comfortable answering. Questions related to eligibility determination and monitoring of safety and treatment response are not optional. If a person

declines to answer these questions, we will advise them that they will not be able to participate.

5. Alcohol monitoring using wrist and ankle monitors: The risk for breach of confidentiality associated with these monitors is very low. The data will be stored in the monitor's data porter and will be downloaded to secure UF drives after each lab session and the field test. Only study ID will be used to link the data.

6. 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 (described above). Additionally, the App will need the study ID to collect data, with no requirement of other personal information (e.g., phone number). To encourage participants to take time every day to complete the assessment, they will receive a bonus ($70 additional to the base payment of $70) for completing at least 80% of the EMA assessments.

8. Possible Benefits:

There are no direct benefits to participants, although some persons enjoy participating in studies that can provide information to help others.

9. Conflict of Interest:

N/A

References

1. Stein M, Herman DS, Trisvan E, Pirraglia P, Engler P, Anderson BJ. Alcohol use and sexual risk behavior among human immunodeficiency virus-positive persons. *Alcohol Clin Exp Res.* May 2005;29(5):837-843.
2. Azar MM, Springer SA, Meyer JP, Altice FL. A systematic review of the impact of alcohol use disorders on HIV treatment outcomes, adherence to antiretroviral therapy and health care utilization. *Drug Alcohol Depen.* Dec 1 2010;112(3):178-193.
3. Pandrea I, Happel KI, Amedee AM, Bagby GJ, Nelson S. Alcohol's Role in HIV Transmission and Disease Progression. *Alcohol Res Health.* 2010;33(3):203-218.
4. Justice AC, McGinnis KA, Tate JP, et al. Risk of mortality and physiologic injury evident with lower alcohol exposure among HIV infected compared with uninfected men. *Drug Alcohol Depen.* Apr 1 2016;161:95-103.
5. Parry CDH, Tomlinson M, Bryant K, Rotherham-Borus MJ. Fresh Perspectives on the Alcohol and HIV Nexus: A Call for Action in an Era of Increased Opportunities and Challenges. *Aids Behav.* Nov 2017;21(Suppl 2):121-125.
6. Szabo G, Zakhari S. Mechanisms of alcohol-mediated hepatotoxicity in human-immunodeficiency-virus-infected patients. *World journal of gastroenterology.* May 28 2011;17(20):2500-2506.
7. Barve S, Kapoor R, Moghe A, et al. Focus on the Liver: Alcohol Use, Highly Active Antiretroviral Therapy, and Liver Disease in Hiv-Infected Patients. *Alcohol Res Health.* 2010;33(3):229-236.
8. Rosenbloom MJ, Sullivan EV, Pfefferbaum A. Focus on the brain: HIV infection and alcoholism: comorbidity effects on brain structure and function. *Alcohol Res Health.* 2010;33(3):247-257.
9. Heinz AJ, Fogler KA, Newcomb ME, Trafton JA, Bonn-Miller MO. Problematic Alcohol Use Among Individuals with HIV: Relations with Everyday Memory Functioning and HIV Symptom Severity. *Aids Behav.* Jul 2014;18(7):1302-1314.
10. Samet JH, Walley AY. Interventions targeting HIV-infected risky drinkers: drops in the bottle. *Alcohol Res Health.* 2010;33(3):267-279.
11. Quanbeck A, Chih MY, Isham A, Johnson R, Gustafson D. Mobile Delivery of Treatment for Alcohol Use Disorders A Review of the Literature. *Alcohol Res-Curr Rev.* 2014;36(1):111-122.
12. Hasin DS, Aharonovich E, O'Leary A, et al. Reducing heavy drinking in HIV primary care: a randomized trial of brief intervention, with and without technological enhancement. *Addiction.* Jul 2013;108(7):1230-1240.
13. Marschollek M, Gietzelt M, Schulze M, Kohlmann M, Song B, Wolf KH. Wearable sensors in healthcare and sensor-enhanced health information systems: all our tomorrows? *Healthcare informatics research.* Jun 2012;18(2):97-104.

14. Patel S, Park H, Bonato P, Chan L, Rodgers M. A review of wearable sensors and systems with application in rehabilitation. *Journal of neuroengineering and rehabilitation.* Apr 20 2012;9:21.

15. Gao W, Emaminejad S, Nyein HYY, et al. Fully integrated wearable sensor arrays for multiplexed in situ perspiration analysis. *Nature.* Jan 28 2016;529(7587):509-514.

16. Steinhubl SR, Muse ED, Topol EJ. The emerging field of mobile health. *Science translational medicine.* Apr 15 2015;7(283):283rv283.

17. Harrison V, Proudfoot J, Wee PP, Parker G, Pavlovic DH, Manicavasagar V. Mobile mental health: review of the emerging field and proof of concept study. *Journal of mental health.* Dec 2011;20(6):509-524.

18. Sharpe JD, Zhou Z, Escobar-Viera CG, et al. Interest in using mobile technology to help self-manage alcohol use among persons living with the human immunodeficiency virus: A Florida Cohort cross-sectional study. *Substance Abuse.* 2017/07/19/ 2017:1-6.

19. Hasin DS, Aharonovich E, Greenstein E. HealthCall for the smartphone: technology enhancement of brief intervention in HIV alcohol dependent patients. *Addiction science & clinical practice.* Feb 17 2014;9:5.

20. Barnett NP. Alcohol sensors and their potential for improving clinical care. *Addiction.* Jan 2015;110(1):1-3.

21. Greenfield TK, Kerr WC. Alcohol measurement methodology in epidemiology: recent advances and opportunities. *Addiction.* Jul 2008;103(7):1082-1099.

22. Ryan P. Integrated Theory of Health Behavior Change: background and intervention development. *Clinical nurse specialist CNS.* May-Jun 2009;23(3):161-170; quiz 171-162.

23. Barnett NP, Meade EB, Glynn TR. Predictors of Detection of Alcohol Use Episodes Using a Transdermal Alcohol Sensor. *Exp Clin Psychopharm.* Feb 2014;22(1):86-96.

24. Simons JS, Wills TA, Emery NN, Marks RM. Quantifying alcohol consumption: Self-report, transdermal assessment, and prediction of dependence symptoms. *Addict Behav.* Nov 2015;50:205-212.

25. Dougherty DM, Hill-Kapturczak N, Liang YY, et al. The Potential Clinical Utility of Transdermal Alcohol Monitoring Data to Estimate the Number of Alcoholic Drinks Consumed. *Addict Disord Treat.* Sep 2015;14(3):124-130.

26. Greenfield TK, Bond J, Kerr WC. Biomonitoring for Improving Alcohol Consumption Surveys: The New Gold Standard? *Alcohol research : current reviews.* 2014;36(1):39-45.

27. Sakai JT, Mikulich-Gilbertson SK, Long RJ, Crowley TJ. Validity of transdermal alcohol monitoring: Fixed and self-regulated dosing. *Alcohol Clin Exp Res.* Jan 2006;30(1):26-33.

28. Bond JC, Greenfield TK, Patterson D, Kerr WC. Adjustments for Drink Size and Ethanol Content: New Results from a Self-Report Diary and Transdermal Sensor Validation Study. *Alcohol Clin Exp Res.* Dec 2014;38(12):3060-3067.

29. Leffingwell TR, Cooney NJ, Murphy JG, et al. Continuous objective monitoring of alcohol use: twenty-first century measurement using transdermal sensors. *Alcohol Clin Exp Res.* Jan 2013;37(1):16-22.

30. Neville FG, Williams DJ, Goodall CA, Murer JS, Donnelly PD. An Experimental Trial Exploring the Impact of Continuous Transdermal Alcohol Monitoring upon Alcohol Consumption in a Cohort of Male Students. *Plos One.* Jun 25 2013;8(6).

31. Dougherty DM, Hill-Kapturczak N, Liang YY, et al. Use of continuous transdermal alcohol monitoring during a contingency management procedure to reduce excessive alcohol use. *Drug and alcohol dependence.* Sep 1 2014;142:301-306.

32. CDC. HIV in the United States: At A Glance. 2016; https://www.cdc.gov/hiv/statistics/overview/ataglance.html. Accessed Feburary 16, 2017.