Protocol

1. Project Title:

A Smartphone App to Capture Inhibitory Control as a Novel Moderate Drinking Tool

2. Investigator(s):

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3. Abstract:

Young adult drinking is a public health issue. Current interventions yield small effect drinking reductions, thus new approaches are needed. Smartphone applications (apps) have great potential for drinking moderation. Almost all young adults own a smartphone and most are open to technology to moderate drinking. There are many drinking apps, but quality varies and there is no evidence any apps are more efficacious than a control condition for young adults. Thus, there is an evidence gap as to which apps may help. Brief interventions have shown that personalized feedback based on motivational interviewing (M.I.) has efficacy, but these interventions give feedback about general patterns only, not drinking and impairment in the moment. Theory and evidence emphasize that slowing pace of drinking is difficult. These findings suggest young adults need more help, preferably while drinking, to slow their pace of alcohol use. Apps have potential for in-the-moment intervention, but there are no efficacious, in-the-moment behavioral interventions for young drinkers. Human laboratory studies support perceived impairment as a focus of an in-the-moment, moderate drinking app. Two studies using different cognitive tasks found heavier drinking young adults underrated impairment more than light drinkers. Simulated driving results in particular suggest serious consequences from misperceived impairment. An app that provides accurate feedback on impairment could increase perceived impairment and reduce drinking. This study will test an app providing in-the-moment feedback on impaired inhibitory control as an adjunct to an existing, M.I.-based, brief web-based intervention that gives feedback on overall drinking. App feedback will be tied to performance on the cued go/no-go task, which tests ability to respond quickly to “go” targets (activation) while withholding responses to “no-go” targets (inhibition). Moderate doses to blood alcohol content (BAC) of .05-.06% reliably lead to inhibition errors, but higher doses are usually needed for “go” reaction time (RT) to slow. Thus, ability to respond remains but ability to inhibit is impaired, which has negative implications. Using M.I. - consonant language, feedback will compare RT and inhibition failures after alcohol to RT and errors pre-drinking, linking performance decrement to consequences like risky sex and driving issues. The experimental app, which will be derived from a larger app in a recent study, will be compared to 2 control conditions in which the task is completed without this novel feedback. Heavy drinking young adults (*N*=99) will be randomized to 1 of the 3 app conditions; attend an individual drinking session and be dosed to BAC=.06%; during which they will use the experimental or a control version of the app. Participants will then attend a group drinking session on a separate day and be dosed to BAC=.06% in small groups in a bar lab; then use the experimental or a control version of the app, followed by opportunity to self-administer more alcohol. Primary outcomes will be differences between study conditions on BAC and alcohol self-administered. During a 4-week period post-session, all participants will use the experimental app in actual drinking

situations for 2 of the 4 weeks, enabling within-subject comparisons of drinking with vs. without the app. This study will yield preliminary data for an R01 to test concurrent use of multiple mobile tools for combined efficacy in reducing drinking.

4. Background

High-risk alcohol use by young adults is a public health issue with over 40% reporting recent heavy drinking[1], which is related to consequences like sexual assault and traffic accidents[2, 3]. Further, heavy drinking at this age can negatively affect the developing brain[4-6]. Driving under the influence (DUI) is more common in 21-25 year olds (18-19% past year prevalence) than any other age[7]. Among 21-30 year-olds killed in crashes, 43% have blood alcohol content (BAC) ≥.08, but risk is not limited to BACs >.08%. Probability of a fatality increases significantly once BAC exceeds .05%[8, 9] and DUI can be charged with signs of impairment even at BACs <.08%.

Young adult heavy drinking warrants targeted intervention. Reviews/meta-analyses[10-14] find current interventions yield small effect reductions, making new approaches critical. Smartphone applications (apps) have potential to moderate drinking. Young adults spend 3-5 hours/day on smartphones[36,37] and 98% report using phones during social events[8, 9]. Fortunately, young adults are open to technology use to moderate drinking[15, 16]. There are many alcohol apps, but quality is poor and there is no evidence that any apps are more efficacious than a control condition for young adults[16-18,40]. There are efficacious apps for treatment-seeking[19, 20] and recovering adults[21] to avoid drinking, but not for young adults to reduce drinking: a very different indication.

Regarding intervention components, personalized feedback based on motivational interviewing (M.I.) has efficacy[11, 14]. Apps with personalized tailoring are more popular and downloaded more[40]. These interventions give feedback based on general patterns though, not drinking and impairment in the moment. With text message interventions[22-47], content still tends to be based on general patterns[23-25] and is limited visually (no graphics)[22]. General feedback has value, but theory and evidence support a need for in-the-moment intervention.

Behavioral economic theory highlights alcohol as immediately available and rewarding[26, 27]. Self-control theory posits that resisting rewards can make later exertion of effort more difficult[28, 29]. For heavy drinkers, the impulse to drink is immediate and compelling, making it hard to exert control. Self-control theory argues that motivation can make up for limited ability[29], but non treatment-seeking young adults may not have enough motivation to control drinking on their own.[30, 31] Accordingly, evidence shows slowing pace of drinking is difficult. Researchers have reported difficulty teaching moderate drinking to older adults[32-35]. Young adults report moderating drinking directly (e.g., counting drinks) less often than ancillary strategies (e.g., designated drivers)[15]. Our recent study found that a web-based intervention was efficacious when it included ancillary strategies, but not when it gave direct strategies to slow drinkin.g[16]. This suggests young adults need more help, preferably while drinking, to slow the pace of drinking and improve decision making while impaired. Apps have great potential in this area.

Past studies suggest actual and perceived impairment are valid targets for an in-the-moment app. Two studies using different tasks found that heavier drinkers underestimate impairment more than lighter drinkers[17-18]. In terms of actual performance, heavier drinkers were equally as impaired as light drinkers (including on a driving simulator). According to self-efficacy theory, decisions are based on perceived ability[36, 37] With low perceived impairment, heavier drinkers may believe that they can drive effectively after drinking and thus, do so[38]. An app giving in-the-moment feedback could increase perceived impairment, and reduce drinking and consequences.

The cued go/no-go (CGNG) task is an ideal choice for in-the-moment impairment feedback. Its instructions are simple; practice effects are minimal; and is sensitive to alcohol[22-31,39]. The CGNG tests ability to respond fast to "go" targets (activation) while withholding response to "no-go" targets (inhibition). Activation/inhibition tension is externally valid. Dual process models[40-43] posit risk behaviors stem from overactive appetitive drives that are compelling and hard to inhibit. Poor CGNG performance post-alcohol has been related to poor simulated driving, enhancing external validity[44]. Moderate dosing to .05-.06% BAC reliably increases inhibition errors[45-51], but slowing reaction time (RT) to "go" cues requires higher doses[44, 46, 47, 52]. RT to go cues often recovers later in a drinking episode (acute tolerance[53]) but ability to inhibit does not. Thus at this BAC, ability to respond remains but inhibition is impaired, which relates to risk behaviors like DUI as young adults underrate impairment[17].

This study (N=99) will test an app giving in-the-moment feedback on impaired inhibitory control as an adjunct to an existing, web-based intervention (US-THRIVE) addressing general drinking patterns, based on M.I.[54-56-21]. US-THRIVE was linked to significant drinking reductions in a sample with low baseline motivation[16]. This new app will give in-the-moment feedback comparing pre- and post-drinking RT and inhibition errors, referring to evidence that poor CGNG response relates to poor simulated driving and willingness engage in risky behavior. After feedback, the app will offer advice on slowing drinking and other options (e.g., a taxi). The experimental app—derived from a larger app (RWJF #73293, PIs: Estrin/Muench)—will be compared to standard (trial-by-trial RT and error information only) and control versions (no information) without feedback. After US-THRIVE, heavy drinking young adults will be randomized to 1 of the 3 apps. They will use this app initially and learn about the relevance of alcohol's effects on CGNG. They will then attend an individual alcohol drinking session where they will be dosed to .06% BAC, followed by app use. After completion of the first session they may be asked to return to the research facility on a different day to take part in a group alcohol drinking session where they will be dosed to .06% BAC in groups of 3, followed by app use, then 1-hr when they can self-administer alcohol up to .12%[57, 58]. They will use the app post-drinking with incentives for fast, accurate performance[44] and learn their number of errors and fast + correct responses. Performance decrement should motivate subsequent app use. Similar to R21AA023368 (PI: Leeman), for 4 weeks post-session, <u>all</u> participants will use the experimental app for 2 weeks in real drinking occasions and not use it the other 2 weeks. Due to the COVID-19 pandemic participants may be asked to complete just the 4 week field use portion of this study.

The proposed study will address a critical knowledge gap: there are no evidence-based smartphone apps for reducing young adult drinking. There are also no efficacious in-the-moment behavioral interventions for young adults, despite supporting theory and evidence. Lab paradigms, often used to test medications, are under-used for behavioral interventions despite their reduced reliance on self-report, time and cost-efficiency[59] and NIAAA's emphasis on their use[60]. The proposed study combines lab with field testing to yield "real world" preliminary efficacy and usability data. We have proof-of-concept and feasibility data, but lack data testing effects of this novel inhibitory control feedback app on alcohol self-administration. Thus, these data are needed for an R01 to test this new app, combined with other mobile tools, for efficacy in reducing drinking.

Preliminary Studies: The studies described below pertain to the validity of the alcohol self-administration paradigm, along with its safety and feasibility; our ability to recruit the proposed sample; and young adults' interest in intervention components pertinent to the proposed study, including a breathalyzer device/app.

PS1: Lab research in heavy drinking young adults at University of Florida, the study site. Dr. Leeman's group is conducting an NIH-funded study to test a smartphone breathalyzer device/app and 2 other forms of alcohol-related technology in a simulated bar lab. Over 17 mos., 130 young adults have enrolled (7.7/month). Enrolled participants have been 52% male and diverse: 54% non-students, and 32% non-White. This study includes a 2-week field period to determine how often participants use the 3 forms of technology in "real" drinking situations. Participants have used the technology an average of 8 times overall (SD=5.5) on 63% of drinking days (SD=27%). They receive $20 for using each of the 3 technologies at least once. No other compensation is tied to technology use. Thus, participants use the technologies "extra" times without compensation. These findings provide strong support for non-treatment seeking, heavy-drinking young adults' motivation to use technology to moderate drinking. Though breathing into the breathalyzer only takes about 1 min., the process entails a waiting period of 15 min. after one's last drink, much longer than the 3-4 min. required for the experimental app in the proposed study. Thus, heavy drinking young adults are willing to use drinking apps even if they require several minutes.

PS2: Experience with alcohol administration paradigm. The proposed paradigm is based on a study by Co-Investigator Corbin and Dr. Kim Fromme[57, 58]. They recruited 174 heavy drinking young adults (50% female) for a lab study with methods resembling the proposed study including administration in a simulated bar lab in small groups; vodka mixed drinks; targeting initial BAC of .06% followed by a free-drinking period up to BAC=.12%. Their ad lib period was only 20 minutes yet there was a range in drinks self-administered (0-3), which will be accentuated due to extension of the free-drinking period to 1 hour in the proposed study.

PS3: CGNG and risk behavior. In a recent pilot study, Dr. Corbin recruited heavy drinking young adults for a lab study, again dosing to BAC=.06% (*N*=21, 43% female). Post-alcohol, participants complete the CGNG, then a modified self-report[61]. CGNG response inhibition failures post-alcohol correlated with risk behavior inclination (*r*=.47), specifically aggression (*r*=.31), drug use (*r*=.32), delinquency (*r*=.31) and risky sex (*r*=.36). Thus poor response inhibition post-alcohol relates to risk for negative behaviors. Along with driving, relations between CGNG and these risk behaviors will inform personalized feedback in the app for the proposed study.

PS4: CGNG Validity. In a placebo-controlled study (*N*=222, 75% male) by Dr. Corbin, CGNG performance post-alcohol (peak BAC=.076%) was related to negative consequences. There was a beverage condition by CGNG interaction, β=.35, *p*=.02. Self-reported consequences were associated with inhibition failures on the CGNG after alcohol, β=.26, *p*=.02, but not placebo, β= -.10, *p*=.44. These findings show impaired inhibitory control has "real world" relevance to outcomes that could be avoided with feedback given by the proposed app.

PS5: Feedback on task performance & perceived intoxication. Dr. Fillmore led a study in which young adult drivers with and without a DUI (*N*=40, 68% male) completed 2 administration sessions with alcohol (peak BAC =.08%) or placebo, then performed simulated driving and rated perceived impairment[38]. They were then given feedback that their driving performance was impaired by alcohol. After feedback, they were retested as in the first 2 sessions. Paralleling prior findings on heavy vs. lighter drinkers[62, 63], those with DUIs initially perceived less impairment than those without. However, post-feedback, those with DUIs reported increased perceived impairment (*p*<.01). These results strongly support that perceived impairment is meaningful to young adult high-risk drinkers and that task performance feedback can have a positive effect in this population.

Figure 2a

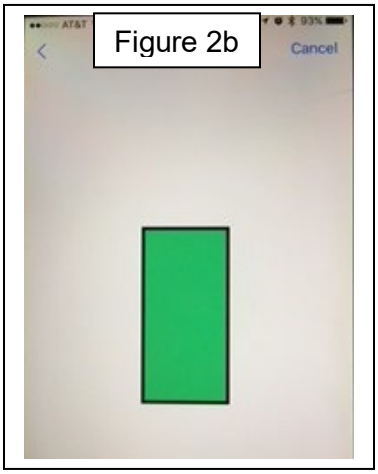


Figure 2b

S6: Preliminary findings: app version of CGNG
In a pilot study (*N*=76, 67% female, 25% non-white, *M* age= 43[*SD*=14]), consultant Muench compared a standard CGNG with the app version in his current study, which required 3 min., on average. This app version of the CGNG will be elaborated in the proposed study. Reaction times (RTs) in the app and computer versions were highly correlated (r=.69, p<.01). The trials in the app version were divided into thirds and mean RTs were correlated to evaluate reliability. RTs among each third were correlated between .89-.95, indicating strong reliability. Correlations of inhibition errors on the computer version and errors on the app were lower, r=.28 (p=.015). This is not surprising as CGNG errors are infrequent when sober. This is actually an advantage as it enhances sensitivity to alcohol effects. Given the promising findings and extensive literature on the CGNG[45-51], we are confident the app version will be sensitive to alcohol. Dr. Leeman included a description of the app in a preliminary study of young adult drinkers (*N*=23). Participants rated the likelihood they would use the app 5.1 (*SD*=1.3) on a 1-7 scale. In a recent web survey of young adults in FL (*N*=72), Dr. Leeman found 66% of heavy drinkers reported scores $\geq$ 3 on a 0-10 scale, indicating agreement they would like to use an app to help reduce drinking, suggesting high interest and a degree of motivation.

Summary: These studies show feasibility; young adults' motivation to use moderate drinking apps even if they take several minutes; our experience with relevant methods; external validity of the CGNG; and reliability and validity of the app version of the CGNG. Thus, the CGNG is a good choice for in-the-moment intervention.

5. Specific Aims

Primary Aim 1: Compare effects of a smartphone app providing feedback on impaired inhibitory control to 2 control conditions on BAC (Aim 1a) and number of alcoholic drinks self-administered (1b) during a 1-hour free drinking period in a naturalistic bar lab that occurs immediately after a fixed alcohol dose targeting BAC= .06%.

Primary Aim 2*:* In a 4-week period post-session, compare, within-subject, number of drinks per occasion during 2 weeks when participants use the app during actual drinking situations vs. 2 weeks when they will not use the app. Also test app satisfaction including number of times used and likelihood of future use.
Hypothesis: Participants will self-administer less alcohol when using the experimental app with feedback.

Secondary Aim: Test increased perceived impairment as a partial mediator of the effects in the prior Aims.
Hypotheses: Participants using the experimental app will report higher perceived impairment, which will mediate relations between app use and lower alcohol consumption in the lab and in the 4-week post period.

Exploratory Aim 1: Test study condition during the lab sessions, amount of alcohol self-administered (operationalized as estimated peak BAC and number of drinks self-administered in separate models) in the group alcohol drinking session and during the field period in the intervention and non-intervention periods as predictors of self-reported alcohol consumption (e.g., drinks per drinking day) and alcohol-related problems self-reported at 6- and 12-months post-session on web-based surveys.

Exploratory Aim 2: Test BACTrack Skyn readings taken during each alcohol administration session as predictors of successive breath alcohol readings taken following alcohol administration/self-administration periods in the alcohol drinking sessions and to predict number of drinks self-administered during the group drinking session.

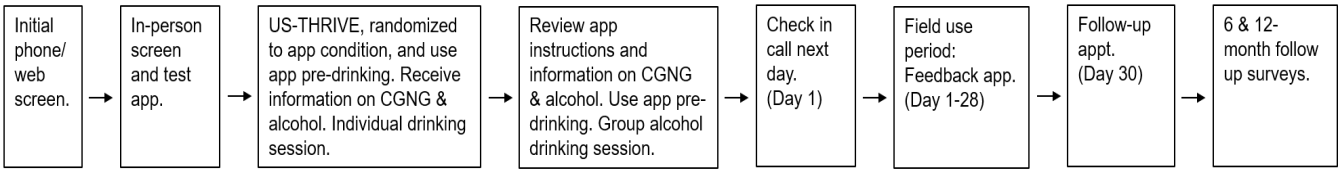
Exploratory Aim 3: Predict scores on self-reported expected involvement in risky behaviors post-alcohol administration based on performance on the app-based cued go/no-go task following a .06% fixed alcohol dose in each alcohol drinking session.

6. Research Plan

Overview

Participants will be otherwise healthy men and women between the ages of 21-25 who frequently engage in heavy alcohol use. This study will test an app based on the cued go/no-go (CGNG) task giving in-the-moment feedback on impaired inhibitory control as an adjunct to an existing, web-based intervention (US-THRIVE) targeting general drinking patterns using M.I. principles. This new app will give in-the-moment feedback comparing pre- and post-drinking RT and errors, referring to evidence that poor CGNG response relates to poor simulated driving and willingness to engage in risky behavior. After feedback, the app will offer advice on slowing drinking and other options to avoid harm (e.g., a taxi). The experimental app—derived from a larger app (Robert Wood Johnson Foundation grant #73293, PIs: Estrin/Muench)—will be compared to standard (trial-by-trial RT and error information only) and control versions (no information) without feedback. After US-THRIVE, heavy drinking young adults will be randomized to 1 of the 3 apps. After initial use of their randomized app, they will then be dosed to .06% BAC during an individual session in a naturalistic lab, followed by app use. After this initial session, on a separate day, participants will attend a group session including 2 other participants. During this group session; they will again be dosed to .06% BAC, followed by app use, then 1-hr when they can self-administer alcohol up to .12%. There will be at least one day between the individual and group sessions and the goal will be for the individual and group session to occur within 7 days of each other. For 4 weeks post-session, all participants will use the experimental app for 2 weeks in real drinking occasions and not use it the other 2 weeks. Participants completing both the laboratory alcohol administration and field testing components of the study can earn up to $450 during the course of study participation. Participants may also be invited to complete only field use of the app due to the COVID-19 pandemic or because they cannot physically come to the study location on campus. Among these participants, some will be invited to complete the four-week field use period as described above (i.e., 4 weeks total, 2 weeks with app access, 2 weeks with not and a brief daily questionnaire each day for the 4 weeks). Maximum possible payment for those chosen to complete only the field use period will be $310. A small subset (up to n= 12 participants) will be selected to complete an ecological momentary assessment based field period of 10 days in which participants will be prompted multiple times per day to either use the app or to complete a brief questionnaire. Maximum payment for those completing the ecological momentary assessment will be $200. We anticipate enrolling 208 participants, of whom 109 will be eligible with a target of 99 individuals completing the study.

Figure 1. Timeline of Study Procedures



Participants

Participants will be recruited through a number of means. Flyers and palm cards will be posted and handed out in and around the various colleges, universities and technical/trade schools in the Gainesville, FL-area as well as in other public areas frequented by young adults. We will also post brief messages on multiple sections of Craigslist. Facebook postings will be made from our dedicated lab account. These ads will direct participants to the study's web address **but will not include an active hyperlink**. Ads will also include the study phone number and email address. Postings made in response to the ad will be monitored with periodic reminders for interested parties to contact the study via phone/text or email. These same brief messages will also be disseminated to students at the local colleges, universities and technical schools in the area via batch emails and list servs. When permitted, brief recruitment talks will be given verbally during class meetings at these local institutions. Verbal recruitment messages will contain similar information as flyers and other advertisements. Copies of flyers and palm cards will also be provided at the conclusion of these brief recruitment talks. We will also recruit participants who have completed the following studies with active protocols: the Smartphone Technology Effects on Alcohol Drinking among Young adults (STEADY) study (IRB201600614, PI: Leeman), A Quasi-experimental Examination of Alcohol use on Game and Non-game Days over Time (IRB201903421, PI: Leeman), and Advancing New Computer-based Health Outreach Regarding Sexual behavior (ANCHORS) Study: UH2 Project (IRB201701367, PI: Leeman).

All enrolled participants will me the following inclusion and exclusion criteria:

Inclusion Criteria:

Each subject must:

1. Be between the ages of 21-25
2. Be able to read English and complete study evaluations
3. Report drinking to an estimated blood alcohol concentration (eBAC) of 0.12% (i.e., the maximum allowable BAC in the alcohol drinking sessions in this study) or higher at least once in the prior 30 days
4. Report at least four days with heavy episodic drinking (i.e., 4 or more drinks for women and 5 or more drinks for men) out of the prior 30 days*
5. Report having consumed at least one alcoholic drink during a minimum of 12 days out of the prior 30 in order to maximize the likelihood that subjects will choose to drink during the self-administration portion of the laboratory sessions.*
6. Meet, at minimum, DSM-5 criteria for a mild alcohol use disorder (i.e., meet at least 2 diagnostic criteria)
7. Perform within 2 standard deviations of normative levels both with regard to reaction time and number of errors on the cued go/no-go task at in-person screening.

8. Have an iphone/iOS-compatible phone that they are willing to use for study-related tasks (field use-only participants from outside of the Gainesville area, only; local participants will have an opportunity to borrow a study phone)

Exclusion Criteria:

No subject may:

1. Be seeking treatment for alcohol or other addictive behaviors or have been in inpatient or intensive outpatient treatment within the past 12 months
2. Have used a smartphone application to facilitate moderate drinking more than 1 time within the past 12 months
3. Provide two positive breath alcohol concentration (BrAC) readings (i.e., > 0.00%) at an in-person screening appointment or on the day of the alcohol drinking session. After participants blow their first positive BrAC, they will be allowed to reschedule and participate at another time, however if they blow a second positive BrAC, they will be excluded from this study and offered referrals for alcohol treatment. **
4. Have positive urine screen results at the in-person screening or on the day of an alcohol drinking session for opiates, cocaine, phencyclidine, amphetamines, methamphetamine, barbiturates, methadone or benzodiazepines. **
5. Meet criteria for current moderate or severe DSM-V Cannabis Use Disorder, or a mild, moderate, or severe DSM-V substance use disorder on any other drug, excluding alcohol.
6. Report current use of psychotropic drugs including anxiolytics and antidepressants. **
7. Have received a prescription for any psychotropic drug in the 30 days prior to study enrollment **
8. Be psychotic or otherwise severely psychiatrically disabled
9. Report a history of a medical condition that would contraindicate the consumption of alcohol (e.g., liver disease, cardiac abnormality, pancreatitis, diabetes, neurological problems, and gastrointestinal disorders).
10. Have a history of clinically significant withdrawal from alcohol, defined as any one of the following: a) a lifetime history of seizures, delirium, or hallucinations during alcohol withdrawal; b) a Clinical Institute Withdrawal Assessment scale (CIWA-Ar, Sullivan et al., 1989) score > 8; c) a report of drinking to avoid withdrawal symptoms in the past 12 months; or d) a lifetime history of medical treatment for withdrawal.
11. A woman who is pregnant, nursing, or engages in sexual activity with opposite-sex partners and refuses to use a reliable method of birth control. **
12. Report disliking vodka or vodka mixed drinks. Vodka is the alcoholic beverage participants to be used in the proposed study**
13. Body weight less than 110 pounds or greater than 220 pounds**
14. Be colorblind
15. Be a Foreign National

* These inclusion criteria do not apply to the EMA field testing scenario. There will be no requirement of 6 or more heavy drinking days for the EMA scenario. Also, the minimum requirement of any drinking days will be only 8 for EMA, rather than 12 in the main study

** These exclusion criteria do not apply to either field testing-only scenario.

Procedures

Preliminary screening: All recruitment methods will direct participants to either call, text message or email the study to find out more information or to go directly to a web page where they can learn basic information about the study and complete the web screening questionnaire. Research assistants fielding requests for information will provide an overview of the study and answer questions. Individuals interested in participating will be directed to complete the confidential web screening questionnaire. Those who follow the link will be taken to an informed consent form for the web screener, which is encrypted and housed at REDCap via UF's site license. They will then proceed to complete the web screen, also housed at REDCap. Neither email address nor any other personally identifiable information will be stored on REDCap, which is a secure website. REDCap complies with privacy standards set forth by HIPAA, and collected data is protected by real-time data replication. If participants do not have web access or would prefer to complete the screener by phone, they may do so.

Interested individuals will indicate consent for the web screener by checking a box or verbally, if screened by phone. They will be advised that they can print out a copy of the web screener consent for their reference. Only those indicating consent will continue on to the screening survey itself. After providing consent by clicking in a box, participants will be asked to think of a code word that would be easy for them to remember but that does not contain any identifying information (e.g., their name). People completing the web screener will be informed of their preliminary eligibility via e-mail. Interested individuals who are eligible on a preliminary basis can then make an appointment for an in-person screening. These individuals are free to ask any questions they would like about the study via phone or email during the time between web and in-person screening.

In-person screening:

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 identity and to ensure that they are between the ages of 21-25. This ensures that no alcohol consumption on the part of individuals under age 21 will take place in this study. At this appointment, the entire consent form will be reviewed in detail in a private, one-on-one setting at one of our research offices. Participants will be told that the purpose of the study is to test alcohol-related smartphone applications designed to provide assistance during actual drinking situations to help young adults reduce their drinking. It will be explained to participants that the apps will be tested both during a laboratory alcohol drinking session and a 4-week period outside the lab in which they can use this technology in actual drinking situations. For those who are asked to complete the 4-week field test only, the in-person screening can be done remotely by phone call or password-protected UF Zoom meeting. For field use-only participants, we will review the informed consent document remotely and they will sign it via eConsent on RedCap.

Risks and potential benefits will be described. Any questions the participant may have will be addressed. If the subject wishes, he/she may take the consent form home (or review the eConsent, if remote) 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, s/he 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 .Field-use only participants who are screened entirely remotely will be prompted to sign the ICF electronically using RedCap. 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-specific procedures at the in-person screening. A breath alcohol concentration (BrAC) reading will be taken immediately after signing of the informed consent. The informed consent will be considered valid and the in-person screening appointment will proceed only if the participant's BAC = 0.00%. Following the BrAC reading, participants will also complete drug and pregnancy tests (women); timeline followback (TLFB)[64] for 30-day alcohol/ other substance use; medical history; diagnostic interview[36] ; and will complete the cued go/no-go task. The screen will take approximately 2 hours, and participants will receive up to $30 via a prepaid debit card.

Eligible participants who are interested in enrolling will be assigned to the earliest possible individual alcohol drinking session. After this individual session, participants may be invited back to complete a group alcohol session on a different day along with two other participants with similar availability. There is a web-based, REDCap questionnaire for participants to complete in conjunction with the in-person screen, however participants complete this questionnaire on their own. However, if participants do not do so between the in-person screening appointment and the individual alcohol drinking session, we will request that participants complete the web-based questionnaire on the day of the individual alcohol drinking session on one of the computers in the research office.

Individual Alcohol Drinking Session:

Preliminary steps: Participants will be asked not to eat for 3 hours pre-arrival. Alcohol drinking will occur in a bar lab located at Yon Hall North in Ben Hill Griffin Stadium at the University Florida campus. Participants will be brought to the bar or simulated laboratory for the session via study-provided transportation: either a professional service such as taxi or Uber or a UF-owned automobile driven by a UF employee. However, if a participant lives within a 0.5-mile radius of the research facility they may walk to the facility rather than being driven. These participants may be walked home by study staff after the end of the alcohol drinking session. Upon arrival, BrAC must=.00% and urine tests will be repeated. Participants registering a BAC > 0.00% or with a positive urine test that leads to exclusion will be dismissed immediately and provided transportation directly home by the study. Participants will complete US-THRIVE, an efficacious, brief, web intervention based on M.I. (i.e., personalized feedback on drinking patterns, behavioral strategies, alcohol facts and resources). Before the alcohol administration, participants may be asked to wear the BACTrack Skyn alcohol wristband monitor, which looks like a fitness tracker or wristwatch and can detect alcohol as it evaporates through the skin. Prior to the session, they will be randomized to 1 of the 3 app conditions. The randomization procedure will be managed by a study staff member/collaborator without direct participant contact. Staff working with participants will not know app assignment.

Instructions: After participants learn their app condition, they will view a presentation on the CGNG and how to use their assigned app. They will be told the app is based on a cognitive game and that they will use it 3 times. They will learn that the task is relevant to real-life as moderate amounts of alcohol affect task success and poor performance has been linked to driving problems and risky decisions. Dr. Leeman has used similar instructions relating alcohol to task performance and pay[65, 66] and seen a range of alcohol use in lab drinking sessions.

Alcohol administration steps: After completing US-THRIVE and using the app, the participant will be given vodka mixed drinks targeting a BAC of .06% based on sex, height, and weight divided into three parts. The participant will have 10 minutes to complete each drink and after

completion of all the drinks they will have a 15-minute absorption period. Participants will consume these beverages with a trained research staff member (graduate or undergraduate research assistant) to add a social aspect. This individual will be introduced as a staff member not a confederate and will not consume any alcoholic beverages [67]. After the drinking portion has ended the participant will use the app again, be given a glass of water, and a BrAC will be taken. After 30 minutes, another BrAC will be taken, followed by self-reports. Drink administration will be conducted per NIAAA guidelines[75] by 3 staff (supervisor, bartender, assistant). The individual drinking session can take place between 11am-7pm and participants should expect to remain on site for at least 2 hours after the drinking portion has ended and will be released when BrAC≤.02%. At that, time transportation will be arranged to take participants to their home address only. Payment for this session will be $10 an hour and payment will be distributed at the follow-up appointment.

Table 1. Summary procedures involved in individual alcohol drinking sessions in the proposed study

Time	Procedures
+0	Arrival. Breath alcohol (BrAC) reading, urine testing, snack, US-THRIVE, app assignment, app information, & instructions, use app.
+60	Alcohol dosing period: dose targeting BAC=.06, divided into three parts, 10 minutes to drink each part of dose
+90	15 minute absorption period, participant drinks small glass of water to rinse alcohol from mouth
+105	BrAC, use app, self-report of perceived impairment & other measures, then BrAC
+135	BrAC, use app, self-report of perceived impairment & other measures.
+165	BrAC. Dismissal once BrAC ≤ .02%

Group Alcohol Drinking Session:

Preliminary steps: Participants who are invited back for a group alcohol drinking session will be asked not to eat for 3 hours pre-arrival. Alcohol drinking will occur either in a bar lab or other room located at Yon Hall North in Ben Hill Griffin Stadium at the University of Florida campus. At around 3:45pm, participants will be brought to the bar or simulated laboratory for the session via study-provided transportation: either a professional service such as taxi or Uber or a UF-owned automobile driven by a UF employee (Table 2). However, if a participant lives within a 0.5 mile radius of the research facility they may walk to the facility rather than being driven. At the end of the session, these participants may be walked home by study staff. Upon arrival at 4pm, BrAC (must=.00%) and urine tests will be repeated (Table 2). Participants registering a BAC > 0.00% or with a positive urine test that leads to exclusion will be dismissed immediately and provided transportation directly home by the study. At this appointment, participants will receive an abbreviated version of the instructions on how to use the app and its value (see below). Participants will also complete baseline self-reports and the cued go/no-go task on the app. Before the alcohol administration, participants may be asked to wear the BACTrack Skyn. Each session will be scheduled with 3 people each assigned to a different app, but if 1 cannot participate, the session may still occur. While it is our preference that this appointment occur at 4pm just before the rest of the drinking session activities, if a participant's schedule does not permit it, the 4pm activities may also be scheduled earlier in the day on the day of the session or the day before. In the case of an appointment the day before, the urine drug and pregnancy test will still occur on the day of the session. Payment for this appointment will be $20 via cash card and will be transmitted on the day of the appointment.

Instructions: The day of the group session participants will be given a brief review of the instructions that were given to them at their individual drinking sessions. Participants will be asked to not share their results on the app with the other participants. Study staff will explain to participants that to incentivize fast, accurate performance (Fig. 2a), they will get $.10 each

correct response if ≤275ms with $.10 penalty per error based on the final CGNG. Dr. Fillmore has seen a range of performance post-alcohol with this procedure[44]. All participants will learn their number of errors and fast + correct responses on the final CGNG. This may increase motivation to use the app in the 4-wk field-use period.

Alcohol Administration/self-administration steps: Starting at 5pm, each participant will be given vodka with juice targeting BAC=.06% based on sex, height and weight divided into 3 parts with 10 min. for each, 15-min. absorption, then BrAC, app use again and perceived impairment rating[62] (how impaired they are; how unsafe driving would be). After these steps and another BrAC, 1-hr free drinking will begin when they can self-administer more alcoholic drinks up to .12% maximum BAC. Drink administration will be conducted per NIAAA guidelines[68] (Table 1) by 3 staff (supervisor, bartender, assistant). After 1-hr, participants will be given water, another BrAC, wait 30 min., BrAC again, then app use, followed by self-reports. Staff will download app data onto a computer and inform participants of their number correct and errors on the last CGNG. They will rate the assigned app for usability including ease; self-consciousness when using; overall value and likelihood of future use[69]. Procedures for the 4-week field period will be explained. In the field period, participants will get the experimental app, regardless of session condition. Participants will remain on-site until at least 11pm and released when BrAC≤.02%. At that time, transportation will be arranged to take participants to their home address only. Participants can earn up to $80 for session participation ($10 per hour for the 6 hours and $20 for adhering to session rules including accepting study-provided payment to and from the session, not completing academic or job-related work during the session, etc.), and payment will be distributed at the follow-up appointment.

Table 2. Summary of procedures involved in group alcohol drinking sessions in the proposed study

Time	Procedures
4pm	Arrival. BrAC, urine testing, snack, review of instructions, and use app.
5pm	Alcohol dosing period: dose targeting BAC=.06, divided into 3 parts, 10 minutes to drink each part of dose
5:30	15 minute absorption period, participant drinks small glass of water to rinse alcohol from mouth
5:45	Breath alcohol (BrAC) reading, use app, self-report of perceived impairment & other measures, then BrAC
6:15	1-hour free-drinking period when participants can self-administer more vodka mixed drinks to max BAC=.12%
7:15	Participant drinks small glass of water to rinse alcohol from mouth, then BrAC
7:45	BrAC, use app, all participants will get feedback on performance, self-reported impairment/other measures
8pm	Food provided, participants' phones returned and staff extracts data from study phones.
10pm	Usability ratings of assigned app, 4-week field period explained, experimental feedback app provided to all
11pm	Earliest possible dismissal once BrAC ≤.02%

App condition: The control version is a smartphone-compatible CGNG. Each trial has this order: fixation cross (250ms); blank (250ms), vertical or horizontal cue (white rectangle) for 1 of 6 stimulus onset asynchronies (100, 200, 300, 400, 500, 750ms); go or no-go target (green or blue rectangle, respectively) until participant responds or 500ms; inter-trial interval (250ms). Participants are told to respond fast to green, not to blue. Cues signal a target at 70% probability (horizontal: go, vertical: no-go). Activation and inhibitory tendencies develop cue-dependence[70, 71]. Go cues speed RT to go targets, which must be overcome for no-go targets.

Inhibition errors are more common after go cues. The app is the same as a computer version except it fits a smartphone (Fig. 2b) with instructions to press the screen directly rather than a keyboard and includes 75, not 250 trials.

The standard version is the same as the control version with the exception that information about performance (correct or incorrect) is displayed along with RT in ms for a correct response during each inter-trial interval.

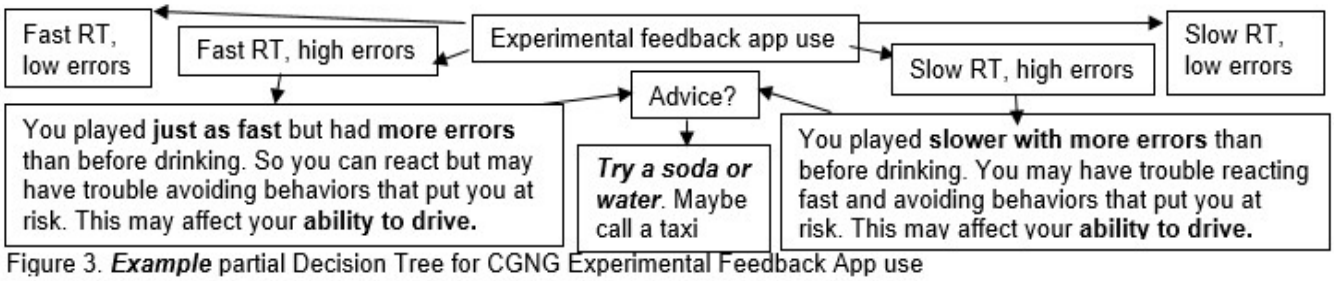


Figure 3. ***Example*** partial Decision Tree for CGNG Experimental Feedback App use

The experimental, feedback version includes the standard plus feedback on RT and inhibition errors compared to pre-drinking (Fig. 3). Based on past findings[45-51], if they react ≥20ms slower and/or make >5% errors, they will get a message summarizing the performance decrement and implications for an outcome, picked randomly among trouble driving, risky sex, drug use, delinquency, or aggression. The app will state that there are simple alternatives with invitation to press a box to view advice, based on research that risk information may increase risky behavior if convenient options are not given[72]. Feedback will be worded non-judgmentally per motivational interviewing tenets.

Post-session field use:

We will collect data for 4 weeks as people engage in usual drinking. The app will be programmed to deploy the CGNG, give related feedback and offer advice for 2 of the 4 wks (counterbalanced), enabling within-subject comparison of alcohol use with vs. without the main component app. The app will prompt 3 times on typical drinking days. Participants can set the app to prompt on other days also. After CGNG and feedback, participants report perceived impairment, the number of standard drinks they have consumed to that point and the extent to which they want and would like more alcohol. During the 2-weeks when the app does not deploy the CGNG task and feedback, participants will answer the questions only. Each morning for the 4 weeks, the app will prompt recording of number of drinks and time spent drinking the prior day. Data collected by the app will not be visible after it is submitted so minimal information about participants will be visible in the app if the phone is stolen, lost, “hacked” or in some other way made visible to another person. Even though task performance and self-report responses are no longer visible after submission we suggest that all participants password protect their phone, and change the auto lock to 1 minute so that the application cannot be accidently accessed by anyone other than the study participant. Participants completing only the field use period will attend a baseline appointment, which can be held remotely via a password-protected UF Zoom meeting. During this baseline appointment participants will be walked through how to download the smartphone application, and shown how to use the app. They will be asked to use the app during the appointment to gather baseline data, and will then be pinged again later that evening or the following morning to use the app again. Compensation for this appointment will be $10. Following their baseline appointments participants will be asked to attend an orientation appointment where they will receive their randomized version of the smartphone application. They will receive $10 for this appointment. Participants completing lab sessions will complete these appointments in the course of their session participation and receive the same

compensation. Participants will be paid $5 per day each day of the field use period for completing the morning assessment on the app with a $5 bonus for completing the assessment 7 out of 7 days ($40 per week). They will also be compensated $10 per week for using the app at least once per week. Thus, participants can earn up to $200 during the field use period, and payment will be given at the follow-up appointment. Participants will also complete the 6 & 12 month follow-up surveys making maximum compensation for those chosen to only complete the field the use period $310.

EMA Field Testing Scenario:

As with main study participants, EMA participants may use their own smartphones or a study phone to complete these tasks in the study. Participants will be prompted 5 times per day for 10 days to complete some type of brief assessment on their phone. On days when participants drink alcohol, they may complete up to 7 assessments. EMA participants will complete the same morning questionnaire via the app as main study participants do. They will then be prompted to use the app including completion of the cognitive task twice (typically, once late morning/early afternoon and once in the mid-late afternoon) each day. Participants will receive a reminder an hour-two hours before the time when they most often begin drinking on a typical day of the week. The reminder will be for participants to complete a brief drinking questionnaire housed on REDCap at the conclusion of each of their first 3 drinks, should they have at least that many. The reminder will be delivered via text message from a study phone and will include the REDCap survey link. This survey will ask about what the participant is drinking, the speed of consumption, the subjective effects of alcohol they are feeling, the social context in which they are drinking, and their location (i.e. at home, bar, restaurant, friend's house, etc.). Participants will then receive another prompt via text from the study phone to complete the end of the day survey just before they go to bed. This prompt will come between an hour to two hours before their typical bed time on a given day of the week. This survey will about their total number of alcoholic drinks for the day/night, what time they finished drinking, the subjective effects of alcohol they are feeling, their perceived impairment, and about perceived impaired control over alcohol use (i.e., difficulty in one's ability to limit drinking). Thus, participants will have input regarding when they will receive each of these prompts. Participants will receive $130 if they complete ≥ 80% of possible questionnaires. Payment will receive a prorated portion of the $130 if they complete less than 80%. For instance 50% completion would earn $65. EMA participants will earn $20 for the in-person screening appointment; $20 for an appointment to train them how to use the app and regarding how the EMA will work, which can occur remotely via Zoom; and $30 for an appointment after they complete the 10-day period, which can also occur remotely though participants using a study phone will have to return it to the research office. Thus maximum compensation for a participant chosen for the EMA scenario will be $200. Typically EMA studies are conducted via special EMA software, however, given that we tend to enroll no more than 12 participants and the duration will only be 10 days, we will conduct the EMA via text messages sent from study staff using a study phone and REDCap surveys.

Follow-up appointment:

After 4 weeks, participants will come to our office for an updated TLFB and give usability and acceptability ratings for the CGNG experimental feedback app based on the 4-week field period. Staff will extract data from the phones, participants will be paid, and clinical referrals will be provided when appropriate. Participants who participate entirely remotely will complete their follow-up appointment via Password-Protected UF Zoom. Participants will receive $30 for attending this appointment. They will receive all other earned compensation at this time via a prepaid debit card.

Six- & 12-month follow ups: At six and twelve-months post completion of the study, participants will be contacted via electronic mail and will be asked to complete a survey comprised of

previously approved measures and items regarding use of alcohol reduction smartphone apps and other means of alcohol use reduction. The survey will be completed through the secure website www.REDCap.com. Payment for completion of each survey will be $25.

Assessments:

Web/phone screener:

Demographic information: This questionnaire assesses basic demographic information, including age, sex, weight, and whether they are a Foreign National or not.

Frequency and quantity of alcohol consumption: Three multiple choice items will be included, which will assess number of drinking days; number of heavy drinking days (5 or more for men, 4 or more for women) and peak number of drinks in a 24-hour period in the past 30 days.

Liking for different alcoholic beverages: An item will be included concerning participants' liking of beer, wine, vodka (straight or in mixer) and rum (straight or in mixer).

General questions regarding other inclusion criteria: Two questions will list several inclusion criteria and ask participants whether or not all of the listed criteria pertain to them. This will provide information regarding inclusion and exclusion to study staff while not requiring participants to provide specific information along these lines as part of the preliminary screen.

In-Person Screening Appointment:

Vital signs (i.e., blood pressure and pulse readings), *height and weight*.

Withdrawal: The *Clinical Institute Withdrawal Assessment for Alcohol (Revised) (CIWA-AR*)[29] will be used to assess withdrawal symptoms. The CIWA is a reliable 10-item instrument designed to assess severity of current withdrawal syndrome.

Medical and psychiatric history: A medical and psychiatric history will be taken from all participants, which will cover the following conditions: hypertension, diabetes, high cholesterol, cardiac abnormalities, pancreatitis, renal insufficiency, cancer, pulmonary disease, thyroid conditions, history of head injury or other neurological problems, stomach or intestinal disorders and liver disease. Participants will also be asked whether they have ever been diagnosed with a psychiatric condition or received treatment for such a condition. Participants will be asked to report all medications, including over the counter medications and those that they are currently taking, including psychotropic medications. The *Structured Clinical Interview for DSM-5* (SCID) will be used to classify patients according to the presence or absence of past or present alcohol and other substance use disorders as well as other psychiatric disorders, as needed.

The *digits backwards* task from the digit span subtest of the Wechsler Adult Intelligence Scale-III[80] will be used to assess working memory.

The *Kirby delay discounting measure* is a 27-item measure that assesses preferences as to whether participants would prefer smaller, immediate or larger, delayed hypothetical monetary amount. Length of delay and amount of hypothetical funds vary across items.

Web-Based Survey Associated with In-Person Screen

Demographics: Participants will be asked to report their birth sex, gender identity, age, race and ethnicity.

Student status: Participants will be asked to report whether or not they are students currently and if so, they will be asked about various aspects of their student status, including full-time versus part-time status, year in school, type of residence and fraternity/sorority membership.

Psychiatric symptoms/conditions: The 42-item *Depression Anxiety Stress Scale (DASS*[85]) will be administered. This measure assesses several negative emotional states, including depression, anxiety and stress to which participants indicate their agreement on a 4-point scale.

Family history of problem drinking: Family history is measured with a subscale taken from the *Addiction Severity Index*[57]. Participants are asked to indicate whether or not four classes of relatives on both their mother's and father's side ever "had a significant problem with alcohol or drugs, one that either lead to treatment or should have led to treatment."

Drinking history: Participants will be asked to report the age when they first started drinking, not counting small tastes or sips of alcohol and their age of first intoxication. They will also be asked to report the highest number of drinks they have ever consumed over a 24-hour period in their lifetimes.

Alcohol-related problems: Participants will complete the long version of the Young *Adult Alcohol Consequences Questionnaire* (*YAACQ*), which is comprised of 48 consequences that may have occurred within the past three months.

Alcohol expectancies: The *Comprehensive Effects of Alcohol* (*CEOA*) measure will be used to assess the extent to which participants report experiencing alcohol-related expectancies (e.g., "After a few drinks of alcohol, I would be more likely to feel dizzy").

Subjective response to alcohol: An adapted version of the *Self-rating of Effects of Alcohol* (*SRE*; Schuckit et al., 1997[92]) will be used at intake to assess the number of alcoholic drinks it took for participants to experience a series of subjective effects (e.g., stimulation, arousal) the first time they drank alcohol, in the past three months and during their period of heaviest drinking. Responses to the adapted SRE will be used to assess self-reported *tolerance* as well. A tolerance score is created by subtracting the score for the first five drinking occasions (α = .83) from the score for the recent drinking experiences (α = .86)[93].

Drinking motives: Drinking motives will be assessed using Cooper and colleagues measure of three types of drinking motives (i.e., social, coping and enhancement or the achievement of pleasurable affect from drinking).

Drinking-induced disinhibition: The *Drinking-Induced Disinhibition Scale*[63] (*DIDS*) is a measure comprised of a series of drinking-related experiences to which participants are asked to indicate agreement on a six-point scale. The DIDS assesses four types of disinhibitory experiences resulting from alcohol use (i.e., euphoric/social, dysphoric, sexual and aggressive).

Impaired control: The *Impaired Control Scale*[33] *(ICS*) consists of three parts including 5 items concerning actual attempts at limiting alcohol consumption (Part 1); 10 items assessing the frequency of past failures at controlling drinking (Part 2) and 10 items assessing beliefs regarding future ability to control drinking (Part 3). Parts 1 and 2 will be administered in this study. The ICS is reliable and has been validated in clinical and community samples. Items are rated on a 0 to 4 scale and summed with higher scores indicating greater difficulty in controlling consumption.

The *Protective Factors Questionnaire* measures frequency of alcohol-related protective strategy use on a 7-point scale. This measure has been used with young adult samples in several studies.

Facets of impulsivity: Impulsivity and risky decision making will be measured using the *UPPS Impulsive Behavior Scale*: a 59-item measure that assesses five subdimensions of impulsivity (premeditation, positive urgency, negative urgency, sensation seeking and perseverance). A *cued go/no-go task*[60] will be administered during the in-person screening appointment. This is a

8-10 minute computerized task which assesses the ability to inhibit a prepotent response. Subjects are instructed to press a key or inhibit pressing a key based on the colors of the shapes presented. The orientation of the shape (horizontal or vertical) before the color appears signals imperfectly the likelihood that the subsequent stimulus will be “go” or “no-go.” Participants receive feedback regarding their accuracy and speed of response.

In-Person Screening Appointment and at Preliminary Appointment Day of the Sessions:

Self-reported alcohol consumption and smoking: The *Timeline Followback Interview* (TLFB) will be administered at the in-person screening and updated at the preliminary appointment. Participants will be given a blank calendar including memory prompts (e.g., holidays), which covers the designated time interval (the prior 30 days at initial screening) and asked to reconstruct their drinking behavior and smoking over that interval. The TLFB has good test-retest reliability and good validity for verifiable events.

Marijuana use: Participants will be asked on how many days they have used any form or marijuana. Participants will be asked to report on the prior 30 days at the in-person screening appointment and since the in-person screening appointment at the appointment on the day of the session.

Urine drug and pregnancy tests: Urine drug dips will be used to detect opiates, cocaine, phencyclidine, amphetamines, methamphetamine, barbiturates, methadone and benzodiazepines. Urine pregnancy tests will also be administered to all female participants. A positive test for any of the above drugs or a positive pregnancy test will lead to immediate exclusion from the study.

Symptoms: Adverse experiences are collected on standardized forms, using the *SAFTEE*. The SAFTEE includes 1) open-ended questions about any changes in physical or health problems, appearance, or activity level, and 2) yes/no responses to a specific list of symptoms for a specified time period. For each symptom reported on the SAFTEE a rater also records the severity (mild, moderate, or severe) and action taken.

Suicidality: The *Columbia Suicide Severity Rating Scale (CSSRS)* is a semi-structured interview that assesses past and current suicidal ideation, intent, and attempts. It will be used to monitor the safety of participants. Any participant reporting current suicidal ideation including intent to carry out a suicide attempt will be excluded from the study and the study physician, Dr. Cook, will be alerted immediately.

Menstrual cycle data: Self-reports will be obtained from all women on their menstrual/gynecological status. We will include women who are cycling normally and/or on birth control pills. Three months of self-report data recording the start of their menses will be obtained prior to the alcohol drinking session. This information will be obtained initially at the in-person screening and updated at the pre-session screening appointment on the day of the alcohol self-administration session.

Brief Smoking Questionnaire: The Brief Smoking Questionnaire is a brief self-report survey that consists of four questions that evaluate current daily cigarette use and likelihood of nicotine dependence. I

Drinking Reduction Form: This is a brief survey consisting of three Yes/No questions. The first question determines whether a potential participant has used a smartphone app to reduce drinking in the previous 12 months. The next two questions determine whether a potential participant plans to take active steps to stop or cut down drinking in the next three months.

Eligibility Checklist: This checklist is used by study staff to determine participant eligibility based on measures taken during the screening appointment to make certain that active evaluations of eligibility and ineligibility are made.

Screening and at Alcohol Administration Sessions:

Breath alcohol concentration: Breath alcohol concentration will be assessed using a hand-held Intoxilyzer breathalyzer unit at the in-person screening; at the preliminary appointment earlier on the day of the alcohol drinking session; at the outset of the alcohol drinking session and then at several points during the sessions.

Alcohol purchase task: This is a simulation measure to assess self-reported alcohol consumption and expenditure were alcohol to cost varying amounts of money. The measure generates a number of variables pertaining to reinforcement from alcohol, including intensity of demand. The purchase task will be administered twice during the in-person screening appointment. One version will assess how many drinks a participant would consume right now at varying amounts of money and a modified version will assess how many drinks a participant would consume on a hypothetical weekend evening. At the alcohol drinking session, the "right now" version of the measure will be administered multiple times at both at baseline and after the drinking period. This will allow a comparison of the amounts of hypothetical money participants are willing to spend on alcohol, a priori, upon arrival at the bar or simulated lab and after consumption of alcohol.

Risk Taking Behavior: The *Cognitive Appraisal of Risk Events* (CARE) and its revised version (CARE-R; Katz, Fromme, & D'Amico, 2000) assess recent negative consequences and expectations that these consequences will occur again in the near future. Of the measure's 4 subscales, we will administer at in-person screen a version of the past frequency subscale that combines the original with the revised version in order to obtain baseline data. Participants will be asked to report how many times in the past 3 months each has occurred. Then after fixed dose in the individual session, we will administer the expected involvement subscale. Items are rated a 7-point Likert scale ranging from "not at all likely" to "extremely likely".

Alcohol Administration Sessions:

Measures of the subjective effects of alcohol, craving, mood and perceived impairment will be administered at the end of the alcohol self-administration period and every hour afterward until the end of the session. Participants will also be asked to estimate their current blood alcohol level and number of alcoholic drinks consumed at the end of the alcohol self-administration period. Craving and mood will also be assessed at the beginning of the session.

The *Probabilistic Choice Questionnaire (PCQ)*[71] is made up of 30 items comparing certain with uncertain hypothetical monetary amounts of varying sizes.

Subjective effects of alcohol: The *Biphasic Alcohol Effects Scale*, a 14-item self-report, unipolar adjective rating scale, will be used to measure the stimulant and sedative effects of alcohol.

Craving: Craving will be assessed using two measures. The *Alcohol Urge Questionnaire (AUQ)* is an 8-item questionnaire, derived from a larger 49-item "Questionnaire of Alcohol Urges" and assesses *desire for a drink, expectation of positive effect from drinking,* and *inability of avoid drinking if alcohol was available.* The AUQ is a reliable and valid scale for the measurement of self-reported alcohol urges and scores have been shown to be strongly related to alcohol dependence severity and to cognitive preoccupation with alcohol. Its brevity and time frame for ratings (i.e., right now) makes it suitable for administration during the alcohol drinking period.

Craving will also be assessed with a *single item assessed using a 100-point visual analog scale*. Participants will be asked to report the extent to which they "want alcohol."

Liking for alcohol: An item from *The Drug Effects Questionnaire*[64] (DEQ) will be used to assess the extent to which participants like the effects of alcohol they are experiencing at the time, rated on a 100-mm line (from "not at all" to "very much"). The DEQ has been utilized in previous alcohol studies[65].

Mood: The *Positive Affect and Negative Affect Scale* (*PANAS*) provides a measure of current mood. Participants indicate their agreement with 20 adjectives, including 10 each to assess positive (e.g., attentive, interested) and negative affect (e.g., hostile, scared). The PANAS has been found to be both reliable and valid.

Perceived impairment: Participants will also rate their perceived level of impairment with three items on 1-10 scales, used by Brumback et al[66]: 1. "how impaired do you think you are at present?", 2. "how unsafe do you think it would be to drive an automobile at present?", and 3. "if I were at work now, others might think I was intoxicated or behaving unusually" with 10-point rating scales for each, anchored at 1 for "not at all" and 10 for "extremely". The use of these items will allow for analyses to address the possibility that misperceived impairment partially mediates an association between self-reported impaired control and ad libitum alcohol consumption.

Social bonding: The *Perceived Group Reinforcement Scale (PGRS)* will be used to evaluate the degree of social bonding participants believe has occurred during the session for those participants who complete alcohol self-administration in a group format. The PGRS is a 12-item measure with items (e.g., "I liked this group) rated for agreement on a 9-point scale. The measure will be administered twice, once right after the end of the drinking period and then again toward the end of the session when the first participant has reached a safe BAC level and is able to leave.

"Real Time" Impaired Control Questions: We will ask a series of questions pertaining to impaired control that are based on some items in the Alcohol Craving Questionnaire[67]. The goal is to get a sense of participants' perceived impaired control at that time if they could drink alcohol without the limitations on drinking in place due to the study: "If I had access to alcohol right now, I would not be able to stop using it;" "I would not be able to control how much alcohol I drank if I had some here now;" "I could not stop myself from drinking if I had some alcohol here." Items are rated on 7-point scales anchored by "strongly disagree" and "strongly agree."

Acceptability and satisfaction with mobile technology: Toward the end of the alcohol drinking session, participants will complete a measure regarding the acceptability of the form of mobile technology to which they were randomly assigned. These items were adapted from an evaluation for computerized cognitive behavioral therapy[36]. Participants will rate satisfaction with their mobile technology; ease of use; self-consciousness while using it; overall value; and likelihood they would use it in the future.

Participant Experience Interview: During the follow-up interview, a study staff member will conduct a participant experience interview to obtain participant input regarding aspects of the study including aspects they liked, disliked and suggested changes for future studies. Questions regarding the drinking session, app use, and advice provided are included in this interview.

EMA Surveys

While drinking survey

Type of drink: Participants will be asked “What type of drink did you consume?” with the options beer, wine, malt liquor, hard liquor shot, and mixed drink.

Speed of Consumption: As soon as possible after completing an alcoholic drink, participants will answer the question “How long did it take you to drink [the beverage]?” endorsing one of the following time increments in minutes: 1 = <2, 2 = 2 to 5, 3 = 6 to 10, 4 = 11 to 15, 5 = 16 to 20, 6 = 21 to 25, 7 = 26 to 30, 8 = 31 to 45, 9 = 46 to 60, and 10 = >60.

Location: Participants will be asked “Where is your current location?” with the following options: home, work, bar/restaurant, outside, other public place, other location, friend’s house, and significant other’s house.

Social Context: Participants will be asked “In the past 15 minutes, who have you been with?” with the following options: no one, romantic partner/spouse, family member, friend/ acquaintance, boss/teacher, coworker, roommate, and other.

Liking for alcohol: An item from *The Drug Effects Questionnaire*[64] (DEQ) will be used to assess the extent to which participants like the effects of alcohol they are experiencing at the time, rated on a 100-mm line (from “not at all” to “very much”). The DEQ has been utilized in previous alcohol studies[65].

Craving: Craving will also be assessed with a *single item assessed using a 100-point visual analog scale*. Participants will be asked to report the extent to which they “want alcohol”.

Subjective effects of alcohol: The *Biphasic Alcohol Effects Scale*, a 14-item self-report, unipolar adjective rating scale, will be used to measure the stimulant and sedative effects of alcohol.

After Drinking Survey

Drink Amount: At the end of the night participants will be asked about how many drinks they have consumed during that day/night, and what type of drinks they were (Beer, wine, hard liquor).

End of Drinking: Participants will be asked to indicate when they completed their last drink for that day/night

Subjective effects of alcohol: The *Biphasic Alcohol Effects Scale*, a 14-item self-report, unipolar adjective rating scale, will be used to measure the stimulant and sedative effects of alcohol.

Perceived impairment: Participants will also rate their perceived level of impairment with three items on 1-10 scales, used by Brumback et al[66]: 1. “how impaired do you think you are at present?”, 2. “how unsafe do you think it would be to drive an automobile at present?”, and 3. “if I were at work now, others might think I was intoxicated or behaving unusually” with 10-point rating scales for each, anchored at 1 for “not at all” and 10 for “extremely”. The use of these items will allow for analyses to address the possibility that misperceived impairment partially mediates an association between self-reported impaired control and ad libitum alcohol consumption.

“Real Time” Impaired Control Questions: We will ask a series of questions pertaining to impaired control that are based on some items in the Alcohol Craving Questionnaire[67]. The goal is to get a sense of participants’ perceived impaired control at that time if they could drink alcohol without the limitations on drinking in place due to the study: “If I had access to alcohol right now, I would not be able to stop using it;” “I would not be able to control how much alcohol I drank if I had some here now;” “I could not stop myself from drinking if I had some alcohol here.” Items are rated on 7-point scales anchored by “strongly disagree” and “strongly agree.”

Liking for alcohol: An item from *The Drug Effects Questionnaire*[64] (DEQ) will be used to assess the extent to which participants like the effects of alcohol they are experiencing at the time, rated on a 100-mm line (from "not at all" to "very much"). The DEQ has been utilized in previous alcohol studies[65].

Craving: Craving be assessed with a *single item assessed using a 100-point visual analog scale*. Participants will be asked to report the extent to which they "want alcohol"

Six and Twelve Month Follow-Up Survey:
Student status: Participants will be asked to report whether or not they are students currently and if so, they will be asked about various aspects of their student status, including full-time versus part-time status, year in school, type of residence and fraternity/sorority membership.

Psychiatric symptoms/conditions: The 42-item *Depression Anxiety Stress Scale (DASS*[85]) will be administered. This measure assesses several negative emotional states, including depression, anxiety and stress to which participants indicate their agreement on a 4-point scale.

Family history of problem drinking: Family history is measured with a subscale taken from the *Addiction Severity Index*[57]. Participants are asked to indicate whether or not four classes of relatives on both their mother's and father's side ever "had a significant problem with alcohol or drugs, one that either lead to treatment or should have led to treatment."

Alcohol-related problems: Participants will complete the long version of the Young *Adult Alcohol Consequences Questionnaire* (*YAACQ*), which is comprised of 48 consequences that may have occurred within the past three months.

Alcohol expectancies: The *Comprehensive Effects of Alcohol* (*CEOA*) measure will be used to assess the extent to which participants report experiencing alcohol-related expectancies (e.g., "After a few drinks of alcohol, I would be more likely to feel dizzy").

Subjective response to alcohol: An adapted version of the *Self-rating of Effects of Alcohol* (*SRE*; Schuckit et al., 1997[92]) will be used at intake to assess the number of alcoholic drinks it took for participants to experience a series of subjective effects (e.g., stimulation, arousal) the first time they drank alcohol, in the past three months and during their period of heaviest drinking. Responses to the adapted SRE will be used to assess self-reported *tolerance* as well. A tolerance score is created by subtracting the score for the first five drinking occasions (α = .83) from the score for the recent drinking experiences (α = .86)[93].

Drinking motives: Drinking motives will be assessed using Cooper and colleagues measure of three types of drinking motives (i.e., social, coping and enhancement or the achievement of pleasurable affect from drinking).

Drinking-induced disinhibition: The *Drinking-Induced Disinhibition Scale*[63] (*DIDS*) is a measure comprised of a series of drinking-related experiences to which participants are asked to indicate agreement on a six-point scale. The DIDS assesses four types of disinhibitory experiences resulting from alcohol use (i.e., euphoric/social, dysphoric, sexual and aggressive).

Impaired control: The *Impaired Control Scale*[33] *(ICS*) consists of three parts including 5 items concerning actual attempts at limiting alcohol consumption (Part 1); 10 items assessing the frequency of past failures at controlling drinking (Part 2) and 10 items assessing beliefs regarding future ability to control drinking (Part 3). Parts 1 and 2 will be administered in this study. The ICS is reliable and has been validated in clinical and community samples. Items are rated on a 0 to 4 scale and summed with higher scores indicating greater difficulty in controlling consumption.

The *Protective Factors Questionnaire* measures frequency of alcohol-related protective strategy use on a 7-point scale. This measure has been used with young adult samples in several studies.

Facets of impulsivity: Impulsivity and risky decision making will be measured using the *UPPS Impulsive Behavior Scale*: a 59-item measure that assesses five subdimensions of impulsivity (premeditation, positive urgency, negative urgency, sensation seeking and perseverance). A *cued go/no-go task*[60] will be administered during the in-person screening appointment. This is a 8-10 minute computerized task which assesses the ability to inhibit a prepotent response. Subjects are instructed to press a key or inhibit pressing a key based on the colors of the shapes presented. The orientation of the shape (horizontal or vertical) before the color appears signals imperfectly the likelihood that the subsequent stimulus will be "go" or "no-go." Participants receive feedback regarding their accuracy and speed of response.

Smartphone app use: Several questions will ask participants about their use of smartphone applications during the past 6-months as a way to moderate or reduce their drinking.

Drinking reduction: Two questions will assess whether participants have taken active (i.e., attending self-help group meetings, beginning psychotherapy, medication use or entering an inpatient facility) steps to change their alcohol and/or other substance use during the past 6-months

Data analyses

Normal probability plots will be reviewed to assess normality and need for transformations. Paired samples *t*-tests will be used to confirm an effect of initial dose on CGNG inhibition errors but not RT. Our analytic strategy will resemble 3 past studies. The main method will be multiple regression with study condition and sex as predictors. Baseline variables that differ significantly by condition will be covaried.

Outcome 1a will be BAC during self-administration. Because we will not interrupt alcohol self-administration with BrAC readings, we will calculate peak estimated BAC (eBAC) based on number of alcoholic drinks, time elapsed, weight and sex. eBAC was sensitive to differences in consumption between study conditions in a prior study conducted by Dr. Leeman. Results will be BrAC-confirmed after the 1-hr free-drinking period. Though not the main focus, we will test 2-way interactions of study condition by RT and inhibition errors post-alcohol to see if more inhibition failures under alcohol predict self-administration. Regressions will be confirmed using multilevel models (MLM) in Mplus with random effect of group (people completing a drinking session together) and other predictors as fixed effects. Since participants will be randomized to different apps, we do not expect strong intra-class correlations, which should result in similar findings in regression and MLMs. In our in-progress study, no group level effects have emerged. A similar strategy will be used for 1b (alcoholic drinks self-administered).

Primary Aim 2 will entail comparisons of alcoholic drinks consumed per occasion between the 2 weeks participants will use vs. not use the app in the 4-week field period post-drinking session. We will retain study condition as a predictor (effects of lab-assigned condition are not hypothesized here) and a random group effect while adding app use vs. non-use period as a within-subjects effect in MLM. *ANOVA* will compare usability and acceptability ratings at the end of the drinking session and 4-week field period across app conditions. For mediation (Secondary Aim), we will test for indirect effects of app condition on self-administration via perceived impairment using MacKinnon's products of coefficients approach with bootstrapped confidence intervals (CIs). This approach accounts for non-normality of the product of

coefficients in calculating indirect effects of IV on DV, operating through a mediator. When the CI does not include 0, an indirect effect is significant at the specified alpha level.

For Exploratory Aim 1, we will test between-subjects study condition during the lab sessions, amount of alcohol self-administered (operationalized as estimated peak BAC and number of drinks self-administered in separate models) in the alcohol drinking session and during the field period in the intervention and non-intervention periods as predictors of self-reported alcohol consumption (e.g., drinks per drinking day) and alcohol-related problems self-reported at 6- and 12-months post-session on the web-based surveys using MLM. Baseline reports of each alcohol-related outcome and participant sex will be entered as covariates. The web-based surveys at baseline, 6- and 12-months post also include measures of several potential covariates that may be entered into these models should they differ significantly across study conditions.

For Exploratory Aim 2, we will use separate MLMs to test BACTrack Skyn readings during each alcohol administration session as predictors of successive breath alcohol readings taken following alcohol administration/self-administration periods in the alcohol drinking sessions and to predict number of drinks self-administered during the group drinking session. Sex and participant weight will be entered into these models as covariates as well.

For Exploratory Aim 3, we will use MLM to predict expected involvement scores on the CARE measure post-alcohol administration based on performance on the app-based cued go/no-go task following the .06% fixed dose as the predictor variable. Baseline expected involvement scores and scores on the other CARE subscales will be held constant in these models. Since the .06% dose will be administered at each session along with cued go/no-go task performance and the CARE, these measures will be entered into the same models as repeated measures. Participant sex and study condition will also be entered as covariates in these models

Sample, power & effect size

Our goal was to power the study for the Primary and Secondary Aims. Roberts and Fillmore's findings speak to the potential impact of task-based feedback (Preliminary Study 5 [PS5]). Perceived ability to drive post-alcohol declined from *M*=46.8(4.7) to 29.7(5.5) in the higher risk DUI group and only *M*=25.8(5.5) to 21.2(4.8) in the no-DUI group: a large effect difference (*d*=1.5). While not the same as a control condition, the no-DUIs were a subgroup in which the intervention had minimal impact, as with a control condition. Our alcohol study in-progress (Preliminary Study 1 [PS1]) is relevant as a test of effects of an app on alcohol self-administration though the methods are not identical. Since our ongoing study does not begin with a fixed dose targeting a specific BAC, results involving number of alcoholic drinks self-administered are more comparable to the proposed study and more appropriate for power and effect size estimation. In our in-progress study, the smartphone breathalyzer device/app was associated with significantly less alcohol self-administration (*M*=3.5 drinks, *SD*=1.3) than a control condition (*M*=4.8, *SD*=1.5), *d*=.89. Considering these findings, we project a large effect size.

Aim 1 power is based on ability to detect a between-subjects effect of app condition. We used an effect size equivalent to our in-process smartphone breathalyzer study for effect of condition (experimental vs. control groups). This estimated effect is much smaller than in Roberts and Fillmore's prior study providing feedback regarding cognitive impairment to a sample of drinkers with and without a prior DUI. Assuming an effect (d=.89) at α=.025 (to account for comparisons between the experimental app and each of the other study conditions: standard and control), the proposed sample of 99 completing the lab session and follow-up period yields .90 power. For Primary Aim 2, the goal will be to compare alcohol use in the 2 weeks participants use vs. do

not use the experimental app. No study condition effect is hypothesized, thus the focus will be on within-subjects comparison. As such, assuming α=.05 at 90% power, we can detect an effect of .33 (small-to-medium). The secondary aim of testing the indirect effect of app condition on drinking via perceived impairment will require the largest sample size as it entails tests of between group differences and tests of indirect effects are underpowered relative to tests of direct effects. In a Monte Carlo simulation, assuming small-to-medium correlation (.35) between perceived impairment and drinks self-administered (DV), power to detect an effect of the IV (study condition) on the mediator and an effect of the mediator on the outcome was >.90 and power to detect an indirect effect was .80 with 33 per condition (N=99 total).

7. Possible Discomforts and Risks

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) and two reviews on this subject (Dolinsky & Babor, 1997; Wood & Sher, 2000). Steps taken to minimize these risks were also developed in accordance with these documents.

Alcohol consumption: 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 as revealed by a medical history taken during the in-person screening will be excluded from the study.

Alcohol self-administration in a research study by individuals who are severely alcohol dependent as evidenced by current withdrawal or a history of withdrawal may pose a risk to their health and safety. Alcohol self-administration in a research study by individuals who are seeking treatment for alcohol use disorder 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 frequent heavy drinkers are selected for the study, thus ensuring that any amount of alcohol consumed during an alcohol drinking session is less than or equal to an amount of alcohol they consume on their own on a regular basis. Also, beyond the initial fixed dose targeting a blood alcohol content of .06%, the subjects determine the amount of alcohol consumed. Subjects can choose not to drink any alcohol at all beyond the fixed dose if they prefer.

Another area of potential risk to subjects under the influence of alcohol involves their safety during the experimental procedures. All subjects 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.

Breath screening and urine collections: Breath screening and urine collections are performed primarily as safeguards and should add no risks other than those normally associated with these procedures.

BACTrack Skyn: The wrist biosensor poses virtually no risk as it is a noninvasive device and is shaped like a fitness tracker with a sensor for alcohol. Utilizing this product will add no risks other

than those normally associated with these procedures, for example, wearing the wrist band too tightly. The device is adjustable for different wrist sizes, and participants will not be required to wear the wrist sensor if they do not want to. Data collected by the Skyn will not include participant identifiers. Readings from the biosensor will be downloaded as a CSV/Excel file and stored on a secured server at UF after each lab session. Data from these devices may be combined with data from another ongoing study (IRB201801188) without identifiers to address relationships between Skyn readings and key variables such baseline self-reported alcohol use and participant sex and weight. These data would be combined to create a larger dataset including parallel measures to yield enhanced statistical power for analyses related to Skyn readings. Data will not be matched to data from individual participants in IRB201801188. The study populations from the two studies are non-overlapping. RB201801188 enrolls participants with a much wider age range and wider range of drinking behavior including a high percentage of lighter social drinkers. Further, approximately half of participants enrolled in RB201801188 are HIV-positive. In contrast, HIV-positive individuals would likely not be eligible for the current study, which enrolls a narrow age range of young adults who engage in frequent heavy drinking behavior. Dr. Wang and Dr. Leeman are investigators on both studies. They are the only investigators privy to identifiers of participants from the two studies.

Interviews, rating scales and questionnaires: The assessments used in this study deal with some sensitive issues including family history of high-risk alcohol use and participants' own experience of alcohol-related problems. 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.

Smartphone app use: We will use smartphone apps as a form of moderate drinking intervention and a data collection tool in the proposed study. During the alcohol drinking sessions, participants will use study-provided smartphones only, however for the 4-week field use period after the drinking session, participants will use smartphone apps on their own personal smartphone or they can continue to use a study smartphone if they prefer. We prefer that participants use their own smartphone during the field use period since it will be easier and more natural for them to utilize the app on their own phone. However, we want to include participants who do not own their own smartphone and we respect the possibility that some individuals may not want to utilize their own phone for study purposes. The apps to be tested in this study will obtain minimal information from users (e.g., study ID number; date and time of logins to the app), however they do not obtain protected health information (e.g., the user's phone number). Consequently, the developers of the apps to be used in the study receive only limited information (not protected health information) about study users. At the follow-up appointment, taking place at the end of the field use period, we will extract data regarding use of the app from participants' own smartphones or the study smartphone, depending on which they used during this period. Study staff will extract the data in the presence of study participants. During the informed consent process, study staff will inform participants about smartphone apps obtaining minimal user data and our extraction of use data from their smartphones after the field use period.

Possible breach of confidentiality: In addition to a breach of confidentiality risk associated with data collected in the study, that alcohol drinking sessions will involve 2-3 participants at a time introduces possible breaches of confidentiality.

Procedures to protect against or minimize potential discomforts and risks

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.

Alcohol drinking sessions will be conducted by the P.I. and by research staff who are experienced with these methods and have been carefully trained. As described above, all subjects 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 in restaurants and bars in Gainesville, FL or in the surrounding cities/towns, this necessitates exclusion of individuals who are currently nicotine dependent as we will not be able to allow them smoking breaks during the alcohol self-administration period and nicotine deprivation may present a confound to the results of this study. All alcohol consumption will end at 7:15pm. Also, no alcohol consumption will be allowed that would lead to an estimated BAC > 0.12% at any point during the session. Estimated BAC will be monitored using an estimated blood alcohol level chart developed for each individual, based on their sex and weight. Participants will be retained at the laboratory faculty until at least 11pm and until their breath alcohol concentration (BrAC) drops to the safe level of 0.02% or lower (according to 2 breathalyzer readings). Participants will wait in the laboratory space while their BrAC goes down. When it is time for dismissal, participants will be placed in transportation provided by the study and taken directly home. Participants will not be allowed to drive themselves home from the lab or to otherwise arrange their own transportation home (e.g., from a friend or family member).

Several protocol features diminish the chance that study participants will leave the 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 also ask participants to refrain from consuming more alcohol and from driving or operating heavy machinery the rest of the night after their dismissal from the session. We reiterate these requirements on the day of the session, just before the beginning of the alcohol administration period.

Finally, several aspects of the study's methods discourage early departure from the lab, including their acceptance of study-provided transportation to the lab. The pay structure of the study also discourages early departure. We pay participants on an hourly basis during the alcohol drinking sessions, thus persons leaving early would forfeit payment for the remainder of

the session. Any participants who depart early would also forfeit a portion of their pay devoted to adherence to study rules. While there is some benefit to participants in the form of personalized information about their drinking and the opportunity to use smartphone apps designed to facilitate moderate drinking, participants in laboratory studies take part primarily for the monetary compensation, making it unlikely that they will intentionally engage in behaviors that reduce their payment.

Nonetheless, it is possible that a participant could elect to leave the lab early. We have procedures in place should this occur. Study staff will ask individuals who wish to end their participation early to remain in the lab until their breath alcohol reaches the safe level of 0.02% or lower. Study staff will offer these participants transportation by cab to their home, paid for by the study, regardless of whether or not they comply with requests to remain in the lab. Given that participants arrived by cab and will not have a car available, we expect that they will accept study-provided transportation to their home.

During a follow-up phone call on the day after the alcohol drinking session, study staff will verify with participants that they have experienced no adverse events related to the alcohol consumption they engaged in for the study. At a follow-up appointment at the end of the field use period, participants will receive brief counseling and information about their drinking. A master's or doctoral-level clinician will provide participants with a summary of their typical frequency and quantity of alcohol use and related consequences. In addition, treatment referrals will be offered to participants as needed based on their level of drinking and stated concern about their drinking levels. These may include relevant randomized, controlled treatment trials; student health services available at the local colleges and universities along with other local treatment resources. Web-based behavior change options will be offered as well, including NIAAA's "Rethinking Drinking" website.

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; Sullivan et al., 1989), to be conducted by trained study staff. 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.

Interviews, rating scales and questionnaires: The major risk of the assessments is potential loss of confidentiality, which we address below. 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.

Smartphone app use: We anticipate that smartphone app use will be acceptable to participants since most young adults own a smartphone and utilize multiple smartphone apps in a day. For these reasons, we also anticipate that the vast majority of participants will opt to utilize their own personal smartphones during the 4-week field use period, however the option to use a study

smartphone is available for those who prefer to do so and for those who do not own a smartphone. Any participants using a study smartphone during the field use period will be asked to use the study phone only in association with drinking occasions. During other parts of their day, they should use their own cell phone. Participants will be advised that any data from their personal use of the study smartphone (e.g., personal text messages, records of recent personal phone calls) will be deleted from the study smartphone at the end of their study participation. During the consent process, participants will also be advised of possible breach of confidentiality associated with loss of the study smartphone during the 4-week field use period and that $50 (approximately half the replacement cost of the phone) will be deducted from their payment should they lose a study smartphone. Only participants who acknowledge this potential confidentiality breach and agree to this penalty will be able to use a study smartphone during the field use period. While study staff will extract use data for the experimental app, we will do so in participants' presence, which should allay any concerns they might have about study staff seeing any personal information on their phones.

Confidentiality: 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 clinical interviews, vital signs, breath alcohol and urine drug/pregnancy screening are recorded by staff members on paper forms using study IDs only. Urine testing 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.

However, 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.

Electronic mail is an invaluable means of communicating with prospective and enrolled study participants. All email communication with participants in this study will be via secure email accounts administered by UF. In the proposed study, electronic mail is an option for prospective participants to self-identify as being potentially interested in the study. Prospective participants also have the option of communicating with study staff by phone or text message. Email communication will be used primarily to schedule appointments and to respond to questions about the study. Telephone and in-person are the preferred methods for conversations regarding protected health information (PHI). Conversations via email regarding PHI will occur only after participants consent to engaging in these conversations via email after being advised of potential risks of breach of confidentiality, which will be minimal given our use of secure email accounts administered by UF.

Some self-report data will be collected via the web, however no protected health information (PHI) will be collected via web-based forms. Participants will be identified on web-based forms either by self-selected code words that do not contain PHI or by a study-issued identification number. Even though no PHI will be collected on these forms, steps will be taken to maintain the confidentiality of this information. A preliminary screening questionnaire to contribute to the determination of eligibility and self-reports by enrolled participants will be completed using a secure web survey software (REDCap), which ensures that data will be kept confidential. Data transmitted from the server will be encrypted and secured within a password-protected file that

will only be accessed by study staff. In order to contact individuals completing the web screener to inform them of their eligibility, participants will identify themselves in the web-based form with the use of an innocuous code word that is personally meaningful but contains no PHI. They will be instructed subsequently to send an email message to a secure UF email account for the study in which they list this code word. This allows study staff to link participant identity to the web-based self-report data. These steps will provide the highest level of security for web-based data in this study.

Data sets not containing any PHI will be stored on the P.I.'s desktop computer in his office at the Florida Gymnasium facility on the UF campus and on space in a secure server maintained by UF HHP. Data for this study that are stored on the secure server will be maintained by the Research Assistant and the P.I. Any data from this study that is shared with collaborators or other qualified individuals from institutions outside UF will first be de-identified. Thus, no investigators outside UF will have access to any protected health information collected in this study. This includes consultants on the proposed study.

To reduce possible breach of confidentiality resulting from multiple participants being involved in each alcohol administration session, steps will be taken to avoid participants knowing the other participants completing the sessions with them. For instance, efforts will be made to avoid scheduling participants who attend the same college/university. As part of the consent process, participants will be told that they will be participating in alcohol administration sessions with other participants and will be asked not to disclose the identities of other individuals who complete the study along with them, nor to disclose the behaviors that these other individuals demonstrate during the sessions (e.g., how much alcohol they consume).

All NIH-funded studies collecting sensitive date 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.

In Case of Injury: If a participant is injured as a direct result of participation in this study, treatment will be provided. The participant and/or his or her insurance carrier will be expected to pay the costs of this treatment. No additional financial compensation for injury or lost wages is available. Participants will not waive their legal rights by participating in this study.

8. Possible Benefits:

Participants may benefit from an awareness of problematic behaviors in which they are engaging, through completion of the interviews and self-reports in this study. They may also benefit from use of the experimental app and moderate their alcohol use. Information about counseling/treatment options will be provided to them as needed. The results of this study could benefit society at large because of the potential public health impact of the proposed app, should it have efficacy in reducing alcohol drinking and related consequences.

9. Conflict of Interest:

None

10. Data Safety and Monitoring Plan:

Designation of Serious Adverse Events:

Dr. Liana Hone, the PI, has primary responsibility for monitoring the data, assuring protocol compliance, and conducting regular safety reviews after each alcohol drinking session has been completed. Dr. Hone will be responsible for distinguishing serious from non-serious adverse events. Dr. Hone has sufficient clinical research expertise to make this distinction.

Reporting of Serious Adverse Events

Dr. Hone will report serious adverse events in writing within 48 hours to the UF IRB 01 following their policies. The investigator will apprise fellow investigators and study personnel of all adverse events that occur during the conduct of this research project through regular weekly study meetings. An annual report will be submitted to UF IRB 01 summarizing all adverse events.

Female subjects:

Women who are pregnant or nursing, or who report engaging in sexual activity with an opposite sex partner and refuse to use a reliable method of birth control (e.g., condoms +spermicide; birth control pills, diaphragm) will not be allowed to participate in this study. Urine pregnancy tests will be completed at the in-person screening appointment and at an appointment at the research office just prior to alcohol self-administration.

Supervision of Alcohol Administration Sessions:

The National Advisory Council on Alcohol Abuse and Alcoholism - Recommended Council Guidelines on Ethyl Alcohol Administration in Human Experimentation - Revised May 2005 will be followed. All alcohol drinking sessions will be supervised by Dr. Hone herself or by a graduate student or other senior research staff member who will be carefully trained in alcohol self-administration methods and this specific protocol. Dr. Hone will either be present at the alcohol drinking session themselves or be readily available on call to make any determination regarding serious versus non-serious adverse events. In addition, the Study Physician Dr. Cook will be available for consultation as needed. In cases of illness or injury where medical treatment is needed, the necessary treatment will be provided.

Follow-up:

At a follow-up phone call the day after both alcohol drinking sessions, study staff will verify with participants that they have experienced no adverse events related to the alcohol consumption they engaged in for the study. Dr. Hone will review reports of all adverse events interviews. In the case of any medical concerns, participants will be seen by the Study Physician or other medical personnel. Participants will then be directed by these clinicians to obtain further treatment as needed. Participants are screened carefully prior to alcohol administration and all prospective participants who present as psychotic or otherwise severely psychiatrically disabled are excluded, along with those who report psychotropic medication use or a prescription for such medications within the prior 30 days. Given these exclusions, the likelihood of serious psychiatric symptoms arising at this appointment is slight, however if such issues arise, participants will be evaluated immediately by the Study Physician and directed for further treatment as needed. Any Serious Adverse Events that occur during this period will be reported as indicated above.

Procedures for Data Quality Assurance and Confidentiality:

Data quality will be ensured through training of research staff, the development of data collection tools, and monitoring of data quality. Study staff will monitor the quality of data after completion of each participant. Right to privacy for participation in this research will be protected through coding of data using study-assigned identification numbers and proper storage of research records. Access will be limited to the P.I. and his designates involved in the study. Data storage and analysis will occur at Yon Hall North or Florida Gymnasium on the UF campus. All private identifiable information about individuals will be stored in locked filing cabinets in a locked room in the research facility in Yon Hall North. A master list linking participants' names to their study ID numbers will be maintained, but it will be stored in a locked cabinet separate from other study materials. Identifiers will be destroyed when all study activities are completed. Protected health information will not be collected or stored electronically. Web-based data collection will be encrypted and stored on secure servers, but will not contain any identifiers. Data from the app will be stored on the Amazons AWS database with no personal identifiers beyond randomly assigned study ID. Amazon's AWS is approved by UF IT as secure and currently has a Business Associate Agreement with the University of Florida. Intermittently, these data will be downloaded by study staff and stored on our secure server and secure desktop computers in the P.I.'s office or lab space. 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.

ClinicalTrials.gov Requirements

This study will be registered on clinicaltrials.gov.

11. References

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