Family-focused vs. Drinker-focused Smartphone Interventions to Reduce Drinking-related Consequences of COVID-19

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Building and pilot testing a couples-based smartphone system to address alcohol use disorder

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REVISION HISTORY

Revision #	Version Date	Summary of Changes	Consent Change?
1	8.19.22	Updates to payment process, survey collection, screening process and ACHESS services.	yes
2	10.25.22		no
3	9.1.23	Add qualitative interview procedure	no
4	9.5.23	Add voicemail/text message scripts	no

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STUDY SUMMARY

Alcohol and other substance use disorders (AUD, SUD) increase the likelihood and consequences of contracting COVID-19.1-3 Conversely, stresses of the pandemic are triggers for drinking and drug use,4-6 even as isolation, distancing, and loss of jobs and health insurance have reduced access to healthcare, including treatment for AUD and SUD.7-9 For minority and marginalized communities, these crises are often compounded by social and systemic inequities. In sum, the combination of COVID and SUD exacerbates a wide range of existing problems, with long-term consequences.3 Interventions are needed to address these problems, which are likely to persist even after widespread availability of COVID vaccines.

In response to PAR 20-243, this R01 project titled “Family-focused vs. Drinker-focused Smartphone Interventions to Reduce Drinking-related Consequences of COVID-19" is a Hybrid II RCT/implementation study to modify and test two of our alcohol smartphone interventions to address the fallout from COVID. We propose a three-arm RCT comparing a smartphone control group vs. a drinker-focused intervention vs. a family-focused intervention. All study arms recruit dyads comprising a person who drinks and a family partner.

Our two interventions are designed for use across a range of alcohol use severity from risky use to disorder, and for any stage or type of recovery including reduction, cessation, or relapse prevention. Both can be used by people with no access to treatment. As such, both are potentially powerful tools to reduce social inequities in the medical, psychological, and relational risks and effects of COVID, including alcohol and substance use.

Our drinker-focused intervention is an extension of our evidence-based Addiction–Comprehensive Health Enhancement Support system (ACHESS10). ACHESS provides support and skills for reductions in alcohol and other drug use. In 2020, we incorporated material from our COVID app providing: 1) clear, simple information about strategies for COVID risk reduction, symptoms, testing, treatments, and vaccinations; 2) resources to help individuals navigate job-seeking, unemployment benefits, and issues of intimate partner violence, housing, and food insecurity; and 3) tools and social support to help individuals cope with the stresses and isolation of COVID. This extended, drinker-focused app is ACHESS-COVID (ACHESS-C).

The current proposal will fund the extension of our new PartnerCHESS app to create a family-focused intervention. Using NIAAA-R34 funding (PI Gustafson), we built and are piloting this smartphone app for romantic partner dyads in which one person has AUD. PartnerCHESS is designed to help with behavior change around alcohol use, relationship problems, and well-being of both partners. PartnerCHESS combines ACHESS with the evidence-based program Alcohol Behavioral Couple Therapy (ABCT).11 Part of the current proposal is to add our COVID content and resources for comorbid drug use to the PartnerCHESS app to create FamCHESS-C, for use by any family dyad (e.g. drinker + adult child).

Both ACHESS-C and FamCHESS-C will provide support and resources to: 1) reduce or eliminate the drinker's use of alcohol and comorbid drugs and 2) improve coping with COVID stresses and risks. Both apps should benefit families coping with the complex, interrelated challenges of alcohol use, comorbid drug use, and COVID, but FamCHESS-C is expected to yield greater benefits for both the drinker and the family partner.

1.0 BACKGROUND & SIGNIFICANCE

As of February 19, 2021, more than 27 million Americans are known to have been infected by COVID-19. Among these, more than 489,000 have died.12 COVID infections, hospitalizations, and mortality have been markedly higher among people of color and lower-income communities, reflecting differential ability to engage in social distancing because of inequities in housing size and occupation safety, and differential effects of infection given inequities in access to well-resourced healthcare.13-15

At the same time, COVID-19 and its stresses have led to increased use of alcohol and other drugs.16 A Rand national longitudinal study17 found an overall 14% increase in drinking days from mid-2019 to mid-2020, with a 41% increase in heavy drinking days and 39% increase in drinking consequences for women. In December, 2020, the CDC issued a health advisory warning of a rapid acceleration in drug overdose deaths since March 2020, when lockdowns and other pandemic mitigation efforts began.18 Recent research suggests that reasons for these spikes in use include: 1) stresses and loss of structure that stem from fear of disease, isolation, and job/income loss4-6 and 2) reduced access to treatment as the pandemic causes clinics to reduce staff/hours and delay treatment initiation and as job loss leads to loss of health insurance.8,9 In addition, drinking and comorbid substance use weaken the immune, cardiovascular, and respiratory systems, putting alcohol and drug users at higher risk for infection and more serious acute and residual COVID-19 illness.3 Future pandemics are likely to have similar effects. For instance, community services (such as behavioral health care) will need to be provided remotely. Families will be asked to play a bigger role in the delivery of these services.

Even before the pandemic, alcohol and substance use disorders afflicted over 20 million American adults age 18 and older.19, 20 Over 50% of treated users return to substance abuse within a year.21 The cost of providing treatment is high, and even the best evidence-based programs cannot address in real time the cravings, conflicts, and emotional states that often lead to relapse.22 During and after the pandemic, the need for interventions that can help address these issues—including for communities that have been underserved and that face the greatest health, financial, and psychological impacts of the pandemic—has only increased.

Importance of Smartphones. Pew nationally representative data indicate that in 2019 over 80% of US adults owned a smartphone and roughly 20% relied on it as their primary means of accessing the internet.23 This reliance was especially common among African Americans and Hispanics, lower-income respondents, and younger adults. As the

pandemic has shifted many critical services online (e.g. medical and therapeutic treatment, unemployment benefits, housing and food resources), access to smartphones is a fundamental tool for mitigating inequities in access to health information and other resources.24-27

Even beyond the basics of smartphone-enabled internet access, a growing research literature indicates that smartphones can play an important role in treatment for AUD and SUD,28 providing anytime/anywhere access to effective care, including assertive outreach,29 monitoring,22, 30, 31 action planning,32 symptom reinterpretation,33-35 peer36, 37 and family support,38 prompts,39, 40 and professional support.22, 41 The use of smartphones to receive help without physically attending recovery meetings and counseling sessions can reduce stigma and increase treatment seeking and retention. Smartphones are portable, and their software can be modified quickly in response to new needs, such as those posed by COVID. Gustafson (PI) has been a leader in developing evidence-based eHealth systems to address the needs of patients and families.

CHESS Interventions. CHESS (Comprehensive Health Enhancement Support System) is the overarching name for a variety of eHealth systems built to support continuing care for chronic diseases. All CHESS systems are based on principles of Self-Determination Theory (SDT), providing tools to enhance coping competence, intrinsic motivation, and social relatedness.42 RCTs have found that CHESS significantly improved: 1) asthma control43; 2) quality of life and cost of care in HIV patients44; 3) quality of life and self-efficacy in breast cancer patients compared with control45 and internet46; 4) risky drinking10; and 5) caregiver burden, symptom distress, and median length of survival in lung cancer patients.47 CHESS for lung cancer was aimed at caregivers as well as patients and was our first to integrate features of cognitive behavior therapy (CBT), which is also a cornerstone of ABCT.47

COVID-19 Wisconsin Connect App. In 2020, we created a smartphone app to help Wisconsin residents cope with the COVID-19 outbreak (please see: https://COVID.chess.wisc.edu). While our research center led its development, it was a collaborative effort with the Wisconsin Department of Health Services and UW's School of Journalism & Mass Communication. Our goals were to promote protective behaviors, counteract misinformation, and help people cope with the effects of isolation caused by the widening gaps in access and care for substance use due to COVID-19. The app employs many of the features of other CHESS apps.

ACHESS-C App and Study Arm. ACHESS-C is a COVID evolution of ACHESS. ACHESS (Addiction–CHESS) is a smartphone app designed to prevent relapse after treatment for AUD/SUD.10 It offers emotional and instrumental support at any time and place. ACHESS began with three grants from the Robert Wood Johnson Foundation to examine the potential of technology to improve addiction treatment. Our meetings48 with patients, family members, and technologists helped us: 1) personalize patient and family needs; 2) predict societal, technological, and treatment evolutions; and 3) envision how technology could improve addiction treatment. NIAAA then funded the development and RCT (N=349) of the ACHESS mobile app for AUD drinkers leaving residential treatment.

In the RCT, ACHESS, compared with usual care, reduced risky drinking days by 47%, improved abstinence by 23%,10 and significantly increased treatment retention at months 8 (OR=1.96, 95% CI=1.09-3.52) and 12 (OR=2.16, 95% CI=1.13-4.12).49 Further, a large (N=198) field test of ACHESS in Appalachia found that individuals with ACHESS averaged more than twice as many treatment service units (780 vs. 343) and remained in treatment more than 50% longer (410 vs. 262 days) versus a non-randomized comparison group.50 An RCT (N=262) in Philadelphia that involved a mainly African American sample of individuals with SUDs found ACHESS to be superior to a pure control.

ACHESS does not involve family members in use of the app. In 2020, we adapted ACHESS to incorporate content from our COVID app, creating ACHESS-C. Our current NIDA-funded RCT is now comparing two implementation models of ACHESS-C throughout Iowa. This ACHESS-C app will be the intervention for the proposed drinker-focused (ACHESS-C) study arm for this proposed study.

PartnerCHESS App. Our ongoing NIAAA R34 funded us to combine ACHESS with a digital adaptation of Alcohol Behavioral Couple Therapy (ABCT)11 to develop PartnerCHESS. Partner support can help prevent relapse because AUD problems and intimate relationships are reciprocally related. Distress in the relationship, along with partner attempts to control the user's drinking and substance use, may prompt craving and trigger relapse; alcohol and drug use are associated with greater relationship conflict, especially under the constraints of COVID mandates.51 Further, recovery can destabilize relationships, as new patterns of interacting need to be negotiated to support each partner's needs.52 Yet many partners do not know how to support recovery or manage their own responses to the user's changed drinking behavior, including symptoms of post-acute withdrawal such as irritability.38 While partners can help loved ones stop drinking or using drugs,53-58 trying to do so may increase their own stress.59-61

ABCT has demonstrated positive outcomes for men and women with AUD.51 Recognizing the reciprocity between intimate relationships and substance abuse problems, ABCT tries to build abstinence support and strengthen the couple relationship. ABCT uses the relationship to reward abstinence and teaches tools for better communication51 and more positive activities. PartnerCHESS includes key aspects of ABCT; the drinker and the romantic partner each receive the smartphone app. In addition to the regular ACHESS components, PartnerCHESS incorporates ABCT elements such as collaborating to identify and deal with triggers and cravings, increase positive activities together as alternatives to drinking and to reinforce abstinence, teach the partner how to be more supportive, and help improve communication.

FamCHESS-C App and Study Arm. FamCHESS-C will expand PartnerCHESS by: 1) adding resources from our COVID app; 2) shifting from exclusive focus on intimate partner+drinker dyads to include any family partner; and 3) adding content from ACHESS to address comorbid use of other drugs that interact with COVID-19 risk and consequences. Like ACHESS-C, FamCHESS-C will be designed to address immediate and longer-term collateral damage of COVID and to enhance access to care. Unique to

FamCHESS-C (vs. ACHESS-C) is that it engages a family member. Family members tend to suffer deeply from a loved one's alcohol and drug use, yet are in a powerful position to support recovery. Family-focused interventions have become more critical than ever as the stresses of COVID, including enforced time together at home during lockdowns, have decreased quality of life62-64 and relationship satisfaction,65-67 and increased rates of intimate partner violence. The FamCHESS-C app will be used in the proposed family-focused (FamCHESS-C) study arm.

2.0 STUDY OBJECTIVES

Aim 1:
Complete refinements to the FamCHESS-C app.

Aim 2:
Conduct a balanced RCT to test the following outcomes: Primary: 1) drinker % heavy drinking days, 2) dyad quality of life. Secondary: 3) dyad relationship satisfaction, 4) dyad psychological/physical conflict, 5) drinker no heavy drinking days, 6) drinker % days alcohol/drug use, 7) dyad COVID vaccination rates, 8) drinker alcohol- and drug-related problems. Exploratory: 9) partner % days alcohol/drug use, 10) dyad crisis healthcare use, 11) dyad technology satisfaction. We hypothesize that outcomes will be more favorable in FamCHESS-C relative to ACHESS-C, and both will be more favorable relative to smartphone control.

Aim 3:
Examine mediation effects of dyad's competence, relatedness, and motivation; drinker's interim change in % days of alcohol and drug use, and extent of app use for comparisons of ACHESS-C and FamCHESS-C. Examine moderation of effects of condition by drinker sex, severity of drinker's baseline alcohol use, drinker engagement in treatment for AUD/SUD, and dyad's baseline relationship satisfaction.

Aim 4:
Conduct a small-scale (20 dyads) formative evaluation using an implementation science model to collect qualitative data on perceptions of difficulties and benefits of ACHESS-C and FamCHESS-C use. In preparation for this R01 submission we have been conducting an NIH- funded R34 study, testing the use of a partner-focused CHESS app and feel that the data from that research study, has fulfilled the needs of Aim 4.

Study Coordination
The UW-Madison Center for Health Enhancement Systems Studies (CHESS) is the coordinating site for this study. The UW study coordinator will oversee all activities at the recruitment site which includes:

- developing site specific recruitment and data collection processes that meet study objectives;
- training site staff on protocol procedures prior to start of recruitment and continuous monitoring to assure compliance with the protocol and human subjects regulation;

- communicating with site staff via weekly conference calls to monitor progress, inform of protocol changes/distribute new version of protocol, and address unanticipated issues or challenges;
- and manage all study data.

3.0 ELIGIBILITY

Patients and Partners: A total of 198 dyads will be recruited from the community.

Drinkers and their family partners must give informed consent; agree to complete interviews at baseline, 4, 8, and 12 months; and not have a mental or physical condition that limits smartphone use. Drinkers must be age 18 or older and meet criteria for risky drinking (for men, >14 standard drinks in a week or >4 in a day; for women, >7 in a week or >3 in a day),76 or meet criteria for AUD (any severity) defined by DSM-5 and have had at least 1 drink in the past 3 months .77 Partner must be a committed romantic partner, spouse, or family member (e.g. sibling, parent, grandparent, adult child age 21 or older).

Exclusion criteria: current (last 6 months) evidence of unstabilized serious mental illness (active psychosis, delusions, hallucinations, active manic phase). We will also exclude dyads if either partner reports serious interpersonal violence in the past year, because of potential safety risk owing to access to a partner's smartphone or computer.

4.0 REGISTRATION PROCEDURES

Patient Recruitment and Consent
Based on our R34 enrollment pace (43 romantic partner couples over 3 months of recruitment), we estimate a recruitment rate of 14–20 dyads per month across 12 months. We anticipate a faster recruitment pace for the proposed study than the R34 because of expansion of inclusion criterion from romantic partner to any family member. The majority of AUD outpatients have at least one family member78; in one large study of AUD outpatients, 86% had a family member or significant other willing to participate in baseline and follow-up assessments.79 Recruitment pace may also increase because data plans will be provided. Finally, there is no need to visit a clinic, and phones can be delivered to homes, a process we have successfully used in the past.

After we receive initial indication of interest, we will call the dyad to describe the study. CHESS staff will speak with each member of the dyad individually and follow the phone screening script to determine eligibility. If only one member of the dyad is available, we will ask for permission to send the other member a letter, or an email or text, with a link to the letter. The letter contains a description of the study and how to contact CHESS staff if interested.

If the drinker and partner are eligible and interested, we will go through the informed consent individually on the phone. Since all recruitment will be done remotely, we will

be collecting verbal consents. A Partial waiver of HIPAA authorization to not require signature of the individual and date (e.g. verbal) will be submitted to UW's IRB, based on the following:

- The use or disclosure of protected health information involves no more than a minimal risk to the privacy of individuals, based on, at least, the presence of the following elements: (Check if "Yes". All must be checked)
    - An adequate plan to protect the identifiers from improper use and disclosure.

The consent process will inform potential subjects of:
(1) the nature and purpose of the study
(2) the types of data that will be collected from FAM-CHESS-C and ACHESS
(3) study risks and measures taken to mitigate
(4) their right to leave the study at any time
(5) the timeline of the study

Verbal consent will be documented on the recruitment form and in REDCap and a copy of the IRB-approved consent form will be mailed to participants for their records. All study data outside of REDCap will be stored in a locked cabinet at the Center for Health Enhancement Systems Studies at the UW.

Baseline interviews will be conducted with the drinker and partner individually over the phone.

Once dyads complete the pretest, the UW team will send phones and train drinkers and partners on the appropriate technology. Dyads will be informed that they will stay in the study if they do not miss two surveys in a row. If the drinker or partner declines, the dyad will be excluded. We will document reasons for refusals and monitor whether refusal rates differ by sex, race/ethnicity, and age. We will also note race/ethnicity and whether partners are of the opposite or same sex.

Recruitment sources. Many couples participating in our R34 PartnerCHESS study were recruited not from AUD/SUD treatment agencies but from advertisements in Craigslist and an email blast sent to faculty and staff at the University of Wisconsin–Madison; this indicates there is a large segment of people not in treatment who want and need help. Ultimately, our approach will be to recruit and serve dyads from addiction treatment agencies, hospitals that identify individuals with AUD, and the wider world where individuals may not have access to treatment or avoid it because of stigma. This will be a nationwide recruitment using platforms such as email marketing, targeted over-the-air advertising delivered through streaming platforms (e.g. Roku, Amazon Fire TV), local broadcast television, Craigslist, Facebook, and an email blast sent to faculty and staff at the University of Wisconsin. to increase awareness of opportunities to get help. We will also purchase advertising in newspapers that traditionally reach African American populations.

Minority recruitment. We will strive to recruit communities of color as they have been disproportionately affected. At the same time, we understand the challenges of minority recruiting and retention. We partner with UW's Collaborative Center for Health Equity and the UW Community Advisors on Research Design and Strategies (CARDS) program to engage and recruit minority groups, including African American and Latinx. Ambassadors from the Collaborative Center facilitate community–academic partnerships and provide culturally tailored training for recruitment and retention. CARDS advisors offer detailed feedback (e.g. on study materials) from a range of racial, socioeconomic, and educational perspectives. We will use CARDS's recruitment management toolkit, including a real-time research registry, to document enrollment and refusal rates. This toolkit includes the National Initiative for Minority Involvement in Clinical Trials website.

Randomization. We will use urn randomization80 after baseline interviews to stratify on drinker's sex, balancing on alcohol use severity (risky drinker, mild, moderate, severe AUD).

Blinding. We will work with the institutional review board (IRB) to blind participants as much as possible to their study arm while maintaining compatibility with guidelines for informed consent. Because all participants receive a phone with some recovery/support-related content, it should be possible to use the same scripts in describing the study arms and expectations for participation. Research staff conducting telephone surveys will be blind to participant condition and study hypotheses, and even when asking about perceptions of the intervention will use standardized questions that apply to any arm (e.g., "How do you feel about the recovery- and support-related content on the phone?"). Data entry will be performed by staff blind to condition.

5.0 TREATMENT PLAN

We will provide an Android smartphone to anyone who does not have one, and we will provide a data plan for 8 months to both partners in all three study arms. If participants already have a smartphone, we will help them download the relevant app onto their phone and pay $50 per month toward internet service. The apps are compatible with both Android and iOS phones. After 8 months, study participants are no longer part of the active intervention and they will no longer be required to use the app. We will conduct a follow-up survey at 12 months to assess results after the active intervention.

Set-up and training. All enrollment, training and baseline data collection will occur over the phone. Participants will have the option to complete 4, 8 and 12 month surveys over the phone, by completing a paper survey and mailing it back to us, or completing the survey using a secure UW-Madison Qualtrics online survey. Participants who wish to complete a paper survey and mail it back will be provided a self-addressed stamped envelope. After completing consents, baseline interviews, and randomization, UW staff will provide relevant training. Drinkers and family partners in the smartphone control condition and family partners in the ACHESS-C study arm will be given standardized suggestions to use the phone to connect to resources to help with the stresses of

COVID and alcohol use, and will be shown the pre-programmed numbers for support (e.g. AA, Al-Anon) and crisis hot lines. Drinkers in the ACHESS-C study arm will be helped to download the app onto the phone, instructed in the services on the app, and taught to personalize the app, including entering high-risk locations and creating a location alert (e.g. a voice-recording from a partner or other key person expressing love and concern about the drinker being in a high-risk location). The same procedures occur in the Fam-CHESS-C study arm, but in addition, staff will help the drinker and partner enter what motivates them to be healthy and what triggers alcohol or other substance use. Dyads will enter at least one recovery-supporting activity and one social activity or fun thing they will do together. Training sessions will be recorded and reviewed for fidelity. Both the ACHESS-C and FamCHESS-C apps will provide ongoing prompts to use different parts of the app, and there are refresher training videos on the phones, reminding participants how to use the functions they were shown.

Data collection. Surveys will be conducted with both members of the dyad in all three study arms every 4 months (baseline, 4, 8, and 12 months). Each participant receives $25 per completed survey. Payments will be processed in 2 ways. If the participant prefers to receive the payment in the mail, we will send cash to the participant within 5 business days of their survey being completed. If the participant prefers to receive payment through a mobile app, we will send them payment through Venmo or Paypal.

UW staff blind to the hypotheses will conduct the surveys. To ensure fidelity and data quality, we will record interviews, and Dr. Epstein will review a subset and provide feedback. All uses of the apps are automatically logged to create measures of use of different services. Survey data will be double-entered into ICTR REDCap and compared to reduce the chance of data-entry errors. Both survey and app data are stored on a UW Division of Information Technology HIPAA-secure server using the Campus Computing Infrastructure. The timing of interviews will be based on enrollment date.

Once the trial begins, we will analyze app use data every 2 weeks to note trends in services used most and differences in use patterns between drinkers and partners. One tool for drinkers in ACHESS-C and FamCHESS-C will be a weekly survey adapted from the Brief Alcohol Monitor (BAM),81 with four COVID-related protective behavior questions added. Our adaptation of the BAM asks about 5 factors that put patients at risk of relapse and 5 factors that protect. Responses help CHESS systems tailor services to individual patients and partners. We will also add questions to the every-4-months interviews. Some app-based questions will change over time as we explore specific issues. For instance, if a service is not used for a month, we will add a question about why. If certain services are used a great deal, we will ask how and why it's useful, to understand if additional related resources are needed.

Keeping patients and partners engaged. Other CHESS studies have increased engagement in 4 ways. We will use all: 1) Monitor and respond to changes in the amount of app use. 2) Examine discussion posts using tools we developed that are based on Linguistic Inquiry and Word Count74 and machine learning82-84 to

automatically predict relapse and intervene (e.g. an alert sent to a counselor). 3) Use ecological momentary assessments and weekly check-in data to identify and act on disconcerting trends (e.g. call to ask how the person is doing; refer users to relevant app services, games, and customized tips to address concerns, e.g. sleep). 4) Like other content-based or social media apps (e.g. NYT.com, FaceBook), relevant new information, resources, and user-generated content across the range of app topics, including alcohol use, couple skills, and COVID-19, is continuously added so that people keep coming back.

If drinkers stop using the app. We will be automatically notified of drinker non-use lasting 2 weeks. The project director will then make contact to resolve problems and encourage use. Those not using their app will still be included in the post-test interviews to understand reasons for stopping.

Dissolution of the relationship. If a family partner and drinker separate, we will encourage both to continue the study. At either's request, we will disengage portions of FamCHESS-C connecting them to each other. If one wishes to quit, we will honor their choice but encourage them to continue answering surveys.

Qualitative interviews. We will conduct qualitative interviews with a subset of participants who were randomized into the FamCHESS arm. Interview questions were developed by the study investigators to fill in the gaps where quantitative data alone may fall short. For example, how they decided to join the study, did they use the app together, did the app spark specific behavior change techniques. We will contact participants by phone or email to see if they are interested in taking part in a 45-minute qualitative phone interview. We will try to reach participants a maximum of three times. This is the script for leaving a voicemail:

"Hi. This is <name of study staff> from the UW Partner Study. I'm checking to see if you'd be interested in doing a phone interview with us so we could learn about your experience using the PartnerCHESS app. It will take about 45 minutes, and we would compensate you $20 for taking part. Call or text if you're interested in finding out more. I'll also send you an email message to see if you're interested. Thanks!"

This is the script for leaving an email message:

Subject Line: UW Interview Opportunity

"Hi. This is <name of study staff> from the UW Partner Study. I'm checking to see if you'd be interested in doing a phone interview with us so we could learn about your experience using the PartnerCHESS app. It will take about 45 minutes, and we would compensate you $20 for taking part. If you're interested, email us back or you can call me at <study staff work phone number>."

We will explain that the interview is voluntary, and they can refuse if not interested. Participants will be paid $20 for completing the interview. To cover a wide range of

experiences with the app, we will look at app use data to find a pool of potential interviewees. Our goal is to interview participants across the spectrum of app use, from very little to very much. Recruitment will continue until thematic saturation has been reached. We define thematic saturation as the point at which additional data lead to no new themes, when the researcher is empirically confident having repeatedly seen similar instances of data, and themes (or patterns in the data) are well-developed with diminishing returns from further data collection. If a participant agrees to the interview but does not want to be audio recorded, we will continue the interview, taking hand-written notes.

Audio recordings will be saved to HIPAA compliant servers managed by UW-Madison's College of Engineering Computer Aided Engineering with restricted access to CHESS study staff. Study staff will create de-identified transcripts for review by researchers. 7 years after study completion, all audio recordings will be destroyed.

Descriptions of the 3 Study Arms.

Summary of smartphone control arm. Both the drinker and family partner will receive a smartphone with pre-programmed contact information for Alcoholics Anonymous (AA), Narcotics Anonymous (NA), Al-Anon, Adult Children of Alcoholics (ACOA), and crisis hot lines.

Summary of ACHESS-C and FamCHESS-C arms. In ACHESS-C, both the drinker and the partner will receive a smartphone, but only the drinker will receive the ACHESS-C app. The partner will receive a smartphone with contact information for standard AUD, SUD, and crisis support. In the FamCHESS-C arm, drinker and partner will both receive a smartphone with the FamCHESS-C app, which contains ACHESS-C services plus ABCT/ PartnerCHESS services. As described below, both the ACHESS-C and FamCHESS-C apps will contain services designed to address relapse factors of lifestyle imbalance, desire for indulgence, urges and cravings, high-risk situations, low self-efficacy, lack of coping responses, previous lapses, and abstinence violations.

ACHESS-C services. ACHESS-C offers the following, which are also available in FamCHESS-C:
COVID content. COVID-relevant materials are incorporated into multiple services: instant library (COVID information), personal stories (how others have prevented or dealt with COVID), risk assessments (evaluate-your-risk simulation), crisis assessments (what to do if infected), warning signs (possible infection or vaccine side effects), healthy/safe/fun things to do together, surveys (adherence to preventive behaviors), and reminders (COVID prevention and vaccine opportunities).
Instant library. Frequently asked questions and brief information on addiction and couples-related issues (e.g. taking care of yourself, financial matters, substance abuse, crisis intervention, referral, medications).
Discussion groups. Forums connect patients or partners with others. Posts are analyzed to predict relapse.

Optional Video Meetings: Regularly scheduled group meetups facilitated by research staff via zoom. Attending video meetings is completely optional and study participants can choose to have their camera on or off, and no one is required to speak. To foster open and honest dialogue, each meeting will be held for each specific group in the study. So, participants in different groups will not be able to attend another group's meeting.
Personal stories. Audio/video of patients and family partners talking about experiences dealing with addiction. The audio/video is not of active study participants, but volunteers willing to share their experiences.
Location monitor. Geo-fencing of areas identified by participants as triggers (e.g. a bar that was frequented) prompts a warning. If the drinker stays in the area, a recorded message encourages him or her to leave. If the drinker does not leave, a supporter is notified. (Our advisors felt that family partners in the FamCHESS-C arm should not monitor drinker location.)
Surveys/ecological momentary assessments. Questions assess immediate needs and trends over time. Partners are asked about their own status and their perspectives on the drinker's status. Advice or referrals to other ACHESS-C or FamCHESS-C services arise from responses to questions as well as from the predictive analytics that examine relapse risk using data, e.g. from discussion groups and surveys.[73]
Guided relaxation. Audio/video to guide mindfulness, relaxation, games, and other help for cravings.
Meeting locator. Drinkers (and family partners) can use GPS to find AA and Al-Anon meetings.
Healthy activities. Database of ideas (e.g. taking a walk) and local recovery-friendly activities.
Crisis button. Relaxation exercises, optional calls to supporters, games for distraction, and other resources.
Skills reminders. Tips and reminders of CBT-based skills (e.g. effective communication, refusal skills).
Predictive analytics. Real-time linguistic analysis,[74] based on research we are conducting, that detects weakened defenses against imminent relapse. Previous ACHESS data analyses found patterns of drinkers' word use in discussion groups (e.g. increase in swear words) that signaled impending relapse (R^2=.40). For ACHESS-C and FamCHESS-C, we propose to modify analyses so that they immediately identify such patterns, allowing us to rapidly push tailored interventions. (This analysis currently occurs offline.)

FamCHESS-C services. The following ABCT services, from PartnerCHESS, will be available in the FamCHESS-C app but not in ACHESS-C:
ABCT tutorials. Interactive e-learning modules explaining key ABCT skills, including: partner helping drinker with triggers and cravings, supporting change, self-care, partner-assisted relapse prevention, enhancing pleasant activities together, and improving communication. Figure 2 shows a sample tutorial screen.
Agreements between drinker and partner to follow key principles.

Trigger identification and removal. During set-up, the drinker and partner enter triggers. FamCHESS-C prompts dyads to identify coming trigger events and reminds them of ways to address each.
Cravings discussion. Ecological momentary assessments track preconditions for relapse, review urge reduction options, and encourage partner discussions on causes and managing urges.
Relapse plan. Monitoring and reminders of steps that have been planned for relapse prevention.
Reminders. Reminders to notice something positive in one's partner, of reasons to stay sober, to take meds, etc.

Structure of FamCHESS-C system. FamCHESS-C will have two complementary versions—one for the drinker, one for the family partner—that in some services will contain different, role-relevant information. For instance, the Instant Library for the partner contains partner-related stories and other material on self-care during crisis. That content does not appear in the drinker version. Additionally, some permissions within services differ by role. For example, partners can communicate with other partners in the discussion group, and patients with other patients, but partners cannot read patients' discussion group posts and vice versa. This enables users to engage in a peer network for more candid interactions.

Drinkers and their family partners can access FamCHESS-C when and how they wish, but the system will also push notifications to them. Thus FamCHESS-C does not rely on user initiative alone to drive engagement. Examples: Drinkers will receive notifications when it is time to take a survey or when they are near a high-risk location. Partners will receive notice of a new post in the partner discussion group, prompts to notice a nice thing, and alerts if the drinker has pushed the crisis button. In the real world, access to FamCHESS-C could be indefinite for ongoing maintenance of recovery and relationship functioning.

AIM 1: FamCHESS-C Refinement (Months 1–6). Aim 1 is to modify PartnerCHESS in 3 fundamental ways to create FamCHESS-C: 1) Add COVID material already in ACHESS-C, information on vaccines, long-term effects of COVID, and heightened risk from AUD/SUD. 2) Expand PartnerCHESS from focus on romantic partner to any family member. 3) Added content targeting comorbid drug use (psychoeducation, tools to stop, tools for partner to help, and psychoeducation on relationship of drugs to COVID risk and sequelae). Our software design team will recruit 10 dyads for evaluation to assure that we offer appropriate content and delivery in the proper style. The 10 dyads will be recruited from colleagues with lived experience and their personal networks. All refinements will employ rapid cycle testing, refining, and retesting based on feedback from the 10 dyads about difficulties and benefits. Both members of the dyad will engage in think-aloud protocol to assess their in-the-moment reactions as they use the app prototype. Throughout the month of pilot use, dyads will be asked about the extent to which the language, presentation style, and structure are understandable, engaging, intuitive, and relevant to their experience. We will use wireframes, mockups, and html to test prototypes, use feedback to quickly make changes, and test again. We will continue

to improve FamCHESS-C throughout the adaptation and pilot phase. Our strategy is based on Shewhart's Plan, Do, Check, Act cycle.[29] Refinements to baseline and follow-up surveys will also be tested with the dyads.

AIM 2: Conduct an RCT to Test Smartphone Control vs. ACHESS-C vs. FamCHESS-C (Months 7-30).

***Study design and outcomes*.** We will conduct a 24-month randomized trial (*N*=198 dyads, 66 in each arm, to yield approximately 180 dyads at 8-month analysis) in which assessment and intervention will all occur remotely. Dyads comprising one person who drinks at risky levels or has AUD (any severity) and one family partner (any family member) will be recruited and randomly assigned to 8 months of either: 1) smartphone control (both drinker and partner receive smartphones with numbers for AA, NA, Al-Anon, ACOA and crisis hot lines); 2) ACHESS-C (drinker receives a phone with ACHESS-C; partner receives a phone with numbers for Al-Anon, ACOA, and crisis hot lines); or 3) FamCHESS-C (drinker and partner receive a phone with FamCHESS-C). In all conditions, both members of the dyad complete baseline assessment plus follow up assessments at 4, 8, and 12 months (i.e. 8-month active app/phone use phase plus follow-up 4 months later).

Primary outcomes: 1) drinker % heavy drinking days, 2) dyad quality of life.

Secondary outcomes: 3) dyad relationship satisfaction, 4) dyad psychological/physical conflict, 5) drinker no heavy drinking days, 6) drinker % days alcohol/drug use, 7) dyad COVID vaccination rates, 8) drinker alcohol- and drug-related problems.

Exploratory outcomes: 9) partner % days alcohol/drug use, 10) dyad crisis healthcare use (ER, 30-day hospital readmits), 11) dyad satisfaction with technology.

Rationale for our primary outcomes: Quality of life captures the physical and socio-emotional impacts of COVID and alcohol and comorbid drug use for drinkers and partners. Reductions in alcohol and comorbid drug use are the primary means by which we hope to improve quality of life.

Hypothesis 1: Outcomes will be more favorable in FamCHESS-C relative to ACHESS-C, and both will be more favorable relative to smartphone control.

AIM 3: Test a Mediation Hypothesis About Processes of Change and Examine Moderation. As illustrated in Figure 3, we will test our mediation hypothesis that increases in SDT constructs of

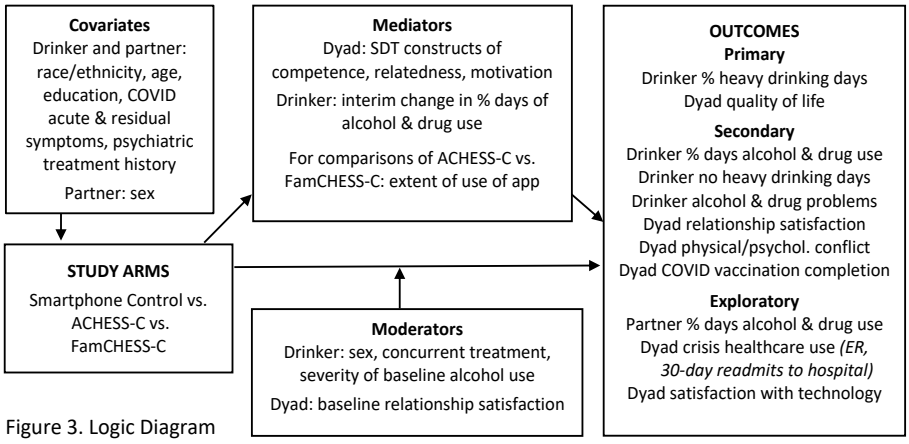

Figure 3. Logic Diagram

competence, relatedness, and motivation for both drinker and partner, together with interim reductions in the drinker's % days with use of alcohol and drugs, will mediate effects of condition on other improvements in outcomes. For comparisons of ACHESS-C vs. FamCHESS-C, we will also test use of the app as a mediator. Further, we will examine moderation of effects of condition by drinker sex, severity of drinker's baseline alcohol use, drinker engagement in treatment for AUD/SUD, and dyad's baseline relationship satisfaction. Details of measures for all variables in the figure are in the Measures section below.

AIM 4: Conduct a Formative Evaluation Using an Implementation Science Model. Using our Organizational Change Model (OCM),[75] we will collect qualitative data from 20 drinkers and 20 family partners in the RCT on perceptions of difficulties and benefits of ACHESS-C and FamCHESS-C use. In preparation for this R01 submission we have been conducting an R34 testing the use of a partner-focused CHESS app and feel that the data from that research study, has fulfilled the needs of Aim 4.

Privacy and Confidentiality:

To mitigate the risk of patient breaches of confidentiality, all subjects will be assigned a code number. A list of subject code numbers will be maintained by the UW project director and stored in a password protected spreadsheet. Participant surveys will be identified by code number only. The UW study coordinators will assist patient subjects in choosing codenames and passwords to use to login to the A-CHESS-C or FamCHESS-C system. Patients will be instructed not to use their real names as a codename and will be made aware of the potential dangers of divulging confidential information (e.g. real names or telephone numbers).

Prior to gaining access to our data, all students, faculty and staff must provide our Data Security Officer a copy of their certificates of completion of the UW Madison Human Subjects online training and the online HIPAA Privacy Rule training. Furthermore, they are required to complete training on Center security procedures and policies and sign a Center Data Security Policy Certification upon completion of this training.

Hard copy data, such as surveys, will not contain identifying information. They will be stored in a locked file cabinet in the study coordinators private office. Electronic data, such as A-CHESS-C or FamCHESS-C use data, will be stored on a secure, HIPAA-compliant UW-Madison DoIT server. Access to this data will be limited by granting individuals access via their UW user log-in. Paper study data, such as surveys and contact information, will be entered into a REDCap system managed by ICTR.

Any data stored on a participant's device are stored in an encrypted file and only accessible by that participant, i.e. participants won't have any other participant data on their phone. These data are only collected after the participant has signed into their account and are removed when the participant signs out of the A-CHESS-C or FamCHESS-C application. Any data transferred to and from CHESS servers are done through an encrypted connection.

A list of subject code numbers will be maintained by the UW study coordinator and stored in an electronic spreadsheet. This data will be kept in a secure, limited access,

password-protected file on CHESS servers which are located in the department of Systems and Industrial Engineering in the Mechanical Engineering building on the 4th floor.

The study coordinator will be the only person with access to both the coded study data and the subject identifiers.

When all study activities are complete identifiable information will be destroyed. De-identified study data will be stored on the secure CHESS servers for potential future unspecified research for which new IRB submissions will be initiated.

Potential Risks:

Regarding risk of misinterpretation of information: Information and resources on the A-CHESS-C/FamCHESS-C apps will be screened by experts from our project team as well as from our Steering Committee for accuracy. Additionally, messages exchanged within the apps will be monitored to make sure the information is accurate and that study participants are using the system for its intended purpose. Inaccurate or harmful statements will be addressed by the CHESS moderator.

Possible breach of confidentiality: All subjects will be assigned a blind code number that will be kept in a locked file in the CHESS office. Data collected from clinic records and smartphone use files will have the name removed and the code number attached by the study coordinator.

Possible break of confidentiality in surveys: Surveys will be conducted by UW staff trained in protecting patient confidentiality. Project staff who have access to the data will not have access to subject names.

Possible risk of being randomized to a less effective treatment group: If it is found that one treatment arm is more effective than an other treatment arm, there is a potential for less effective results for those randomized to the less effective arm. Potential study subjects are notified of this during the consent process.

Possible breach of confidentiality in smartphone use: There is a risk that information provided on the A-CHESS-C/FamCHESS-C apps will be used to the detriment of the subjects. Particular sources of risk include messages written within the discussion groups or personal profiles. Patients will select code names and passwords to use on the apps. They will be instructed to not use their real name as a code name and will be warned of the potential dangers of divulging confidential information (e.g. real names or telephone numbers). Divulging real names could lead to a loss of anonymity and un-wanted contact from study participants outside of the app. The smartphone will automatically collect data on how often and for how long a subject uses each of the A-CHESS-C or FamCHESS-C services.

A-CHESS-C/FamCHESS-C data will be collected by subjects' codename only and will not be attached to real names or identities. Patients will also be asked to set up a pass code on the phone to protect their information in the event someone else finds the phone.

Possible psychological stress regarding sensitive issues: Reporting on sensitive

issues (such as drug and alcohol use and mental health) while using the FamCHESS-C recovery support program may cause anxiety, distress, embarrassment, or feelings of sadness.

Possible risk of economic burden: If a participant uses their own smartphone during the study, CHESS will pay the participant $50 per month to put toward the cost of their personal cellular plan. Depending on the cost of the participants' cellular plan, the $50 may not cover the entire monthly charge. The participant would be responsible for paying any amount over **$50.** Participants are made aware of this during the informed consent process.

For the potential psychological stress regarding sensitive issues: Participants do not have to answer any questions that make them uncomfortable. In addition, study participants can change their minds and choose not to participate at any time.

Findings of Depression/Self-harm/Harm to Others: If a patient subject is determined to be in danger of self-harm, suicide or harm to others when on the phone with a participant during a survey or by reviewing a discussion group post on the smartphone, a crisis intervention plan will be implemented. The UW researchers will contact appropriate others to intervene (e.g., the subject's health care team, and/or their emergency contact).

If potential harm to others is identified, then it may be necessary for us to contact local authorities to ensure your protection or the protection of others. In addition, as researchers, we may be required to report or voluntarily report child abuse to the authorities if the issue arises during the course of this research. Some states have laws requiring or permitting reporting of substance abuse during pregnancy, and if those laws apply, we may be required to report or voluntarily report such information to the appropriate authorities. It is also possible that other users of the app may report substance abuse during pregnancy or other information shared in the app. Participants in this study are not required or expected to share information about pregnancy status in ACHESS-C or FamCHESS-C.Discussion group posts are monitored by study staff daily. If a participant posts a message on A-CHESS-C/FamCHESS-C, we send a message through the app and will try to call the participant. We will ask them if they feel like they are in danger. And provide them a set of resources in their local community.

Mental health referrals will be made when symptoms of major depression, acute anxiety, etc. are indicated in discussion group messages or in the daily or weekly A-CHESS-C/FamCHESS-C survey. If evidence arises that a participant is contemplating suicide, a 4-step protocol will be initiated that includes the following steps: (1) a CHESS staff person will break the code to make identification and emergency intervention possible (e.g., by calling the subject and appropriate authorities); (2) initiate crisis intervention to disengage the writer from a suicide method, engage in stabilizing techniques, and connect the subject with appropriate support; (3) document and follow-up as appropriate.

If there is evidence of abuse or of a smartphone user being engaged in criminal activity (e.g., a discussion group being used to sell an illegal drug), we may need to inform an

appropriate authority. Hence our consent form will include the following statement: “I understand that subject anonymity and data confidentiality cannot be maintained if A-CHESS-C or FamCHESS-C finds evidence of abuse, suicidality, or criminal activity.”

If participants are incarcerated, no research activities would occur during the time of incarceration. Participants can contact the UW study coordinator if they are released during the original study period and would like to continue on study.

The researchers may also take participants out of the study, even if they want to continue, if they use the phone in an inappropriate manner (i.e. messages including nudity, threats, racism, bigotry), research staff will delete the inappropriate messages and follow up with the participant. If the behavior continues, research staff may decide to withdraw the participant from the study without their consent for their best interest as well as others on the study

If participants experience any crises during the study period, they will be instructed to contact their clinician if currently in treatment. If participants have crises after hours, they will be instructed to call 911 for imminent risk or go to a local emergency room crisis center. All participants will be provided with a listing of crisis hotline numbers and community resources that participants may access 24/7, such as the National Drug Abuse Hotline (800-662-4357), the National Domestic Violence Hotline (1-800-799-7233), or a Crisis Hotline for any crisis (800-233-4357).

Lost or Stolen Smartphone: Participants will be informed that if the phone is in the hands of another person there is the potential that someone might see the information they stored on the phone (personal contacts, text messages). Participants are advised to make their phone password protected to reduce the risk of someone being able to see their information if the phone is lost or stolen.

Phone service for the study phone is terminated at the end of the 8-month intervention period. Participants may feel some loss when they no longer have that service. The study coordinator will explain this prior to informed consent and will inform the participants well in advance of the service ending so they have time to get their own service if they wish.

If study phones are lost or stolen they will not be replaced.

To help us further protect participant privacy, we will obtain a Certificate of Confidentiality from the National Institutes of Health.

Potential Benefits

A potential benefit may be a reduction in heavy drinking days for your family partner and improvement in quality of life for you and your family partner.

Although taking part in this research may not benefit you directly, it may benefit other people in the future by helping us learn more about how a smartphone with a recovery support system can improve patient and family partner quality of life and improve the

health care given to others with substance abuse problems.

6.0 MEASUREMENT OF EFFECT

Variables reflect the conceptual model (see Figure 3, above) and study aims. Measures chosen have good psychometric properties with similar populations. Where possible, we used PhenX and PROMIS measures (e.g. PROMIS 29.2) so that results are comparable to other studies.[85] Our primary outcome is percent days of heavy drinking, but given 2015 FDA draft guidelines we also include number of patients with *no* heavy drinking days per period as a secondary outcome.[86] Table 2 lists our measures, number of questions, and sources, with references to validation studies where relevant. In the R34, we collected much of the same data we propose to collect in the RCT. Survey completion time averaged about 90 minutes.

Table 2: Proposed Measures, Scales, and Sources for Study Outcomes and Other Variables

MEASURE	WHO	SOURCE	REFERENCE	# QUEST	TIME (MONTH)
Primary Outcomes					
% days heavy drinking	Drinker	Timeline Follow Back[87]	Johnston et al.[88]	7	0, 4 , 8, 12
Quality of life	Dyad	PROMIS 29.2	Hamilton et al.[85]	29	0, 4, 8, 12
Secondary Outcomes					
Relationship satisfaction	Dyad	OQ-45.2[89]	Beckstead et al.[89]	45	0, 4 , 8, 12
Physical/psychological conflict	Dyad	Rev. Conflict Tactics	Straus et al.[90]	20	0, 4 , 8, 12
No heavy drinking days	Drinker	Timeline Follow Back[87]	Johnston et al.[88]	7	0, 4 , 8, 12
% days alcohol or drug use	Drinker	Timeline Follow Back[87]	Johnston et al.[88]	7	12
COVID vaccination completion	Dyad			1	0, 4 , 8, 12
Drinking/drug problems	Drinker	Clinical evaluation guide	Spitzer et al.[91]	5	0, 4 , 8, 12
Exploratory outcomes					
Crisis healthcare use (ER, 30 day readmits)	Dyad	Treatment Services Reviews	McCollister & French[92]	3	0, 4 , 8, 12
% days alcohol or drug use	Partner	TLFB last 60 day	Collins et al.[87]	11	0, 4 , 8, 12
Satisfaction with technology	Dyad	Tech Accept Model[93]	Szajna[94]	26	4, 8, 12
Mediators					
Competence	Dyad	CCQ / # of skills used	Schroder & Ollis[95]	11	0, 4 , 8, 12
Relatedness	Dyad	Revised Important People	Zwiak et al.[96]	14	0, 4 , 8, 12
Motivation	Dyad	Brief Self Control Scale	Tangney et al.[97]	13	0, 4 , 8, 12
Reductions over 8 months % days alcohol or drug use	Drinker	Timeline Follow Back[87]	Johnston et al.[88]	7	0, 4 , 8
For ACHESS-C vs. FamCHESS-C: use of app	Dyad	Smartphone data	N/A	0	0, 4 , 8, 12
Moderators					
Sex	Drinker			1	0
Concurrent treatment services	Drinker	TSR	McLellan et al.[98]	10	0, 4 , 8, 12
Severity baseline alcohol	Drinker	Smartphone data	N/A	0	0, 4 , 8, 12
Baseline relationship satisfaction	Dyad	Smartphone data	N/A	0	0, 4 , 8, 12
MEASURE	**WHO**	**SOURCE**	**REFERENCE**	**# QUEST**	**TIME (MONTH)**
Covariates					
Age	Drinker & partner			1	0
Education	Drinker & partner			1	0
Race/ethnicity	Drinker & partner			2	0

Psychiatric treatment history	Drinker & partner	Question (PhenX tier 1)	Collins et al.[87]	1	0, 4, 8, 12
COVID acute & residual symptoms	Drinker & partner	Acute and Persistent Symptoms: COVID-19	Carfi et al.[99]	17	0, 4, 8, 12
Sex	Partner			1	0

7.0 STUDY PARAMETERS

198 dyads will be recruited, 66 in each of 3 conditions to yield approximately 180 dyads at 8-month analysis.

They will be allowed to keep the phone, so that they could continue to use those interventions if they had other ways to access the two systems. Partners in the A-CHESS group will not have access to either app.

8.0 STATISTICAL CONSIDERATIONS

Data Analysis Plan. The analysis will: 1) explore differences among the three arms over the 8-month active intervention phase and then the 4-month follow-up phase of the RCT; 2) explore the conceptual model (see Figure 3) that considers the relations between the primary and secondary outcomes, and drinker and partner mediators, moderators, and covariates; and 3) examine how the dyad's demographic characteristics (e.g. young drinker and older partner) affect intensity and length of ACHESS-C and FamCHESS-C use and SDT mediators of relatedness, motivation, and competence on study outcomes.

Assumptions and randomization effect. We will report descriptive statistics for all demographic and clinical variables in both arms to ensure that randomization produced comparable groups; if not, variables with significant differences will be included as covariates in a sensitivity analysis. Sensitivity analyses (with and without covariate adjustment) will determine the robustness of covariate-related error control. All outcome variables will be examined using standard summary statistics, visualizations, and tests for normality and homoscedasticity. Data will be transformed for continuous outcomes that do not meet the assumptions of a normally distributed outcome.

Effects of study arm on primary and secondary outcomes (Aim 2). Linear mixed effects models (LMEM)—which account for dependence among successive observations on the same drinker and can address incomplete data—will be used to examine effects of study arm (FamCHESS-C vs. ACHESS-C vs. control, a between-subjects factor) on drinker outcomes over time. We will conduct specific treatment X time contrasts both between and within groups to test time-based effects. For binary, count, and other non-normal data, generalized linear mixed effects models will be used.

Mediation of effects of study arm on primary outcomes (Aim 3). Structural equation modeling (SEM) will explore the effects of mediation on the relation between study arms and our two primary outcomes. We anticipate that the impact of study arm on drinker heavy drinking days and dyad quality of life will be mediated by SDT (competence, relatedness, and motivation) and by drinker's interim change in percent alcohol and drug use days. SEMs involving app use will be run separately for only the ACHESS-C and FamCHESS-C arms.

Moderation of study arm on primary outcome (Aim 3). We will test whether the four variables listed in Figure 3 moderate the effects of the intervention on outcomes. The moderators will be entered as interaction terms in the models described above for the primary outcomes, testing each moderator separately. We will conduct exploratory analyses on whether these moderation effects are also observed for secondary outcomes.

Power. Our primary outcome used to power the study is reduction in percent of heavy drinking days. In our prior study of ACHESS with drinkers coming out of inpatient treatment for AUD, we found an effect size of ACHESS vs. usual care of d=.31 for this outcome.[100] Since then, ACHESS has been improved, and in the proposed study we will incorporate COVID-related content to help drinkers cope with pandemic stresses. Given this, we expect an effect size of d=.40 for the comparison of smartphone control vs. ACHESS-C.

We powered the analysis to be able to detect an effect size of d=.40 for smartphone control vs. ACHESS-C, and then the same magnitude of effect for ACHESS-C vs. FamCHESS-C. It is reasonable to expect an effect of roughly d=.80 for FamCHESS-C vs. smartphone control, given the strong effects observed in an RCT of ABCT, where the effect size for reductions in percent risky drinking days was d=.79.[101]

We ran the power analyses two ways, based on two different estimates of likely attrition. In prior ABCT and ACHESS studies, 10–21% attrition at 9 and 8 months, respectively, was observed. [101] As the analyses below indicate, an initial sample of 198 dyads would give us adequate power at either rate of attrition.

Starting with a sample of 198, 10% attrition would mean a sample size at 8 months of 180. Across 10,000 LMEM simulations, with post-attrition N=180, we would have power >90% to detect the study arm X time interaction. Starting with a sample of 198, 21% attrition would mean a sample size at 8 months of 159. Across 10,000 LMEM simulations, with post-attrition N=159, we would have power >85% to detect the study arm X time interaction. We will recruit 198 dyads.

Qualitative Analyses (Aim 4). Transcripts of qualitative interviews concerning perceived difficulties and benefits of app use will be examined using Braun and Clarke's[102] six-phase procedure for thematic analysis: 1) familiarization with data, 2) generation of initial codes, 3) identifying instances of themes, 4) review of themes, 5) defining and naming themes, 6) production of findings. To improve consistency and accuracy, coders will work separately using NVivo software; findings will be compared and discussed until consensus is reached.

Interim Analyses and Stopping Plan. The interim analyses are solely to check whether the stopping plan needs to be implemented. They will not be reported as tests of our hypotheses and thus will not inflate Type 1 error. We will engage in the following practices: 1) We will report any fatalities as they occur, as required by the university IRB. 2) Our statistician will conduct interim analyses at months 18 and 27 after the start of the study (9 and 18 months after recruiting begins), examining our primary outcome of substance use days in the two arms. She will share the results with UW's independent Data Safety and Monitoring Board but not with the PIs unless instructed to do so by the Board. Because all of our prior research has been designated low-risk by

the IRB, we anticipate the same designation in this case. Barring exceptional disparities in outcomes between conditions, we do not anticipate stopping the trial. As an *a priori* rule, we believe we should stop if our primary outcome of functional health shows a T-score difference greater than 6 (averaged across components of the PROMIS-29). A T-score of 6 is at the very upper end of the clinically meaningful differences for PROMIS-29 components (e.g. physical function, pain, fatigue).[22,30] We have no reason to anticipate such an occurrence. We will follow Data Safety Monitoring Board guidance on this matter.

Missing Data. In previous RCTs, we completed about 85% of interviews through 12 months and kept missing data on core interview items to about 2%. We expect these rates in this study. We will identify missing data patterns and use pattern-mixture modeling to test the sensitivity of our analysis to missing data assumptions.[103-106] We will conduct other sensitivity analyses after imputing missing data with a range of plausible values based on assumptions for the missing data (e.g. best-case, worst-case; with and without multiple imputation).[107-109]

Intention-to-Treat and Subject Noncompliance. Standard intention-to-treat (ITT) estimates the average treatment effect by comparing outcomes based on assignment of the treatment, but ignoring use of the treatment. Because ITT effect estimates do not represent treatment efficacy under noncompliance (e.g. a drinker is randomized to FamCHESS-C but does not use the system), we will also estimate noncompliance by estimating treatment effects only for compliers, using As-treated, Per-Protocol[110] and CACE.[111]

9.0 RECORDS TO BE KEPT

The following records will be kept during the course of the study.

- Subject Intake
- Subject Demographics
- Subject Consent Forms
- HIPAA Authorization Form
- Baseline and follow up survey data
- A-CHESS-C and FamCHESS-C use data using coded identifiers collected during this study.

10.0 DATA SECURITY AND PRIVACY MONITORING PLAN

Data and Safety Monitoring Committee

The Center uses the Data Monitoring Committee (DMC) located in the University of Wisconsin's Institute for Clinical and Translational Research (ICTR). The ICTR DMC will provide services to ensure appropriate measures are in place to promote subject safety, research integrity and compliance with federal regulations and local policies. The DMC members will review protocol-specific reports created by statisticians using data pulled from the Research Electronic Data

Capture (REDCap) data management tool. These standard reports will include an overview of study objectives, a review of actual and projected accrual rates, an evaluation of patient demographics for balance of randomization, and a summary of the number and seriousness of adverse events. An interim analysis of study results may be performed and source documents may be reviewed to allow the board to independently judge whether the overall integrity and conduct of the protocol remain acceptable based on data provided and reported by the Principal Investigators. The board will make recommendations to the Principal Investigator that could include actions of continuation, modification, suspension, or termination.

In providing oversight for the conduct of this study, the ICTR DMC will meet annually during the 3-year study. Additional meetings may be scheduled as determined by the DMC or as requested by the PIs.

We will record events that are deemed to be 'possibly, probably, or definitely' related to the study intervention, and communicate to NIAAA, DMC and UW IRB in accordance with the following guideline.

What Event is Reported	When is Event Reported	By Whom is Event Reported	To Whom is Event Reported
Fatal or life-threatening unexpected, suspected serious adverse reactions	Within **7 calendar days** of initial receipt of information	Investigator	Internal IRBs NHLBI and/or DMC
		Sponsor or designee	FDA (if IND study)
Non-fatal, non-life-threatening unexpected, suspected serious adverse reactions	Within **15 calendar days** of initial receipt of information	Investigator	Internal IRBs/ Institutional Officials NHLBI and/or DMC
		Sponsor or designee	FDA All participating investigators
Unanticipated adverse device effects	Within **10** working days of investigator first learning of effect	Investigator	Internal IRBs NHLBI and/or DMC
		Sponsor or designee	FDA (if IDE study)
Unanticipated Problem that is not an SAE	Within **14 days** of the investigator becoming aware of the problem	Investigator	Internal IRBs/Institutional Officials, NHLBI and/or DMC
All Unanticipated Problems[2]	Within **30 days** of the IRB's receipt of the report of the UP from the investigator.	IRB	OHRP
		Investigator	Internal IRBs and DMC

Data Security and Privacy Monitoring Plan

In accordance with the Health Insurance Portability and Accountability Act (HIPAA), CHESS has adopted the following Data Security and Privacy Monitoring Plan.

I. Appointment of Center Data Security Officers.

A. Gina Landucci and Matt Wright are the security officers for the Center.

B. Responsibilities of the security officers include:

- Developing information technology (IT) security policies
- Increasing security awareness and providing training for all Center faculty and Team Members
- Providing virus protection for IT resources
- Maintaining security patches on computing equipment
- Developing and implementing back up procedures
- Performing periodic vulnerability scanning on computers
- Reviewing and updating firewall strategies and policies
- Enhancing the physical security of IT resources
- Performing annual review of staff policies and procedures contained in this document
- Conducting formal HIPAA Risk Assessment Inventory per requirements of the UW HIPAA Office; last review completed summer 2018.

II. Policy for Orientation and Training

A. All Center students, faculty, and staff are required to complete the UW-Madison **2019-20 HIPAA Privacy & Security Training** course online which is offered in Canvas at https://canvas.wisc.edu/courses/173269. Contact Judy Ganch if you do not have the HIPAA training on your Canvas dashboard. Please email Judy when you have completed the training. You will need to retake this course annually.

B. All Center students, faculty, and staff that are involved in human subjects research are required to complete the UW-Madison CITI Human Subjects training online at https://my.gradsch.wisc.edu/citi/index.php. Register with your NetID. Select the training for the **UW Social & Behavioral Course.** Please email Judy Ganch when you have completed the training. You will need to take a refresher course every three years.

C. All Center students, faculty, and staff that are involved in human subjects research are required to complete the UW-Madison CITI Human Subjects training online at https://my.gradsch.wisc.edu/citi/index.php. Register with your NetID. Select the training for the **GCP—Social and Behavioral Research Best Practices for Clinical Research.** Please email Judy Ganch when you have completed the training. You will need to take a refresher course every three years.

D. Successful completion of the CITI and HIPAA training is required before any team member is allowed access to Protected Health Information (PHI) or Research Data.

E. All Center Team Members are required to complete training with Judy Ganch on Center security procedures and policies.
F. Sign (on the last page) the "Center Data Security Policy and Privacy Monitoring Plan" upon completion of this training and return to Judy Ganch.

III. Workstation Policy

A. All workstations will require login with a unique user name and password.
B. All workstations are required to be joined to the ENGR domain under the control of the College of Engineering. Access to specific folders on the Center network will be approved by the Center Management team or the study Project Director.
C. All workstations are required to use anti-virus software that can be remotely administered from the College of Engineering domain.
D. Users will log-out from or lock workstations when leaving them unattended.
E. Screen savers will be configured to require a password and to activate after ten minutes of workstation inactivity.
F. Users requiring remote access to the Center network will only do so with computers specifically certified by a Center Data Security Officer.
G. Study coordinators or support personnel using desktops in private or public areas must have screens adjusted so that visitors cannot read the screen upon entering the space in case PHI or other confidential information is displayed.
H. Access to the network or center work stations along with any on-line systems will be terminated immediately following an employee's last day of work at the Center.

IV. Password Policy

A. Users will require a password to access any computer connecting to the Center network.
B. Passwords must meet the requirements of the Computer Aided Engineering department (CAE). CAE password construction help can be found here: https://kb.wisc.edu/cae/page.php?id=8143.
C. Ideally the best practice is to re-set your password on a semi-annual basis.
D. Passwords may not be stored in proximity to the workstation and may not be shared by others.

V. Policy for the Use of Email

A. Patient Identifiable, Confidential, or Personnel Data may only be included in an encrypted attachment and should never be sent in the body or subject line of an email message.
B. Team Members who need to send encrypted attachments should contact a Center Data Security Officer to schedule a training session.

VI. Policy for Storage, Retrieval, and Disposal of Protected Information

A. Effective 1/1/14 any new studies must use the REDCap environment for

study participant information. Contact Matt for start-up and access information.

B. Any Patient Identifiable, Confidential, or Personnel Data in electronic form will be stored on secure servers only and **may not** be stored on individual workstations, laptops, or any other endpoint devices. Currently, the only place such information can be stored is the R: Drive for studies prior to 1/1/14 or REDCap.
C. Study coordinators will have printers in their office for printing any materials that include PHI and/or names of study participants.
D. All paper-based files will be stored in locked rooms inside locked file cabinets with limited access.
E. Any offices that contain PHI must be locked when leaving a room.
F. Servers containing Patient Identifiable, Confidential or Personnel Data must be located within physically secured server rooms which can only be accessed by authorized personnel.
G. The Center Data Security Officers will be responsible for assigning and restricting access to shared resources on Center servers.
H. Patient Identifiable, Confidential, and Personnel Data as a general rule may not be copied to or stored on the Center's publicly accessible servers at any time. However, in some studies, patient's name, disease state, and physician are stored within Center applications only accessible via a secure connection using a codename/password.
I. Remote access to files on secure Center servers will be provided in a very limited case only through a connection from a certified Center Workstation (see Center Workstation policy above for details).
J. Storage media containing Patient Identifiable, Confidential or Personnel Data will be rendered unusable before disposal.
K. All back up media will be stored in locked rooms with limited access.

VII. Policy for the Use of Endpoints (e.g. Workstation Smartphone, Laptop, Thumb Drive, External Hard Drive) Accessing Patient Identifiable, Confidential, and Personnel Data

A. Staff are not allowed to access or store any PHI data on any endpoint unless the endpoint is provided by a Center Data Security Officer ensuring that the endpoint is protected and secured. In addition, *any PHI data residing on an endpoint must also be encrypted with the oversight of a Center Data Security Officer.*
B. All endpoints accessing PHI must be owned and provisioned by the Center.
C. Patient Identifiable, Confidential, and Personnel Data files may not be transported from the Center unless the device/medium is monitored for physical security at all times and the data is encrypted on the mobile device.
D. Remote access to PHI data must be conducted using a secure encrypted end-to-end connection implementing modern security best practices either over HTTPS or using the WiscVPN connection.

VIII. Policy Governing the Storage and Use of Audiovisual Materials

A. Audiovisual media containing Patient Identifiable, Confidential, and Personnel Data are governed by the same policies and procedures that apply to handling and use of computerized data, including disposal, storage and access to media.
B. Such audiovisual media may not be transported from the Center unless the material is monitored for physical security at all times.

IX. Policy Governing the Transmission of Information via Fax

A. All outgoing correspondence via fax must be stripped of confidential information.
B. Before confidential information is transmitted to the Center via fax, sender must notify the appropriate Center Team Member to ensure the recipient is available to pick up the fax document.

X. Field Hardware Policy

A. Device provided for study participants will require log-in information to access the device.
B. Upon their return, all Center study computers, smartphones, or other devices that have been used in the field will have all data wiped from the hard drive in compliance with DOD standards.
C. Field computers will be stored at the Center in a wiped state.

XI. Study Participant Information

A. Center Team Members will not share or talk about confidential information regarding the CHESS study participant with anyone who is not directly involved in the management of the CHESS Project.
B. Confidential or other sensitive information regarding the study participant cannot be left in an unsecured place where others may see it.
C. Copies of written correspondence about the study participants with anyone other than CHESS management cannot be provided, unless specifically authorized to do so by the Project Director.
D. Access to study participant's PHI will be approved by the Project Director in coordination with the PI for the project. As noted in Section VI, studies beginning after 1/1/14 must use REDCap to enter participant information electronically.

XII. User Responsibilities

A. All Center Team Members are responsible for adhering to the Center Data Security and Privacy Monitoring Plan Policies at all times. In addition, all Center Team Members are responsible for adhering to the UW-Madison IT policies detailed at https://it.wisc.edu/about/office-of-the-cio/it- policies/ at all times as well.
B. All Center Team Members will be given a comprehensive briefing session upon hire.
C. Usernames and passwords are not to be shared with others.

D. No equipment may be connected to the Center network without specific prior certification by a Center Security Officer.
E. Specifically, no wireless access points may be deployed or connected to the network under any circumstances.
F. The Center Data Security Officers will maintain records to insure that all Center Team Members have been briefed.
G. The Center Data Security Officers will provide periodic refresher sessions to all Center Team Members.

XIII. In case of a PHI breach, Center Security Officer and/or PI reports incident to UW HIPAA Security Office, the UW Health Sciences IRB or other IRB of record, the ICTR Data Monitoring Committee, and sponsor as required.

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