CBT Texts for PTSD & Hazardous Drinking (Project Better)

NCT05372042

Document Date: 03/12/2024

Study Protocol

Materials & Methods

This study was registered with ClinicalTrials.gov (NCT05372042) and was reviewed and approved by the University of Washington (UW) Institutional Review Board (IRB). Recruitment and data collection began in October 2022 and is expected to be completed by April 2024.

Trial Design

This study uses a 3 (message framing: gain framing vs. loss framing vs. no framing) x 2 (mindset: growth mindset vs. simple reminder) design to evaluate whether message framing and growth mindsets enhance the efficacy of the brief CBT-based text-message intervention. Following eligibility screening, participants are verified, and block randomized to intervention conditions. Assessments consist of self-report measures and will be completed at baseline, post-intervention, 1-month, and 3-months post-intervention. See Figure 1 for the study flow diagram.

Participants

The study will enroll 500 participants, age 18 years or older, who reside in Washington (WA) State, and who endorse heavy episodic drinking and exposure to a DSM-5 Criterion A traumatic event with accompanying PTSD symptoms (i.e., a score of 33+ on the Posttraumatic Stress Disorder Checklist, Civilian Version, DSM-5 [PCL-5; Weathers et al., 2013]). Additional study inclusion criteria are in Table 1. There are no exclusion criteria for study entry to maximize sample generalizability.

Recruitment

Participants will be recruited in WA State via Craigslist ads posted in all 10 statewide categories, the UW-affiliated Institute of Translational Health Sciences (ITHS) website, and the Clinical Trials website (clinicaltrials.gov). Flyers will be distributed locally in community

centers, college campuses, and businesses. A social media ad campaign (i.e., Facebook, Instagram) will be launched state-wide and will be used to target specific demographics (e.g., gender, race, ethnicity) to boost sample diversity and representation.

Measures

Measures will be exclusively self-report questionnaires to minimize participant burden and have practical remote study procedures. Demographics including age, race/ethnicity, gender, income/work status, weight (for blood-alcohol-concentration calculation), verification of cell phone ownership and willingness to receive messages, certification of English fluency, and current residential zip code (to verify WA State residency) will be assessed at screening. Trauma exposure will be assessed at screening and at 3-month follow-up (intervening trauma exposure). We will use the Life Events Checklist (LEC; Weathers et al., 2013), a 16-item measure that queries on lifetime experience of commonly reported traumatic events (e.g., sexual assault, natural disasters) and identifies the most impactful, worst event in the person's lifetime.

Co-Primary Outcome Measures. Co-primary outcome measures will be given at screening or baseline and at all follow-ups. Power calculations were based on the heavy episodic drinking outcome (see power analysis section).

Drinking behavior will be assessed via well-validated measures that provide details on drinking patterns. Heavy episodic drinking over the past month (HED: 4/5 or more drinks per single occasion for women/men) will be assessed with the Quantity Frequency scale (QF; Baer, 1993) that asks about past month peak drinking occasion, how many drinks were consumed on that occasion, and over how many hours the drinks were consumed. Typical weekly alcohol consumption will be assessed using the Daily Drinking Questionnaire (DDQ; Collins et al., 1985); participants will report the number of drinks they typically consume each day. Negative

alcohol-related consequences will be assessed via the Short Index of Problems (SIP; Miller et al., 1995), which corresponds with longer measures of drinking consequences (Forcehimes et al., 2007).

PTSD symptom severity will be assessed using the PCL-5 (Weathers et al., 2013). The PCL-5 uses the event selected as the "worst" on the LEC to index PTSD symptoms to a target trauma. The PCL-5 is commonly used and has good test-retest reliability (rs = .82-.84) and strong convergent validity (rs = .85-.87) with other PTSD measures (Blevins et al., 2015).

Secondary Outcome Measures. Secondary measures will be given at baseline and 3-month follow-up. They include the Alcohol Use Disorders Identification Test (AUDIT; Babor et al., 2001), the Depression Anxiety Stress Scales (DASS-21; Lovibond & Lovibond, 1995), the Customary Drinking and Drug Use Record (CDDR; Brown et al., 1998), the Drug Abuse Screening Test (DAST-10; Skinner, 1982), and treatment services received. A study reactions questionnaire will be given at post-intervention and 3-month follow-up to assess satisfaction with the texts and study and skill use. This measure will be used for descriptive purposes to assess the intervention's feasibility and acceptability.

Enhancement Measures. Measures assessing avoidant coping and mindsets will be included to allow for secondary analyses to test mechanisms of action for the enhancements (Framing: approach; Mindsets: growth mindset). The 7-item avoidant coping scale assesses the extent to which individuals endorse avoiding problems and challenges (Ottenbreit & Dobson, 2004). For mindsets, a 3-item scale based on work by Dweck (1999, 2006) will assess beliefs about the changeability of PTSD symptoms, AM, and coping strategies.

Moderator Measures. To assess whether severe psychopathology associated with PTSD+ AM is a predictor of intervention response, we will assess severe mental illness and suicidality at

baseline. We will include a 4-item history of bipolar disorder and schizophrenia screening measure (Unutzer et al., 2001) and the 2-item screening version of the Columbia Suicide Severity Rating Scale (C-SSRS; Posner et al., 2011).

Procedures

Participants will follow a link included in the study advertisements to an online screening survey. The survey will start with an information statement to obtain consent, followed by self-report questionnaires assessing inclusion criteria. Participants deemed eligible from screening will be scheduled for a 5-minute verification phone call to review study procedures, allow the participant the opportunity to ask questions, obtain verbal consent, and verify participant identity. Immediately after verification, we will send baseline assessment via email. Participants will have 7 days to complete it to be officially enrolled in the study.

Once the participants complete the baseline assessment, they will be randomized using a web-based custom program. Participants are entered into the program by the project coordinator. Randomization will use stratified permuted block randomization in 8 strata with three stratified variables: PTSD severity (PCL-5 scores of 33-60 vs. ≥ 61), risk of alcohol use disorder (AUDIT scores < 20 vs. ≥ 20), and gender identity (male vs. any other gender identity). Within strata, conditions assignments are based on prior assignments to ensure balanced numbers across intervention conditions. Stratification aims to control representation of factors commonly related to intervention response across conditions.

Starting the Monday following randomization, intervention texts will be sent 3 days a week (Tuesday, Wednesday, Friday) for 4 consecutive weeks. Each participant will receive 2 texts, back-to-back, each day based on intervention condition (see below). The participant chooses what time of day they receive the texts.

A post-intervention assessment will be emailed the day after the last text has been received, and a follow-up survey will be sent 1-month and 3-months post intervention. Regular reminders will be sent to maximize completion of the follow-up surveys. All measures, procedures, and intervention delivery are done via automated text message or self-report computerized survey: study investigators and staff are not aware of individual participant intervention conditions.

Participants will be compensated for completing baseline and follow-up assessments. Compensation will be $20 at baseline, $25 at post, $30 at 1-month, and $35 at 3-month follow-up, given as Amazon gift cards. Gift card drawings after each of the follow-up assessments (five, $50 Amazon gift cards) will be used to further encourage assessment completion. Participants will not be compensated for screening or for receiving messages.

Fraud Detection

Because this is an online study except for the verification phone call, we have thought carefully about best practices to detect possibly fraudulent participant enrollments and responses (e.g., Teitcher et al., 2015). First, we have procedures to discourage fraudulent enrollment, including masking eligibility criteria in study advertisements and screening measures and not providing compensation for completing screening. Second, we will review screening data for potential fraudulent responses prior to the verification call. This review will include use of the Qualtrics survey platform's built-in fraud detection features to identify responses potentially generated by "bots," and duplicate submissions. We will also use a reverse phone number search to identify those using Voice Over Internet Protocol (VOIP) service. We will not verify or enroll VOIP users because, based on our pilot work and early data collection in this study, they are significantly more likely to be fraudulent. Additionally, prior to verification and enrollment, we

will search participants' address, city, and zip code to confirm that the address is legitimate and within WA State. Third, the verification call serves as both a fraud deterrent and detection method. In this call, we will ask participants to provide, not confirm, their name, age, location, and contact information and will check for a match with their screening data. The call also verifies that the phone number is functioning. These procedures should decrease the likelihood of fraudulent participants enrolling.

Interventions

The CBT text-message intervention was adapted from our pilot (Bedard-Gilligan et al., 2022) in which participants received a weekly CBT skill message focused on addressing PTSD symptoms, AM, or their co-occurrence (e.g., sitting with memories and feelings [imaginal exposure – example below], approaching avoided activities [in vivo exposure—the link between traumatic events and subsequent behavioral avoidance is explained, and participants are asked to identify and engage in activities they used to enjoy], testing out activities to increase connection, pleasure, and/or competence [behavioral activation—the link between traumatic events and isolation, low mood, low self-efficacy is explained, and participants are asked to identify and engage in a new activity that can lead to positive mood, higher self-efficacy, and/or social connectedness, and reducing drinking to cope [increasing adaptive coping skill—the link between trauma symptoms and drinking to reduce them is explained, and participants are asked to identify and engaged in alternative coping strategies]). Here, participants will receive 3 messages per week for 4 weeks. All messages are one-way; participants cannot respond. Each week, participants receive a message with a skill described above, and based on randomization assignment, they will receive additional enhancements (framing and/or mindsets) via a 3 (message framing: loss vs. gain vs. no framing) x 2 (mindset: growth mindset reminder vs. not

[simple reminder]) factorial design. The additional messages were first drafted by the principal investigators (MBG & KPL) and then refined via consultation with an applied social psychologist with expertise in social psychological theories and intervention development to improve self-regulation and (mental) health. Participants' condition is held constant throughout the intervention.

Consistent with the pilot, texts will begin with a greeting from the study team (e.g., "Greetings from Project Better!"). Messages are broken into two parts to allow for more characters if participants do not have a smart phone. The first message introduces a CBT skill/coping strategy (e.g., "This week we're focusing on painful feelings and memories, which are common after stressful events. Approaching – feeling and sitting with them can actually reduce their impact. How can you approach your feelings & memories this week?" [imaginal exposure]). The second text—sent one day later—includes the message framing manipulation. Participants receive additional information about the skill, and it is framed in terms of *avoiding* future losses (e.g., "The impact of stressful events can be very difficult. To prevent things from getting worse, remember to sit with your feelings and memories this week."); *maximizing* future gains ("The impact of stressful events can be very difficult. To help make things better, remember to sit with your feelings and memories this week.") or will have *no framing* (e.g., "The impact of stressful events can be very difficult. Remember to work on sitting with your feelings and memories this week."). The third and final text – sent two days later –will include the mindset enhancement. Participants in the *growth mindset* condition receive information about our ability to change symptoms and distress, and it normalizes setbacks (e.g., "Sitting with your emotions and memories can help you change how you think and feel. Remember that setbacks are a chance to learn—you can develop these coping skills!); those in the *no mindset [simple*

reminder] condition receive a reminder to use their skills (e.g., "Sitting with your emotions and memories can help you change how you think and feel. Remember to practice the skills."). Text messages range in length from 124 to 265 characters. No additional resources on CBT skills are offered to participants beyond the messages.

Analysis Plan

Decision Rules

A priori decision rules will be applied to select the intervention condition that is most effective and the simplest to undergo further testing in a subsequent RCT. Consistent with best practices for studies aiming to select the most effective combination of intervention elements using a factorial design, we will use a process of elimination rather than hypothesis-testing approach in applying our decision rules (Collins, 2018). In this approach, a series of criteria will be applied, and intervention elements that fail to meet minimum criteria for efficacy will be ruled out until the strongest set of elements remains (Collins, 2018). Because Type I error is less of a concern in this approach than Type II error, significance will be defined as $p < .10$.

Decision rules are based on co-primary and secondary outcomes and do not include intervention completion rates. This decision reflects both the type of intervention (texts are passively delivered) and pilot findings (no participants withdrew from the pilot), thus non-completion rates are not expected to be a concern.

Decision rules will be as follows:

1. We will first examine main effects for PTSD and HED in a model without interaction terms. We will retain any enhancements for further consideration in Step 2 that have significant negative main effects for both outcomes. If none exist, we will retain enhancements with significant negative main effects on PTSD or HED alone.

2. We will then examine interaction effects (framing x growth mindset x time) for PTSD and HED among any enhancements with significant negative main effects. If there is one or more negative interaction terms, we will examine linear contrasts among the combinations of enhancements that are part of the interaction to determine whether adding specific enhancements leads to improvement. If this does not yield a clear conclusion in terms of the combination of effects to select, we will examine the direction and magnitude of the main and interaction effects for these conditions on secondary outcomes and participant satisfaction data. If there are no negative interaction terms, we will select any enhancements that had significant main effects and no evidence for negative impacts on outcomes.
3. If there are no positive significant interactions or main effects for either PTSD or HED, we will repeat step 1 and 2 with other co-primary and secondary outcomes in the following order: alcohol use consequences (SIP), typical weekly alcohol consumption (DDQ), depression (DASS), and anxiety (DASS).
4. If effect sizes across conditions do not differ significantly from control (no framing, simple reminder), we will choose the control given that it is the simplest condition.

Power

The co-primary outcomes for this study are HED and PTSD symptom severity. Power calculations were conducted for HED, as its lower expected average values and non-normal distribution was expected to generate a more conservative estimate of sample size relative to PTSD symptom severity. Considering a base rate of 5.93 episodes of HED per week (based on our pilot data) and $\alpha = .05$, we determined that a sample size of $N = 500$ *(*$n = 75$ per condition; *n*

= 150 per comparison) would yield >.80 power to detect an 18% or greater difference in number of HED episodes between any two conditions (i.e., count ratio of 0.82).

Decision rules were revisited in response to reviewer feedback when submitting our protocol for potential publication. We realized that our original approach was not fully aligned with our power analysis or our overarching goal of identifying the most efficacious *and* simplest condition. We realized that a process-of-elimination approach starting with main effects was more in line with our goal (rather than first testing the hypothesis that the combination of growth mindsets and loss-framing would be the most efficacious condition). We thus altered our decision rules from what was originally submitted to the funder and will be testing main effects (rule 1) first, followed by interaction effects (rule 2). Further, given our process of elimination approach (vs. hypothesis testing), a *p*-value cut-off of 0.10 is appropriate (Collins, 2018). The power analysis was reviewed with these changes, and we anticipate having >.80 power to detect even smaller main effects (i.e., a count ratio of .89).

Assessing Differences by Condition

We will use an intent-to-treat approach to analyze results and retain all available data. For each outcome, we will explore change over time by condition visually, using within-group pre-post effect sizes (d = (Mpost-Mpre)/Sdif), and in generalized linear mixed effects models. In mixed-effects models, we will test main effects for each enhancement (i.e., framing enhancements with no framing as the reference, growth mindset with no growth mindset as the reference) and time (baseline, post, 1-month, 3-month), and a 3-way interaction term for framing x growth mindset x time. We will evaluate the need for random effects for time, different specifications for time (e.g., linear, quadratic), and count regression forms of the mixed-effects model (e.g., Poisson, negative binomial, zero-inflated).

Missing Data

Mixed-effects modeling should yield unbiased estimates in the presence of missing data assuming data are missing at random—that is, missingness is only related to observed data, but not the unobserved data. We will explore missing data patterns according to baseline (time-fixed) values of variables and consider the inclusion of additional covariates that show strong associations with missingness above and beyond any other planned covariates Should sensitivity analyses suggest that the findings may be dependent on unobserved data, we will consider the need for approaches to missing data (e.g., using the pattern-mixture approach to combine effects across missing data patterns to yield unbiased results).

References

Babor, T.F., Higgins-Biddle, J.C., Saunders, J.B., & Monteiro, M.G. (2001). *The Alcohol-use disorders Identification Test (AUDIT): Guidelines for use in primary care (2nd ed.). World Health Organization, Department of Mental Health and Substance Dependence.*

Bedard-Gilligan, M. A., Dworkin, E. R., Kaysen, D., Ojalehto, H. J., Stappenbeck, C. A., & Lindgren, K. P. (2022). A pilot study on the feasibility, acceptability, and preliminary efficacy of a brief text message intervention for co-occurring alcohol misuse and PTSD symptoms in a community sample. *Journal of Anxiety Disorders*, *91*, 102615.

Blevins, C. A., Weathers, F. W., Davis, M. T., Witte, T. K. & Domino, J. L. (2015). The posttraumatic stress disorder checklist for DSM-5 (PCL-5): Development and initial psychometric evaluation. *Journal of Traumatic Stress, 28*, 489–498. DOI: 10.1002/jts.22059

Collins, L.M. (2018). *Optimization of Behavioral, Biobehavioral, and Biomedical Interventions: The Multiphase Optimization Strategy (MOST)*. Cham, Switzerland: Springer.

Dweck, C. S. (2000). *Self-theories: Their role in motivation, personality, and development*.

Forcehimes, A. A., Tonigan, J. S., Miller, W. R., Kenna, G. A. & Baer, J. S. (2007). Psychometrics of the Drinker Inventory of Consequences (DrInC). *Addictive Behaviors, 32*, 1699–1704. https://doi.org/10.1006/obhd.1998.2781

Ottenbreit, & Dobson, K. S. (2004). Avoidance and depression: The construction of the Cognitive–Behavioral Avoidance Scale. *Behaviour Research and Therapy, 42*(3), 293–313. https://doi.org/10.1016/S0005-7967(03)00140-2

Posner, Brown, G. K., Stanley, B., Brent, D. A., Yershova, K. V., Oquendo, M. A., Currier, G.

W., Melvin, G. A., Greenhill, L., Shen, S., & Mann, J. J. (2011). The Columbia–Suicide Severity Rating Scale: Initial validity and internal consistency findings from three multisite studies with adolescents and adults. *The American Journal of Psychiatry, 168*(12), 1266–1277. https://doi.org/10.1176/appi.ajp.2011.10111704

Teitcher, J. E., Bockting, W. O., Bauermeister, J. A., Hoefer, C. J., Miner, M. H., & Klitzman, R. L. (2015). Detecting, preventing, and responding to "fraudsters" in internet research: Ethics and tradeoffs. *Journal of Law, Medicine & Ethics*, *43*(1), 116-133. doi: 10.1111/jlme.12200

Unutzer, J., Katon, W., Williams, J.W. Jr., et al. (2001). Improving primary care for depression in late life: the design of a multicenter randomized trial. *Medical Care ,39*(8), 785–99. https://doi.org/10.1097/00005650-200108000-00005

Weathers, F.W., Litz, B.T., Keane, T.M., Palmieri, P.A., Marx, B.P., & Schnurr, P.P. (2013). The PTSD Checklist for *DSM-5* (PCL-5). Scale available from the National Center for PTSD at www.ptsd.va.gov.