TITLE: Study of a Transdiagnostic, Emotion-focused Group Intervention for Young Adults With Substance Use Disorders

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Pilot study of a transdiagnostic, emotion-focused group intervention for young adults with substance use disorders

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DETAILED PROTOCOL
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I. BACKGROUND AND SIGNIFICANCE

SUDs among young adults: SUDs, defined as all alcohol and drug use disorders (minus nicotine and caffeine), are among the most common and burdensome public health problems in the United States. The prevalence of SUD is especially high among young adults.[1] Recent national surveys indicate that approximately 17% of 18 to 25 year-olds meet SUD criteria, compared to about 7% of individuals ages 26 and older and 5% of adolescents.[2] Young adults also have the highest rates of specific risky (or potentially life-threatening) substance use behaviors, including illicit drug use, binge drinking, and heavy drinking.[2] Given these statistics, it is no surprise that a large proportion of the overall health and economic burden of SUD can be attributed to this cohort.[3,4,5]

Young adults have been shown to benefit from evidence-based treatments for SUD, such as cognitive-behavioral therapy (CBT), certain medications in combination with psychotherapy, and mutual-help organizations.[6] However, young adults consistently have a less robust response than both adolescents and older adults, *and* tend to be more difficult to retain in SUD treatment.[1] The latter may be at least in part due to lower readiness to stop (or change) substance use.[1] Thus, there is still room for improvement of outcomes and retention associated with existing SUD treatment approaches for this high-need group.

SUDs and emotional distress: Epidemiological studies have observed high comorbidity rates for SUDs and the affective/emotional disorders (i.e., anxiety, depressive, and related disorders) across adults and adolescents.[7,8,9] The risk of suicidal and nonsuicidal SITBs (e.g., suicide ideation and attempts, nonsuicidal self-injury [NSSI]), manifestations of acute emotional distress especially prevalent among young adults,[10,11] is also elevated among individuals with SUD.[12,13,14] Unfortunately, the presence of an emotional disorder (especially more severe conditions, such as recurrent MDD and bipolar disorder) has a negative impact on SUD treatment outcome.[15,16] SITBs are high risk, difficult to treat, and can complicate SUD treatment. In sum, young adults with SUD and comorbid emotional distress are a sizeable, challenging population for whom a novel treatment approach could have a large public health impact.

Emotion dysregulation as a transdiagnostic treatment target: To this end, we propose to target core psychopathological processes related to emotion dysregulation that underlie SITBs and commonly co-occurring emotional disorder pathology. One such process is the frequent experience of intense negative affect coupled with aversive reactivity to emotional experiences when they occur (i.e., neuroticism).[17] These aversive reactions result in efforts to avoid, control, or suppress emotional experiences, which lead to rebound effects in which emotions return with greater frequency and intensity,[18] resulting in symptom maintenance/recurrence. This temperamental factor has been implicated in the onset and maintenance of anxiety, depressive, and other emotional disorders such as OCD and PTSD,[17] as well as in SITBs.[19] For example, neuroticism has been shown to predict suicidal ideation, attempts, and deaths[20,21] and leading

evidence-based theories point to the role of overwhelming negative affect in contributing to suicidal behavior.[22,23] It is also well-established that NSSI is most often enacted to relieve acute negative affective states.[24,25]

Although not necessarily conceptualized as a prototypical emotional disorder, emotion regulation difficulties have also been implicated in the development and persistence of SUDs.[26] For example, people with alcohol use disorder (AUD) report elevated emotion dysregulation,[27] neuroticism,[28] and negative emotionality.[29] Impaired emotion regulation is also associated with poorer AUD treatment response.[30,31] Emotion dysregulation increases vulnerability to cue-induced craving and impulsive responding—constructs relevant to *all* SUDs.[32] Alterations in emotion regulation neural circuitry (e.g., hypoactivation of the rostral anterior cingulate cortex/ventromedial prefrontal cortex) have been observed for example in those with cocaine and opiate use disorders.[26] Finally, distressing emotional states are precipitants of drug and alcohol use,[33,34] leading some researchers to conceptualize problematic substance use as a maladaptive strategy for down-regulating negative affect,[35,36] often colloquially termed "self-medication".

The Unified Protocol: The Unified Protocol for Transdiagnostic Treatment of Emotional Disorders (UP[37,38]) is an evidence-based psychological intervention designed to be applied across anxiety, depressive, and any other disorder in which emotion dysregulation is central. Rather than focusing on diagnosis-specific symptoms, the UP seeks to target shared temperamental vulnerabilities to emotional disorders (namely, neuroticism) through five emotion-focused CBT strategies: increasing mindful emotion awareness, increasing cognitive flexibility, countering emotion-driven behaviors, and conducting interoceptive/emotion exposure exercises. Given its transdiagnostic format, the UP has the potential to address comorbidity among the emotional disorders (and other functionally similar problems such as SUDs) simultaneously and more comprehensively than single-diagnosis treatments. This approach also has notable implications for dissemination and training, as clinicians could learn only one CBT protocol to flexibly utilize across many presentations.

PRELIMINARY STUDIES

The UP has shown efficacy in treating heterogeneous anxiety and comorbid unipolar depressive disorders in multiple randomized controlled trials (RCTs), including a recent large-scale RCT (N=223) in which the UP was shown to be equally efficacious to "gold-standard," single-diagnosis CBT protocols for social anxiety disorder, generalized anxiety disorder, obsessive-compulsive disorder, and panic disorder .[39,40] Initial findings also support its use for primary MDD,[41] bipolar disorder,[42] PTSD,[43] borderline personality disorder,[44] and NSSI.[45] An adapted version of the UP also demonstrated initial feasibility and acceptability for suicidal inpatients in a recent pilot study.[19]

Regarding applications of the UP to SUD, the one published RCT to date (N=81) found the UP to significantly reduce heavy drinking in adults with AUD and anxiety.[46] To our knowledge, the UP has not yet been evaluated in those with a range of SUDs, though the framework is theoretically applicable to any substance use that functions as a maladaptive response to negative emotion. In the UP, problematic substance use is conceptualized as an avoidant coping response that reciprocally increases the frequency and intensity of negative emotions such as anxiety, sadness, anger, etc. Because young adults may be more motivated to change emotional disorder symptoms than substance use,[1] it is also possible that an integrated, emotion-focused treatment like the UP may be associated with less dropout than SUD-specific protocols, while still delivering concepts relevant to reducing problematic substance use.

POTENTIAL BENEFITS OF THE PROPOSED RESEARCH

The greatest potential eventual implication of the proposed research is to improve the standard of care for a sizeable population in need of improved treatment approaches: young adults with SUD and emotional distress. If the adjunctive UP proves incrementally effective when added to TAU, it will contribute to evidence-based treatment guidelines for this underserved population. Effectively treating this group would reduce long-term disability and costs, improving overall functioning and reducing public health burden. By delivering adaptive strategies for emotional responding, this transdiagnostic group intervention offers a low cost, easily implemented treatment that may provide greater and more broad-based benefits than existing pharmacological and single-diagnosis therapies, and perhaps help prevent future SUD relapse. Eventual findings may be used to inform the development of guidelines for treatment of young adults (and potentially, other cohorts) with SUD and co-occurring emotional distress. This pilot study is the first, necessary step in obtaining preliminary data for future grant applications (e.g., K awards) to conduct a larger randomized trial adequately powered to examine short- and long-term efficacy, as well as intervention moderators (e.g., SUD type) and mediators.

II. SPECIFIC AIMS

We propose to conduct a pilot randomized controlled trial comparing a cognitive-behavioral, transdiagnostic, emotion-focused group intervention plus treatment as usual (UP + TAU) to TAU alone to within an existing comprehensive outpatient program for young adults with SUD and comorbid emotional distress (N=50). Participants will be randomized in a 2:1 ratio to UP + TAU or TAU alone conditions.

Specific Aim 1: To evaluate the acceptability and feasibility of adding a transdiagnostic, emotion-focused group intervention (16 twice-weekly UP sessions) to TAU in a comprehensive outpatient program for young adults with SUDs and elevated emotional distress (N=50).

Hypothesis 1a. UP participants will report high satisfaction with and acceptability of the UP per Client Satisfaction Questionnaire (CSQ-8[47]) and semi-structured clinical feedback interview.

Hypothesis 1b. UP participants will be less likely to drop out from treatment at the outpatient program during the study period than those in control condition.

Specific Aim 2: To explore the adjunctive intervention's acute efficacy in treating emotional distress (anxiety, depression, suicidal ideation, NSSI) and indices of SUD (commitment to sobriety, craving, quantity and frequency of substance use).

Hypothesis 2a. UP participants will evidence greater decreases in Overall Anxiety Severity and Impairment Scale (OASIS) and Overall Depression Severity and Impairment Scale (ODSIS) from pre- to post-treatment than the those in the control condition.

Hypothesis 2b. UP participants who report past month suicidal thoughts at baseline will evidence greater reductions in Beck Scale for Suicidal Ideation (BSI[49]) scores from pre- to post-treatment than those in the control condition.

Hypothesis 2c. UP participants who report past month NSSI urges or episodes at baseline will report a lower frequency of NSSI urges and episodes in a one-month period on the Self-Injurious Thoughts and Behaviors Interview-Clinician Rated [SITBI-CR[50]]-

and on the Self-Injurious Thoughts and Behaviors Interview-Self-Rated [SITBI-SR[50]]at post-treatment than the control.
Hypothesis 2d. UP participants will evidence greater increases in Commitment to Sobriety Scale (CSS[51]) and decreases in Craving Scale[52] scores from pre- to post-treatment than the control.
Hypothesis 2e. UP participants will report lower quantity and frequency of substance use during the study period than those in the control condition.

III. SUBJECT SELECTION

We propose to conduct a pilot randomized controlled trial for young adults with SUD and comorbid emotional distress who are entering into or currently engaged in treatment within a comprehensive outpatient program (ARMS at MGH). We plan to enroll 50 young adults (ages 18 to 26) with SUD and comorbid emotional distress from ARMS. They will be randomized in a 2:1 ratio to one of two conditions: 16 twice-weekly sessions of a transdiagnostic, group-based CBT intervention (the Unified Protocol [UP]) plus usual services at ARMS (UP + TAU condition) or treatment as usual at ARMS (TAU; control condition). All potential subjects must satisfy the following inclusion/exclusion criteria upon the study screening visit:

Inclusion criteria:
1. Young adults ages 18 to 26, inclusive
2. English language proficiency
3. Ability to provide written, informed consent
4. Ability to attend in-person, outpatient sessions
5. Has provided consent to receive or is currently undergoing treatment at the MGH Addiction Recovery Management Service (ARMS) program (i.e., is a new or existing ARMS patient)
6. Documented DSM-5 SUD diagnosis (limited to alcohol use disorder; cannabis use disorder; phencyclidine or other hallucinogen use disorder; inhalant use disorder, opioid use disorder; sedative, hypnotic, or anxiolytic use disorder; stimulant use disorder; other (or unknown) SUD)
7. Current elevated emotional distress, as evidenced by ANY ONE of the following:
    a. Score at least in the moderate range on the self-report anxiety questionnaire administered by ARMS clinicians during the routine clinical evaluation or by study staff during the screening visit
    b. Score at least in the moderate range on the self-report depression questionnaire administered by ARMS clinicians during the routine clinical evaluation or by study staff during the screening visit
    c. Report of suicidal thoughts in the past week on the SITBI-CR
    d. Report of engagement in NSSI in the past week on the SITBI-CR
8. Not expected to require inpatient level of care within the next two weeks (as judged clinically)

Exclusion criteria:
1. Documented psychotic disorder (or current, clinically significant psychotic symptoms) that render the patient inappropriate for outpatient level of care or participation in group therapy (as judged clinically by study staff)

2. Current imminent suicide or homicide risk (as judged clinically by study staff)
3. Unwilling or unable to provide consent for study staff to access subject's medical records and coordinate care and exchange data with ARMS clinical staff
4. Unwilling or unable to identify an emergency contact

Recruitment: Subjects will be recruited exclusively through the ARMS program at MGH. ARMS is an outpatient, dual diagnosis clinic comprising a multidisciplinary team of psychiatrists, clinical psychologists, and masters-level social workers who are trained to work with adolescents and young adults with substance-related problems. ARMS provides comprehensive outpatient individual therapy, group therapy, and outpatient psychiatry consultation and follow-up. The investigators have obtained commitment from the Clinical Director of ARMS (James McKowen, PhD) to support recruitment of young adult patients at ARMS, and to facilitate delivery of the group-based experimental intervention. The ARMS program conducts evaluations with approximately 180 new patients per year, the majority of whom also present with comorbid depression or anxiety. We will collaborate with the ARMS Clinical Director and staff in order to recruit through study flyers and direct referrals from the ARMS clinicians (psychiatrists, psychologists, social workers) who conduct routine clinical evaluations.

Clinicians who conduct the routine clinical evaluation for treatment at ARMS will identify potentially eligible participants based on information obtained during the routine evaluation, which includes assessment of DSM-5 criteria for SUD. If a patient has already voluntarily provided written consent to be contacted about research opportunities during the ARMS intake process, study staff may contact them via phone call to provide more information about the study and, if interested, schedule a screening visit. Alternatively, during either the routine ARMS evaluation feedback session or the routine ARMS treatment recommendations session, which occur either in the same visit or over the course of two visits, potentially eligible participants may be presented with information about the study (including a study flyer) by an ARMS clinician. Additionally, existing ARMS patients may also be presented with information about the study by their ARMS clinician. Potentially eligible subjects who express interest in participating in the study will then be approached by a study clinician at the end of a routine ARMS clinical session to conduct a brief (under one hour) in-person study screening visit, which may take place at ARMS, the MGH Depression Clinical and Research Program (DCRP), or the MGH Center for Addiction Medicine (CAM). Study staff may walk participants between ARMS and the DCRP or CAM as needed. If a study clinician is unavailable or the participant cannot stay to complete the study screening visit after a routine ARMS visit, the participant will be contacted to schedule a separate in-person study screening visit. When presenting the study to interested participants, ARMS clinicians will ask for their preferred method(s) of communication (phone call, email, and/or text message), which study staff will then use to contact participants to schedule the screening/baseline visit. Up to five consecutive (unanswered) contact attempts will be made to interested participants to schedule the screening/baseline visit.

IV. SUBJECT ENROLLMENT

A total of 50 subjects who have a documented current DSM-5 diagnosis of SUD and elevated emotional distress (operationalized as: score in at least the moderate range on self-report

measures of anxiety or depression used for clinical purposes at ARMS, and/or report of suicidal thoughts or NSSI in the past week) will be enrolled in the study. An ARMS clinician will determine possible subject eligibility based on information obtained during the routine clinical evaluation for ARMS treatment. Those who are deemed potentially eligible and express interest in the study will then undergo a brief in-person screening visit with a study clinician. The screening visit, which will take about 60 minutes, will consist of a meeting with a study clinician to provide informed consent and confirm study eligibility (via review of information obtained during routine ARMS clinical care and completion of the SITBI-CR). For participants who report suicidal thoughts in the past week or having made a suicide plan or suicide attempt in the past year on the SITBI-CR, a clinical risk assessment (including severity of ideation and presence of plan, intent, and access to means) will be conducted during the visit in order to ensure participant safety and eligibility for the study (i.e., no imminent suicide risk). The study clinician conducting the screening visit will consult the ARMS Clinical Director (or, if Dr. McKowen is unavailable, another licensed clinician on-site) immediately regarding risk in any questionable cases to determine the appropriate action, per usual ARMS clinical procedures. Eligible participants will then complete the Timeline Follow Back (TLFB[53,54]) as an interview, in which participants recall the quantity and frequency of substance use during a specified time window (e.g., past month) using a calendar, and several self-report questionnaires, including the BSI, CCS, and Craving Scale (see Table 1). The study clinician will also fill out a concomitant treatment log to identify the participant's overall treatment plan, including medication and therapy. Data obtained at this screening visit will be considered the "pre-treatment" assessment. After eligibility criteria are determined and participants have completed the screening/baseline assessment, participants will be randomly assigned to UP+TAU or TAU only conditions using a permuted block randomization procedure. The permuted block randomization schedules will be generated by an independent biostatistician from the MGH Biostatistics Center prior to enrolling the first subject into the study. Groups, or "blocks," of 5 individuals will be randomized at a time to one of the two treatment conditions (UP+TAU or TAU alone) using a 2:1 randomization scheme, defined as 2 blocks randomized to UP + TAU for every 1 block randomized to TAU alone. Randomizations will be conducted using a web-based randomization program developed by the MGH Biostatistics Center. The randomization code will be generated within the web-based program by study staff only when the randomization occurs, i.e. once the last participant of each group has completed baseline. Participants will then be contacted by study staff via their preferred method of communication to notify them of their study condition.

Study staff will be masters and doctoral-level staff members from ARMS and/or the MGH Depression Clinical and Research Program (DCRP) who donate time to conduct assessments and/or deliver treatment for research studies. Masters-level advanced practicum students at ARMS or DCRP may also contribute to the study as part of their training. ARMS and DCRP clinicians (psychologists, psychiatrists, licensed clinical social workers, research/clinical fellows, advanced practicum students) will be included as study staff and able to conduct assessments and, as long as they have also received training in the protocol, deliver the UP treatment (see *Study Intervention*). All study procedures will be conducted with a licensed clinician on-site at ARMS, the DCRP, or CAM who can conduct additional risk assessment and/or help facilitate transfer to the Acute Psychiatry Service in the MGH emergency room if needed.

Procedures for obtaining informed consent:
Informed consent will be obtained at the time of the screening visit, prior to the collection of any data for the study. Before or upon meeting with the study clinician, subjects will receive a written copy of the consent form that includes an easy-to-read description of the protocol, risks and benefits, privacy concerns, and provisions for subjects who decide to discontinue the study. Subjects will be informed that they may voluntarily discontinue participation in the study at any time. A study clinician then review the consent form with the participant and provide the opportunity for the subject to ask questions. Participation in this study is voluntary and subjects may withdraw from the study at any time. The IRB-approved informed consent document will be signed and dated by the subject and the clinician obtaining consent.

In addition to consent for study participation, subjects will be asked to provide consent to coordinate care and share clinical data with/from the ARMS program, including review of medical records (e.g., routine ARMS clinical evaluation) to confirm inclusion/exclusion criteria, extract relevant clinical data obtained during the routine ARMS clinical evaluation from the medical record (e.g. diagnoses, treatment history, family history of substance use), track treatment engagement at ARMS, and facilitate good clinical care during the study. Subjects who are unable or unwilling to provide such consent will not be eligible for further participation. Subjects will also be asked to provide consent for audio-recording of group treatment sessions. The purpose of audio-recording, measuring therapist adherence to the treatment protocol, will be explained. Subjects who decline consent to audio-record their sessions will not be enrolled in the study. On the consent form, subjects will also be asked to list their preferred methods of communication between sessions (regarding scheduling and other logistical issues) and will be presented with pertinent information about the risks of the various methods of communication. Participants will be asked to provide consent to be contacted via e-mail and/or text messaging over the course of the study for scheduling purposes and appointment reminders.

V. STUDY PROCEDURES

TAU condition: After randomization, participants randomized to the TAU condition will undergo usual care at ARMS for the next 8-10 weeks. Usual care at ARMS typically consists of a combination of up to 3 group therapy sessions per week, individual weekly therapy, and/or psychopharmacology appointments as needed. Some ARMS patients are offered and choose to engage in all three treatment modalities (group therapy, individual therapy, and psychopharmacology), whereas others only engage in one treatment modality. No requirements will be placed on TAU participants with regard to TAU dosage and TAU will be consistent with each participant's clinical treatment plan at ARMS; however, TAU attendance (e.g., number of appointments) for all participants will be tracked by study staff. Four to 6 weeks after randomization, TAU participants will complete a mid-treatment assessment, during which they will complete the same self-report questionnaires (plus TLFB and concomitant treatment log with a study clinician) administered at the screening/baseline visit (see *Measures*). Eight to 10 weeks after randomization, they will repeat the same measures for the in-person "post-treatment" assessment. During both the mid- and post-treatment assessments, should a participant report suicidal thoughts in the past week on the SITBI-SR or clinically significant increases in NSSI, a clinical risk assessment (including severity of ideation and presence of plan, intent, and access to means) will be conducted by a study clinician in order to ensure participant safety and that the

participant remains stable to be treated in an outpatient setting. After completing the post-treatment assessment, their study participation will be complete.

UP + TAU condition: After randomization, participants randomized to the UP + TAU condition will undergo TAU at ARMS and be offered 16 additional, twice-weekly group UP sessions, also at ARMS (see *Intervention*). Participants in the UP + TAU condition will undergo the same mid- and post-treatment assessments as the TAU condition, plus the CSQ-8 and a semi-structured interview to collect feedback about the intervention (see *Measures*). The mid-treatment assessment will occur after each participant's 8th UP session OR between 4-6 weeks after randomization, and the post-treatment assessment will occur within two weeks after each participant's 16th UP session. The same risk assessment procedures for mid- and post-treatment assessments used in the TAU condition will also apply to the UP + TAU condition. Should a UP + TAU participant condition have two consecutive unplanned absences from a UP group session, up to three attempts to contact will be made regarding their absence. There will not be a maximum number of missed UP sessions warranting a participant to step out of the 16-session group protocol. After completing the post-treatment assessment, their participation in the study will be complete.

Group UP sessions will take place at the ARMS program at MGH. Study assessment visits (screening/baseline, mid-treatment, and post-treatment) may take place at the ARMS program, the Depression Clinical and Research Program (DCRP), or the Center for Addiction Medicine (CAM) at MGH. Study staff may walk participants between ARMS and the DCRP or CAM as needed.

In sum, the proposed study involves the following points of contact: (1) obtaining informed consent and screening/baseline assessment, (2) mid-treatment assessment involving self-report questionnaires and TLFB, (3) post-treatment assessment involving self-report questionnaires and TLFB (primary endpoint), and (4) 16 twice-weekly group UP sessions for those randomized to the UP + TAU condition.

If participants are unable to complete the clinician-rated measures in-person at their mid- or post-treatment assessments, they will be given the option to complete this portion of the visit via phone call with a study clinician. Should any risk issues arise, the clinician will complete a risk assessment while on the phone with the participant. A licensed clinician will always be on-site for consultation as needed during assessments conducted over the phone.

If participants are unable to complete the self-reported measures in-person at their screening/baseline, mid-treatment, or post-treatment assessments, they will be e-mailed a link to the self-report battery in Redcap to complete remotely. Study staff will review the completed SRQ assessment in Redcap within 24 (business) hours of submission for report of suicidal thoughts, and within one week to assure their completeness. Should a participant report suicidal thoughts in the past week on the SITBI-SR, a clinical risk assessment (including severity of ideation and presence of plan, intent, and access to means) will be conducted over the phone by a study clinician to ensure participant safety and that the participant remains stable to be treated in an outpatient setting. Additionally, a clinical risk assessment will be conducted over the phone by a study clinician in response to reports of increased NSSI that are deemed clinically

significant. Up to three attempts to contact will be made for this risk assessment before calling a participant's designated emergency contact.

Participants may receive recruitment and scheduling messages, as well as appointment reminders via e-mail or text message over the course of the study, depending on their preferred method of communication. Up to three consecutive (unanswered) contact attempts to the participant will be made for participants in both conditions to schedule mid- and post-treatment assessments. If a participant misses the mid-treatment assessment, but is still responsive to contact attempts, they will still be able to complete the post-treatment assessment. If a participant in either condition is unresponsive to three consecutive unanswered contact attempts within a three-week period at any point within the 10-week study, they will be considered dropped out from the study and no further follow-up will be made; the ARMS clinical team will also be notified.

Participants will make $100 for completion of the three assessments ($25 for the pre- and mid-treatment assessments, and $50 for the post-treatment assessment) and up to an additional $80 for session attendance. Session attendance will be compensated as follows: participants will receive $5 per session attended (up to 16 UP sessions in the UP+TAU group and up to 16 TAU sessions in the TAU along group). This amount represents approximate cost of travel to/from up to two sessions per week. In the TAU group, the number of possible sessions a patient can attend a week varies depending on the patient's individualized (clinical) treatment plan at ARMS; thus, receiving $5 per session attended (for up to 2 weekly sessions) is appropriate given individual patients' variable session time commitment as part of TAU. Payment for study assessments will take place in the form of a check, which can take between 4 to 8 weeks to process. Payment for UP group and TAU session attendance will be in the form of $5 gift cards to stores that do not sell alcohol or contain a pharmacy (e.g., Dunkin Donuts), which will be provided on an ongoing basis throughout the study.

The following list includes descriptions of each measure being used in the proposed study.

Client Satisfaction Questionnaire (CSQ-8[47]). This 8-item self-report questionnaire will be given to participants in the UP + TAU condition only at the post-treatment assessment to acceptability of and satisfaction with the UP group treatment.

Demographics Questionnaire. This measure assesses age, sex, gender, ethnicity, education, and employment, and will be administered at the screening/baseline visit only.

Beck Scale for Suicide Ideation (BSI[49]). This 19-item self-report measure will be used to measure intensity of attitudes, behaviors, and plans to die by suicide over the past week at pre-, mid-, and post-treatment assessments.

Commitment to Sobriety Scale (CSS[51]). This 5-item, psychometrically valid self-report measure will be used to assess participants' commitment to sobriety at pre-, mid-, and post-treatment time points.

Craving Scale[52]. This self-report measure, which is made up of three items rated on a visual analogue scale from 0-10 and has been validated for use across multiple substances, will be used to assess craving at pre-, mid-, and post-treatment time points.

Emotion Regulation Questionnaire (ERQ[55]). The ERQ is a 10-item self-report measure assessing two emotion regulation strategies—cognitive reappraisal and expressive suppression. It will be used at the three assessment points to capture changes in emotion regulation during the study.

Brief Experiential Avoidance Questionnaire (BEAQ[56]): The 15-item BEAQ is a modified, briefer version of the original 62-item Multidimensional Experiential Avoidance Questionnaire (MEAQ), self-report measure of six experiential avoidance domains: behavioral avoidance, distress aversion, procrastination, distraction/suppression, repression/denial, and distress endurance. It will be used at the three assessment time points to capture changes in experiential avoidance.

Overall Anxiety Severity and Impairment Scale (OASIS[57]). This is a 5-item, self-report measure assessing the anxiety-related severity and impairment in the past week. It will be administered at each of the three assessment points to participants in both conditions. Participants in the UP + TAU condition will also complete it at the start of each UP session, per the treatment protocol[37].

Overall Depression Severity and Impairment Scale (ODSIS[58]). This 5-item, self-report measure captures severity and impairment of depression in the past week. It will be administered at each of the three assessment points to participants in both conditions. Participants in the UP + TAU condition will also complete it at the start of each UP session, per the treatment protocol[37].

Self-Injurious Thoughts and Behaviors Interview-Clinician-Rated Version (SITBI-CR[50]). This clinician-rated measure will be used to capture suicidal thoughts and behaviors and NSSI over lifetime, past year, past month, and past week at the screening/baseline visit.

Self-Injurious Thoughts and Behaviors Interview-Self-Report Version (SITBI-SR[50]). This self-report measure will be used to capture suicidal thoughts and behaviors and NSSI in the past month at the mid-treatment and post-treatment assessments.

Timeline Follow Back (TLFB[53,54]). The TLFB will be administered as an interview at all three time points in order to determine frequency and quantity of substance use, as well as percent days abstinent, since the last assessment (or at pre-treatment, over the past month). For the TLFB, participants mark the days on which they used a substance and indicate which substance(s) (and how much) they used.

Patient Health Questionnaire (PHQ-9[63]): A nine-item measure of depressive symptoms. It will be administered at each of the three assessment points to participants in both conditions.

Generalized Anxiety Disorder Assessment (GAD-7[64]): A 7-item measure of generalized anxiety symptoms. It will be administered at each of the three assessment points to participants in both conditions.

Short Version of the UPPS-P Impulsive Behavioral Scale (SUPPS-P[65]): A 20-item version of the original UPPS-P Impulsive Behavior Scale that assess five distinct facets of impulsivity: negative urgency, sensation seeking, lack of premeditation, lack of perseverance, and positive

urgency. It will be administered at each of the three assessment points to participants in both conditions.

Emotion Reactivity Scale (ERS[66]): A 21-item self-report measure of emotion sensitivity, intensity, and persistence. It will be administered at each of the three assessment points to participants in both conditions.

Drug Use Motives Questionnaire (DUMQ[67, 68]): An adapted version of the original Drug Use Motives Questionnaire; a 17-item measure to assess reasons or motives for using substances. It will be administered at the screening/baseline visit only.

Concomitant Treatment Log: A log that captures overall treatment plan, including therapy and medication, as well as the corresponding start and stop dates for each treatment. A study clinician will complete the log at the screening/baseline visit, and update the log at the mid- and post-treatment assessment visits.

Study clinicians and subjects will complete all measures on paper copies. Data collected will then be entered directly into REDCap by study staff.

Table 1 (below) outlines the schedule of assessments for the study.

Table 1. Schedule of Assessments

Assessment	Screen /Baseline	Week 1	Week 2	Week 3	Week 4 / Mid-treatment	Week 5	Week 6	Week 7	Week 8 / Post-treatment
Informed Consent Form	X								
Demographics/ Contact Info	X								
Inclusion/ Exclusion	X								
Adverse Events Tracking Form					X				X
Concomitant Treatment Log	X				X				X
PHQ-9	X				X				X
GAD-7	X				X				X
SUPPS-P	X				X				X
ERS	X				X				X
DUMQ	X								
SITBI-CR	X								
SITBI-SR					X				X
BSI	X				X				X
CSS	X				X				X
Craving Scale	X				X				X
TLFB	X				X				X
ERQ	X				X				X
BEAQ	X				X				X
OASIS	X	X (UP + TAU only)	X (UP + TAU only)	X (UP + TAU only)	X	X (UP + TAU only)	X (UP + TAU only)	X (UP + TAU only)	X
ODSIS	X	X (UP + TAU only)	X (UP + TAU only)	X (UP + TAU only)	X	X (UP + TAU only)	X (UP + TAU only)	X (UP + TAU only)	X
CSQ-8 and Feedback Interview									X (UP + TAU only)
Approximate Time Estimate	< 60 min	< 5 min	< 5 min	< 5 min	45 to min	< 5 min	< 5 min	< 5 min	45 (TAU) to 60 min (UP+TAU)

Study Intervention

Study Therapists and Training: Masters- or doctoral-level clinicians at ARMS and/or the DCRP will deliver the UP treatment. One to two therapists will (co-)lead each group session. All study therapists will be trained in the protocol by Kate Bentley (co-investigator), who has been extensively trained and certified in delivering the UP by a treatment developer. Study therapists will meet weekly with Dr. McKowen (ARMS Clinical Director) for clinical supervision, or more frequently as needed. A licensed clinician will be on-site at ARMS and available for consultation and risk management as needed whenever a UP group is conducted. Consistent with routine clinical practice at ARMS, should a participant present with clear alcohol or drug intoxication or spontaneously disclose suicidal or homicidal ideation during a UP group session, a study clinician will meet individually with the participant for a clinical risk assessment. If needed, a transfer to the MGH emergency room will be facilitated immediately.

Treatment Fidelity: Recommendations suggested by the NIH Behavior Change Consortium workgroup on treatment fidelity will be implemented. Therapists will be trained on the UP treatment, and adherence to the manual will be monitored. Group sessions will be audio-recorded in order to facilitate supervision and manual adherence. A random selection of audiotapes will be rated for adherence using scales adapted from a previous, large-scale grant-funded UP trial[40]. Study therapists will meet at least monthly to discuss adherence to the protocol, or more frequently as needed.

Description of the UP Treatment

The UP was originally designed as a time-limited, CBT protocol to be delivered in 12 to 16 individual outpatient therapy sessions[37]. Previous studies have demonstrated that the original UP can be successfully modified for administration in other formats (e.g., 12 2-hour weekly outpatient group sessions[60], 5 one-hour individual inpatient sessions[19]). For this study, the UP will be delivered over the course of 16, 1-hour twice-weekly sessions, delivered over an 8-week period, in order to be consistent with the length of existing group treatment session (1 hour) and average group treatment engagement (8 weeks) at ARMS.

Each of the original 8 UP modules (motivation enhancement, functional assessment of emotions, mindful emotion awareness, cognitive flexibility, countering emotion-driven behaviors, interoceptive exposure, emotion exposure, relapse prevention[37]) will be delivered to a small group of up to 10 participants. See Table 2 for weekly session content. One UP group will be running at any point in time within ARMS, Admission will be partially rolling, such that new study participants can enter the group intervention at any point through UP Week 5 (and then, for example, would attend UP Weeks 1-4 after UP Week 8). If a participant beginning the group treatment during UP Week 5 misses one of the two UP Week 5 sessions, they will undergo an individual "catch-up" session before UP Week 6 in order to ensure that they have received all the UP Week 5 material before proceeding to UP Week 6. Participants will not be permitted to begin the group during UP Weeks 6-8 as these sessions (interoceptive and emotion exposure exercises) are contingent upon learning the emotion management skills presented during UP Weeks 1-5. Should a group of five participants be randomized to the UP + TAU condition during UP Weeks 6-8, they will wait up to attend their first UP group session until UP Week 1 begins again (up to

4 weeks). During this waiting period, they will still be encouraged to engage with usual ARMS services. It is also possible that, if there are not currently enough other people enrolled in the study to form a group, participants may be asked to wait to attend the group. In this case, participants may be given the opportunity (but will not be required) to have brief individual meetings with a study clinician until enough participants are enrolled to form a group. When a participant attends their first UP group session, the first few minutes of the session will be spend orienting the new participant to the structure and logistics of the group, as well as delivering a brief introduction to the overall goal of the UP treatment (i.e., modify emotion regulation strategies as a way to help decrease the intensity and frequency of maladaptive emotional experiences with the goal of improving functioning). Homework will be assigned at each session, including worksheets and handouts adapted from the UP client workbook.[38]

See Table 2 below for weekly session content of the UP group.

Table 2. UP Session Content

UP Week #	UP Session #	Point of entry to group?	Session Content
Week 1	Session 1	Yes	*Motivation enhancement (UP Module 1):* -Discuss importance and fluctuation of motivation during treatment -Conduct decisional balance exercise (i.e., identify pros and cons of change, address ambivalence) -Identify goals for treatment in goal-setting exercise
Week 1	Session 2	Yes	*Functional assessment of emotion (UP Module 2):* -Discuss nature and function of emotions -Introduce three-component model of emotion (thoughts, physical sensations, behaviors/ behavioral urges) -Introduce ARC of emotion (antecedents, responses, consequences)
Week 2	Session 3	Yes	*Mindful emotion awareness (UP Module 3):* -Discuss utility of present-focused, nonjudgmental awareness of emotions -Introduce and practice mindful emotion awareness through experiential exercises
Week 2	Session 4	Yes	*Cognitive flexibility (UP Module 4):* -Discuss interactive relationship of thoughts and emotions -Introduce negative automatic thoughts -Practice using cognitive challenging strategies to generate more flexible, balanced interpretations
Week 3	Session 5	Yes	*Countering emotion-driven behaviors (UP Module 5):* -Discuss short-term and long-term consequences of emotion-driven behaviors (EDBs) -Identify common maladaptive EDBs -Present rationale for countering EDBs with alternative actions -Generate examples of adaptive alternative actions
Week 3	Session 6 *(Repeat Session 3)*	Yes	*Mindful emotion awareness (UP Module 3):* -Discuss utility of present-focused, nonjudgmental awareness of emotions -Introduce and practice mindful emotion awareness through experiential exercises
Week 4	Session 7 *(Repeat Session 4)*	Yes	*Cognitive flexibility (UP Module 4):* -Discuss interactive relationship of thoughts and emotions -Introduce negative automatic thoughts -Practice using cognitive challenging strategies to generate more flexible, balanced interpretations
Week 4	Session 8 *(Repeat Session 5)*	Yes	*Countering emotion-driven behaviors (UP Module 5):* -Discuss short-term and long-term consequences of emotion-driven behaviors (EDBs) -Identify common maladaptive EDBs -Present rationale for countering EDBs with alternative actions -Generate examples of adaptive alternative actions
Week 5	Session 9	Yes	*Review of UP Modules 2 and 3:* -Re-introduce concept of functional nature of emotions and three-component model -Re-introduce and practice mindful emotion awareness

Week 5	Session 10	Yes	*Review of UP Modules 4 and 5:* -Re-introduce negative automatic thoughts and generating flexible, balanced interpretations -Re-introduce countering EDBs with adaptive alternative actions
Week 6	Session 11	No	*Interoceptive exposure (UP Module 6):* -Discuss the important role of physical sensations in emotional experience -Present the rationale of improving objective awareness and tolerance of distressing physical sensations -Conduct in-session interoceptive exposure exercises
Week 6	Session 12	No	*Emotion exposure (UP Module 7):* -Present the rationale for conducting emotion exposure exercises (including the natural course of emotion) -Conduct emotion exposure exercise as a group (e.g., imagining an emotional situation, listening to emotion-provoking music, or watching an emotional video while practicing new emotion management skills)
Week 7	Session 13 *(Repeat Session 11)*	No	*Interoceptive exposure (UP Module 6):* -Discuss the important role of physical sensations in emotional experience -Present the rationale of improving objective awareness and tolerance of distressing physical sensations -Conduct interoceptive exposure exercise(s) as a group
Week 7	Session 14 *(Repeat Session 12)*	No	*Emotion exposure (UP Module 7):* -Present the rationale for conducting emotion exposure exercises (including the natural course of emotion) -Conduct emotion exposure exercise as a group (e.g., imagining an emotional situation, listening to emotion-provoking music, or watching an emotional video while practicing new emotion management skills)
Week 8	Session 15	No	*Relapse prevention (UP Module 8):* -Review key treatment concepts and emotion management skills -Identify ongoing opportunities for skills practice -Identify long-term goals
Week 8	Session 16	No	*Relapse prevention (UP Module 8):* -Review key treatment concepts and emotion management skills -Identify ongoing opportunities for skills practice -Identify long-term goals

VI. BIOSTATISTICAL ANALYSIS

Power: The proposed pilot study is the first, necessary step in obtaining preliminary data to justify future larger, randomized trials. Although we will test for statistical significance, the primary aim is to obtain usable feasibility and acceptability data, as well as to estimate the adjunctive intervention's effect size in order to conduct more adequately powered studies in the future. As such, a formal power analysis was not conducted *a priori*; however, the proposed N (50 subjects) is in line with other recent pilot RCTs examining the feasibility and preliminary efficacy of cognitive-behavioral group interventions for young adults[61] and teens[62] with SUD.

Preliminary analyses will describe the participants' demographic and clinical characteristics. Comparisons will be made using Mann-Whitney or chi-square tests to determine if the

randomization provided a balanced sample and if participants who dropped out differ from those who did not. All analyses will be conducted using the SPSS and/or Stata statistical packages.

Specific Aim 1: We will use descriptive statistics to report satisfaction ratings with the UP intervention (total CSQ-8 score; *Hypothesis 1a*) and number of UP sessions attended. We will use chi-square tests to evaluate differences in the proportion of participants in each condition who drop out of treatment at the ARMS program during the study period (*Hypothesis 1b*).

Specific Aim 2: Analyses will be intention-to-treat, such that participants will be analyzed as part of their allocated group irrespective how much treatment was received. Continuous variables (OASIS, ODSIS, BSI, CSS, and Craving Scale scores, frequency of NSSI urges and episodes captured by the SITBI, quantity and frequency of substance use, percent days abstinence [PDA]) will be analyzed with generalized mixed effect modeling, which imputes missing values based on maximum likelihood estimates of missing parameters (*Hypotheses 2a, 2b, 2c, 2d, 2e*). Time-by-condition interactions will be analyzed to test the efficacy of the adjunctive intervention. Known confounding variables (e.g., age, gender) will be included as covariates in these analyses. Effect sizes between the two conditions will also be reported. Although we will test for statistical significance, as previously noted, the primary aim of this pilot study is to estimate the intervention's effect size before conducting larger, more adequately powered future studies.

VII. RISKS AND DISCOMFORTS

There are some potential risks and burdens to participating in the study. Risks and discomforts associated with receiving psychotherapy are generally considered modest, but can include a worsening of psychiatric symptoms as well as psychological discomfort associated with discussion of one's difficulties and potentially emotionally-provoking experiential exercises. For group psychotherapy specifically, participants may also feel uncomfortable sharing personal information in front of others and experience a triggering of distressing thoughts and feelings while listening to others discuss sensitive issues related to substances use and emotional health. Participants will be given telephone numbers of the clinicians involved in the study if they would like to talk about any discomforts and will be able to stop the study intervention at any time without penalty. All group leaders are also skilled in delivering group therapy and navigating group discussion of sensitive topics. Second, answering detailed questionnaires and undergoing clinician interviews regarding substance use and psychological problems may create a mild degree of discomfort. For the possibility of subjective discomfort from answering questions, distress will be minimized by assurance that participants can refuse to answer any question that they do not feel comfortable addressing and may withdraw from the study at any time without penalty. Further, study clinicians are skilled in talking about sensitive information with subjects, and subjects may decide to end an interview at any time. Third, coming in for UP group sessions and/or assessments may be seen as time-consuming and inconvenient. For study visits involving assessments and not treatment, we have provided compensation for subjects' time, commensurate with hourly compensation for non-treatment studies being conducted at MGH. We have also provided compensation for up to two weekly treatment sessions, commensurate with the approximate costs of travel.

Breach of confidentiality is possible, though highly unlikely because all information will be identified with a numeric code only and stored in a locked file cabinet or on encrypted computerized databases. An enrollment database linking names and study identification numbers will be kept in a secure folder separate from other subject data sources. Only study staff will have access to this database. All staff are or will be fully trained in relevant ethical principles and procedures, including confidentiality. All assessment and treatment procedures will be supervised by the PI. Audiotapes will be erased upon completion of data analysis. We will ask all UP group participants to keep the information that others share during the groups confidential.

Subjects will be informed of all of the aforementioned risks during the consent process.

VIII. POTENTIAL BENEFITS

It is possible that the participants may not receive any direct benefit from participation in the study. However, it is hoped that the experimental intervention could provide relief from substance use related problems, emotional disturbances, and improve the level of functioning exhibited in young adults with SUD and co-occurring emotional distress.

Subjects participating in this study may experience individual benefits from receiving the adjunctive group intervention. The intervention, which will be conducted by a master's or doctoral-level clinician, will be provided to the participants at no charge. Participants will make $100 for completion of the three assessments and up to an additional $80 for session attendance. If patients do not complete the full screening visit due to ineligibility, compensation will not be provided as it is anticipated that inclusion/exclusion criteria will be determined within the first 15 minutes of the visit; in addition, every effort will be made to conduct the screening visit immediately following the subject's routine ARMS evaluation feedback or treatment recommendations sessions so that the subject need not travel back to MGH for a separate screening visit. Participants will not be compensated for treatment sessions.

Benefits to future patients, researchers and clinicians could include the development of more effective and efficient treatment for substance use-related problems and emotional distress experienced by young adults.

IX. MONITORING AND QUALITY ASSURANCE

Safety Monitoring: Participants' suicidality and homicidality will be assessed by a study clinician for degree of immediate risk (plan of harm, intent to harm, means to harm) at each assessment visit. If a participant is determined to be at imminent risk of harm, a transfer to the MGH emergency room will be facilitated immediately for further evaluation. If additional treatment is warranted (e.g., inpatient hospitalization), the PI will assess the appropriateness of the participant's continuation in the study based on the exclusion criteria and clinical well-being of the individual. The PI will continue to monitor the mental status of participants and/or discontinue participation in the study if appropriate. Participants will be dropped from the study for unstable mental health rendering them inappropriate to be treated in an outpatient setting (e.g., new onset SI/HI with intent and/or plan) and/or severe noncompliance with study procedures.

Continued drug use and alcohol consumption is to be expected to some degree with outpatient treatment, including at ARMS specifically. This will be monitored throughout the treatment period. If a participant presents with acute alcohol or drug intoxication to a study assessment visit or UP group session and is determined (by a study clinician) to require emergency services, a transfer to the MGH emergency room will be facilitated immediately. Participants' involvement in the study will not be disclosed to emergency services.

General safeguards consistent with good clinical practice will be in place for all subjects enrolled in the study. As part of routine clinical care at ARMS, all subjects will have an ARMS clinician contact who they can access by pager 24 hours a day, 7 days per week for emergencies. During the informed consent process and as needed throughout the study, subjects will be encouraged to page their ARMS clinician contact in the event of a crisis. As part of the MGH, all research subjects can access the Acute Psychiatry Service in the emergency room at any time of the day or night. The PI will be responsible for monitoring the safety of the study and complying with the reporting requirements. Continuous, close monitoring of participant safety will include prompt and frequent reporting of safety data (i.e., adverse/serious adverse events) to the MGH IRB and/or appropriate study staff with oversight responsibility. Serious adverse events (SAEs) will be reported to the Data Safety and Monitoring Board (DSMB) members. SAEs will also be reviewed by the PI every 6 months during progress reports as well as during the written report required by the IRB as part of the annual IRB renewal process.

Data Safety and Monitoring Board (DSMB): A DSMB will be assembled prior to the start of the study. This will consist of three independent staff-level investigators; one will have expertise in clinical interventions with individuals with SUD; the second will have expertise in clinical trial design; the third will have expertise in biostatistical analysis. The DSMB will meet every six months during the study to review progress, address any difficulties with recruitment, and address any safety related matters that may arise. The DSMB will be provided with unblinded data from the study so as to determine whether that risk to subjects outweighs the potential benefits. If at any time during the course of the study, the DSMB judges that risk to subjects outweighs the potential benefits, the DSMB shall have the discretion and responsibility to recommend that the study be terminated. In addition to the IRB, all DSMB members will be informed of any serious adverse events occurring during the study.

Adverse Event Reporting: Consistent with good clinical practice, safety will be closely monitored by study staff. The PI will oversee all study activities including self-report and clinician ratings. All procedures have been designed to minimize subject discomfort, and no subject will be asked to engage in research procedures not outlined in the consent form. Subjects will be monitored for adverse events at each assessment visit by a study clinician. All adverse events (including unexpected and serious AEs) will be recorded and reported in accordance with Partners HealthCare guidelines. A subject may be dropped from the study at any time due to adverse events. We will follow and adhere to all guidelines as defined and outlined on the Partners Human Research Committee web site: http://healthcare.partners.org/phsirb/adverse.htm.The PI will be responsible for ensuring that adverse events are reported to the local IRB in compliance with local and federal requirements. Any changes to the protocol will be made in accordance with MGH IRB policies.

Data Monitoring: The PI will be responsible for ongoing quality control, including data integrity and protocol compliance. All clinician-rated data will be collected on paper and entered into Redcap. All self-report data that is collected on paper will be entered into Redcap. If a participant is unable to complete self-report measures in person, the data will be entered directly into Redcap remotely by the participant. To ensure usability of self-report data, a member of study staff (whoever is conducting the assessment) will review all self-report measures within one week of submission to insure their completeness. All self-report assessment forms and clinician-administered instruments will be reviewed by study staff within one week of their completion to assure that they are being completed correctly. Any errors in completion will be reviewed to determine if directions or procedures for the assessments need to be altered. In this case, permission from the IRB will be requested to change any procedure. The group sessions will also be audiotaped (with subjects' permission) and a random selection will be rated for competence and adherence to the protocol. This will also ensure the usability of the data.

Confidentiality:

Sources of materials. Research material will be obtained from living human subjects. Data will be collected directly from participants using self-report questionnaires and clinician interviews measuring demographic variables, psychiatric symptoms, and history and current pattern of alcohol and other drug use. Diagnostic status and other information on mental and physical health conditions will be obtained from the routine ARMS clinical evaluation for the purpose of confirming inclusion/exclusion criteria. As noted in the study exclusion criteria, participants will also be required to provide consent for study staff to access the participant's medical records and exchange data with ARMS staff in order to track treatment engagement at ARMS and facilitate good clinical care.

Linkages and access to identifying information. All research-related records initiated as a result of a subject's participation in this study that reveal the subject's identity, will remain confidential except as may be required by law. Participant names and contact information will be maintained in a recruitment/enrollment database during the course of the study. Once individuals enroll in the study, names will be linked to study ID number in this database, which will be kept in a restricted access folder on a secure server. Signed consent forms will be kept in a locked file cabinet, separate from any other study data. Once data collection is completed, the corresponding recruitment/enrollment database will be deleted as it will then be unnecessary to maintain the link between participant identity and study data. Subjects will only be contacted regarding future studies if they indicate that they are interested in being contacted by initialing in the specific section of the consent form.

De-identified data. Research data collected from this study will not identify the subjects individually, and will be linked to an ID number. Data obtained from our studies may be published, but published data will not identify individual participants. Original research-related records may be reviewed by the Partners Human Research Committee, and regulatory authorities for the purpose of verifying clinical trial procedures and/or data. De-identified study data will be kept either in a restricted access folder on a secure server or in a locked file cabinet. All information collected as part of this study will be accessible only to research staff who have completed mandatory training in the protection of human subjects.

X. REFERENCES

1. Bergman, B. G., Kelly, J. F., Nargiso, J. E., & McKowen, J. W. (2016). "The age of feeling in-between": Addressing challenges in the treatment of emerging adults with substance use disorders. *Cognitive and Behavioral Practice, 23*(3), 270-288.
2. Substance Abuse and Mental Health Services Administration (2014a). *Results from the 2013 National Survey on Drug Use and Health: Summary of National Findings*. NSDUH Series H-48, HHS Publication No. (SMA) 14–4863 Rockville, MD: Substance Abuse and Mental Health Services Administration.
3. Gore F. M., Bloem P. J. N., Patton G. C., Ferguson J., Joseph, V., Coffey, C., & Mathers, C. D. (2011). Global burden of disease in young people aged 10–24 years: A systematic analysis. *The Lancet*, *377*(9783), 2093-2102.
4. Rehm, J., Dawson, D., Frick, U., Gmel, G., Roerecke, M., Shield, K. D., & Grant, B. (2014). Burden of disease associated with alcohol use disorders in the United States. *Alcoholism: Clinical and Experimental Research, 38*(4), 1068–1077.
5. Substance Abuse and Mental Health Services Administration (2014b). *Treatment Episode Data Set (TEDS). 2002–2012. National Admissions to Substance Abuse Treatment Services*. BHSIS Series: S-71, HHS Publication No. (SMA) 14–4850 Rockville, MD: Substance Abuse and Mental Health Services Administration.
6. Substance Abuse and Mental Health Services Administration (2016). SAMHSA's National Registry of Evidence-Based Programs and Practices. Retrieved from http://www.nrepp.samhsa.gov/01_landing.aspx
7. Grant, B. F., Goldstein, R. B., Saha, T. D., Chou, P., Jung, J., Zhang, H., … Hasin, D. S. (2015). Epidemiology of DSM-5 alcohol use disorder: Results from the national epidemiologic survey on alcohol and related conditions III. *JAMA Psychiatry, 72*(8), 757-766.
8. Grant, B. F., Saha, T. D., Ruan, W. J., Goldstein, R. B., Chou, S. P., Jung, J., … Hasin, D. S. (2016). Epidemiology of DSM-5 drug use disorder: Results from the national epidemiologic survey on alcohol and related conditions III. *JAMA Psychiatry, 73*(1), 39-47.
9. Kessler, R. C., Avenevoli, S., McLaughlin, K. A., Green, J. G., Lakoma, M. D., Petukhova, M., … Merikangas, K. R. (2012). Lifetime comorbidity of DSM-IV disorders in the NCS-R Adolescent Supplement (NCS-A). *Psychological Medicine, 42*(9), 1997-2010.
10. Centers for Disease Control and Prevention. (2014). Web-based Injury Statistics Query and Reporting System (WISQARS) [online]. Retrieved from http://www.cdc.gov/injury/wisqars/leadingcauses.html
11. Swannell, S. V., Martin, G. E., Page, A., Hasking, P., & St. John, N. J. (2014). Prevalence of nonsuicidal self-injury in nonclinical samples: Systematic review, meta-analysis and meta-regression. *Suicide and Life-Threatening Behavior, 44*(3), 273–303.
12. Brausch, A. M., & Boone, S. D. (2015). Frequency of nonsuicidal self-injury in adolescents: Differences in suicide attempts, substance use, and disordered eating. *Suicide and Life-Threatening Behavior, 45*(5), 612-623.
13. Nock, M. K., Joiner, T. E., Gordon, K. H., Lloyd-Richardson, E., & Prinstein, M. J. (2006). Nonsuicidal self-injury among adolescents: Diagnostic correlates and relation to suicide attempts. *Psychiatry Research, 144,* 65-72.
14. Nock, M. K., Hwang, I., Sampson, N. A., & Kessler, R. C. (2010). Mental disorders,

comorbidity and suicidal behavior: Results from the National Comorbidity Survey Replication. *Molecular Psychiatry, 15,* 868-876.
15. Bogenschutz, M. P., Rice, S. L., Tonigan, J. S., Vogel, H. S., Nowinski, J., Hume, D., & Arenella, P. B. (2014). 12-step facilitation for the dually diagnosed: A randomized clinical trial. *Journal of Substance Abuse Treatment, 46*(4), 403–411.
16. McHugh, R. K. (2015). Treatment of co-occurring anxiety disorders and substance use disorders. *Harvard Review of Psychiatry, 23*(2), 99-111.
17. Barlow, D. H., Sauer-Zavala, S., Carl, J. R., Bullis, J. R., & Ellard, K. K. (2014). The nature, diagnosis, and treatment of neuroticism back to the future. *Clinical Psychological Science, 2*(3), 344-365.
18. Wegner, D. M., Schneider, D. J., Carter, S. R., & White, T. L. (1987). Paradoxical effects of thought suppression. *Journal of Personality and Social Psychology, 53*(1), 5-13.
19. Bentley, K. H., Sauer-Zavala, S., Cassiello-Robbins, C., Conklin, L. R., & Homer, D. (in press). Treating suicidal thoughts and behaviors within an emotional disorders framework: Acceptability and feasibility of the Unified Protocol in an inpatient setting. *Behavior Modification.*
20. Tanji, F., Kakizaki, M., Sugawara, Y., Watanabe, I., Nakaya, N., Minami, Y., Fukao, A., & Tsuji, I. (2014). Personality and suicide risk: The impact of economic crisis in Japan. *Psychological Medicine*, 45(03), 559-573.
21. Wedig, M. M., Silverman, M. H., Frankenburg, F. R., Bradford Reich, D., Fitzmaurice, G., & Zanarini, M. C. (2012). Predictors of suicide attempts in patients with borderline personality disorder over 16 years of prospective follow-up. *Psychological Medicine*, *42*, 2395-2404.
22. Joiner, T. E. (2005). *Why people die by suicide*. Cambridge, MA: Harvard University Press.
23. Shneidman, E. S. (1993). Suicide as psychache. *Journal of Nervous and Mental Disease*, 181, 147-149.
24. Nock, M. K., & Prinstein, M. J. (2004). A functional approach to the assessment of self-mutilative behavior. *Journal of Consulting and Clinical Psychology, 72*, 885–890.
25. Bentley, K. H., Nock, M. K., & Barlow, D. H. (2014). The four-function model of nonsuicidal self-injury: Key directions for future research. *Clinical Psychological Science, 2*(5), 638-656.
26. Wilcox, C. E., Pommy, J. M., & Adinoff, B. (2016). Neural circuitry of impaired *emotion* regulation in substance use disorders. *American Journal of Psychiatry, 173*(4), 344-361.
27. Petit, G., Luminet, O., Maurage, F., Tecco, J., Lechantre, S., Ferauge, M., ... & Timary, P. (2015). Emotion regulation in alcohol dependence. *Alcoholism: Clinical and Experimental Research, 39*(12), 2471-2479.
28. Jackson, K.M., & Sher, K.J. (2003). Alcohol use disorders and psychological distress: A prospective state-trait analysis. *Journal of Abnormal Psychology, 112*(4), 599-613.
29. Martin, C. S., Lynch, K. G., Pollock, N. K., & Clark, D. B. (2000). Gender differences and similarities in the personality correlates of adolescent alcohol problems. *Psychology of Addictive Behaviors, 14*(2), 121.
30. Berking, M., Margraf, M., Ebert, D., Wupperman, P., Hoffman, S. G., & Junghanns, K. (2011). Deficits in emotion-regulation skills predict alcohol use during and after cognitive-behavioral therapy for alcohol dependence. *Journal of Consulting and Clinical Psychology, 79*, 307-318.
31. Charney, D. A., Zikos, E., & Gill, K. J. (2010). Early recovery from alcohol dependence: Factors that promote or impede abstinence. *Journal of Substance Abuse Treatment, 38,* 42-

50.
32. Thompson, R. A. (1994). Emotion regulation: A theme in search of definition. *Monographs of the Society for Research in Child Development, 59,* 25-52.
33. Baker, T. B., Piper, M. E., McCarthy, D. E., Majeskie, M. R., & Fiore, M. C. (2004). Addiction motivation reformulated: An affective processing model of negative reinforcement. *Psychology Review, 111*(1), 33-51.
34. Buckner, J. D., Zvolensky, M. J., Crosby, R. D., Wonderlich, S. A., Ecker, A. H., & Richter, A. (2016). Antecedents and consequences of cannabis use among racially diverse cannabis users: An analysis from ecological momentary assessment. *Drug and Alcohol Dependence, 147,* 20-25.
35. Aldao, A., Nolen-Hoeksema, S., & Schweizer, S. (2010). Emotion-regulation strategies across psychopathology: A meta-analytic review. *Clinical Psychology Review, 30,* 217-237.
36. Blevins, C. E., Abrantes, A. M., & Stephens, R. S. (2016). Motivational pathways from antecedents of alcohol use to consequences: A structural model of using alcohol to cope with negative affect. *The American Journal of Drug and Alcohol Abuse, 42*(4), 295-403.
37. Barlow, D. H., Farchione, T. J., Fairholme, C. P., Ellard, K. K., Boisseau, C. L., Allen, L. B., & Ehrenreich-May, J. (2011). *The unified protocol for transdiagnostic treatment of emotional disorders: Therapist guide*. New York: Oxford University Press.
38. Barlow, D. H., Ellard, K. K., Fairholme, C. P., Farchione, T. J., Boisseau, C. L., Allen, L. B., & Ehrenreich-May, J. (2011). *The unified protocol for transdiagnostic treatment of emotional disorders: Client workbook*. New York: Oxford University Press.
39. Farchione, T. J., Ellard, K. K., Boisseau, C. L., Thompson-Hollands, J., Carl, J. R., Gallagher, M. W., & Barlow, D. H. (2012). Unified Protocol for Transdiagnostic Treatment of Emotional Disorders: A randomized controlled trial. *Behavior Therapy, 43,* 666-678.
40. Barlow, D. H., Farchione, T. J., Bullis, J. R., Gallagher, M. W., Murray-Latin, H., Sauer-Zavala, S. E., … & Cassiello, C. Equivalence evaluation of the Unified Protocol for Transdiagnostic Treatment of Emotional Disorders compared to diagnosis-specific CBT for anxiety disorders. Manuscript under review.
41. Boswell, J. F., Anderson, L. M., & Barlow, D. H. (2014). An idiographic analysis of change processes in the unified transdiagnostic treatment of depression. *Journal of Consulting and Clinical Psychology, 82,* 1060-1071. http://dx.doi.org/10.1037/a0037403
42. Ellard, K. K., Deckersbach, T., Sylvia, L. G., Nierenberg, A. A., & Barlow, D. H. (2012). Transdignostic treatment of bipolar disorder and comorbid anxiety with the Unified Protocol: A clinical replication series. *Behavior Modification, 36*(4), 482-508. doi:10.1177/0145445512451272
43. Gallagher, M. W. (in press). *Application of the Unified Protocol for Transdiagnostic Treatment of Emotional Disorders to posttraumatic stress disorder*. In T. J. Farchione & D. H. Barlow (Eds.), Applications of the Unified Protocol for Transdiagnostic Treatment of Emotional Disorders. New York: Oxford University Press.
44. Sauer-Zavala, S. E., Bentley, K. H., & Wilner, J. G. (2015). Transdiagnostic treatment of borderline personality disorder and comorbid disorders: A clinical replication series. *Journal of Personality Disorders, 29,* 179.
45. Bentley, K. H., Nock, M. K., Sauer-Zavala, S., Gorman, B., & Barlow, D. H. (2017). A functional analysis of two transdiagnostic, emotion-focused interventions on nonsuicidal self-injury. *Journal of Consulting and Clinical Psychology, 85*(6), 632-646.
46. Ciraulo, D. A., Barlow, D. H., Gulliver, S. B., Farchione, T. J., Morisette, S. B., Kamholz, B.

W., … Knapp, C. M. (2013). The effects of venlafaxine and cognitive behavioral alone and combined in the treatment of co-morbid alcohol use-anxiety disorders. *Behaviour Research and Therapy, 51,* 729-735.
47. Larsen, D. L., Attkisson, C. C., Hargreaves, W. A., and Nguyen, T. D. (1979). Assessment of client/patient satisfaction: Development of a general scale. *Evaluation and Program Planning, 2*, 197-207.
48. Lovibond, P.F., & Lovibond, S.H. (1995). The structure of negative emotional states: Comparison of the Depression Anxiety Stress Scales (DASS) with the Beck Depression and Anxiety Inventories. *Behaviour Research and Therapy, 33*, 335-343.
49. Beck, A. T., & Steer, R. A. (1991). *Manual for the Beck Scale for Suicide Ideation*. San Antonio, TX: Psychological Corporation.
50. Nock, M. K., Holmberg, E. B., Photos, V. I., & Michel, B. D. (2007). Self-Injurious Thoughts and Behaviors Interview: Development, reliability, and validity in an adolescent sample. *Psychological Assessment, 19*(3), 309-317.
51. Kelly, J. F., & Greene, M. C. (2014). Beyond motivation: Initial validation of the Commitment to Sobriety Scale. *Journal of Substance Abuse Treatment, 46*(2), 257-263.
52. Weiss, R. D., Griffin, M. L., & Hufford, C. (1995). Craving in hospitalized cocaine abusers as a predictor of outcome. *American Journal of Drug and Alcohol Abuse, 21,* 289-301.
53. Sobell, L. C., & Sobell, M. B. (1992). Timeline follow-back: A technique for assessing self-reported alcohol consumption. In R. Z. Litton & J. P. Allen (Eds.). *Measuring alcohol consumption: Psychosocial and biochemical methods* (pp. 41-72). Totowa, NJ: Humana Press.
54. Robinson, S. M., Sobell, L. C., Sobell, M. B., & Leo, G. I. (2014). Reliability of the Timeline Followback for cocaine, cannabis, and cigarette use. *Psychology of Addictive Behaviors, 28*(1), 154-162.
55. Gross, J.J., & John, O.P. (2003). Individual differences in two emotion regulation processes: Implications for affect, relationships, and well-being. Journal of Personality and Social Psychology, 85, 348-362.
56. Gamez, W., Chmielewski, M., Kotov, R., Ruggero, C., Suzuki, N., & Watson, D. (2014). The brief experiential avoidance questionnaire: Development and initial validation. Psychological Assessment, 26(1), 35-45.
57. Campbell-Sills, L., Norman, S. B., Craske, M. G., Sullivan, G., Lang, A. L., Chavira, D.A., … Stein, M. B. (2009). Validation of a brief measure of anxiety-related severity and impairment: The Overall Anxiety Severity and Impairment Scale (OASIS). *Journal of Affective Disorders, 112*, 92–101. doi:10.1016/j.jad.2008.03.014
58. Bentley, K. H., Gallagher, M. W., Carl, J. R., & Barlow, D. H. (2014). Development and validation of the Overall Depression Severity and Impairment Scale. *Psychological Assessment, 26*(3), 815-830.
60. Bullis, J. R., Sauer-Zavala, S., Bentley, K. H., Thompson-Hollands, J., Carl, J. R., & Barlow, D. H. (2015). The Unified Protocol for Transdiagnostic Treatment of Emotional Disorders: Preliminary exploration of effectiveness for group delivery. *Behavior Modification, 39*(2), 295-321.
61. Davis, J. M., Mills, D. M., Stankevitz, K. A., Manley, A. R., Majeskie, M. R., & Smith, S. S. (2013). Pilot randomized trial on mindfulness training for smokers in young adult binge drinkers. *BMC Complementary and Alternative Medicine, 3*(13), 215.
62. Esposito-Smythers, C., Hadley, W., Curby, T. W., & Brown, L. K. (2017). Randomized pilot

trial of a cognitive-behavioral alcohol, self-harm, and HIV prevention program for teens in mental health treatment. *Behaviour Research and Therapy, 89,* 49-56.
63. Kroenke, K., Spitzer, R. L., & Williams, J. B. (2001). The PHQ-9: Validity of a brief depression severity measure. Journal of General Internal Medicine, 16(9), 606-613.
64. Spitzer, R. L., Kroenke, K., Williams, J. B., & Lowe, B. (2006). A brief measure for assessing generalized anxiety disorder: The GAD-7. *Archives of Internal Medicine, 166*(10), 1092-1097.
65. Cyders, M. A., Littlefield, A. K., Coffey, S., & Karyadi, K. A. (2014). Examination of a Short Version of the UPPS-P Impulsive Behavior Scale. *Addictive Behaviors*, *39*(9), 1372–1376.
66. Nock, M. K., Wedig, M. M., Holmberg, E. B., & Hooley, J. M. (2008). The emotion reactivity scale: Development, evaluation, and relation to self-injurious thoughts and behaviors. *Behavior Therapy, 39*(2), 107-116.
67. Thornton, L. K., Baker, A. L., Lewin, T. J., Kay-Lambkin, F. J., Kavanagh, D., Richmond, R., … Johnson, M. P. (2012). Reasons for substance use among people with mental disorders. Addictive Behaviors, 37(4), 427–434. https://doi.org/10.1016/j.addbeh.2011.11.039
68. Thornton, L. K., Baker, A. L., Johnson, M. P., Kay-Lambkin, F., & Lewin, T. J. (2012). Reasons for substance use among people with psychotic disorders: Method triangulation approach. Psychology of Addictive Behaviors, 26(2), 279-288.