Study Title: Combined Smoking Cessation and Cognitive Processing Therapy for PTSD

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Protocol and Statistical Analysis Plan, 1/9/2017

Title: Combined Smoking Cessation and Cognitive Processing Therapy for PTSD

Background: The present study seeks to gather data to determine the efficacy of a smoking cessation intervention implemented as part of individual cognitive processing therapy (CPT) for the treatment of posttraumatic stress disorder (PTSD). CPT is based on a social cognitive theory of PTSD that includes primary emotional responses to traumatic events such as fear, anger, and sadness, as well as secondary emotions resulting from a patient's faulty interpretations of the traumatic event. CPT addresses PTSD by facilitating affective expression so that affective components of the trauma memory can be altered. In addition, faulty beliefs about the trauma are challenged and modified using Socratic questioning.

A number of studies of CPT have provided empirical supported of its efficacy in reducing PTSD symptoms (Monson, et al., 2006). Consequently, recent VA guidelines mandating that patients have access to empirically supported treatments have led to CPT being broadly implemented within the VA system. The original CPT protocol devoted a portion of the intervention to patients writing descriptions of their traumatic events to be read both during and outside treatment sessions. An alternative version of the protocol removes the written trauma accounts while retaining the cognitive processing component (Cognitive Processing Therapy – Cognitive version; CPT-C). A recent dismantling study comparing the original CPT protocol to the CPT-C found that the CPT-C was equally effective in reducing PTSD symptoms, and the reduction of PTSD symptoms occurred by the end of session six (Resick, et al., 2008). Individual CPT for PTSD typically consists of 12 sessions that each last 50 minutes. Research suggests that the 12 session protocol is feasible and has a relatively low dropout rate (Resick, et al., 2008). In a personal communication with Dr. Patricia Resick, co-developer of CPT, she suggested that the study utilize the 12-session CPT-C protocol. Based on this suggestion, and because the 12-session protocol is most often used by clinicians in the VA system and is evidence-based, we plan to utilize the 12-session CPT-C protocol.

In addition to the symptoms of PTSD, several problems are frequently comorbid with PTSD. Among these, one prominent problem associated with significant medical morbidity is cigarette smoking. Many veterans with PTSD smoke cigarettes. Epidemiological data indicate that 45% of those with PTSD smoke cigarettes (Lasser, et al., 2000). Although smoking is prevalent in veterans with PTSD, many report interest in quitting smoking, with one recent study indicating that, at the time of assessment, 50% of smokers were contemplating quitting smoking and another 21% were preparing to make a quit attempt (Kirby, et al., 2008). Approaches to improving care and access to care for smokers with PTSD may be particularly useful considering the tendency for psychiatric groups to be socially isolated (Schroeder, 2008) and undertreated for smoking cessation (Prochaska & Velicer, 2004). By integrating smoking cessation interventions with mental health treatment, a greater proportion of those with psychiatric illness will receive treatment and quit smoking. In addition, research suggests that PTSD symptoms are related to smoking behavior (Beckham, et al., 2005).

Despite this connection, interventions seeking to assist people with PTSD in smoking cessation have not traditionally targeted PTSD symptom reduction. Integration of smoking cessation with PTSD treatment could reduce symptoms and provide patients with strategies for managing symptoms without using cigarettes.

In order to adequately examine the unique effects of CPT-C combined with integrated smoking cessation care, we will utilize a randomized controlled trial design. Both interventions will employ extensive smoking cessation treatment, including counseling, pharmacotherapy, and text messaging (described below) to assist in the quit attempt. One group will be randomized to receive CPT-C alongside the smoking cessation intervention. The other group will be offered to have 12 sessions of CPC-C post participation in the active smoking cessation portion of the study.

Objectives:

The primary aim of the proposed study is to evaluate the integration of CPT-C and smoking cessation treatment in an individual 12-session PTSD protocol as compared to a protocol including the same smoking cessation treatment for individuals with PTSD, but without CPT-C. This intervention will be evaluated with the following hypotheses:

1) Compared to the smoking cessation alone protocol, the smoking cessation + concurrent CPT-C protocol will result in reduced frequency and intensity of PTSD symptoms.

2) Compared to the smoking cessation alone protocol, the smoking cessation + concurrent CPT-C protocol will result in reduced depressive symptoms.

3) The smoking cessation + concurrent CPT-C protocol will result in decreased smoking rates, relative to published data on VA smoking cessation usual care.

4) Greater PTSD symptom reduction during the smoking cessation + concurrent CPT-C treatment will result in longer duration to smoking lapse and relapse.

5) Exploratory research question: Will use of automated text messaging as an adjunct to smoking cessation be feasible, and will it impact quit rates?

Methods:

Recruitment

Participants will be recruited from among outpatients at the Durham VAMC clinics, including OEF/OIF/OND program, Access Clinic, Women's Health Clinic, Primary Health Care and PTSD Clinics. Participants will be recruited through IRB approved flyers, brochures, and letters advertising a study on PTSD and smoking cessation posted in the VA Medical Center. We will place IRB-approved recruitment materials in the community in places such as grocery stores, restaurants, etc. We will also advertise via the closed

circuit television system within the VA Medical Center and in local newspapers and online classified services such as www.craigslist.com. Also, upon approval from the Public Affairs officer, we will host informational tables in the medical center. At these informational tables, IRB-approved recruitment materials from the study (and from other studies run in the Traumatic Stress and Health Research Laboratory) will be made available to interested veterans, and study staff members may be on site to answer questions about the research studies. Study information may also be posted on the Durham VA's Facebook page with approval by the VA Public Affairs Officer. No participants will be consented or screened at these public locations.

In conversations with clinicians from several clinics in DVAMC, we have been provided the feedback that they strongly prefer to provide potential participants' names and contact information. Clinicians have reported that they Veterans often indicate that they prefer that their names and contact information be provided directly to study staff. We'd like to make it easy for interested Veterans to get involved in research, while protected the privacy of those Veterans who are not interested in research. Towards that end, we have developed a system whereby clinicians can more directly identify potentially eligible participants. We will ask that the clinician or provider provide basic information about the study to potentially eligible Veterans; clinicians will be provided IRB-approved recruitment materials to assist this patient education. If the Veteran is interested in learning more about participation, the clinician or provider will provide a "Contact Me" information sheet to the Veteran for him/her to complete. We will request that all "Contact Me" sheets will be completed by the Veteran, not by the provider. The information sheet includes options for contact by the study staff (e.g., send me information, call me, send me information and call me). If any Veteran prefers to receive information by mail, he/she will be sent the IRB-approved recruitment letter. Any Veteran who prefers to receive information by phone will be contacted using the IRB-approved telephone script. This information sheet will provide "…written documentation that the subject is willing to be contacted by telephone about the study," as outlined in VHA Handbook 1200.5. "Contact Me" sheets will be delivered to study staff members via secured means (e.g., internal VA snail mail, encrypted Outlook emails with pdf attachments, personal delivery). Any sheets sent via internal VA mail will be placed inside a sealed and addressed envelope that is THEN put into the snail mail envelope. This plan has been reviewed with local privacy and information security officers.

We will also recruit veterans from the Traumatic Stress and Health Laboratory's "Contact Database," IRB #1080; this database contains information about previous lab study participants who have agreed to be contacted about other studies for which they may qualify. A list of potential veteran participants for receipt of recruitment letters will be obtained by using the VA's Fileman system to produce a list of veteran smokers with PTSD. In addition, we will obtain a list of potentially eligible participants from the VISN 6 Mental Illness Research, Education, and Clinical Center (MIRECC) Post-Deployment Mental Health Data Repository (IRB# 01706). Application to recruit from the Re-Contact

Database of the VISN 6 MIRECC Post-Deployment Mental Health Data Repository will be made to the VISN 6 MIRECC Director (Dr. John Fairbank) in accordance with IRB and R&D approved data repository procedures.

As recommended by Dillman, Smith, and Christian (Dillman, Smyth, & Christian, 2009), we will recruit participants by sending a series of four letters to those veterans who are smokers with PTSD who are registered at the Durham VA Medical Center. Based on social exchange theory, Dillman and colleagues recommend that the second letter be sent with a small token of appreciation. This token incentive serves two functions – it will encourage respondents to respond based on the principles of social exchange theory, and more importantly, it will bring additional attention to the request for participation so that it will be more readily considered. As recommended, letter two will be sent with a small selection (i.e., monetary value less than $2) of commemorative stamps. After participants have received the second letter describing the study in detail, a study coordinator may contact them about participation. This information is included in letter 2. Only veterans who are identified via the VA's Fileman system or the MIRECC repository will be sent letters described above. Study staff members will perform random spot-checks of names and addresses on 50% of all letters prior to mailing. This will capture any sorting error that may have occurred during the preparatory procedures. Any person who contacts the study coordinator for more information about the study (whether it be through flyers, word of mouth, etc.) will be informed about the study using the IRB-approved telephone screen script. Participants who drop out will receive partial reimbursement for the time they donate. Participants will be paid up to $545 for their complete participation. Study costs will be paid using funds from Dr. Dedert's Clinical Sciences Research & Development (CSR&D) Career Development Award. Screening is completed following the endorsement of informed consent and HIPAA form by the participant.

Population

The proposed study will recruit seventy male and female veterans ages 18 to 75 for participation in the CPT-C and smoking cessation treatment. Based on data from other similar clinical trials run in the Traumatic Stress and Health Research Laboratory, we estimate that we will need to recruit 120 participants in order to reach an enrollment goal of at least fifty participants.

Participants will be screened for good health by the study physician. If any participant indicates a medical problem that is a possible contraindication to nicotine replacement therapy (NRT), medical clearance to participate in the study will be obtained from their primary care provider and/or other treating physician (e.g. psychiatrist). If the request is denied or not returned, potential participants will be excluded from the study. We are seeking medical clearance rather than excluding participants based on self-report to ensure that we are not prematurely ruling out participants who may be eligible. We are consulting with their primary physician to determine if the use of NRT is appropriate and safe given their current physical status and medication regimen. This medical consult is

a way to further protect the participant and also give them an opportunity to take part in the study if their physician deems it appropriate and safe. At the initial screening, any participant with a primary care physician and/or psychiatrist external to VA will be asked to sign a release of information allowing us to contact a primary care physician or other treating physician (including psychiatrist when applicable) regarding participation in the study. In the screening session, if a participant indicates a medical problem that is a contraindication to NRT or bupropion, as determined by the study physician, we will contact the physician(s) identified in the signed releases of information. Physician(s) external to VA will be contacted by fax using an approved cover sheet and an IRB—approved physician letter. If the physician identified in the release of information is a physician located on site at the Durham VA Medical Center, we will contact the physician via email (as is consistent with existing privacy policies at the medical center). Physicians will be asked to email or fax back their approval of participation to a fax machine located in Dr. Beckham's research laboratory. Only members of the research staff listed on the staff listing for this protocol have access to this fax machine. If the request is not returned within two weeks, the study physician will determine eligibility.

Any participant who will not be stable on their medications for the study period, has a history of myocardial infarction in the past 6 months, has a contraindication to NRT and is unable to get medical clearance from their primary care provider will be excluded. If potential participants use any other forms of nicotine such as cigars, pipes, or chewing tobacco, they will be excluded from participation. For safety and informed consent reasons, fluent conversational English will be required of all participants. Adolescent smoking is a phenomenon worth investigating but given both ethical and feasibility issues, we will not include children or adolescents under age 18 in this study.

Summary of Inclusion Exclusion Criteria

To be enrolled in this study, participants must have the following characteristics:

- Veteran
- Be current cigarette smokers of at least ten cigarettes a day.
- Meet criteria for current PTSD.
- Speak and write fluent conversational English.
- Be between 18 and 75 years of age.
- Be willing to attempt smoking cessation.

Potential participants will be excluded from participating in this study for the following reasons:

- Screened participants will not be stable on their medications for the study period
- Screened participants who have a history of myocardial infarction in the past 6 months
- Screened participants who have a contraindication to NRT and are unable to get medical clearance from their primary care provider will be excluded.

- Screened participants who use any other forms of tobacco such as cigars, pipes, or chewing tobacco and are unwilling to stop using.
- Pregnancy
- Inability to complete study measures and tasks independently
- Dementia or other brain disorder, schizophrenia, current manic syndrome, or substance abuse/dependence in the preceding 3 months.
- Currently receiving trauma-focused psychotherapy.
- Currently enrolled in another smoking cessation trial.
- Currently living in court-ordered residential substance abuse treatment.

Procedures
Participants will be recruited to participate in an intervention consisting of the smoking cessation + CPT-C or smoking cessation without concurrent CPT-C. Potential participants will complete a phone screen with study personnel to rule out those who are likely ineligible. Participants will be asked to attend a total of 15 study sessions, including a screening session, counseling and/or assessment sessions (a total of 12 counseling sessions and a 1-week post-treatment follow-up in each condition), and a 6 month follow-up to verify smoking abstinence and complete assessments.

Screening Session
Potential participants will complete a phone screen to determine whether they might be eligible for the study. Remaining potential participants will be scheduled for a full screening session, lasting approximately 5 hours total (30 minutes consent; 4.5 hours study procedures). For the screening session, participants will meet a member of the research team at the Nicotine Research Laboratory at the Durham VA. The study will be explained in detail, and the participants will provide informed consent.

As indicated in the informed consent form and HIPAA authorization, the following information will be collected: Name; address; phone number; age; birth date; social security number; dates of study visits; dates of traumatic events; current health and mental health conditions; alcohol/drug abuse current status and history; medical history information; current medications; smoking status; number of cigarettes smoked per day; pregnancy; traumatic event; veteran status; lab results (saliva analysis, urine drug screen, pregnancy screen); questionnaires; structured clinical interviews; descriptions of traumatic life events; medical chart review, and traumatic data collected at each session during study participation.

Urine samples will be collected for drug screen urinalysis and will be disposed after we obtain the urinalysis chemistry report. Urine drug screens will be used to corroborate self-report of substance use; the presence of substance use disorders is determined by clinical interview (see below). The participant will then provide a breath sample in order to assess CO level and a saliva sample for assessing salivary cotinine, a metabolite of nicotine. Study staff will measure the participant's height and weight in order to

establish a baseline to determine post-quit weight gain. Blood tests will be conducted to rule out pregnancy in pre-menopausal or peri-menopausal women. The Structured Clinical Interview for DSM-IV Diagnosis (SCID-IV) and the Clinician Administered PTSD Scale (CAPS; Weathers, Blake et al., 2013) will be administered in order to determine participant eligibility. Participants will complete the Traumatic Life Events Questionnaire (TLEQ; Kubany, Haynes et al. 2000) and the Trauma-Related Guilt Inventory (TRGI; Kubany, 1996) to provide a thorough trauma history and evaluation of its impact. If any participant indicates a possible contraindication to the use of nicotine replacement therapy, authorization to participate in the study will be obtained via medical clearance from their primary care provider. The Good Health Screening Measure and Letter to Physician for Medical Clearance are included in Appendix A: Study Measures. Participants who will be unable to complete study measures and tasks independently will also be excluded. To maximize ecological validity, participants will not be excluded if they are already receiving PTSD treatment unless it is a trauma-focused psychotherapy.

Blood samples will be collected to test for pregnancy in female participants of childbearing potential. There is minimal risk associated with venipuncture, including the possibility of infection, superficial hematoma, bleeding, clotting, and fainting. All blood samples will be analyzed at the Durham VA Medical Center and will not be transported off site.

As part of the screening session, participants will be asked to fill out several questionnaires: PTSD symptom severity will be measured by the PTSD Checklist (PCL) (Weathers, Litz, et al., 2013), depressive symptoms will be measured by the Beck Depression Inventory (BDI-II) (Beck, Steer, & Brown, 1996), and perceived Self-Efficacy will be assessed with the Relapse Situation Efficacy Questionnaire (RSEQ) (Gwaltney, et al., 2001), and affective states will be assessed by the Positive and Negative Affect Schedule (PANAS) (Watson, Clark, & Tellegen, 1988). Information about minority, racial and marital status, medications, medical history, years of education and age will be collected. Participants' socioeconomic status will be measured using the Objective Socioeconomic Status measure (OSS; Adler, Epel, et al, 2000). General life satisfaction will be measured with the Quality of Life Inventory (Frisch et al., 1992). Information about nicotine dependence using the Fagerström Test of Nicotine Dependence (FTND) (Heatherton, Kozlowski, Frecker, & Fagerström, 1991), a stages of change measure (Prochaska and Diclemente, 1983), a question regarding motivation to quit smoking, and the Minnesota Nicotine Withdrawal Scale (MNWS) (Patten & Martin, 1996). General desire to smoke will be measured using the 32-item Questionnaire on Smoking Urges (QSU) (Tiffany & Drobes, 1991). Subjects will report about general smoking exposure history using the Smoking Exposure Questionnaire, and will report regarding electronic cigarette use on an internally designed measure. Participants will complete the Connor-Davidson Resilience Scale (CD-RISC). The CD-RISC is comprised of 25 5-point Likert-type items designed to measure an individual's range of abilities to manage different types of stress (Connor and Davidson 2003). In order to evaluate sleep quality and sleep problems, we will ask participants to complete the Pittsburgh Sleep Quality Index with

PTSD Addendum (PSQI-A; Buysse, Reynolds, Monk, Berman, & Kupfer, 1989; Germain, Hall, Krakow, Shear, & Buysse, 2005). Participants will also complete the Anxiety Sensitivity Index-R (ASI-R), a 36-item 4-point Likert scale measure that assesses an individual's concerns about the emotional *and physical* consequences of experiencing anxiety symptoms. In addition, participants will complete the Cook-Medley Hostility Scale, a measure of hostile attitude, and a basic needs questionnaire designed to measure financial stability. History of head injury will be assessed with the OSU-TBI-Short Form, a short structured interview designed to detect multiple forms of traumatic brain injury (Corrigan & Bogner, 2007). Participants will be paid $50 for screening.

With subjects' written consent, contact information containing identifying information such as name, address, phone number, and dates of research participation along with diagnostic information will be added into a "Contact Database". The purpose of this database is to re-contact potential subjects about future studies for which they may qualify. Potential participants will only be contacted about future studies under the direction of Dr. Beckham and her staff. Only Dr. Beckham and her research staff will have access to this database, which will be housed on the VA Network's S:\ Drive (path S:\Nicotine Research\Study Information\Study Logbooks).

Diagnostic, demographic, and questionnaire data and other information collected as part of this study will be added to a larger database entitled 'Trauma Database.' Data coding and complete confidentiality of all subject information in the "Trauma Database" will be accomplished in a three-step process. First, information from this study will be coded and will only be linked by an assigned random study number. Second, information collected from other protocols run by Dr. Beckham will be coded and linked by the random study number. Lastly, the information will be merged into the larger "Trauma Database" which will be used for future research. Information collected from many study participants (500 or more) from different studies will then be examined to inform researchers about the topic they are trying to learn more about. Topics of research change over time and for that reason, the development of a combined research database is particularly useful. The purpose of combining information collected from numerous studies is to increase the power of the statistical analysis of genetic, diagnostic, questionnaire and other assessment data. Each study that deposits data into the 'Trauma Database' repository will not include any of the 18 individual identifiers under the Privacy Rule.

Ecological Momentary Assessment

Participants will monitor smoking for a total of three weeks: the first week of treatment, the first week of the quit attempt, and the first week following the end of treatment. Participants will be paid $25 per week for monitoring. Participants will also have the opportunity to earn an extra $25 per week in incentive pay for returning fully completed electronic diaries. During the monitoring period, participants will record any smoking lapses on the electronic diary (ED), immediately after smoking. Smoking lapse assessments will be accompanied by a "situational assessment" including situation,

activity, smoking craving, mood, and PTSD symptoms. In addition, participants will complete situational assessments on at least five occasions per day selected at random by the ED. Random occasion assessments will be stratified every 2.5 hours. The timing of these assessments will be random with the constraint that no prompts will be given for 10 minutes after a cigarette entry.

Prompting will cover all waking hours. When the diary is not completed, up to 3 reminder signals will be emitted at 1-minute intervals and then the diary program will become inaccessible until the next scheduled occurrence. Smokers will be instructed to stop what they are doing when they hear the signal or plan to smoke a cigarette and complete a diary record, which will take about 1 minute. They will be told to ignore any signal that occurs during an incompatible activity (e.g., driving). To increase adherence, participants will be allowed to suspend prompting when responding would be too costly (e.g., church, driving). In previous research using similar methodology, participants suspended prompting only 2 times per week. Additionally, participants will be able to delay an assessment with a 5-minute delay function. Daily start and stop times will be programmed individually according to each participant's usual sleep pattern and entries will be time-stamped.

At the end of each weekly period of monitoring, participants will be asked to bring their assigned EMA device (see below for device description) to the laboratory. The study coordinator will upload all diary information onto secured server space owned by Duke University Medical Center (B: Beckham Research Lab). This server is located in Duke University Medical Center's main campus, and is only accessible to staff members with especially approved access (i.e., only staff members on Dr. Beckham's team). Data will be uploaded to the Duke server because Duke has an Entryware license, whereas the VA does not. Although the drive itself is within Duke's PHI zone, data being uploaded onto this server contains neither any of the 18 types of PHI nor any other types of PII. Only Dr. Beckham and her study staff have access to this secured server space, which is encrypted at rest.

Electronic Diary System Hardware and Software

The electronic diary (ED) system will be implemented on PalmOne Treo 650 handheld computers (PalmOne, Inc.), with a 4 line, 20-character per line bright CSTN backlit color display. The computer contains a 144 MHz processor with 32 megabytes of memory. It is 4.4 in. X 2.4 in. x .9 in., weighs 5.9 ounces, and is powered by a rechargeable lithium ion battery. All other computer functions will be locked out. Customized programming has been developed specifically for this project using Entryware software (Techneos Systems, Inc., Vancouver, Canada). All assessment data will be collected by means of structured input. This electronic diary procedure ensures total confidentiality, even if a palmtop is misplaced. It also ensures temporal accuracy because participants cannot delay or clump their entries. The proposed electronic diary procedure is consistent with state of the art methodology for collecting ambulatory data assessing smoking and smoking lapse.

Electronic Diary Training
Several steps will be taken to train participants to use the electronic diaries (ED). Participants will be introduced to the handheld computers at session 2, watch a 20-minute instructional video, and be given an instruction manual that details the procedure and reviews specific items and decision rules. Participants will practice diary entries during the session and receive immediate feedback regarding their data. Participants will be given the Medical Center toll-free number and appropriate extension and will be encouraged to call at any time with questions or problems. Data will be downloaded at each laboratory visit. Our pilot data and data collected during the current merit review period suggest that this procedure is highly effective in producing high participant compliance.

Risks and Data Security
Subjects' identifying information will only be available to Dr. Beckham and her research staff. Data that links participants to information collected in the course of a given study will be kept separately from identifying information. This includes elements of dates, including dates of sessions. All study data will be kept in a secured file to which only study investigators will have access, S:\Nicotine Research\Study Information\Study Databases. Hard copy paper records will be stored in a locked filing cabinet in the study coordinator's locked office, within this research lab at the Durham Veterans Affairs Medical Center (DVAMC). Information from the interview and/or the questionnaires may be entered into a computerized database. This database will be stored on a VA secured computer server that is password-protected, and only accessible by Dr. Beckham and study staff. If data analysis software is not available locally, a de-identified dataset will be sent to VINCI for analysis using VA-owned data analysis software (SAS). Access to data will be limited to a small number of project staff who have been trained to preserve participant confidentiality. The key linking code numbers and identifying information will be kept in a locked office in the Durham VA, and will be maintained on password-protected computers behind the VA firewall on the VA secured server (S:\Nicotine Research\Study Information\Study Logbooks). Currently, VA records control requirements dictate that all research data, including keys for identifying data, are not destroyed. All data will be stored in accordance with this policy. For study personnel who leave the research team, removal of access to research study data will be accomplished immediately. Any information security or privacy incidents will be reported to the facility's PO and ISO immediately.

To protect against potential side effects of medications used as part of this study, patients' physicians will be consulted to determine appropriateness for this trial if any potential contraindications to these medications are reported during the screening visit. In order to monitor possible side effects associated with NRT, participants will be instructed to report any side effects as soon as possible to research staff. At each session following initiation of the nicotine replacement therapy, participants will also be questioned about any side effects to further monitor any adverse reactions. All adverse

events will be closely monitored by the PI, Dr. Jean Beckham, and the designated medical monitor (Dr. Scott Moore). Dr. Moore will evaluate patient reports of adverse events to determine whether they are study related. Serious adverse events will be promptly reported to the VA Institutional Review Boards as required. Potential risks will be minimized by carefully screening participants according to the inclusion/exclusion criteria, closely monitoring symptom levels, and following established laboratory procedures.

Safety monitoring for adverse events (AEs) will be conducted in real time by Dr. Dedert, his primary mentor, Dr. Beckham, and the project coordinator. All adverse events will be indicated on the source documentation for the study, and on the specific adverse event report form (required by the Durham VAMC IRB). The following information about adverse events will be collected: 1) the onset and resolution of the AE, 2) an assessment of the severity or intensity (use existing grading scales whenever possible), 3) an assessment of the relationship of the event to the study (definitely, probably, possibly or not related), and 4) action taken (e.g., none, referral to physician, start or increase concomitant medication). The PI will determine the severity of the event, will assign attribution to the event, and will monitor the event until its resolution.

All serious adverse events (SAEs) will be reported to the DSMB and the Durham VAMC IRB within 24 hours of the investigative team learning about them. The initial report will be conducted by phone, email or fax. This initial contact will later be followed by a written report to the IRB (using their SAE reporting form).

Intervention Protocol

If screened potential participants are deemed eligible to participate in the study, participants will be randomized to participate in either a 12-session CPT-C with concurrent smoking cessation treatment or a smoking cessation treatment including 6 individual smoking counseling sessions, to be followed (if desired) by CPT-C six months after the quit date. Both arms of the study will include text messaging to support the quit attempt (smokefree VET), pharmacotherapy for smoking cessation, and brief monthly follow-up phone contacts by therapists to support the quit attempt. The complete randomization sequence will be generated a priori and performed centrally by the study staff.

Although participants will attend a total of 15 sessions for this study, not all study sessions will include therapy. In the CPT-C and smoking condition, participants will receive 12 sessions of combined PTSD and smoking therapy. The first 50 minutes of each session will be devoted to the randomized therapy and the last 25 minutes will be devoted to the manualized integrated smoking cessation treatment by McFall and Saxon (McFall & Saxon, 2005). Sessions 7 through 12 of the treatment sessions will include 50 minutes of the randomized therapy, and brief (five to ten minutes) check-in regarding smoking relapse prevention and/or renewed quit attempts. In the smoking cessation without concurrent CPT-C condition, there will still be 15 total study sessions, with 6

including therapy for smoking cessation and lasting 25 minutes. If, during the course of treatment, a participant is lost to contact, the study coordinator will send an IRB-approved "no-contact letter" to increase the likelihood that we re-establish contact.

It should be noted that per the study protocol, the smoking quit date is scheduled to occur on Session 7 of the study; however, we have found that participants sometimes wish to quit smoking earlier than is called for in the study protocol. The treatment manual, which was not designed specifically for this study, indicates that changing the quit date to occur earlier is reasonable if it's based on participant preferences. Per Dr. Miles McFall, a national VA expert in integrated smoking cessation, it is reasonable in cases in which, after strong recommendations from the therapist to stick to the recommended quit date, the participant still wishes to quit earlier than recommended to allow them to, and to make modifications to the skills acquisitions components of treatment (in accordance with the manual) and change medications to coincide with the participant's preferred quit date.

If a participant is randomized to receive CPT-C, consistent with the CPT-C protocol, smokers will focus on the cognitive processing treatment components. These sessions include writing a trauma impact statement, followed by the identification of "stuck points", problematic beliefs that are believed to interfere with recovery from PTSD. In addition, patients will complete A-B-C (Activating Event, Belief, Consequence) worksheets and Challenging Questions worksheets.

Therapists who are not experienced in providing the CPT-C intervention will be allowed to attend a CPT training workshop. For each therapist, he/she will be asked to provide CPT (after training) to two participants, and the therapist's fidelity ratings will be closely reviewed (see paragraph below). Eligible therapists may elect to participate in the CPT certification process, which requires ongoing consultation telephone calls provided by certified CPT trainers within VA, and administration of both CPT and CPT-C versions of the therapy (between which the only difference is the trauma account present in CPT). Consistent with recommendations in the CPT treatment manual, standard training and clinical practice of CPT in VA is for therapists to learn both forms of the treatment (CPT with written trauma account and CPT-C with more time devoted to cognitive restructuring). Because certification of therapists is important to the quality of the therapy provided in this project, therapists choosing to undergo certification processes will be encouraged to do so. In order to facilitate certification, any therapist who is beginning the certification credentialing will be allowed to provide CPT (not CPT-C) treatment for one of his/her first two assigned therapy cases.

To ensure that PTSD symptom assessments and treatment components are consistently implemented, all CAPS interviews and treatment sessions will be videotaped using digital videotaping equipment for participants who provide consent on VA Form 10-3203. A Sony Handycam DCR-SR80 will be used to collect the videorecordings. Because the Handycam has a miniUSB to USB connector, and VA computers do not allow use of

USB drives for data transfer (unless encrypted flash drives are used), the video recordings will be moved temporarily to a stand-alone computer that is not connected to any networks and does not have Internet capability. From this stand-alone computer, the recordings will be transferred to a VA computer using an IronKey encrypted flash drive issued to a study staff member. After transfer, existing copies of data will be immediately removed from the stand-alone computer, the Handycam (using instructions in the User Manual for deletion of movies), and the IronKey device. A fidelity checklist covering CPT-C has been developed in conjunction with treatment mentor Dr. Resick. Twenty percent of videotapes will be randomly selected to be reviewed by an onsite mental health professional who has had formalized training in CPT provision. The reviewer will provide feedback to the PI. In addition, recordings will be rated for CPT treatment adherence using an adherence checklist constructed with input from treatment consultants. This treatment adherence checklist will be retained as part of the treatment manual to assist in ensuring treatment fidelity during dissemination. These video recordings will be randomly chosen with the same ratios. Because the Integrated Smoking Cessation protocol is flexible and readily adapted to fit the participants' needs, ratings of fidelity to the manual would not be useful. For this reason, we will plan only to rate the fidelity of the CPT interventions. All video collected in this manner during this study will be stored electronically on the VA-secured server in a folder to which only the study staff have access (path: S:\\VHADURMUL23\Groups1\Research\DEDERT CPT\Videorecordings OR S:\Nicotine Research\Study Information\Study Logbooks\CPT\Temp. Moved). After study videos have been reviewed for fidelity, or if the storage folders listed above are full, approved study staff members will move videorecordings to DVDs that are encrypted using Symantec Endpoint Encryption. Encrypted DVDs will be stored in a locked filing cabinet in a locked office suite in Bldg 1, C10006. All video recordings will be kept indefinitely as is consistent with VA records control policy.

Text Messaging to Support Smoking Cessation

As part of both interventions, participants will be invited to utilize SmokefreeVET, a mobile text messaging service for military Veterans trying to quit smoking. SmokefreeVET was developed by a joint effort of the National Cancer Institute and the U.S. Department of Veterans Affairs. The program was created to provide 24/7 encouragement, advice, and tips to help smokers quit smoking and stay quit. It is a 6 to 8 week program, depending on when you set your quit date. Users will receive 1-5 messages per day and can receive additional quit support at critical points in the quit process by using one of SmokefreeVET's keywords (URGE, STRESS, or SMOKED). Participants can opt out of supportive text messaging at any time by sending the keyword STOP. Consistent with the structure of SmokefreeVET, participants interested in utilizing it will be assisted in signing up for the program within two weeks before their planned quit date. Participants will not be required to use the texting program. If a participant prefers to use his/her own text-capable telephone to receive these texts, then he or she will be allowed to do so. However, any participant who does not have a text-capable telephone or would prefer not to use his/her own phone will be loaned an

inexpensive telephone (Samsung Gusto 2).. Participants will be informed that there may be an added privacy benefit to using the loaned phones, as any text messages would not be received on a personal phone line, and would not be associated with any personal identifying information. Any participant who chooses to use the loaned telephone will be allowed to use it for the entire treatment period. SmokefreeVET is an (up to) eight-week program, so all participants will have equal opportunity to use the texting program in its entirety. As is true with the PDA device loaned for collection of EMA data, the telephone will not contain any identifying information, and will not even contain any key connecting the device with a participant. Rather, we will track which participant has which telephone by an electronic log connecting serial number to study ID number. This electronic log is kept on a VA secured server at S:\Nicotine Research\Study Information\Study Databases.

Text messaging is a very accessible technology for phone-based health interventions, with an estimated 56% of American adults owning a smart phone (Center, 2013). In addition, data from 2010 indicate that one in six people were using their mobile phone for health-related topics (Fox, 2010). As a push technology that requires very little effort on the part of the patient, text messaging can be very useful for reminding patients of their health goals, providing timely education and coping responses, and accessing customized feedback. Preliminary research on text messaging to assist smoking cessation suggests that it is useful (Haug, 2009).

Assessments After Screening

Prior to each session, participants will complete questionnaires to assess psychiatric symptoms and smoking variables. These include the PTSD checklist (PCL), questions about smoking behavior in the past week, and the Beck Depression Inventory (BDI-II). In the final two sessions, participants will also complete the ASI, QOLI, TRGI, PSQI-A, CAPS, treatment satisfaction, Cook Medley Hostility Scale, e-cigarette use measure, and a question about current non-study psychotherapy. In session 8, participants will complete measures of treatment credibility and expectancy using the Reaction to Treatment Questionnaire (Borkovec & Nau, 1972). At the beginning and end of treatment, therapists will rate their level of allegiance to the therapy they are using with a single question asking “Which treatment do you think leads to better outcomes?” In the final treatment session, participants will also complete measures of SmokeFreeVet usability, and the nicotine dependence stages of change measure. In session 14 (after the final treatment session), participants will be interviewed with the CAPS.

Abstinence and relapse will be monitored by ED entries and at visits 7-14. Participants will provide breath samples for carbon monoxide (CO) analysis at every laboratory visit following their quit date. The first verification of smoking abstinence will occur on the morning following their quit date. Smoking abstinence will be obtained by self-report and verified by comparing CO levels to the level obtained at the baseline visit. The chart below lists the sliding scale of CO values that will be considered validating. At the six month follow-up visit, salivary cotinine will also be used to confirm self-reported

smoking abstinence. The formula in Table 1 below uses the participant's CO reading at the screening visit to determine the threshold that will be considered as confirming smoking abstinence after the quit date for each participant.

Table 1. Carbon Monoxide Thresholds for Validating Smoking Abstinence		
CO SCREENING	AM CO LIMIT	
14-15	15	AM CO Limit after Overnight Abstinence AM CO Limit Formula: [14 + (.25 * (1.33 * (SCREENCO -14)))]
16-18	16	
19-21	17	
22-24	18	
25-27	19	
28-30	20	
31-33	21	
34-36	22	
37-39	23	
40-42	24	
43-45	25	
46-48	26	
49-51	27	
52-54	28	
55-57	29	
58-60	30	
61-63	31	
64-66	32	
67	33	

After saliva samples are returned to the research laboratory, they will be sent for analysis to the University of California at San Francisco Pharmacology Laboratory for analysis. Should this laboratory discontinue salivary assay analysis, or should the PI determine use of another lab is warranted for this purpose, another lab will be identified to provide this service and this new lab will be reported to the IRB. Coded samples will be sent by trained study team members in accordance with the standards of practice outlined in Research Transporting and Shipping Biological Specimens, SRS SOP 202. Saliva samples will be analyzed for the presence of cotinine using a standard cut point off 10 ng/ml to determine abstinence. A blind sample of 5% will be run again to assure test accuracy of saliva samples. Secondary smoking outcomes will include 7- and 30-day point prevalence abstinence at each assessment, where abstinence is defined as no tobacco use in the prior 7 or 30 days respectively (McFall et al., 2010)

Any participant who is unable to remain abstinent from smoking after their quit date will be encouraged to make additional quit attempts. Participants will be allowed to make as many quit attempts as necessary during their study enrollment until they are successful or until they have completed their study enrollment. There will be no additional sessions provided for those participants who do not remain abstinent.

Consistent with guidelines for Integrated Care for Smoking Cessation, participants will continue to receive brief care for smoking cessation for as long as they remain in therapy for PTSD. In the CPT-C and smoking condition, this means that study session 8 will be the first session of smoking cessation counseling that will focus on relapse prevention and encouraging those who have relapsed to make an additional attempt to stop smoking. In sessions 8-13, participants will complete questionnaires to assess psychiatric symptoms and smoking variables and continue to receive smoking cessation follow-up counseling. In the smoking cessation condition, participants will complete the six sessions included in the Integrated Care for Smoking Cessation manual, as well as completing brief smoking counseling when completing assessments at study sessions following the quit attempt.

The smoking cessation intervention is based on the research and publication efforts of Miles McFall, Ph.D., and Andrew Saxon, M.D. It includes assessment of smoking history and motivation for smoking cessation, pharmacotherapy, setting a quit date, stress management techniques, and behavioral strategies to use on the quit date.

Nicotine Replacement Therapy

All participants will receive nicotine replacement therapy in session 6, and will be asked to begin using NRT on their quit date (just prior to session 7). Participants will be provided with detailed information and education regarding the use of the nicotine skin patches. This educational component will include a rationale for using the patches, proper placement of the patch, when to use them, possible side effects, and how to report side effects to research staff as they may occur in the course of the study. All participants will also be given the option of one NRT rescue method of their choosing (nicotine gum, lozenges or inhalers).

Medications will be distributed under the consultation of study physician, Scott Moore, M.D., Ph.D. Dr. Moore prescribes smoking cessation pharmacotherapy for the Durham VA specialty smoking cessation clinic. Dr. Moore is familiar with standard smoking cessation pharmacotherapy and side effects. He will determine initial nicotine dosage levels and consult on any adjustments to medication dosage. For example, patients only smoking 10 cigarettes a day would likely not benefit from 21mg/day nicotine patches, and will begin NRT at 14mg/day. Recent research has suggested that for heavy smokers (i.e., smokers with CO readings higher than 30 ppm), smoking cessation efficacy is greater when high dose (42 mg) nicotine patches are used in the pre-cessation phase (Rose, personal communication; Rose, 2010). The side effect profile for heavy smokers using a 42 mg patch is low. Rose (personal communication) reports that 2.5% of heavy smokers using a 42 mg. patch pre-quit report vomiting (as compared to 0.4% with the 21 mg. patch). No other adverse effects were reported. Smokers in this study were allowed to use their usual brand of cigarettes. Taken together, these studies suggest that pretreatment with nicotine patch while smoking cigarettes is safe and tolerable.

Heavy smokers (as defined by CO readings greater than 30 ppm) will be prescribed 42 mg. patches. Two weeks after their quit date, participants will lower the dose of the prescribed nicotine patch (i.e., participants receiving 21 mg initially will lower to 14 mg, and those receiving 42 mg will lower to 21 mg). At three weeks after the quit date, any participant who initially received the 42 mg patch will lower the patch dose further to 14 mg. At four weeks post-quit, all participants will replace the 14 mg patch with a 7 mg patch, to be worn for two weeks. All NRT, including both the patch and rescue method, will end 6 weeks after the target quit-smoking date. If any participant has been unable to maintain abstinence during the follow-up period, he/she may be allowed to re-initiate NRT during the follow-up period in order to make a renewed quit attempt. Dosage of NRT will be decided by the study physician at this time point, and will depend upon the participant's most recent smoking patterns and CO reading.

Table 2. Study Tasks and Procedures

Session	Tasks		Payment
	CPT-C + Smoking Intervention	**Smoking Intervention**	
Phone	• **Phone screen** • **Scheduling screening session**		**None**
1	• **Consent** • **Screening (Clinical Interviews, Questionnaires)** • **Height/Weight Measurement**		**$50 visit**
2	• **CPT + smoking treatment 1** • **Questionnaires** • **Introduction to smokefree VET** • **Review EMA practice and begin EMA data collection**	• **Smoking treatment 1** • **Questionnaires** • **Intro to smokefree VET** • **Review EMA practice and begin EMA data collection**	**$20 visit**
	2 hr, 15 min	***55 min***	
3	• **CPT + smoking treatment 2** • **Questionnaires**	• **Smoking treatment 2** • **Questionnaires**	**$20 visit; $25 for EMA; $25 incentive pay**
	1 hr, 45 min	***55 min***	
4	• **CPT + smoking treatment 3** • **Questionnaires**	• **Smoking treatment 3** • **Questionnaires**	**$20 visit**
	1 hr, 45 min	***55 min***	

Session	Tasks		Payment
5	• **CPT + smoking treatment 4** • **Questionnaires**	• **Smoking treatment 4** • **Questionnaires**	**$20 visit**
	1 hr, 45 min	***55 min***	
6	• **CPT + smoking treatment 5** • **Questionnaires** • **Receive NRT + rescue method; instructed not to use until quit date** • **Begin bupropion**	• **Smoking treatment 5** • **Questionnaires** • **Receive NRT + rescue method; instructed not to use until quit date** • **Begin bupropion**	**$20 visit**
	1 hr, 45 min	***55 min***	
7	• **CPT + smoking treatment 6** • **Questionnaires** • **QUIT DATE/Relapse Prevention** • **Begin patch NRT + rescue method** • **EMA data collection**	• **Smoking treatment 6** • **Questionnaires** • **QUIT DATE/Relapse Prevention** • **Begin patch NRT + rescue method** • **EMA data collection**	**$20 visit**
	1 hr, 45 min	***55 min***	
8	• **CPT 7 + Relapse Prevention/Renewed Quit Attempt** • **Verify Smoking Abstinence** • **Questionnaires** • **Continue 21 or 42 mg patch NRT + rescue method**	• **Smoking treatment 7** • **Verify Smoking Abstinence** • **Questionnaires** • **Continue 21 or 42 mg patch NRT + rescue method**	**$20 visit; $25 for EMA; $25 incentive pay**
	1 hr, 45 min	***55 min***	
9	• **CPT 8 + Relapse Prevention/Renewed Quit Attempt** • **Verify Smoking Abstinence** • **Questionnaires** • **Step down to 21 or 14 mg patch NRT + rescue method**	• **Smoking treatment 8** • **Verify Smoking Abstinence** • **Questionnaires** • **Step down to 21 or 14 mg patch NRT + rescue method**	**$20 visit**

Session	Tasks		Payment
	1 hr, 45 min	***55 min***	
10	• **CPT 9 Relapse Prevention/Renewed Quit Attempt** • **Verify Smoking Abstinence** • **Questionnaires** • **Continue or step down to 14 mg patch NRT + rescue method**	• **Smoking treatment 9** • **Verify Smoking Abstinence** • **Questionnaires** • **Step down to 21 or 14 mg patch NRT + rescue method**	**$20 visit**
	1 hr, 45 min	***55 min***	
11	• **CPT 10 + Relapse Prevention/Renewed Quit Attempt** • **Verify Smoking Abstinence** • **Questionnaires** • **Step down to 7mg patch NRT + rescue method**	• **Smoking treatment 10** • **Verify Smoking Abstinence** • **Questionnaires** • **Step down to 7mg patch NRT + rescue method**	**$20 visit**
	1 hr, 45 min	***55 min***	
12	• **CPT 11 + Relapse Prevention/Renewed Quit Attempt** • **Verify Smoking Abstinence** • **Questionnaires** • **Continue 7mg patch NRT + rescue method**	• **Smoking treatment 11** • **Verify Smoking Abstinence** • **Questionnaires** • **Continue 7mg patch NRT + rescue method**	**$20 visit**
	1 hr, 45 min	***55 min***	
13	• **CPT 12 + Relapse Prevention/Renewed Quit Attempt** • **Verify Smoking Abstinence** • **Questionnaires** • **End of NRT** • **Continue bupropion** • **Weight measurement** • **Begin 1 week of EMA**	• **Smoking treatment 12** • **Verify Smoking Abstinence** • **Questionnaires** • **End of NRT** • **Continue bupropion** • **Weight measurement** • **Begin 1 week of EMA data collection**	**$20 visit**

Session	Tasks		Payment
	data collection		
	1 hr, 15 min	***30 min***	
14	• **End EMA data collection; Return study equipment** • **Verify Smoking Abstinence** • **CAPS**		**$20 visit; $25 for EMA; $25 incentive pay; $35 equipment return**
	60 min		
15 (6 mos. after quit date)	• **Verify Smoking Abstinence** • **If Not Abstinent, Timeline Follow Back** • **Questionnaires** • **End bupropion** • **Weight measurement** • **CAPS**		**$50 visit**
	60 min		
16-27	**Not applicable**	**CPT-C (if desired), at 60 minutes per session over three months**	**None**
Total			**$545**

Nicotine toxicity

There are minimal risks associated with wearing a nicotine patch including skin irritation, dizziness, lightheadedness, increased heart rate or blood pressure, nausea or vomiting. Despite this low risk, side effects from the combination of NRT and *ad lib* smoking may occur. Rare side effects associated with nicotine toxicity may include: dizziness, lightheadedness, nausea, vomiting, excessive saliva, stomach pain, sweating, headache, dizziness, confusion, weakness, fainting, difficulty breathing, seizures, rapid/weak/ irregular heartbeat, blurred vision, diarrhea, and hearing problems. In previous trials of pre-treatment with 21mg/day nicotine patch there was no evidence of nicotine toxicity even among those smoking regular brand cigarettes (Rose, Behm, Westman, & Kukovich, 2006). In addition, there has been no evidence of serious nicotine toxicity associated with the tailored dose of nicotine patch therapy despite using nicotine patch dosages up to 44 mg/24 hours. Others have used dosages of up to 63 mg/24 hours in smokers without signs of nicotine toxicity.

Bupropion

Consistent with standard clinical care for smoking cessation pharmacotherapy, all participants who have no contraindications or are medically cleared will be offered bupropion to assist in the quit attempt. Participants with a history of renal failure, hepatitis, cirrhosis, non-alcoholic fatty liver disease, or liver cancer will not be offered

bupropion as part of this study. Since the efficacy of bupropion is well established, we proposed this procedure for each participant to maximize best practices. Beginning one week prior to their quit date, given that they are medically eligible, participants will be prescribed bupropion SR 150 mg to be taken on days 1-3 with an increase to 300 mg beginning on day 4. Participants will continue to receive bupropion until 6 months after their quit date, when they will attend the final study session. These participants may consult their psychiatrist or primary care provider to determine whether they will continue to take bupropion, but this medication will no longer be prescribed through the study after the 6 month follow-up visit. Participants who decline bupropion will remain eligible to complete the study.

Relapse

All participants will complete the intervention protocol, regardless of smoking relapse. Participants who relapse will have the option of completing the intervention so they can continue to apply smoking cessation skills to subsequent quit attempts. Once the intervention and smoking protocol is completed, participants who relapse will be encouraged to make additional quit attempts until the end of the study at the 6-month follow-up appointment. Relapse will be defined as smoking at least 5 cigarettes a day for 3 consecutive days.

In the follow-up session, if a participant reports an inability to attain or maintain abstinence, we will utilize the Timeline Followback (TLFB) method, which was designed by National Institute on Alcohol Abuse and Alcoholism (NIAAA) to retrospectively evaluate substance use. In this interview, which will last approximately 15 minutes, participants will provide retrospective estimates of their smoking behavior over the time period since their participation. This information will be used to evaluate smoking rates post-quit and relapse incidence among the sample.

CPT-C Post Follow-Up

In order to ensure that all participants have access to evidence-based treatment for PTSD, all participants who were randomized to participate in the smoking cessation without concurrent CPT-C group will be offered the option of receiving 12 sessions of CPT-C following the 6-month follow-up session (i.e., session 15). Treatment will be provided by the same group of therapists who provided CPT-C in the smoking cessation + concurrent CPT-C group. Participants will not be provided smoking cessation counseling during these sessions, and smoking cessation medications will not be provided. In addition, participants will not be paid for participating in these study visits, as they have been previously paid to participate in smoking cessation counseling visits. Participants can choose not to participate in this portion of the study. Any participant who is offered and choose this treatment will continue to complete the PCL and BDI at each visit, as is consistent with CPT-C provided in a clinical setting. No other study measures will be required. Adverse event monitoring, data security, and other risk protections will continue during this portion of the study for those participants.

During this study, it is anticipated that participants will miss scheduled appointments, either through cancellation or no-shows. This does not necessarily constitute a protocol deviation. If a no-show or a missed appointment causes interruption in study activities (such as more than 2 days of missed medications), we will report the missed appointments to the IRB as protocol deviations. Otherwise, the missed appointments will be recorded in electronic study log books as necessary. Also, throughout the study, study staff may contact enrolled participants regarding study-related concerns, scheduling/rescheduling appointments, or appointment reminders.

Data Analysis and Hypotheses:

The following variables will be described for the sample as a whole: minority status, marital status, age, trauma exposure, negative affect level, PTSD symptom severity, nicotine dependence, mean pack years, nicotine cigarette brand, and mean number of cigarettes smoked daily.

Because one of the aims of this study is to assess the efficacy of the combined CPT-C and smoking intervention on smoking cessation, we will analyze these variables to determine whether they change over time.

1) Compared to the smoking cessation alone protocol, the smoking cessation + concurrent CPT-C protocol will result in reduced frequency and intensity of PTSD symptoms.

2) Compared to the smoking cessation alone protocol, the smoking cessation + concurrent CPT-C protocol will result in reduced depressive symptoms.

3) The smoking cessation + concurrent CPT-C protocol will result in decreased smoking rates, relative to published data on VA smoking cessation usual care.

4) Greater PTSD symptom reduction during the smoking cessation + concurrent CPT-C treatment will result in longer duration to smoking lapse and relapse.

5) Exploratory research question: Will use of automated text messaging as an adjunct to smoking cessation be feasible, and will it impact quit rates and symptom severity?

Hypothesis 1. **Compared to the PTSD Coach and smoking cessation protocol, the CPT-C and smoking cessation protocol will result in reduced frequency and intensity of PTSD symptoms.** The change in PTSD symptoms over time will be analyzed using repeated-measures ANOVA, utilizing data provided at baseline, post-treatment, and 6-months post-quit. We will evaluate the potential influence of several potential psychosocial covariates on smoking abstinence, including: 1) demographics (age, race, socioeconomic

status), 2) psychiatric variables (PTSD symptom severity, depression, substance abuse/dependence), 3) smoking variables (self-efficacy, motivation to quit, social support, smokers in social group), and 4) treatment process variables (therapeutic alliance, satisfaction with treatment, attendance at sessions, homework adherence).

Hypothesis 2. **Compared to the PTSD Coach and smoking cessation protocol, the CPT-C and smoking cessation protocol will result in reduced depressive symptoms.** Analysis procedures for Hypothesis 2 will be the same as those used for Hypothesis 1.

Hypothesis 3. **The CPT-C and smoking cessation protocol will result in decreased smoking rates, relative to published data on VA smoking cessation usual care.** An outcome variable denoting the proportion of subjects abstinent at Week-6 will be regressed on the group proxy and included covariates using standard logistic regression procedures. A secondary analysis will explore cessation rates at the 6-month follow-up.

*Hypothesis 4.***-The level of PTSD symptom reduction during the intervention will be related to longer latency to relapse.** PTSD symptom change scores will be used to evaluate the degree of PTSD symptom reduction. We will fit Cox proportional hazard regression models to the data to evaluate effects of PTSD symptom reduction on the time to relapse.

Hypothesis 5. **Exploratory research question: Will use of automated text messaging as an adjunct to smoking cessation be feasible, and will it impact quit rates and symptom severity?** This will be evaluated by examining proportion of participants choosing to utilize text messaging, retention rates, and usage rates.

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