

**Cover Page**  
**Study Protocol and Statistical Analysis Plan**

**Title:** Evaluation and Treatment of Substance Abuse in Veterans with PTSD Service-Connection Claims

**NCT Number:** NCT01597856

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## **Protocol**

**Grant Title:** Evaluation and Treatment of Substance Abuse in Veterans with PTSD  
Service-Connection Claims

**Principal Investigator:** Marc I Rosen, MD

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## **Background**

There are high rates of PTSD among returning OEF/OIF Veterans, and high rates of comorbid substance use

Recent estimates are that 1.7 million Veterans will have returned from OEF/OIF by 2012 and that a significant proportion of them will develop PTSD. A study in the New England Journal of Medicine of returning OEF/OIF combat troops indicated that between 12 and 20% met screening criteria for PTSD (Hoge, Castro et al. 2004), and an analysis of a broader sample of returning OEF/OIF personnel identified 9.8% who met the screening threshold for PTSD (Hoge, Auchterlonie et al. 2006).

Substance use, especially alcohol use, is also a highly prevalent problem in returning service members, despite aggressive attempts to reduce use of alcohol and illicit drugs in the service (Jacobson, Ryan et al. 2008). Nineteen percent of the returning OEF/OIF combat troops described in the New England Journal of Medicine article indicated that they “wanted or needed” to cut down on their drinking (Hoge, Castro et al. 2004). In another large cohort described in JAMA (Milliken, Auchterlonie et al. 2007), approximately 13% of soldiers interviewed six-months post-deployment reported at least one alcohol-related problem, but few soldiers had been referred to substance abuse treatment (fewer than 1%). Rates of alcohol use have been high in VA-based studies that consider treatment-seeking OEF/OIF Veterans. Unfortunately, OEF/OIF Veterans have particular difficulty engaging in mental health treatment (Hoge, Castro et al. 2004; Calhoun, Elter et al., 2008), especially if confidentiality is not assured (Warner et al., 2011).

A diagnosis of PTSD has been associated with at least double the risk of developing alcohol problems (Jacobson, Ryan et al. 2008). The high prevalence of substance use among people with PTSD has been described in VA and community populations (Mansell, Penk et al. 2006). A review of consecutive Veterans presenting for PTSD treatment at the Minneapolis VA found that 57% had evidence of an Alcohol Use Disorder and 36% indicated hazardous or harmful alcohol use on the AUDIT (Erbes 2009). A troubling ancillary finding was that 65% of those identified as harmful or hazardous drinkers reported on one year follow-up that they had not received any treatment for alcohol use at the VA or elsewhere.

The importance of Compensation examinations as a gateway to VA treatment for PTSD

To apply for benefits, a Veteran sends a claim to the Veterans Benefits Administration, where staff ask the local VA treatment facility to arrange a Compensation examination. The examiner reviews the existing records, conducts a psychiatric interview and writes a report outlining the examiner’s conclusions concerning diagnosis, functional impairment, and relationship of impairment to military service. The examiner’s report is reviewed by a Veterans Benefits Administration claims officer who determines whether an award is warranted and if so, the percentage of full disability benefits that should be awarded.

Based on the number of claims that have been filed to date, a full 50% of OEF/OIF Veterans are expected to apply for service-connection, a percentage only slightly higher than the 44% of Gulf War Veterans who applied (Bilmes 2007). It is likely that a large proportion of those who apply are actually those who are at least partially disabled. As of 2005, 88% of OEF/OIF Veterans who applied for disability were awarded it, percentages that are comparable to those among Veterans of the Gulf War. Award rates ranging from 33-72% for PTSD were

reported in an older study (Murdoch, Hodges et al. 2005). Dr. Rosen's group recently reported that 55.6% of 2400 recent PTSD claims were awarded (Rosen, 2010), and unpublished data suggest that 80% of PTSD claims for service-connection are eventually awarded after appeals.

OEF/OIF Veterans undergoing disability examinations for PTSD are at a critical juncture in their lives, with the disability decision having far-reaching implications for their financial and work status (Murdoch, Sayer et al., 2011). The profound effects of this designation have been described in the psychiatric literature: "Becoming formally designated as *disabled*...has replaced long-term hospitalization as a crucial social factor shaping the course and direction of disablement. Getting disability income can be viewed as the intervention of longest duration and most potential impact" (Estroff, Patrick et al. 1997). Successful rehabilitation at this stage can have far-reaching benefits. Qualitative data and surveys of Veterans applying for service-connection for PTSD indicate that for the majority, the motivations for seeking service-connection are complex (Sayer, Spoont et al. 2004), with financial gain being only one of many motivations.

A 2007 Institute of Medicine report was commissioned to address concerns about how PTSD evaluations were being conducted, and this report highlighted the inattention to substance abuse during this critical juncture (Committee on Veterans Compensation for Posttraumatic Stress Disorder 2007). The Institute of Medicine report noted the importance of comorbidity, including substance abuse. The Report noted that for clinicians conducting Compensation examinations, "*There is no scientific guidance addressing the separation of symptoms of comorbid mental disorders for the purpose of evaluating their relative contributions to subject's condition*" (page 5). The Institute of Medicine recommended that mental health clinicians conducting the examinations get more guidance concerning evaluation of co-morbid disorders.

#### The relationship between compensation examinations and engaging in VA treatment

A substantial proportion of Veterans presenting for Compensation examinations have not received VA services before, making this a crucial opportunity to engage them in treatment. The most direct study of this issue was a review of 452 Veterans who obtained service-connected benefits for PTSD of whom only 112 were using mental health services before initiating their claim (Sayer, Spoont et al. 2004). Surprisingly, service use was not associated with having more severe self-reported symptoms of PTSD (Sayer, Clothier et al. 2007).

A number of retrospective reports have suggested that Compensation-seeking alters treatment attendance in counter-productive ways. It has been asserted that patients applying for service-connection disproportionately exaggerate symptoms (Frueh, Elhai et al. 2003; Arbisi, Murdoch et al. 2004) and are not motivated to engage in and respond to treatment. A *seemingly* incompatible claim is that there are Veterans who engage in mental health treatment to further their disability claims and then immediately disengage from treatment after the claim is awarded (Office of Inspector General, 2005).

There is countervailing evidence from retrospective analyses that awards of service-connection for PTSD are not associated with poorer treatment outcomes or less treatment attendance (Marx, Miller et al. 2008). Treatment drop-out was not suggested by two groundbreaking prospective studies considering the course of treatment attendance and self-reported PTSD severity among disability claimants (Spoont, Sayer et al., 2008; Sayer, Spoont et al, 2008). These two studies analyzed data from 101 Veterans applying for service-connection. These studies were not powered or designed to determine whether Veteran-specific factors such as substance abuse and attitudes about Compensation exams were related to outcomes; that is what is proposed in this study.

It is also unknown whether the extant studies (cited above) of treatment engagement and compensation status apply to OEF and OIF Veterans because only a small proportion of the Veterans in these studies were OEF/OIF Veterans. Large majorities of Veterans in those

studies were Vietnam-era Veterans whose outcomes were complicated by accumulated physical, psychiatric and substance use comorbidities. Only a prospective, adequately-powered study of a representative sample of Veterans presenting for Compensation examinations can address basic questions concerning the relationship between applying for disability and service use in OEF/OIF Veterans.

The proposed studies relating Veteran attitudes towards the Compensation process build on pioneering work conducted primarily by researchers at the VA in Minneapolis. Dr. Nina Sayer and colleagues developed the Disability Application Appraisal Inventory, a reliable, valid rating scales for measuring attitudes towards Compensation examinations (Sayer, Spont et al. 2004). They have also described, in qualitative work, Veterans' perspectives on the decision to apply for disability (Sayer, Spont et al., 2004) and to engage in treatment or not (Sayer, Friedman-Sanchez et al., 2009). However, Veterans' perspectives on how they decide to cope with disability would be of far more policy-making importance if it could be shown that Veterans' attitudes and beliefs relate directly to clinical outcomes.

#### SBIRT Fills the Need for a Brief Assessment and Intervention at Compensation Examinations

SBIRT (Screening, Brief Intervention, and Referral to Treatment) is an approach to identifying and treating patients with substance abuse issues who are presenting for purposes other than substance abuse treatment. SBIRT was developed for use in settings such as emergency rooms, and primary care clinics where patients were not seeking substance abuse treatment but had issues potentially related to substance abuse. It involves Motivational Interviewing, which has been a remarkably consistently effective approach to facilitating engagement in substance abuse treatment in Veterans (Davis, Baer et al. 2003) and other populations. Length of time in treatment is arguably the most important predictor of good substance abuse outcomes (Moos, Finney et al. 2000) and Motivational Interviewing that fosters attendance at VA facilities is an efficient way to target substance use.

The evidence for SBIRT's efficacy in reducing alcohol use is compelling. A randomized controlled trial published in *JAMA* of 774 primary care patients with problem alcohol use who received SBIRT or a minimal control intervention found that patients who received SBIRT had less recent alcohol use, less binge drinking and remarkably, fewer days hospitalized at 12-month follow-up (Fleming, Barry et al. 1997). Other trials have demonstrated reduced alcohol use after SBIRT interventions (Kaner, Beyer et al. 2007). The evidence for SBIRT's efficacy for other drugs is less definitive (Bernstein, Bernstein et al. 2005; McCambridge, Strang et al. 2004).

Because it is relatively simple to implement, SBIRT is being disseminated in a large service program initiated by SAMHSA (<http://sbirt.samhsa.gov/index.htm>). A recent paper described considerably less substance abuse six months post-intervention than before in a population of 560,000 healthcare consumers who received SBIRT, attesting to the feasibility of SBIRT in a wide range of healthcare programs and among heterogeneous populations (Madras, Compton et al. 2009). Another quality favoring the dissemination of SBIRT is that in populations with high rates of illness, it can be cost-effective.

#### The Importance of Referral to Available VA Treatment for Substance Abuse and PTSD

The "RT" (Referral to Treatment) in "SBIRT" takes advantage of the range of effective substance abuse and PTSD treatments available for OEF/OIF Veterans at VA, and can have a large impact by engaging Veterans in those available treatments. VA facilities typically offer a wide range of substance abuse treatments and there is evidence that at VA, as is true elsewhere, the extent of participation in substance abuse treatment is associated with achieving abstinence (Moos, Humphreys et al. 1999).

Engaging Veterans in substance abuse treatment may help PTSD too. In an intriguing pharmacological clinical trial targeting both alcohol abuse and PTSD, participants' alcohol use

improved before PTSD symptoms did (Back, Brady et al. 2006). SBIRT referrals to substance abuse treatment do not preclude concomitant PTSD treatment; surveys of VA clinicians in substance abuse treatment settings show that they usually screen for PTSD and may then refer Veterans who screen positive for PTSD to specialized PTSD treatment providers (Young, Rosen et al. 2005). The large sample in this study will allow for cross-lagged analyses to determine the relative time course of changes in substance abuse with changes in PTSD symptoms and treatment attendance.

It is likely that some Veterans who attend SBIRT will insist on PTSD treatment instead of substance abuse treatment, and, consistent with a Motivational Interviewing approach, Veterans who insist on PTSD treatment after weighing their options will be supported in their choice. Fortunately, treatment focused on PTSD can also ameliorate substance abuse (Brady, Sonne et al., 2005). In uncontrolled studies, substance-using Veterans who received PTSD treatment were more likely to be abstinent than those who did not (e.g. Ouimette, Moos et al. 2003) and PTSD improvement has been associated with reduced alcohol use in clinical trials settings too (Back, Brady et al. 2006). The current standard of care is that *integrated treatment* be offered to people with concomitant substance abuse and psychiatric disorders (Morrissey, Jackson et al. 2005) and both VA Connecticut and the Tennessee Valley Healthcare Systems have clinicians based at their PTSD clinics who are specially trained to offer such integrated treatments.

It is also noteworthy that the recommended treatment *for PTSD* at VA is a cognitive behavioral approach, Cognitive Processing Therapy. A number of small studies have suggested that approaches that combine cognitive behavioral approaches to both PTSD and substance abuse treatment are effective (e.g. Brady, Dansky et al. 2001; McCarthy 2009).

#### Significance of Proposed Studies:

The proposed studies are significant because they address a large population of returning OEF/OIF Veterans. Veterans with PTSD comprise a significant and increasing proportion of the one million Veterans who file Compensation and Pension claims each year (Committee on Veterans Compensation for Posttraumatic Stress Disorder 2007). The reviewed literature suggests that 10% of returning OEF/OIF Veterans will have PTSD, and given the fact that PTSD is associated with a two to four-fold increase in the risk for substance abuse, approximately 30% of the 10% will meet criteria for risky alcohol or substance abuse (Kessler, Crum et al. 1997). Early intervention is particularly important for this group because of the comorbidity associated with chronic PTSD. The proposed model involves assessment and treatment at a critical time for these Veterans. The proposed studies are responsive to the HSR&D Priorities for Investigator-Initiated Research for FY 2011: "HSR&D has a special interest in innovative approaches to improve earlier identification and treatment of post-traumatic stress disorders and suicidality, enhance the continuum of care for substance use disorders..."

Given the high prevalence of substance abuse among OEF/OIF Veterans with PTSD and the exacerbation of PTSD by substance use, it is likely that some of the morbidity and sporadic treatment attendance that has been described is related to substance use. The analysis of the impact of substance abuse on the course of PTSD and attendance at treatment will suggest what complications in the treatment of dually diagnosed OEF/OIF Veterans might effectively be targeted by addressing their substance abuse.

The proposed Evaluative Component analyses of Veteran attitudes about Compensation examinations and their relationship to outcomes are of more than academic interest. Such opinions and beliefs are likely to be important determinants of outcome (Sayer, Clothier et al. 2007), and these beliefs are modifiable. One hypothesis that will be tested is the following: Veterans who believe that engaging in substance abuse treatment reduces a Veteran's likelihood of getting benefits are less likely to engage in substance abuse treatment (for fear of being denied benefits). A belief by Veterans that substance abuse treatment reduces the

chances of getting benefits is potentially modifiable. The Social Security Administration addressed the accurate perception by Social Security beneficiaries that working would result in irretrievably losing disability benefits by implementing and publicizing a Ticket to Work program to foster the transition from disability to employment (Tremblay, Smith et al. 2006). Such agency responses to claimants and disabled people are potent means to socially-desired ends.

There is considerable public pressure to improve the process of evaluating Compensation claims and engaging Veterans in treatment. In widely publicized testimony to the House Committee on Veterans Affairs, Linda Bilmes called for something very much like the proposed approach for returning OEF/OIF Veterans: "VBA should shift its focus away from claims processing and onto rehabilitating and reintegration of Veterans" (House Committee on Veterans Affairs).

Finally, if SBIRT is effective, it may suggest the utility of a similar integration of assessment and treatment for other Compensation examinations. The study's finding among Veterans applying for PTSD-related Compensation may be generalizable to Veterans applying for service-connection for other disabilities, and to other disability evaluations. The study results may hasten the day that a Compensation examination is routinely seen as an opportunity for both evaluation and treatment for returning OEF/OIF Veterans.

The proposed study will test a new approach that melds the Compensation evaluation process to treatment tailored to the results of an evaluation. It is the first study to target treatment to patients at the crucial stage of the Compensation examination. It is the first to analyze the relationship between the disability application process and treatment outcome in a prospective clinical trial. The proposed Clinical Trial Component study would be among the first if not the first adequately-powered randomized controlled trial of a behavioral intervention designed for Veterans with PTSD and substance use.

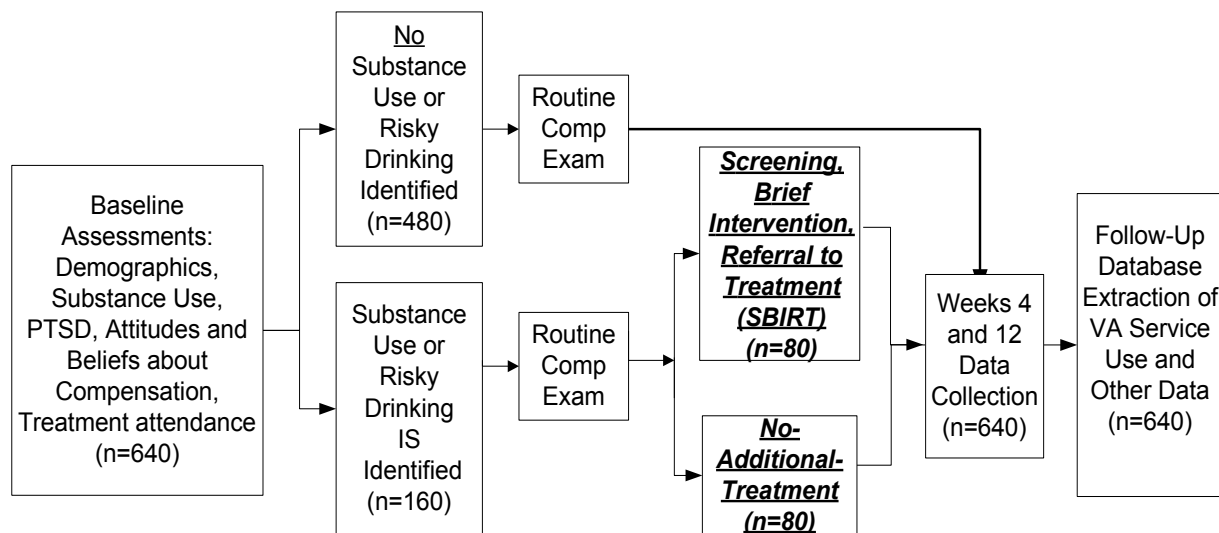
Despite the controversies swirling about disability claims and their obvious importance, only a few pioneering groups have focused research on the claims process; even fewer have gone beyond controversies about whether claimants are malingering to address questions concerning optimal treatment approaches. The proposed study is the first to determine how a Veteran's beliefs about Compensation impact outcome, and will suggest ways to help these Veterans.

### **Specific Aims**

The Compensation examination that determines if a Veteran is entitled to any disability payments related to military service is a crucial gateway to accessing VA care for returning OEF/OIF/OND Veterans. However, researchers and oversight agencies have noted that examiners typically do not have guidelines for evaluating comorbid conditions like substance abuse and for referring patients to treatment.

In the Evaluative Component of this study, OEF/OIF/OND Veterans presenting for Compensation evaluations for PTSD will be approached to undergo a paid battery of confidential substance use, PTSD, service use and attitude assessments prior to their scheduled Compensation examinations. The batteries will be collected again twice, four and twelve weeks after the Compensation examinations. Long-term follow-up data will be extracted from VA databases including diagnoses, the results of the Veterans' Compensation evaluations, award determination, use of VA services and attendance at mental health and/or substance abuse treatment.

In the Clinical Trial Component of this study, one hundred sixty Veterans identified during the baseline evaluation as having a substance use disorder will be randomly assigned to a session of Screening, Brief Intervention and Referral to Treatment (SBIRT) or to No-Additional-Treatment.



#### Hypotheses for Evaluative Component:

1. Veterans with substance use disorders randomized to No-Additional-Treatment will have worse PTSD over time compared to Veterans without substance use disorders and will attend fewer weeks of mental health and/or substance abuse treatment, after accounting for baseline differences between substance users and non-users.
2. Attendance at treatment will be predicted by Veterans' perceptions that obtaining and maintaining VA benefits depends on attending PTSD treatment. Attendance at treatment will be negatively associated with the perception that VA benefits are more likely to be denied if a Veteran receives substance abuse treatment.
3. Long-term attendance at treatment (before Compensation exam to post-award notification) will be significantly impacted by the occurrence of the Compensation examination and determination of award. The effect of attitudes about how disability benefits are awarded will be significantly moderated by these time-varying covariates.

#### Hypotheses for Clinical Trial Component:

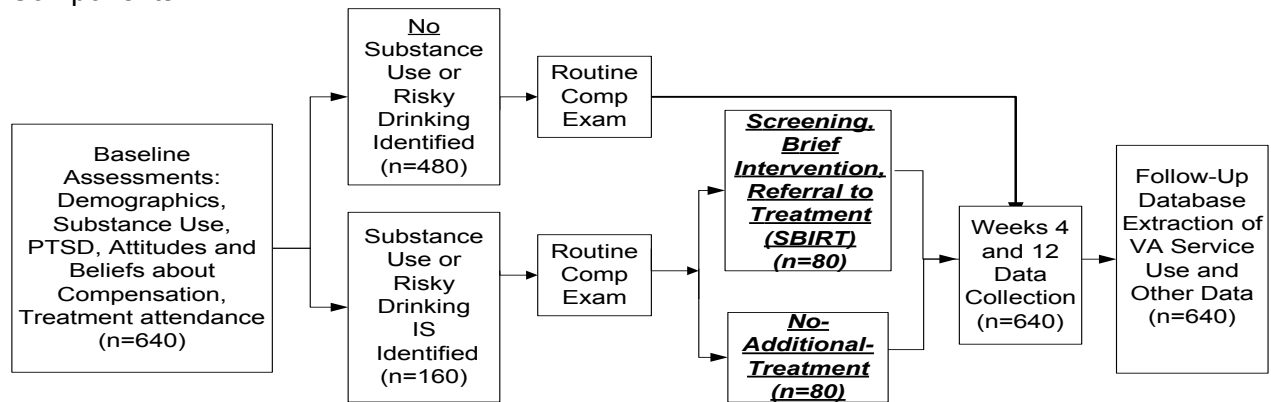
1. Veterans with substance use disorders receiving SBIRT will attend more weeks of substance abuse and/or mental health treatment and will have fewer days of substance use in the twelve weeks after the Compensation examination than Veterans assigned to No-Additional-Treatment. Secondary outcomes will include: (i) weeks attending any mental health treatment; (ii) proportion days using any alcohol, proportion days drinking to intoxication and (iii) PTSD as measured by the CAPS.
2. Preliminary analyses will determine whether the effect of SBIRT on outcomes is moderated by beliefs about disability.

Together, the findings will determine the effects of substance use and other factors on outcome and treatment engagement among Veterans presenting for Compensation evaluations for PTSD, and will determine the efficacy of an intervention to foster treatment engagement and abstinence.

#### **D. Research Design and Methods:**



## A. Design for the Proposed Evaluation and Clinical Trial Components



### Sampling of Patients with Substance Use and/or Risky Drinking:

The sampling frame will be the population of OEF/OIF/OND Veterans being evaluated at the participating sites for PTSD who are not already service-connected for it. We will use systematic sampling procedures to define the sample (Cochran, 1977), and will stratify the sample to ensure equal representation of patients from the Tennessee and Connecticut sites. A sampling interval will be estimated to achieve the recruitment rate, and extra recruiting will be included to account for Veterans who refuse to participate and/or are found to be ineligible after approach. The sampling interval will be adjusted after the first six months based on rates of participation from this phase. If the rate of participants meeting substance use criteria for randomization is below the anticipated rate of 25%, we will initiate a brief pre-screen for substance use prior to enrollment and oversample Veterans who pre-screen positive for substance use. This oversampling will allow for sufficient substance-using Veterans to be enrolled in the randomized clinical trial of SBIRT.

As is indicated in the Figure on the preceding page, all Veterans who screen positive for substance use disorders or risky alcohol use will be enrolled in the Clinical Trial Component. A conservative estimate was made that 160 veterans (25% of the sample) would be randomized to SBIRT or No-Additional-Treatment.

### Justification for Combining Evaluative and Clinical Trial Components in a Single Study:

There are scientific and financial advantages to combining the Evaluative and Clinical Trial Components in a single study. The main scientific advantage is that the findings from the two Components can be considered together. The evaluation study and the control group in the clinical trial will be used to describe predictors of outcome in a naturalistic design; the clinical trial will consider whether these outcomes can be altered with a specific intervention. There are financial efficiencies to conducting a study with two integrated sets of aims, in that the study infrastructure (staffing, investigators, etc.) is not funded twice.

The main concern in combining the two components is that the two will interfere with each other, either by having procedures during the Evaluative Component influence the Clinical Trial Component, or vice versa. The study design was carefully considered to minimize such interference.

With regard to preventing the Evaluative Component from interfering with the Clinical Trial Component, the assessments are interrogative, and contain no implication that treatment is needed. The volume of assessments (taking approximately two and quarter hours) and multiple topics assessed make it unlikely that any particular treatment message will emerge from them. The question of whether there is an "assessment effect" was addressed in an imaginative clinical trial in which 775 patients presenting to an emergency room received either brief screening for substance use or screening and more in-depth assessment; no effect of

assessments was found (Daeppen, Gaume et al. 2007). Settings in which conducting assessments have been associated with reduced substance use have generally involved assessment by decisionmakers (e.g. judicial system personnel) or physicians taking a smoking history, and not assessments clearly delineated as confidential research assessments. The large multisite clinical trial of behavioral therapies for alcoholism, Project MATCH, involved an assessment battery that was long relative to the study interventions. Nevertheless, a variety of outcomes associated with receiving different types of interventions could be discerned (e.g. Ilgen, McKellar et al. 2006).

Standard procedures will be employed to see that the delivery of the study therapy and the collection of study data are separated. The Evaluative Component and Clinical Trial Component will be carried out by a different staff member for each Veteran. After the data collector completes the assessments of the Veteran eligible for randomization, the data collector will enter the information for urn randomization into the computer program, but the study therapist will actually give the software command to conduct the urn randomization and generate group assignment. All outcome evaluations will be conducted by the data collector, and Veterans will be asked not to tell the data collector whether SBIRT was delivered. In summary, the clinical trial is not adversely impacted by the presence of a preceding Evaluative Component.

It also is unlikely that the Evaluative Component will not be interpretable because of the Clinical Trial Component. The 480 Veterans who are not randomized (because they do not have risky alcohol use and/or substance use) will be compared to the 80 substance users randomized to No-Additional-Treatment, using a prospective observational design to determine effects of substance use. Both groups will receive serial assessments that are not likely to impact outcomes.

2. Power Analysis for Analysis of the Effects of Substance Use on Outcomes: The effects of substance abuse on outcomes will be analyzed by random effects regression analyses. The treatment attendance outcome will yield a value for each week (attendance or not) and PTSD severity will be assessed at three time points (baseline, 4 and 12 weeks). In the primary analysis, these repeated-measures outcomes will be regressed on substance use, with covariates included that represent potentially confounding differences between Veterans with and without substance use disorders. The proposed sample of 560 participants receiving No-Additional-Treatment, of whom 80 are substance users, has power  $> .80$  to detect standardized mean differences in linear slopes as small as  $\delta = .25$ , allowing for potential downward bias in effects from nonrandom group assignment (Optimal Design software version 1.77), and partial  $\eta^2$  of  $< .1$ , correcting for non-sphericity (G\*Power 3.1.2, Buchner et al., 1992-2009).

3. Power Analysis for Clinical Trial Component: This study is powered to determine whether Veterans assigned to SBIRT have greater probability of attending substance abuse treatment than those assigned to No-Additional-Treatment. A sample size of 128 is sufficient to detect a standardized effect size of the difference in linear trends in probability of treatment attendance by week between treatment and control groups of  $\delta = .50$  with power =  $.80$  and  $\alpha = .05$  (Optimal Design software, version 1.77). Only minimal attrition is expected because VA service use data will be available for Veterans who do not attend any follow-up assessments, although the sample size allows for loss of 20% of participants.

At least a moderate effect size on treatment attendance is expected because Veterans who agree to substance abuse treatment can be escorted to substance abuse treatment at the time of SBIRT therapy. As described in detail in the Facilities Section, the VA facilities in West Haven and Nashville have comprehensive substance abuse treatment and dual PTSD-substance abuse treatment available on demand.

Assuming a conservative standardized effect of .50 on probability of daily substance abuse, a sample size of 128 is sufficient and allows for 20% attrition. An effect size of 0.5 is within the range of effects on substance abuse outcomes reported for SBIRT interventions (Kaner, Beyer et al. 2007). The effect of the SBIRT intervention on slopes of substance use is likely to be substantial if Veterans assigned to SBIRT preferentially avail themselves of available substance abuse and/or PTSD treatment at VA. It is noteworthy that studies of behavioral interventions for PTSD and concomitant substance use reported large effect sizes. For example, Brady and colleagues reported pre- to post-treatment effects of 1.26 for substance use severity when Exposure Therapy was provided to people with PTSD and cocaine abuse (Brady, Dansky et al. 2001). Mean differences and SDs were used to compute a pre-post effect size of .94 for days of alcohol use in a behavioral intervention targeting PTSD and alcohol use among Veterans (Donovan, Padin-Rivera et al. 2001).

## B. Experimental Participants

### 1. Recruitment of Veterans Presenting for Compensation examinations for PTSD:

The recruitment strategy involves identifying OEF/OIF/OND Veterans who have submitted requests for initial PTSD Compensation examinations.

Veterans applying for initial Compensation and Pension exams will be sent a letter by Express mail from Dr. Rosen describing the study and notifying them that research staff will call with more information about the study in about six days. Up to three attempts will be made to contact the Veteran for recruitment before we will stop attempting. The letter will include a phone number to call to opt not to receive the research call. No phone calls will be made to Veterans calling to opt out.

We will also supply brochures and flyers to the Compensation and Pension office to make available to potentially eligible Veterans.

The reason to follow these recruitment procedures is that it is not feasible to recruit Veterans at the time they come for their Compensation examinations because the Veterans and examiners are too busy to complete the full research evaluations if they are recruited on-the-spot at the Compensation examinations, and the assessments are designed to be collected before the Compensation examination.

The proposed letter recruitment strategy, which was used in the QUERI study, a multi-site study of the Compensation and Pension process directed by Theodore Speroff, the Nashville site P.I. for this study, was effective. Of the 119 Veterans who were approached for study participation at West Haven, 16 who were called refused to participate and 10 returned opt-out letters, leaving the vast majority (n=93) who participated in this study. There were no adverse events associated with recruitment or with any of the study procedures. Most importantly, the QUERI study demonstrated Veterans' willingness to participate in a study of the Compensation process, even one that manipulated the very interview itself and involved audiotaping. It is noteworthy that only \$10 was provided for participation in the QUERI study (because it involved little additional time), and substantially more is being offered for participation in the proposed study.

### 2. Inclusion and Exclusion Criteria

#### a. Inclusion Criteria

- Veteran of OEF/OIF/OND?
- Not currently receiving VBA Compensation for PTSD
- Able to participate psychologically and physically, able to give informed consent and complete assessments, and participate in study procedures
- Between the ages of 18-65 years old.

b. Exclusion Criteria: Will not be able to attend the week 4 or 12 appointment because of anticipated incarceration or move

3. Criteria for Randomization to SBIRT or Control: All Veterans who complete the assessments and meet the substance abuse criteria (below) will be randomized except:

a. Those who will not be able to attend the follow-up assessments because of planned incarceration or move

b. Those enrolled in substance abuse treatment meeting three or more times per week.

The substance use criteria for randomization are:

**Either risky alcohol use OR self-reported use of an illicit drug within the last 28 days.**

i. Risky alcohol use will be defined by standard criteria: >14 drinks/week or >4 drinks/occasion for men 65 or younger; >7 drinks/week or >3 drinks/occasion for women) (Saitz 2005). A standard drink will be 0.5 oz of absolute alcohol, equivalent to 10 oz of beer, 4 oz of wine, or 1 oz of 100-proof liquor

ii. Self-reported use of an illicit drug on at least two days in the preceding 28 days.

*Veterans who use opioids will be eligible for randomization if any of the following apply to the opioids:*

*--the opioids were not prescribed to the Veteran*

*-- the Veteran describes obtaining the opioids from more than one provider (other than coordinated care)*

*-- the Veteran endorses the SCID screening question indicating use of the drug for non-medical purposes (First, Spitzer et al. 1996)*

Veterans who use medical marijuana will be eligible for randomization. Justification: Veterans sometimes only use medical marijuana for medical reasons, sometimes use medical marijuana for reasons other than what it was prescribed for (e.g. to relax and not for pain relief), and sometimes have a medical prescription but also use marijuana from other sources. Regardless, medical marijuana use puts someone at risk for future misuse of cannabis or other drugs. Furthermore, medical marijuana is not legal in some states or federally. Randomized clients will be counseled about the risks if cannabis is used in ways other than how it is prescribed.

#### Justification for Broad Inclusion Criteria and Few Exclusion Criteria:

The inclusion criteria for randomization require that Veterans have enough substance abuse for there to be room for improvement. Veterans with physiological dependence are not excluded because they may benefit from detoxification services available at the participating VA facilities. Veterans who are using drugs or alcohol and are currently in treatment (< 3 times per week) will be randomized because their recent use places them at particularly high risk for discontinuing treatment (Simpson 1982), absent further intervention. Thus they have room to both reduce their substance use and improve their expected treatment attendance.

#### Justification for Enrolling Veterans with Comorbid TBI:

Histories of TBI will be inextricably intertwined with histories of PTSD in OEF/OIF Veterans with PTSD. TBI, PTSD and substance abuse frequently co-occur and intoxication predisposes people to both TBI and PTSD (Parry-Jones, Vaughan et al. 2006). The prevalence of *possible* Traumatic Brain Injury among returning OEF/OIF Veterans was 19.5% in one 2008 survey and 15.2% in a widely cited study of army infantry soldiers returning from a one-year deployment in Iraq (Hoge, McGurk et al. 2008). The impact of TBI on outcomes is controversial, with one study in the New England Journal of Medicine noting that much of the impairment in one year follow-up of soldiers who had experienced TBI was accounted for by comorbid PTSD and depression (Hoge, McGurk et al. 2008). However, other analyses have suggested that even mild TBI is related to physical symptoms years after the initial injury (Vanderploeg,

Belanger et al. 2009). The cognitive effects of mild TBI are difficulties with processing speed, multitasking, and sustained effort; the behavioral effects of TBI are relatively non-specific.

When Veterans undergo baseline assessments with the data collector, a questionnaire used in VA to make a preliminary diagnosis of TBI will be administered (TBI Clinical Reminder). In addition, the Montreal Cognitive Assessment (MOCA) will be administered to determine the extent of cognitive impairment. A history of TBI, with or without cognitive impairment on the Montreal Cognitive Assessment, will be determined and will be included as a covariate in outcome analyses.

#### 4. Feasibility:

a. Feasibility of Identifying People Applying for Service Connection for Compensation Exams: At both VACT and TVHS, the Compensation and Pension Clinic schedules Veterans who apply for Compensation for examinations, making this clinic an efficient place to identify potential study participants. We have established procedures to recruit Veterans presenting for Compensation examinations in our previous studies.

b. Feasibility of Enrolling 480 Veterans in the Evaluative Component:  
Tennessee: During 2009, TVHS was the site for 299 initial PTSD Compensation examinations for OEF/OIF Veterans, including 22 women.

VA Connecticut: After obtaining IRB approval, our group reviewed the VA charts and Compensation examination reports of 62 consecutive OEF/OIF Veterans who underwent Compensation examinations at VA Connecticut for the six-month period between 7/1/08 and 12/31/08 to estimate rates of substance use and service use. The fact that 62 OEF/OIF Veterans presenting for new PTSD examinations were examined during a six-month period at VA Connecticut, suggests a rate of 124 per year. According to CPRS, between 5/1/12-8/1/12 there were a total of 376 mental health exams scheduled of which 117 were for people not currently service-connected.

i. A rule-out or definitive diagnosis of alcohol abuse was made in eighteen Veterans and two additional Veterans had a substance abuse diagnosis for a total of 32% with an alcohol and/or substance abuse diagnosis. This likely underestimates the rates of substance use and risky drinking because chart review is an insensitive way to identify Veterans with substance use problems (Hawkins, Kivlahan et al. 2007). Only 3% of claimants had received any substance abuse treatment at VA during the three months before the evaluation and only 47% had received any mental health treatment. Altogether, 61% were diagnosed with PTSD on the Compensation examinations and 39% were not.

These results suggest that there is a high prevalence of substance use among OEF/OIF Veterans applying for PTSD-related Compensation, an unmet need for substance abuse treatment, and a range of PTSD-symptom severities.

As noted earlier, 78% (93/119) of the initial Veterans approached agreed to enroll in that more invasive (the Compensation exam itself was altered), lower-paying study, and enrollment in this study is expected to be similarly high. Thus, sufficient OEF/OIF Veterans are evaluated to enroll 200 per year across the two sites. As discussed in the Human Subjects section, participation is not arduous and Veterans will be paid substantially for completing assessments to avoid disproportionately enrolling impoverished Veterans.

c. Feasibility of Randomizing 160 Veterans in the Clinical Trial Component: The above numbers suggest that 423 OEF/OIF Veterans (299 Nashville and 124 West Haven) will undergo an initial Compensation examination for PTSD each year or 1269 over a three-year recruitment period. Based on the high rates of risky alcohol use and other substance use among Veterans with PTSD, we estimate that 25% of Veterans with PTSD claims (n=268) will be eligible for randomization based on risky alcohol and/or drug use. Thus, identifying 160 Veterans who go on to random assignment is feasible.

d. Feasibility of Randomizing Veterans to Therapy that Begins After the Compensation Exam:

Dr. Rosen is the P.I. of an RR&D-funded study in which patients who were presenting for Compensation examinations were randomly assigned to one of two types of counseling focusing on vocational rehabilitation. As of June 2011, 75 patients had been randomly assigned of whom 96% attended at least one scheduled therapy session. This demonstrates the feasibility of the proposed model in which patients are referred to attend therapy after their Compensation examinations and the likelihood that Veterans who complete assessments will attend SBIRT if they are assigned to it.

4. Balancing the study groups: Participants will be randomized using an urn randomization procedure in order to increase the likelihood of balanced allocation of participants to the two interventions on variables that may affect outcome. In urn randomization, an algorithm modifies ongoing randomization probabilities based on prior composition of treatment groups, maximizing multivariate equivalence of treatment groups (Stout, Wirtz et al. 1994). Thus, urn randomization offers the benefits of balancing allocation of important prognostic variables in treatment groups, while still retaining other benefits of random assignment. A different urn will be used at each site, thus stratifying by site. The factors in the urn will be those that literature has suggested may be related to outcomes in Veterans with PTSD and alcohol use:

- Self-reported illicit drug use in last 28 days
- Days of self-reported alcohol use in the last 28
- Current enrollment in VA psychiatric or substance abuse treatment (yes/no).
- Gender: Women have a telescoped course of substance abuse with adverse

effects developing sooner after their substance use than in men but despite this rapid worsening, women appear to wait longer before seeking substance abuse treatment than similarly afflicted men (Arfken, Borisova et al. 2002). Men and women in this study will differ in that more women will have experienced Military Sexual Trauma (Kimerling, Gima et al. 2007). VA facilities screen for and treat Military Sexual Trauma (Kimerling, Gima et al. 2007) and both participating facilities have dedicated women's clinics with expertise in treating female Veterans with PTSD arising from sexual assault. The effectiveness of cognitive-behavioral treatment for women Veterans with Military Sexual Trauma was convincingly demonstrated in a large multi-site clinical trial of CBT for PTSD (Schnurr, Friedman et al. 2007). The SBIRT intervention will include modules to address issues that have been shown to concern women with substance use disorders or PTSD – child-care, abusive or disapproving family members, pregnancy, and concurrent mood and anxiety disorders. Although there are considerable differences in the issues and course of treatment in male and female Veterans, meta-analyses do not show gender differences in response to SBIRT interventions (Kaner, Beyer et al. 2007), and at this phase of research, enrolling both genders is appropriate.

C. Single Patient Flow Chart

\_\_\_\_ Veteran receives mailed letter explaining that a telephone call will be coming and allowing the Veteran to opt-out of receiving it

\_\_\_\_ Telephone call inviting participation. The research assistant asks the Veteran questions to determine eligibility. Following a script, the research assistant describes the study to the Veteran and schedules an appointment for informed consent and baseline data collection. Appointments will be scheduled on the day of the Compensation examination or up to two weeks before it.

\_\_\_\_ Informed consent

\_\_\_\_ Evaluative Component: Data collector conducts assessment. If the Veteran meets the substance use and other criteria for randomization, the data collector contacts Dr.

Anne Black (or her back-up) with the information Dr. Black needs to conduct the urn randomization.

\_\_\_\_ Randomization and Scheduling of Next Appointments: The data collector arranges for the Veteran to telephone Dr. Black in a separate room from the research assistant. The data collector asks the Veteran not to tell him/her about any appointments other than the four week follow-up visit.

Dr. Black tells Veterans randomized to SBIRT about the assignment and explains how to make contact with the study therapist. This will happen by all of the following that the Veteran agrees to and/or are feasible: (1) giving the Veteran the therapist's name and telephone number, (2) giving the therapist the Veteran's name and telephone number, (3) giving the Veteran directions to the therapist's office to schedule an appointment. Therapists will schedule therapy sessions immediately after the Compensation exam if feasible and if not, will offer times in the subsequent two weeks.

Regardless of what condition the Veteran is randomized to, Dr. Black will schedule the Veteran's week 4 follow-up appointment with the data collector using a shared online calendar (but no client identifiers).

\_\_\_\_ Veteran undergoes standard Compensation examination

\_\_\_\_ Substance use patients randomized to SBIRT receive counseling.

\_\_\_\_ Weeks 4 and 12: Data collector administers assessments

#### **Justification for flexible scheduling of first data collection visit and first SBIRT**

**counseling:** Our experience in the ongoing Benefits Counseling study has been that Veterans vary in how able and willing they are to schedule appointments before and immediately after Compensation examinations, depending on what time the examination is scheduled, how far the Veteran travels to the examination, and what other obligations the Veteran has. Flexible scheduling of the first data collection up to two weeks before the Compensation examination and SBIRT within two weeks after it balances feasibility and experimental rigor.

#### D. Major Sources for the SBIRT-VA manual

1. The SBIRT manual for this proposal, SBIRT-VA, was adapted from an existing SBIRT manual (Babor 2001). The SBIRT-VA manual codifies basic substance abuse screening, treatment, Motivational Interviewing and referral procedures. It is designed for providers with minimal substance abuse expertise and is easy for experienced substance abuse providers to deliver.

2. The SBIRT-VA manual borrows from Benefits Counseling manual (Dr. Rosen's study funded by RR&D). Benefits Counseling requires the therapist to engage a Veteran who has presented for a Compensation examination into a broader discussion of the Veterans' vocational goals. The SBIRT intervention involves a similar transition. SBIRT requires the therapist to engage a Veteran who has presented for a Compensation examination into a broader discussion of the Veterans' treatment goals and potential need for substance abuse treatment. The therapist talks to the Veteran about how the Veteran came to apply for service-connected disability to build a therapeutic alliance and ascertain the Veterans' goals.

3. The barriers to attending treatment that are addressed using standard motivational interviewing methods were drawn from barriers identified in a qualitative study of OEF/OIF and older veterans (Sayer, Friedemann-Sanchez et al., 2009).

E. Description of SBIRT/Therapy Procedures: A manual describing SBIRT-VA is attached as Appendix 1.

##### 1. Logistics

a. Setting: The therapist will contact participants to schedule the therapy. If the Veteran does not want to come for face-to-face counseling, the therapist will offer to conduct the counseling by telephone. The counseling by telephone will have the same content as the face-

to-face counseling, except that Veterans will be asked to verbally indicate the values that are most important to them instead of sorting physical cards with this information. Although less compelling than the data for face-to-face counseling, SBIRT has been conducted effectively by phone and allowing for counseling by phone is feasible and allows for Veterans who otherwise would not get study counseling to get it.

- b. A videotape will be set up to rate the study therapist (described later)
- c. Frequency: Therapy will be conducted in a single 60-minute session.

2. Therapist Stance: There are several acronyms (OARS, FRAMES) to describe the methods Motivational Interviewers are asked to follow. Key features of Motivational Interviewing are

- a. Expressing Empathy: The therapist will elicit and empathize with the emotions that accompany the Veteran's disability application. Veterans experience considerable distress during Compensation examinations (Sayer, Spont et al. 2005).

- b. Supporting Self Efficacy: The therapist will reinforce any belief the Veteran has that change is possible, that reduced substance use is achievable, or that substance abuse treatment works. For example, the therapist can point out the initiative the Veteran has taken in facing his or her disability

- c. Rolling with Resistance: The therapist does not argue with the Veteran's resistance, but "rolls with it." The therapist will use the Veteran's "momentum" to further explore the Veteran's views. By allowing the Veteran full-throated expressions of resistance to change ("I like to drink and nobody can tell me not to"), the therapist may amplify and subtly undermine the Veteran's statement "You feel you like to drink so you will, no matter what anyone says." A response by the Veteran reflecting change talk would be "Well, I don't drink at work," which would be followed up by inquiries about work-related concerns.

- d. Developing Discrepancy: The therapist works to develop a discrepancy between where the Veteran is and where the Veteran wants to be by helping the Veteran examine his or her current behavior and future goals.

- e. Using Motivational Interviewing procedures in the SBIRT manual including:

- (i) Identifying the Veterans' values through a card sort,
- (ii) The change ruler, on which the Veteran rates his/her willingness to change current behavior
- (iii) Listing the pros and cons of changing.

3. Overview of Session: The therapist will try to adhere to the following sequence --- each step is discussed in more detail below:

- a. Explain purpose of therapy.
- b. Inquiry about Veteran's experience of Compensation examination. Ask if Veteran has questions about the next steps in the disability determination process. Therapists have to be equipped to directly address Veterans' concern that obtaining substance abuse treatment may impact their claim. There are complicated issues (United States Court of Appeals, 1997; Rosen and Rosenheck 1999) that will be summarized to the Veteran as follows:

<b>Reason obtaining substance use treatment may hurt your claim</b>	<b>Reasons obtaining substance abuse treatment may NOT hurt your claim</b>
--Substance abuse may appear to be your problem and not PTSD	--You may have both PTSD and a substance abuse problem; many Veterans do. --Your substance abuse may be reduced by treatment, thus making it is easier to discern the effects of PTSD



c. Discuss the relationship between PTSD and substance use (substance use as temporary coping). Veterans are told the ways in which alcohol and other drugs may temporarily relieve distress from PTSD symptoms. However, they are told that in the long-term, substance use is a form of avoidance that prevents Veterans from coping with symptoms of PTSD and is a barrier to recovery from PTSD. This approach was drawn from a version of Cognitive Processing Therapy that showed promise in a pilot study of Veterans (predominantly OEF/OIF) with concomitant alcohol and substance abuse problems (McCarthy 2009).

d. Explain that this is an opportunity to consider if there is any other treatment the Veteran needs; administer screening, provide feedback

e. Motivational interview concerning seeking substance abuse treatment, abstaining

f. Referral to primary substance abuse or PTSD treatment. The SBIRT therapist will encourage Veterans to consider a referral to substance abuse treatment but will support Veterans who are determined to attend PTSD treatment instead.

4. Explain purpose of therapy: The purpose of this therapy is to help the Veteran cope with the disability application process and obtain any treatment he/she needs.

5. Inquiry about Veteran's experience of Compensation examination. The purpose of this inquiry is to ascertain the Veteran's immediate goals, gain insight into the Veterans' values, and build an alliance with the Veteran.

6. Explain that this is an opportunity to consider if there is any other treatment the Veteran needs; administer screening, provide feedback. The screening instrument for this SBIRT is the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) (Group 2002). The ASSIST takes five minutes to administer. It consists of eight questions concerning use of alcohol and or drugs, mostly within a three-month timeframe. It includes inquiries about amount of use, and incorporates questions that are somewhat indirect such as whether anyone else asked the Veteran to cut-down on use (Ewing 1984). The ASSIST has excellent reliability (Group, 2002) and validity (Humeniuk, Ali et al. 2008).

A weakness of the ASSIST is that it does not include questions concerning the amount of alcohol imbibed at a single setting, an important question to detect risky drinking. Therefore, to supplement the ASSIST, the therapist will administer the three-item version of the Alcohol Use Disorders Identification Test (Bohn, Babor et al. 1995), the AUDIT-C. Several studies have suggested that the three-item AUDIT-C is as good a screen for alcohol use as the 10 item AUDIT (Kriston, Holzel et al. 2008). Both the AUDIT and the AUDIT-C have very good psychometric properties (Reinert, Allen et al. 2007) and high accuracy (approximately 0.90) in people with psychiatric disorders (Dawson, Grant et al. 2005). The ASSIST and AUDIT come with pictures illustrating the relationship between scores and need for treatment.

7. Motivational Interview concerning engaging in substance abuse treatment and attempting abstinence. Standard Motivational Interviewing approaches have been modified to address issues that are specific to Veterans presenting for PTSD examinations. The therapist will be prepared to address barriers specific to this population including: Veterans' concerns about addressing their PTSD (Sayer, Friedemann-Sanchez et al. 2009), barriers predominantly faced by women (need to arrange child-care, having abusive or disapproving family members, pregnancy); concurrent depression and anxiety; and concern about the effect of seeking treatment on the Compensation Process.

Some Veterans will already be attending treatment, although the fact that randomized Veterans are engaged in risky drinking or substance use suggests there is some room for improvement. The therapist will explore the current treatment arrangement to determine if the Veteran is attending regularly, adhering to all recommended treatment or just some of it, or in need of further treatment. The therapist will also explore whether the treatment the Veteran is attending is addressing the Veteran's substance use, as it has been asserted that substance

abuse treatment is often not addressed in PTSD-focused treatment (Kosten 2008), absent some additional intervention.

Some patients will be engaged in risky drinking and will not want to pursue abstinence. For these Veterans, a harm reduction approach will be taken. The therapist will attempt to negotiate with the Veteran a plan to drink fewer drinks per occasion, or drink on fewer days, but not necessarily strive for abstinence.

8. Content: Referral to Treatment

a. Review Eligibility: OEF/OIF Veterans, with few exceptions, are automatically eligible for VA care for five years after their discharge from military service. Thus, Veterans will have access to usual treatment at participating facilities. However, Veterans may have non-VA health insurance (e.g. from work or a family member). The SBIRT therapist will facilitate engagement in those treatments as well (e.g. determine what services are covered by the insurance plan and assist the Veteran in scheduling an appointment). Veterans will be referred to both PTSD and substance abuse treatment. The substance abuse treatment referral will be made first.

b. Offer concrete actions: Offer to walk Veteran to clinic, make phone call with Veteran.

E. No-Additional-Treatment Control Condition:

As noted in the Single Patient Flow Chart, veterans assigned to the control condition will not receive any study-related therapy. A Veteran who completes a Compensation examination ordinarily has no further treatment, referral or debriefing as part of the Compensation examination.

G. Assessments

1. Separation of Therapies from Assessments: Veterans will be instructed during the assessments not to tell the research assistant if they are receiving study counseling. To determine if the blind was maintained, we will ask the research assistant to rate for each client the condition the Veteran was assigned to and the research assistant's certainty about the randomization on a 0-100 visual analogue scale with 0 being no certainty and 100 being absolute certainty.

2. Data Collection Procedures: Participants will be asked at the beginning of enrollment for the names and telephone numbers of three people who can find them if the research assistant has difficulty reaching them over the course of study participation. Within two days of an upcoming appointment, participants will receive a reminder call and/or a short message service reminder (text message). If a participant misses a scheduled appointment, the research assistant will call to reschedule. If the participant cannot be reached, staff will call up to three identified contacts to locate the participant.

Research staff will call the Veteran up to three times over a three week period. If, after talking to a contact, the research staff member learns that there is another telephone number that should be used to reach the patient, that number will be called up to twice over a two-week period.

3. Location: Research staff may offer to meet Veterans at a convenient location for data collection visits, including Veteran Centers, local VA clinics, or public places. These visits will occur in a private room and this arrangement will be verified in advance of the visit with both the participant and the facility. Research staff will keep identifiable patient information and study data in separate folders. All information will be transported by research staff in a locked bag and will be brought directly back to the VA for filing after study visits.

3. Schedule of Assessments:

Visit	Domain	Assessment
BL	Characterize Participants	Baseline Questionnaire (including TBI screen) MOCA
BL	Beliefs about Compensation	Disability Application Appraisal Inventory Disability Beliefs Scale
BL	Substance Use	SCID substance abuse module
BL,4,12	Substance Use	Substance Use Calendar
BL, 12	Alcohol Use	Ethyl Glucoronide
BL	PTSD	Life Events Checklist and Military Sexual Trauma Screen
4	Process	Veterans' understanding of the study assessments and their relationship or lack thereof to the C&P exam
BL,4,12	PTSD	CAPS
BL,4,12	Other Psych	Beck Depression Inventory II
BL,4,12	Service Use	Service Use Calendar
BL,4,12	Process	Stage of Change
BL,4, 12	Other Psych	Response to Stressful Experiences Scale
At Rx	Process	Satisfaction with Therapy
End-of-Study	Chart Review and Database Extraction	Review of Service Use and Diagnoses from VA Databases; Reports from Compensation Examinations; Disability Determination by VBA; Distance between Veterans' addresses and VA site

**Justification for Schedule of Assessments:** The initial 4-week assessment follow-up date was chosen because results of Motivational Interviewing interventions have been detectable this quickly in other studies (Burke, Arkowitz et al. 2003); the later, week 12 assessment will allow for detection of later-emerging effects of other VA treatments preferentially attended by Veterans who received the SBIRT intervention.

The end-of-study service use assessments will be conducted in the middle of year 4. Virtually all of the last cohort of study participants will have service use data for the three months after claims adjudication available at that time; the highly-publicized delays in the awarding of benefits generally are caused by delays prior to the Compensation evaluation.

**Time to Complete Assessments:** The baseline assessment will take approximately two and a quarter hours to complete. Approximately 45-60 minutes are allotted for the CAPS and Life Events Checklist; ten minutes for each of the baseline questionnaires, SCID substance abuse module, and service use calendar; and twenty minutes for each of the other baseline assessments.

#### 4. Demographics and Other Characteristics

a. **Baseline Characteristics Questionnaire:** A questionnaire to characterize study participants has been culled from the questionnaire used in a prior multi-site study (Morrissey, Calloway et al. 2002) and in our current Benefits Counseling study. It is included as Appendix 2. It covers the following domains: demographics, military history, psychiatric history, employment, and legal status. It will also include a six-item measure of social support and the 10 items from the Attitudes Toward Seeking Professional Psychological Help Scale-Short Form (Elhai et al., 2008). This widely-used scale consists of two factors, one reflecting openness to

seeking treatment for emotional problems and the other reflecting value of seeking treatment and need for it.

Social support is measured as the number of people from six categories that would loan clients \$100, provide them with a ride to an appointment or provide them with emotional support if they were suicidal (Lam and Rosenheck, 1999).

The Questionnaire also includes the VA four-question screen for a presumptive diagnosis of TBI. A presumptive diagnosis of TBI is made when the Veteran responds positively in each of four domains:

- i. History of Potential Head Injury (e.g. blast, vehicular accident, wound above shoulders)
- ii. Symptoms Immediately After Injury (e.g. being dazed, not remembering event)
- iii. Problems Afterwards (e.g. memory problems or lapses, light sensitivity)
- iv. Problems in the Past 7 Days (e.g. memory problems, balance problems, headaches)

b. Montreal Cognitive Impairment Test (MOCA): The holders of the MOCA copyright allow its use within VA for non-commercial purposes. It is sensitive to impairment in domains prominently impacted by TBI such as visuospatial/executive functioning, attention, abstraction and in fact contains several items from the Core Brief Neuropsychiatric Battery (TBI Clinical Reminder) used at VHA to screen for TBI. A score of <26 indicates substantial cognitive impairment (Nasreddine, Phillips et al. 2005).

## 5. Assessments of Attitudes and Beliefs about Compensation

a. The Disability Application Appraisal Inventory's test-retest reliability, internal consistency, factor structure and validation against selected MMPI subscales were tested and the measure has good reliability and construct validity (Sayer, Spont et al. 2004). The Inventory asks the Veteran to rate his/her reasons for seeking service connection. Factor analysis has yielded three subscales reflecting different reasons for seeking Compensation (Sayer, Spont et al. 2004). The "validation" subscale involves seeking benefits to "show that there is a reason for my problems," "feel like justice has been served," and "feel less like I am to blame for my problems." The "Self-Other Acceptance Scale" largely reflects interpersonal issues such as "My family wants me to become service-connected for PTSD." The "Financial Benefits" subscale items reflect seeking compensation to obtain money.

b. It has been assumed that Veterans have attitudes that can be paraphrased as "A Veteran who attends mental health treatment is more likely to get service-connected benefits than one who does not," "A Veteran who reports using illegal drugs is less likely to get service-connected than one who denies using, and "A Veteran who works is less likely to get service-connected than one who does not." Existing rating scales do not fully capture the belief that a Veteran's receipt of Compensation benefits is influenced by whether the Veteran (a) attends treatment, (b) recovers from the disabling illness, or (c) is judged to have alcohol or drug-related problems.

The Disability Beliefs Scale (attached as Appendix 3) asks Veterans to indicate how much a Veteran would affect his or her chance of getting Compensation Benefits on a scale from "Much Less Likely to Get Benefits" to "Much More Likely to Get Benefits" if the Veteran was in any of the following categories (a) engaged in VA treatment, (b) symptomatic from PTSD, and (c) abstinent from drugs and/or alcohol. For example, the Veteran is asked to rate on an interval scale whether the following treatment-related situation would make it more or less likely a Veteran would be awarded Compensation Benefits: "The Veteran takes medication for a psychiatric condition," "The Veteran is attending mental health treatment regularly," and "The

Veteran's symptoms have gotten better with treatment." A confirmatory factor analysis will be conducted of the Disability Beliefs Scale to determine if the anticipated three factor structure emerges, and continuous subscale scores for each factor will be considered separately in the data analyses.

Items for the Disability Beliefs Scale were drawn from existing measures that rate related constructs. The items concerning the relationship between treatment and receipt of disability payments were adapted from items used in a completed study of supportive employment at VA (Rosenheck and Mares 2007). Items were also drawn from the "Negative Expectations" subscale of the Disability Application Appraisal Inventory (not the same scale that rates reasons for seeking disability payments).

6. Substance Use Calendar and Ethyl Glucuronide (ETG): The timeline follow-back Substance Use Calendar assesses substance use on a daily basis. The use of a calendar format prompts participants to remember key dates. It allows for collection of data points for participants who miss evaluation sessions and thus prevents missing data and problems associated with overlap of data points. Timeline follow-backs have been sensitive to change in research settings (Weiss, Greenfield et al. 1998) and can be valid in patients with concomitant psychiatric illness (Petrakis, Poling et al. 2005).

Ethyl Glucuronide is produced and equilibrates throughout nail beds, thus allowing measurement by any nail sample of sufficient weight. Approximately 10mg of nail is required for analysis, which can be obtained from 10mm (a quarter's width) of nail from each of ten digits. Nail-clippers soaked for 10 minutes in 70% rubbing alcohol are used for the actual clipping. Nail levels of ETG have correlated with self-reported number of drinks among college-aged women at .51 and men at .64, with the lower correlation among women possibly reflecting greater use of nail care products (Jones, Jones, et al., 2011).

M. Jones, J. Jones, D. Lewis, C. Plate, M. Fendrich, L. Berger, & D. Fuhrmann. (2011, June). Correlation of the alcohol biomarker ethyl glucuronide in fingernails and hair to reported alcohol consumed. Poster session at the annual conference for the Research Society on Alcoholism, Atlanta, GA.

Samples will be processed at the United States Drug Testing Laboratories (Illinois) with no identifying information other than the study number. After processing, samples will be destroyed following a standard storage period.

#### 7. PTSD Assessments

a. The Life Events Checklist (Weathers, Keane et al. 2001) inquires about whether the Veteran has had exposure to each of 17 classes of traumatic events. Veterans will be asked to identify the trauma causing the most current distress. Military sexual trauma will be defined by having had a sexual experience during military service that was unwanted and involved force or threat of force.

b. Clinician Administered PTSD Scale (CAPS): The CAPS is an extensively validated (Forbes, Creamer et al. 2001; Monson, Gradus et al. 2008) clinical interview used to derive a rating of PTSD symptom severity and diagnosis. It consists of 17 ratings of the frequency and severity of PTSD symptoms listed in DSM-IV-TR. Cluster subscales can be derived for the PTSD symptom clusters of hyperarousal, avoidance/numbing, and re-experiencing.

The CAPS takes 45-60 minutes to administer and requires a data collector with clinical experience. The CAPS is widely considered to be the gold standard measure of PTSD severity, and agreement between the CAPS and self-report measures such as the PTSD Checklist–Military has been variable (Monson, Gradus et al. 2008). Only the CAPS is observer-rated. The CAPS is more specific for PTSD than the PTSD Checklist because unlike the Checklist, the CAPS only rates emotional numbing and hyperarousal symptoms if they are not

accounted for by another disorder.

8. Beck Depression Inventory II is the updated iteration of the older Beck Depression Inventory. Respondents rate 21 statements reflecting the previous two weeks. The Beck includes items reflecting DSM IV somatic symptoms of depression and more cognitive factors associated with depression, and is thus well-suited to depression measurement among people with a high prevalence of somatic symptoms related to substance use. It showed excellent receiver-operating characteristics in identifying depressed Veterans from a cohort of Veterans with TBI and frequent comorbid PTSD (Homaifar, Brenner et al. 2009). Depression has been strongly associated with function among people with PTSD (Hoge, McGurk et al. 2008).

9. The Response to Stressful Experiences Scale contains 22-items describing the respondent's characteristic methods for dealing with stressful experiences. Each item is rated on a 5-point scale indicating the extent to which the item describes a method used by the respondent. Variability among participants in the availability and use of methods to deal with stressful experiences has accounted for variance in severity of PTSD symptoms in military samples (Johnson, Polusny, Erbes et al., 2011).

11. Self-Reported Service Use: A timeline-follow-back method will be used to determine service use during the preceding 60 days. An important benefit of this approach over summary measures is that it minimizes problems associated with information being collected twice for the same service, such as detoxification counted as a medical hospitalization and as substance abuse treatment, and it minimizes problems associated with overlapping data points. The questions about service use will be drawn from the Treatment Services Review (McLellan, Alterman et al. 1992) and the Program and Client Cost-Substance Abuse Treatment (PACC-SAT). The Treatment Services Review includes inquiries about each of the 7 domains explored in the Addiction Severity Index. The PACC-SAT was adapted from the DATCAP and involves questions about different types of services received.

The Service Use calendar has been modified to address analyses that will be conducted in the proposed studies. Specifically, the data collector will code services by non-substance use providers by whether they addressed substance abuse. As shown in the chart review of OEF/OIF Veterans who sought Compensation at VA Connecticut, more OEF/OIF Veterans with PTSD claims received mental health services than specialty substance abuse services. However, VA service use data cannot be used to determine whether people with substance use problems are having those issues addressed if they attend mental health treatment. Therefore, the service use calendar we will be using for self-reported treatment attendance includes inquiries concerning whether substance abuse was addressed during other mental health treatment.

The service use calendar also had questions added to determine what non-VA treatment Veterans received. Data will also be coded by whether it reflects VA or non-VA treatment. Additional questions have been added to determine satisfaction with VA services. Veterans are asked how satisfied they are with the VA services they receive on a 6 point scale.

#### 12. Process Measures:

a. A three-item Motivation for Change scale will be used that taps alcohol or drug use likelihood ("How likely are you to use alcohol or drugs, even a little, ever again?") problem recognition ("How big of a problem is your drug use?"), and treatment motivation ("How interested are you in treatment right now?"). Respondents answer each item using an analogue scale coded from 1 to 100. Scores for the three items are averaged after reverse scoring for the drug-use likelihood item. This simple scale has been sensitive to change in a clinical trial

(Ondersma, Svikis et al. 2007) and a similar scale predicted behavior change in an observational study (LaBrie, Quinlan et al. 2005). Stage of Change measures are of interest because they are one mechanism by which SBIRT may operate. The relationship between Stage of Change and outcome has not been consistent because stage of change is confounded with illness severity but appears to change with brief Motivational Interviewing interventions (Dunn and Ries 1997).

b. Satisfaction with Counseling will be rated on Likert-scaled items that are combined to yield a composite score. *Veterans will be asked to indicate their satisfaction with the amount of attention to PTSD on a Likert-scale anchored by “too much” and “too little.”* The ratings form will be handed to the Veteran, placed in a sealed envelope, and sent to the data manager.

c. Qualitative data concerning the impact of study participation on the examination will be obtained during the week 4 evaluation, first with an open-ended probe: “Tell me any ways the assessment you completed four weeks ago affected you later.” Follow-up probes will address whether the CAPS interview impacted the C&P exam specifically, and whether Veterans believed study participation impacted their service-connection evaluation.

#### H. Chart Review and Database Extraction

1. Therapy Attendance and Service Use Outcomes. Episodes reflecting use of VA substance abuse, specialized PTSD and other mental health treatment will be collected from VA administrative records as described previously (Harpaz-Rotem, Rosenheck et al. 2009). The investigators have extensive experience analyzing VA service use data. Robert Rosenheck is a national authority on service use analyses.

The Austin Information Technology Center provides the service use data for Dr. Rosenheck’s analyses. The Austin databases hold data from all Veterans who received any services from anywhere in VA. The Patient Treatment File contains all episodes of inpatient care delivered within the VA system. The Outpatient Encounter File documents all outpatient VA service use. VA bed section codes indicate hospitalization on specialized units and VA clinic codes indicate outpatient treatment in specialized clinics. In a recent manuscript, Dr. Rosenheck describes analysis of psychotherapy service use codes from these databases (Hunt and Rosenheck, 2011), which will be extracted as psychotherapy participation may reflect a more specific measure of engagement in treatment than broader measures.

Service use data will be collected from three months before the Compensation claim was filed until three months after claims adjudication. We will also collect the date Veteran was separated from military service to determine when VA services became available to each Veteran.

2. Compensation examinations of each Veteran will be reviewed by research assistants who will complete a chart extraction form. The extraction form collates the following information:

i. Clinician diagnosis from C&P exam

ii. Alcohol Use

-- Level of detail describing alcohol use (No mention, Impression but no number of drinks, or number of drinks—including a statement that there has been no recent use).

-- Amount of alcohol reported used in drinks/drinking day

-- Alcohol Use Consequence (no mention, consequences listed)

-- Alcohol Use Disorder Diagnosed (no diagnosis; use noted but no judgment that it is a problem, or merits intervention; rule-out alcohol use diagnosis made; alcohol use diagnosis made)

iii. Other Substance Use (characterized as for alcohol, with delineation of particular drugs)

3. Award determination by VBA: Award determination will also be the dependent measure in proposed secondary analyses. The data collected will be whether any benefit was awarded, and the percentage service connection awarded.

4. The VA databases will be used to identify all non-exclusive psychiatric diagnoses, as defined in the DSM-IV and DSM-V, ICD 9 and ICD 10.

5. Distance from VA: Veterans' addresses collected upon enrollment will be converted into distance from the nearest VA facility using Global Information System (G.I.S.) mapping (Fortney 2000). Participants and VA treatment facilities will be geocoded by street level (the G.I.S. will use the street address) to calculate driving distance as a measure of treatment accessibility. Distance from treatment has been associated with receipt of fewer services (Rost, Fortney et al. 2002).

6. Chart review to determine presence of a substance abuse disorder at time of Compensation.

#### I. Measures Collected from Therapists after SBIRT Counseling Sessions

1. Overview: It is important to measure the fidelity and skill with which SBIRT is delivered, and to measure non-specific but potentially important ingredients such as general supportiveness of the therapist. Each therapists' first eight Veterans treated with SBIRT will be videotaped except if the Veteran asks not be videotaped. Subsequently, a random sample of 10% of sessions will be videotaped and rated. Therapists will set up the recording equipment and sound-amplifying microphone. The camera will be trained on the therapist.

2. Rating of Therapy Videotapes: Videotapes will be rated using ratings drawn from the Yale Adherence and Competence Scale (Carroll et al., 2000) and the current Benefits Counseling study. Standard procedures will be used to rate the videotaped sessions. Two raters blind to the study design will be trained by the P.I. and will rate sessions. During rater training, raters will review the rating form, anchor points, and procedures to rate the sessions. They will then view a videotape, rate it, and review the ratings with the P.I. Discrepancies between the raters will be reviewed and the process will be repeated for successive tapes until adequate inter-rater reliability is achieved. After the two raters have been trained, they will together rate 20% of the collected videotapes.

3. Videotape Rating Scale: Raters will indicate the frequency and extensiveness with which an element of the therapy is covered during a session using a Likert scale anchored by 1- not at all and 7- extensively, with descriptions of what constitutes meeting these anchors. A second scale rates therapist skill level at covering the element (if covered) on a scale anchored by 1- very poor to 7- excellent. The dimensions of adherence and competence are only modestly correlated and thus reflect different aspects of treatment (Carroll, Nich et al. 2000).

The subscales and items will determine:

- i. if essential elements of SBIRT were delivered (assessment, feedback, referral)
- ii. use of Motivational Interviewing (empathy, developing discrepancy, rolling with resistance)
- iii. general factors (optimism, discussion about VA, general inquiries)
- iv. proscribed elements (convey value judgments concerning disability, substance use)

4. Time Spent Providing Counseling: A contact log will be completed for each phone or face-to-face encounter, including scheduling. The contact log will document whether there was a scheduled contact that was not attended, the date and time of contact, type of contact (face-to-face, phone, cancelled appointment), and time spent in minutes.

#### J. Data Analysis for Evaluative Component:



1. Sample Analyzed for Evaluative Component: The effects of substance abuse on outcomes will be analyzed in the sample of 560 participants who did not receive SBIRT, 80 of whom report risky alcohol/substance use and 480 who did not.

2. Data Reduction: Substance use disorder, PTSD diagnosis, and treatment attendance measures are being collected from more than one source. It is important to reduce the data prior to subsequent analyses to identify the outcomes that will be used in the analyses. These data reduction approaches are shown below:

a. The presence or absence of an Alcohol Use disorder at the time of the Compensation examination will be determined by the best estimate procedure developed by Spitzer and colleagues for validating DSM diagnoses (Spitzer, 1983). This procedure involves reviewing all available sources of information, which for this measure will include the SCID interview, Compensation examination report, substance use calendar, chart review and ICD-9 diagnoses.

A sensitive definition of alcohol use disorder will be employed, and the Principal Investigator will review all cases for which the Compensation Examination and SCID diagnosis are discordant. The reasons to use a sensitive but possibly less specific definition of alcohol use disorder are that an extensive literature documents that there are few “false positive” reports of alcohol and other substance abuse (Kosten and Rounsaville 1992). In a population of Veterans applying for PTSD-based disability, Veterans drinking substantial amounts of alcohol are likely to meet criteria for either Abuse or Dependence, and people with PTSD are particularly vulnerable to the psychological disruptions caused by drugs of abuse (Back, Brady et al. 2006). The same approach will be taken to arriving at best estimate diagnoses for other substances of abuse. The stability of the results will be determined by substituting alternate definitions of the substance use construct.

Descriptive analyses will be conducted to describe the agreement between the different sources of information. For example, the definition of alcohol-use disorders will be compared between the SCID Diagnoses during the assessment battery and the Compensation examinations. Preliminary descriptive and ROC analyses will be conducted of the accuracy of the Compensation examinations for determining alcohol use disorders with the validating criterion being the best estimate diagnosis.

b. Treatment attendance will be determined from Austin databases and from the self-reported Service Use calendar. Self-report data will be used for outcomes that cannot be determined from the Austin databases---use of non-VA services, and whether substance abuse was addressed during a counseling session.

Because *sustained* attendance has been more strongly associated with benefit from substance abuse treatment than intensity of treatment (Ritsher, McKellar et al. 2002; Moos and Moos 2003), attendance at treatment will be determined as a dichotomous variable on a week-by-week basis. The extent of therapy attendance will be determined separately for three types of treatment: Mental Health in PTSD specialty clinics, Mental Health in non-specialty clinics, and Substance Abuse specialty treatment.

Each category of therapy contacts will be subdivided as treatment with and without psychotherapy, creating six total therapy attendance measures. Analyzing the subset of contacts representing psychotherapy visits will cull for visits that represent willingness to discuss the problem behavior/symptoms. Dr. Rosenheck has utilized methods identifying psychotherapy stop codes in the Austin databases in a completed service use analysis (Hunt and Rosenheck, 2011).

c. Exploratory analyses will be conducted concerning the agreement of Compensation examination PTSD diagnoses and CAPS-generated PTSD diagnoses. ROC analyses will be conducted on the accuracy of the Compensation examination diagnoses of PTSD with the

validating criterion being a diagnosis derived from the CAPS interview. The CAPS interview, like the Compensation examination, measures the specific DSM IV criteria for PTSD, so concordance is expected to be high. A diagnosis of PTSD will be derived from the CAPS using the “1/2” rule, in which (1) a core PTSD symptom is counted as present when its frequency is rated as a ‘1’ or greater and its intensity is rated as a ‘2’ or greater; and (2) total CAPS severity  $\geq 45$  (Schnurr, Friedman et al. 2005). This strategy ensures that the DSM-IV symptom criteria are met and that severity is sufficiently high. Exploratory analyses will examine characteristics associated with discordance between Compensation examination and CAPS interview diagnoses (diagnosis on CAPS but not on Compensation examination and vice versa).

3. Approach to Missing Data: We will first determine whether data are missing completely at random using Little’s (1988) test. If data are not missing at random, we will characterize study drop-outs in terms of differences in mean scores on relevant variables. Variables determined to be related to missingness or to the incomplete variables (missing data correlates) will be included in models to improve estimation.

For analyses involving hierarchical linear modeling, maximum likelihood estimation techniques permit missing data on the dependent variable. Valid parameters are estimated from all available data from all cases under the assumption that data are missing at random. To improve the plausibility of the missing-at-random assumption, we may include missing data correlates in the model.

For normal models (ANOVA, Regression), if data are not missing-at-random, we will use NORM software to multiply impute missing values. We will combine parameter estimates and estimate standard errors according to Rubin’s rules (cited in Schafer, 1997).

4. Analysis of the Effect of Substance Use on PTSD, Treatment Attendance (Evaluative Specific Aim 1-- Veterans with substance use disorders randomized to No-Additional-Treatment will have worse PTSD over time compared to Veterans without substance use disorders and will attend fewer weeks of mental health and/or substance abuse treatment):

The principal strategy for assessing the effect of substance use on outcomes (CAPS score, weeks attending any mental health and/or substance abuse treatment) will be random effects regression, also called HLM or hierarchical linear modeling. An individual’s behavior on the outcome variable is modeled as a function of an individual growth trajectory (and thus does not require all participants to have data at all measurement points), and then, at a between participants level, the parameters of the individual trajectories are analyzed by group. The focus of these analyses will be the ‘substance use status by time effects’ for each hypothesis. These effects will evaluate whether the slopes, or rates of change, of one group differ from the slopes of another group. The effects of (site) and (site X substance use) status will be modeled.

Because substance use is not randomly assigned, potentially confounding baseline covariates will be considered in the analyses. Baseline level of the dependent variable, e.g. CAPS-rated PTSD severity, will be included in the analysis as a covariate. Other covariates will be included that have been associated with substance use that also might potentially be associated with the outcomes being studied, i.e. PTSD severity and treatment attendance. The covariates will include gender, education level (years of study), current employment status, depression severity (as assessed by the BDI), response to stressful experiences, and meeting criteria for TBI (as assessed by the baseline questionnaire).

We will also examine the within-subjects relationship between the substance use and PTSD outcomes. We hypothesize that improvements in substance use will correspond with improvements in PTSD as evidenced by a significant positive correlation between the slopes of substance use measures (e.g. abstinence, heavy drinking days) and CAPS scores. We also plan to utilize a Structural Equation Model that has the combined benefits of latent curve, autoregressive, and time-specific lagged effects analyses (Bollen & Curran, 2004). We will

analyze the immediate and lagged effects of substance use on CAPS scores. The same approach will be applied to elucidate the relationship between substance use and treatment attendance. Additionally, we will analyze the nature of the effect of each outcome at the previous time point (time t-1) on the value of the same outcome at the current time point (time t). In this manner, we will determine the unique and combined effects of all influences on PTSD symptoms and treatment attendance.

#### 5. Analyses of the Relationship Between Attitudes About Compensation examinations and Outcome

*(Evaluative Specific Aim 2: Attendance at treatment will be predicted by Veterans' perceptions that obtaining and maintaining VA benefits depends on attending PTSD treatment):*

We hypothesize and will test in HLM regression models whether attendance at substance abuse and/or mental health treatment (and other outcomes) are predicted by the following, after accounting for appropriate covariates:

a. Veterans' perception that obtaining and maintaining VA benefits depends on treatment. Veterans' perceptions concerning the linkage between their status and receiving benefits will be derived for the three scales of the Disability Beliefs Scale which reflect perceived linkage of benefits to: (i) engagement in VA mental health treatment, (ii) being symptomatic from PTSD, and (iii) being abstinent from drugs and/or alcohol. Other scales will be analyzed if the factor analysis of the Disability Beliefs scale reveals another factor structure.

b. Subscales indicating that (i) Validation, (ii) Self-Other Considerations and (iii) Financial concerns were Veterans' reasons for seeking Compensation, as rated on the Disability Application Appraisal Inventory (Sayer, Spoont et al. 2004). We hypothesize that Veterans who rate themselves higher in having applied seeking "Validation (of being ill)" will be more likely to attend treatment, and that Veterans with higher ratings in "Self-Other (e.g. someone else urges Veteran to seek award)" or who applied for financial gain would be less likely to attend treatment.

c. Interactions between Disability Application Appraisal and Disability Beliefs Scale subscale variables. Reasons for seeking benefits and beliefs about disability application appraisal may interact to make treatment attendance more or less likely.

Covariates in these analyses will include those reflecting three main domains that have been associated with treatment attendance (Koenen, Goodwin et al. 2003):

- Predisposing factors: demographic variables (age, gender)
- Enabling factors that facilitate access to treatment: study site, distance between home and medical center calculated using G.I.S. mapping
- Need for treatment: Substance Use, PTSD severity (CAPS total score) and depression severity (Beck Depression Inventory).

#### 6. Analyses of the Relationship between Application Status (before Compensation examination vs. after, before receiving claim judgment vs. after) and Treatment Attendance (Evaluative Specific Aim3: Long-term attendance at treatment will be significantly impacted by the occurrence of the Compensation examination and determination of award):

Attendance at treatment will be regressed on time-varying covariates reflecting having had a Compensation examination, and having had a Compensation claim approved by the Veterans Benefits Administration. A secondary analysis will consider whether these time-varying covariates will significantly interact with attitudes concerning how disability is awarded.

#### 7. Exploratory Analyses of Predictors of Compensation Award: Secondary analyses will be conducted to determine factors associated with receipt of award. Anticipated factors associated with receipt of award include site, demographic factors, depression and CAPS severity. A supplementary analysis will determine whether Veterans' likelihood of obtaining Compensation is impacted by behaviors around the time of the examination. The independent contribution of

each of the following to receiving Compensation will be considered in a regression analysis, after covarying for demographic and other factors: i) not having substance use noted in the medical chart before the Compensation examination, ii) attendance at VA mental health treatment before the Examination, iii) attendance at non-VA mental health treatment before examination, iv) having been prescribed psychotropic medication.

8. Other Exploratory Analyses: The covariates in the analyses of outcomes are of interest and will be considered in more in-depth secondary analyses. If suggested in bivariate analyses, the independent contribution of such factors as gender, age, depression, legal status, social support, employment and cognitive function will be described in separate analyses.

We will describe the rates of HIV risk behaviors among the study population, both with and without substance use. Knowing these rates will give policymakers some information about the extent of the problem of HIV-risk behavior, and the usefulness of focusing interventions on these Veterans. We will also determine the independent contribution of substance use, PTSD severity, and attendance in treatment on engaging in HIV-risk behaviors over time, using random effects regression, as outlined in #4 above.

As psychiatric symptoms and substance use predict higher rates of sexual risk behavior, we will also explore whether changes in those variables are associated with change in sexual risk behavior.

#### K. Data Analysis for Clinical Trial Component:

1. Primary Dependent Measures are defined a priori to reduce the likelihood of Type 1 error.

a. The first primary outcome measure will be days using any substance. Within the subgroup of Veterans with substance use, the probability of use over time will be compared across treatment groups.

i. Secondary analysis will consider days of alcohol use and drinks per drinking day.

ii. Exploratory analyses will consider differences across groups in total drinks consumed each day (as IU/Liter).

iii. Days of use of specific drugs will be considered in exploratory analyses.

b. The second primary outcome is weeks attending any substance abuse and/or mental health treatment. Attendance at treatment during a week will be defined as having any service use data (VA or self-reported use of non-VA services) indicating use of mental health and/or substance abuse services. The difference in probability of attendance over time will be compared across treatment groups.

c. PTSD severity is a secondary outcome that will be measured as the overall CAPS score.

i. Secondary outcomes will include each of three symptom clusters of the CAPS.

To determine the proportion of patients meeting criteria for PTSD, a PTSD diagnosis will be established by the "1/2 rule" described previously (Schnurr, Friedman et al. 2007).

Change in symptom severity will be compared between treatment groups.

2. Evaluation of Treatment Effects:

Evaluation of comparability of baseline characteristics of the two client groups will be conducted using chi-square tests for categorical variables and t-tests for continuous variables. If an unexpected difference is found and is related to the outcome, the potentially significant confounding variable will be added to the primary outcome analysis as a covariate.

The principal strategy for assessing the efficacy of the study treatments will be random effects regression, as described for the analysis of the effects of substance use on other outcomes. The focus of these analyses will be the 'treatment group by time effects' for each

hypothesis, and whether the slopes, or rates of change, of Veterans assigned to SBIRT differ from the slopes of those assigned to No-Additional-Treatment. The model will include appropriate covariates and the contrasts of SBIRT versus Control. The effects of site and the site-by-treatment interaction will be determined.

Our principal data analyses will be conducted on the intention-to-treat sample. We will attempt to follow all participants for assessments regardless of their retention in treatment. Intention-to-treat analyses will be supplemented by analyses to describe the consistency of findings across different definitions of the sample: e.g., treatment-exposed and treatment completers.

Secondary analyses will be conducted to account for the possibility that days without substance use data (scored as missing) are not randomly distributed. In these analyses, variables that distinguish people with missing substance use data from those with complete data will be included in the analyses as covariates or auxiliary variables (Graham, 2003).

A linear effect of time on outcome variables is being hypothesized but ancillary analyses will be conducted to determine if the effect of SBIRT treatment is better explained by a quadratic function, given the possibility of deceleration in rate of change.

### 3. Evaluation of Therapy Processes that Mediate Treatment Outcomes

The first set of analyses will evaluate whether the CAPS score mediates treatment response using methods described by Angell and colleagues (Angell et al., 2007). Mediation by the CAPS will be tested by adding it to a model in which proportion substance use days is regressed on group assignment. If there is an effect of treatment that is suppressed by adding the CAPS score to the regression equation, then CAPS score is a mediator of the treatment effect (Baron & Kenny, 1986).

### 4. Evaluation of Factors Associated with Treatment Effects

To determine what factors are associated with response to any kind of counseling, potential predictor variables will be entered into the primary outcome analyses as covariates. Potential predictor variables include gender, type of trauma, use of an illicit drug, baseline PTSD severity as measured by the CAPS, depression as measured by the BDI, a history of TBI, and cognitive impairment as evidenced by a score below 26 on the MOCA. As noted in the data analysis plan for the evaluative component, other potential moderator variables will include attitudes concerning Compensation exams (Veterans' reasons for seeking Compensation on the Disability Appraisal Inventory, and beliefs about whether Compensation is influenced by treatment attendance, continuing symptoms, and substance use on the Disability Beliefs Scale).

### 5. Evaluation of Process Measures

Group X Time random effects regression analyses will be conducted to determine differential effects of time on Stage-of-Change, which is collected at multiple time points. The Likert-scaled therapy process ratings and other measures reflecting single values (e.g. duration of therapy sessions) will be compared between groups using ANOVAs.

## Human Subjects

### A. Consent Procedures

1. Recruitment: A waiver of written informed consent and HIPAA authorization will be obtained to review the names and contact information of OEF/OIF/OND Veterans requesting a new PTSD examination [we will secure lists of new applicants either directly from VBA or from the Compensation and Pension office, as provided by VBA], and to review electronic medical charts for basic eligibility criteria, including age, theater of military service, and percent service connection for PTSD. The waiver will allow for the collection of basic demographic information

concerning Veterans screened for study participation to determine if Veterans who consent to study participation differ systematically from those who do not.

Letters explaining the study will be sent Express mail to Veterans applying for a PTSD examination. The letter explains that a member of the research team will telephone the Veteran to invite the Veteran to participate in the study, but that the Veteran can opt out of receiving this telephone call by calling a confidential telephone number. If the Veteran does not opt out within 6 days of the mailing, the Veteran will be called, and the study will be explained to him/her. Up to three attempts will be made to contact the Veteran for recruitment before we will stop attempting. Interested Veterans will be invited to complete a consent form and begin the Evaluative Phase and baseline evaluations of the study.

2. Consent: Voluntary informed consent will be obtained from all Veterans prior to participation. Consent will be obtained by one of the investigators or his/her designee after the research procedures and risks associated with participation have been explained to the candidate. A signed copy of the consent form will be provided to all potential Veterans.

Participants will be asked several questions to be certain they understand the risks associated with study participation. Only participants who correctly answer all the questions (with a second chance to answer questions if incorrectly answered the first time) will be enrolled. The questions will be the following:

a. What topics will you be asked about?

Answer should mention PTSD and substance use.

b. Will the things you tell the research assistant be told to the VA people who decide on your service-connection?

No.

c. Can you drop out of this study whenever you want?

Yes.

## B. Risks

Risks associated with participation in the study include risks associated with:

1. *Completing questionnaires*: Administration of study instruments may be boring, frustrating, or upsetting.

2. *Becoming upset while discussing traumatic events*: There is a risk that individual Veterans will become upset by discussing their traumatic events during assessments or therapy. Veterans report drinking to manage their PTSD symptoms, so there is a risk that upset from discussing traumatic events could lead to increased substance use (Bremner, Southwick et al. 1996). In practice, study-related adverse events in clinical trials of PTSD treatments among Veterans have been very rare (Schnurr, Friedman et al. 2007; Monson, Gradus et al. 2008). Research assistants will emphasize that answering questions is voluntary and will allow Veterans to answer questions at their own pace and without duress

3. *Information from the counseling being told to participants' clinicians at the VA or to someone who reviews their disability application*. The counseling is unlikely to impact the Veteran's disability. The therapist will not volunteer any non-emergent information in the Veterans' chart or to other clinicians, as this is contrary to the voluntary, Motivational Interviewing stance that is integral to SBIRT. The therapist will write a note in the Veteran's VA chart after therapy indicating that the participant was in a research study and met with the therapist.

Nevertheless, the SBIRT therapist is going to convey information to other VA clinicians if the Veteran indicates information during the therapy that requires emergent intervention by another VA clinician. If the Veteran indicates information suggesting imminent danger to the Veteran or to others, the SBIRT therapist will share this information with other VA clinicians so

they can take appropriate action. Therefore, veterans will be told the risk that information that they tell the study therapist may be told to their VA clinicians and would then become available to someone who reviews their disability application.

Even if the emergency disclosure includes disclosing the presence of a substance use disorder, this is unlikely to prevent receipt of service-connected disability. Veterans who have substance use disorders may still be judged to have service-connected PTSD. In light of the frequent comorbidity between PTSD and substance abuse described earlier, it would be unreasonable for VBA to insist that a Veteran be abstinent to be diagnosed with PTSD. In an oft-cited “Allen” court case decided by the Federal Appeals Court (Allen v. Principi Judicial Decision 99-7199), the court ruled that substance use, when it was a consequence of service-connected PTSD, could in fact itself be an additional, reimbursable consequence of military service.

4. *The three people whose names the Veteran provides may find out that the Veteran is in a research study.* If we are unable to contact the Veteran directly for assessment visits, we will contact the three people whose names the Veteran gave us and ask them if they know how to contact the Veteran. If a member of our staff contacts any of these people, the staff member will say that he (or she) works on a research study at VA. Therefore, we will inform Veterans that if they do not want anyone they know to be called by someone identified as being from a VA research project in order to contact them, then they should not participate in this study.

### C. Protection of Participants

1. Confidentiality: All research information is considered confidential. Limits to confidentiality include only disclosure of acute suicidality, homicidality, or abuse of a minor, as is standard in clinical practice. Suicidal ideation will be revealed to clinical staff if a Veteran selects either of the following on the Beck Depression Inventory: “I would like to kill myself” or “I would kill myself if I had the chance.” *If a Veteran reports any of the following, the person it is reported to (therapist or data collector) will contact the site investigators and if the investigator is not available, the clinician handling intakes for the respective PTSD firms.*

Both study sites have emergency room facilities and a suicide prevention coordination team. The participant’s condition will be assessed by a VA provider. The RA will attempt to facilitate this by contacting the clinical intake coordinator. The PI will also be contacted. The RA will accompany the Veteran to an immediate evaluation by a clinician or assessment in the Emergency Department. Part of the RA training will be learning where these facilities are located.

Research data will be identified by code number and will not include names, although enrollment records must also be kept and these records will include names. Our study forms have been designed to avoid collecting identifiable information; no Protected Health Information (PHI) will be collected on study forms. We generally collect only protocol session dates. These dates are changed to ‘number of sessions completed’ when data sets are anonymized and released to other investigators. Research data, containing no PHI, are brought to the West Haven VA for scanning and outputting to databases using Teleforms Software. All computers used by research staff are password protected.

Study data will be stored and analyzed in the VA Informatics and Computing Infrastructure (VINCI). VINCI is a Department of Veterans Affairs (VA) Health Services Research & Development (HSR&D) resource center that provides a secure, central analytic platform for performing research and supporting clinical operations activities. It is a partnership between the VA Office of Information Technology (OI&T) and the Veterans Health Administration Office of Research and Development (VHA ORD). VINCI includes a cluster of servers for securely hosting suites of databases integrated from select national VA data sources. VINCI servers for data, applications and virtual sessions are physically located at the VA Austin Information Technology Center (AITC), located in Austin, Texas. This secure enclave

with 105 high-performance servers and 1.5 petabytes of high-speed data storage has multiple layers of security and disaster recovery to prevent data loss. To ensure the protection of Veteran data, VINCI maintains compliance with the guidelines set forth by Veterans Health Administration (VHA) Handbook 1200.12, Use of Data and Data Repositories in VHA Research, and all other applicable VA and VHA policies and regulations. In addition, VINCI has undergone all security certification activities in support of obtaining an Authorization to Operate (ATO). Access to VINCI resources are approved in accordance with the requirements of National Data Systems (NDS), VHA Handbook 1200.12, Use of Data and Data Repositories in VHA Research, and all other applicable VA and VHA policies and regulations. All data transferred from VINCI is subject to audit for compliance. VA-credentialed research staffs are granted access to study-specific data along with tools for analysis and reporting in the secure, virtual working environment through a certified VHA network computer within the VA. If not working within a VA or VHA hosted office environment containing VA network access, researchers may apply for and then access VINCI through an approved Virtual Private Network (VPN) and Remote Desktop application. The remote computing environment enables data analysis to be performed directly on VINCI servers, offering a number of advantages: uniform security standards for access; a common point of entry for all investigators who use the data; tools for analysis and reporting; tighter and more consistent control of data quality; and the ability to standardize and update terminology and format as technology and methodology improve.

Personal identifiers will be retained to obtain VA service use data from Austin in year 4 of the study. The personal identifiers will be used to identify service use by study participants from the Outpatient Encounter File and Patient Treatment Files. After the data is extracted, the identifiers will be removed from the Austin files to create files with de-identified data for subsequent analyses.

All possible precautions will be taken to prevent a breach of confidentiality. Study IDs will be assigned at the time of recruitment and replace names and record numbers. Clinical enrollment records are kept separate from research data, and are not available without a Veteran's written consent. Participants' names will appear only on the consent form, HIPAA authorization form, and "key" form kept by the site PI. At the conclusion of the study, all locator data will be destroyed. The crosswalk file will be stored separately from all other study data on VA secure network computers. Data Security will be insured via the servers, which all reside completely behind the VA firewall. All systems utilize Secure Socket Layer (SSL) technology for internet protocol data transfer, which encrypts all network transmissions and transmits only within the VA network backbone. There is no public internet access. Another layer of protection for sensitive information is ascribed to the system by use of granular access privileges. Only site-specific authorized staff will have data access. Study managers have the capability of granting access and read-write privileges to users. All systems undergo daily backup and 24-hour security.

Outcome data will be collected on paper forms that will be scanned into PDFs that are in turn outputted to study databases by Teleforms software using object-character recognition. Forms will be labeled by study numeric ID; names and other Personal Health Information identifiers such as social security numbers will not be used on study material. The forms will be scanned at each site into electronic PDF files and electronically uploaded to the study data repository. Naming conventions will be instituted for all files using study ID codes. The commitment of data from the forms to SPSS databases will be carried out at West Haven using Teleforms software. Source documents (e.g. Compensation and Pension examinations) are stored on VA clinical servers behind a secure firewall, and will not be stored with research data.

All paper forms will be stored and secured in a locked file cabinet under the jurisdiction of the site P.I. The site PI will be responsible for oversight of local data collection.

The research records will be used to prepare reports that do not include patient identification.



All research staff and therapists receive annual Good Clinical Practice, Human Subjects Protection, HIPAA, and VHA privacy training through the VA. Our data collection and management procedures are fully compliant with HIPAA.

To reduce the possibility of identifying participants and associating outcomes with their identities, nail samples will be coded with non-informative ID numbers.

A Certificate of Confidentiality has been obtained to minimize the risk of forced disclosure in a legal or other proceeding. The Certificate, and the study consent form, will indicate the exceptions to confidentiality in which information may be disclosed without a patient's consent.

2. Confidentiality of Videotapes: To assure the confidentiality and protection of participants with respect to videotaping, the following steps will be taken:

- Participants will provide informed consent for videotaping. Participants will be allowed to participate in the study and refuse the videotaping. Participants who do consent to videotaping will be informed that they have the right to stop taping at any time during the session.

- Therapists will videotape their own sessions to eliminate the need for a technician in the room.

- As therapist behavior is of primary interest, the camera will be directed at the therapist. The participant's voice will be recorded on the videotape.

- Video recordings will be treated as confidential research records. The videotape, labeled with a unique study ID code will be uploaded to a secure network VA server, separate from other study data. The file name will use study ID codes.

- Access to videotapes will be limited to members of the investigative team including trained research raters who will rate the tapes according to the therapist adherence and competence rating systems and only the research staff will have access to the recordings. A separate file will link the videotape file code to the participant's unique identification code, the therapist name, and the date of the session.

3. Testing. Subjects will be given breaks during the test battery to minimize frustration, fatigue, and psychological discomfort. The research assistant administering these tests will be trained in the use of these standardized instruments and knowledgeable about cultural differences within the study population.

4. Training of Study Therapists: The risk of angering or alienating Veterans is very small because of the non-confrontational nature of SBIRT. The risk will be further minimized by hiring staff who have experience with the study population. Study therapists will be trained to adopt a collaborative approach. Study therapists will also be taught where the emergency facilities are including the location of emergency rooms, VA and public police and crisis services. Study therapists will also receive training in de-escalating agitated Veterans.

5. Training of Study Data Collector: Data collectors will also be taught where the emergency facilities are including the location of emergency rooms, VA and public police and crisis services. Data collectors will also receive training in de-escalating agitated Veterans.

#### D. Data Safety Monitoring Plan:

##### 1. Data Management Plan

Careful training of evaluators will precede study initiation. The main instruments on which training is needed are the baseline Substance Abuse and Service Use Calendar, CAPS

and MOCA. Training of new personnel to conduct the CAPS will contain review of audiotaped ratings as described previously. Training to conduct the MOCA will consist of a training lecture. Training to conduct the Substance Use and Service Use calendars will involve at least five supervised ratings.

Our research group uses Teleforms® software to create, clean and enter data. Forms are created with barcodes that are scanned using Teleforms' object character recognition software. Data is extracted and automatically inputted to an SPSS database.

All forms and samples collected from Veterans will have a study code number but no identifying information. Registration records including the signed consent form will be stored separately from these study records.

Data will be scanned at the site where it is collected at. Dr. Black will import the PDF data uploaded to the study server into central databases at VA Connecticut monthly utilizing Teleforms software. Random patient data will be keypunched into a blank database independently and compared to the scanned data to check for systemic errors. Key data will be independently verified by the research assistant to insure the software is working correctly. Filters flag data that needs to be re-checked by a person such as unclear characters, out-of-range variables and logical inconsistencies. Dr. Black will scan files monthly so that errors can be readily corrected and consequential differences between treatment types (e.g., different levels of attrition) can be monitored closely.

Data quality will be monitored by random inspection of the completed forms by Dr. Black and any problems detected will be discussed with the P.I. Therapists will receive standardized training on the interventions. Adherence to therapies will be monitored using supervision.

## 2. Safety Monitoring Plan:

Participants in Evaluative Component: The risk to Veterans participating in the Evaluative Component who only receive assessments and are not randomized to SBIRT or control is minimal. Only study-related adverse events or study-related serious adverse events impacting these evaluation-only patients will be reported to Dr. Rosen and if he is unavailable, to Dr. Speroff. Reports to Dr. Rosen will include a description of the event and a summary of recent contacts with the patient. Dr. Rosen will report these to the IRB within three working days.

Participants Randomized in Clinical Trial Component: The risk to Veterans who do go on to be randomized to SBIRT or no-additional-treatment is low (greater than minimal). Veterans with PTSD have a high frequency of medical and psychiatric difficulties. Therefore, changes in medication regimen, the presence of medication side effects and symptom exacerbations are not untoward and do not constitute adverse events. Anticipated adverse events include complaints about the study procedures and the counseling, and any occurrence in which the patient attributes discomfort, harm or disability to the study procedures.

In the clinical trial, assessment for adverse events will be a routine part of every study and therapy visit. SAEs and AEs will be screened for in the timeline follow-backs. Any report that a patient required overnight treatment in any facility (emergency room, detoxification, and hospitalization) will constitute an SAE, as will any report of death or serious disability. Hospitalization or death of another individual due to direct action of patient will also be considered an SAE. When an AE or SAE is reported by a participant, we will refer to the medical chart for additional information.

Any SAEs will be immediately reported to Dr. Rosen and, if he is unavailable, to Dr. Speroff. Reports to Dr. Rosen will include a description of the event and a summary of recent contacts with the patient. This summary will include any warning signs of the adverse event, the patient's general state and any information suggesting a causal link between study participation and the event. Dr. Rosen will report these to the IRB within 3 working days.

The New England MIRECC's D.S.M.B. will be the D.S.M.B. for this study. The faculty who will be currently on the board are Sherry McKee, David Fiellien and Declan Barry. All three are NIH-funded investigators with research experience. The D.S.M.B. will be contacted within 3 days about all significant study-related adverse events.

The main risks of the study are frustration with the study procedures, conflict with the study therapist, and exacerbation of PTSD symptoms and/or alcohol use. Because the risk that either therapy would worsen outcomes, no a priori stopping criteria are proposed. Every year, Dr. Rosen and the D.S.M.B. will review study information on a standardized form. Board members will review recruitment, retention, and follow-up rates for the study-to-date, SAEs and AEs and other data as the D.S.M.B. deems necessary.

Based on this report, each DSMB member will complete a form making one of two recommendations: 1) continue recruitment as planned; or 2) schedule formal DSMB meeting immediately. If any DSMB member recommends a meeting, this will be scheduled within one week, minutes will be kept, the report will be reviewed with the PI, and the committee will vote on whether the study should: 1) continue recruitment unchanged; 2) continue with a protocol amendment; 3) stop recruiting pending further investigation. If, after this meeting, any DSMB member votes to stop recruitment or requests a protocol modification, the Yale IRB will be informed.

A written summary including this information will be provided to the IRB with the protocol renewal. Because the sample size for the Clinical Trial Component study is modest, we are not proposing a preliminary analysis of accumulating efficacy data by treatment assignment.

#### D. Potential Benefits

1. Benefits to the Participants: There are no direct benefits to participants in the Evaluative Component. The potential benefits to participants in the Clinical Trial Component is that they may receive referral and treatment for substance use.

2. Benefits to Society: The Evaluative Component will provide invaluable information concerning the substance abuse and other factors that determine whether Veterans applying for Compensation improve and attend treatment. It may suggest modifications to existing VA Compensation Examination procedures that will facilitate engagement in treatment. The Clinical Trial Component will determine the efficacy of an intervention for Veterans burdened by PTSD and comorbid substance abuse.

#### E. Risk/Benefit Ratio

All participants will receive financial compensation for completing study assessments. The study has the potential to further the development of effective treatment for people who have PTSD and use alcohol. Consideration of the risks and benefits mentioned above suggests that potential benefits for both the participants and science outweigh the risk of minor harm associated with the study procedures.

#### F. Payments

Financial Compensation to Participants for Completing Assessments: It is our usual practice to compensate participants for studies like this one that require considerable time completing forms and ratings that are not a part of routine clinical care. Compensation offsets the inconvenience of these procedures. Participants will be paid \$70 for each of the three outcome assessment sessions. They will also be reimbursed 57.5¢ per mile traveled from the Veterans' residence to and from the assessment sessions. The payment amount compensates Veterans for the inconvenience of the extra trips to attend assessment sessions. The payment is comparable to what participants would be paid in similar studies.

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