VA Cooperative Studies Program Protocol #589

Veterans Individual Placement and Support Towards Advancing Recovery (VIP-STAR)

STUDY PROTOCOL

Version 2.1

August 17, 2015

Study Chair: **Lori L. Davis, M.D.**

Table of Contents

Letters of Submittal

Principal Proponent

Director: Cooperative Studies Program Coordinating Center, West Haven

Director: Cooperative Studies Program Clinical Research Pharmacy Coordinating Center

DEPARTMENT OF VETERANS AFFAIRS

Tuscaloosa VA Medical Center

3701 Loop Road East

Tuscaloosa, AL 35404

April 30, 2012

Timothy J. O'Leary, MD, PhD
Director, Clinical Science Research and Development (125)
VA Central Office
810 Vermont Avenue, NW
Washington, DC 20420

Dear Dr. O'Leary:

We are very pleased to submit the protocol for VA Cooperative Studies Program #589, "Veterans Individual Placement and Support Towards Advancing Recovery (VIP-STAR)" for review by the Cooperative Studies Scientific Evaluation Committee meeting in Washington, DC in July 2012. The primary objective of this multisite, prospective, randomized, controlled study is to evaluate the effectiveness of Individual Placement and Support (IPS), a supported employment approach, compared to the VA standard care Transition Work Programs (TWP) in the recovery of Veterans with posttraumatic stress disorder (PTSD) in a large geographic and urban-rural diverse Veteran population. The primary hypothesis is that IPS would be significantly better than TWP for Veterans with PTSD in terms of the proportion of study participants who become steady workers, defined as holding a competitive job for at least 50% of the follow-up period. The secondary hypothesis is that IPS supported employment will lead to greater income and occupational outcomes, enhance community reintegration and quality of life, and improve the Veteran's self esteem and mental health. We will also explore the differences between groups in terms of occurrences of negative health outcomes.

The importance of this study is based on the fact that Veterans with PTSD represent a substantial proportion of the VHA patient population, consume a great deal of VHA health care resources and disability payments, and are disproportionally unemployed. The current vocational rehabilitation treatments are not adequately meeting their needs. Thus, new and improved vocational rehabilitation approaches need to be rigorously studied. Over the past

two decades of studies involving individuals with serious mental illness, defined as schizophrenia, schizoaffective disorder, bipolar disorder, and major depression with psychotic features, IPS has yielded remarkably robust and consistent outcomes. Overall, approximately two-thirds of participants in clinical trials who receive IPS achieve competitive employment. However, the clinical characteristics and occupational challenges of Veterans with PTSD differ greatly from Veterans with SMI, and thus, one cannot automatically assume that a rehabilitation approach that works best for individuals with an SMI is going to have the same effectiveness for persons with PTSD.

Serving as the first study in a PTSD population, a recent single-site pilot study found that IPS was superior to the conventional VA vocational rehabilitation program in getting unemployed Veterans with PTSD back to work (Davis et al 2012). During the 12-month study follow-up period, 76% of the participants randomized to IPS gained competitive employment, compared to 28% of those randomized to conventional vocational rehabilitation program. Together with the evidence base accumulated in the SMI population, these significantly positive results of the pilot study support the rationale to conduct a VA Cooperative Study and definitively evaluate the effectiveness of IPS in Veterans with PTSD.

CSP #589 plans for a 1 year recruitment period of 540 participants across 15 sites and 1.5 years of participant follow-up. The proposed CSP #589 will yield valuable findings. A positive finding for IPS would provide the generalizable evidence required for VHA to guide evidence-based vocational rehabilitation treatments for PTSD. A negative IPS finding would equally inform the stakeholders and prevent the implementation of an ineffective program in VHA. Conducting a large multisite study is the next logical step in evaluating IPS as a vocational rehabilitation program for Veterans with PTSD.

We look forward to the careful review by CSSEC, and we hope that the protocol is met with enthusiasm and support.

Sincerely,

Lori L. Davis, M.D.
Principal Proponent

DEPARTMENT OF VETERANS AFFAIRS
VA Connecticut Healthcare System
950 Campbell Avenue
West Haven, CT 06516

COOPERATIVE STUDIES PROGRAM COORDINATING CENTER

In Reply Refer To: 689/151A

May 30, 2012

Timothy J. O'Leary, MD, PhD
Deputy CRADO, Director CSR&D Service (125)
VA Central Office
810 Vermont Avenue, NW
Washington, DC 20420

Dear Dr. O'Leary:

Attached is the submission for CSSEC review of CSP #589, "Veterans Individual Placement and Support Towards Advancing Recovery (VIP-STAR)" from the Principal Proponent, Lori L. Davis, MD and the Study Biostatistician, Tassos Kyriakides, PhD.

The study is designed to answer the important questions of whether a supported employment approach, which has been shown to be effective in numerous studies of persons with a serious mental illness and one small single site posttraumatic stress disorder (PTSD) study, will improve the recovery of veterans with PTSD compared to the VA standard care Transition Work Programs.

Study Design
CSP #589 is a multi-center, randomized trial of Individual Placement and Support (IPS), a supported employment approach, compared to the VA standard care Transition Work Programs (TWP) in the recovery of veterans with posttraumatic stress disorder (PTSD). The primary outcome will be achieving 'steady worker' status, defined as holding a competitive job for at least 50% of the 18-month follow-up period. Second outcomes are other occupational measurements, PTSD symptoms, self esteem, social integration, and quality of life.

The target population of the study will be Veterans with a current diagnosis of PTSD who are unemployed and expressing interest in competitive employment. To maximize recruitment and provide the most generalizable results, the study has relatively simple entry criteria. PTSD affects more than 600,000 US Veterans and is the most common psychiatric condition for which Veterans seek VA disability benefits. PTSD is a chronic illness that often results in occupational dysfunction and unemployment in a disproportionate number of Veterans. Although many Veterans with PTSD are college educated, few have jobs and almost 40% are impoverished.

The target sample size is 540 participants (270 per treatment group) enrolled over 1 year from 15 VA medical centers. All participants will be followed in clinic every 3 months for a total of 18 months. This sample size will provide 90% power to detect an odds ratio of 2.15 for achieving 'steady worker' competitive employment status with IPS treatment and will provide ample power to identify clinically meaningful differences between interventions for the secondary outcomes.

The primary outcome, the proportion of 'steady workers', will be analyzed using a chi-square test statistic at a two-tailed alpha-level of 0.05. All analysis will be done according to the intention-to-treat principle.

Budget

The total cost of the study is estimated to be $12,505,418. The estimated budget is based on 12 months of participant intake and 18 months of participant follow-up. The total study duration will be 2.5 years excluding start-up, and close-out phases.

This study will answer an important question: can supported employment help Veteran's with PTSD to become competitively employed and reintegrate into society? Given the increasing number of Veterans seeking services for PTSD, the proportion who are unemployed, and the potential chronic debilitating course of the condition, this study could improve the lives of many thousands of Veterans over the long term.

Sincerely,

Peter Guarino, MPH, PhD
Director, WH-CSPCC

Department of Veterans Affairs
VA Cooperative Studies Program
Clinical Research Pharmacy Coordinating Center (151-I)
2401 Centre Avenue SE
Albuquerque NM 87106-4180

May 9, 2012

501/151-I
In Reply Refer To: CSP #95/ #589
File: STD_DOC

Timothy J. O'Leary, M.D., Ph.D.
Director, CSR&D
VA Central Office
810 Vermont Ave., NW
Washington, DC 20420

Dear Dr. O'Leary:

SUBJ: CSPCRPCC Issues Letter for CSP #589 "Veterans Individual Placement and Support Towards Advancing Recovery (VIP-STAR)"

The protocol for CSP #589 is being submitted for CSSEC review.

There are no PCC issues related to this study. The PCC will provide safety monitoring and MedDRA coding for the duration of the study. The study does not require either an IND or IDE application.

A CSP policy decision was made to require (i) Good Clinical Practices (GCP) training for study personnel (nurse coordinators and site investigators) at study initiation meetings, and (ii) in addition to central monitoring, periodic site monitoring/auditing of all CSP studies regardless of whether the study is to be conducted under an IND or IDE. A site initiation visit, annual site monitoring, and closeout visits were used in formulating the outline of the GCP training and monitoring/auditing plan included in the submission. The personnel and travel costs for providing GCP training and for the monitoring/auditing of sites are in the Site Monitoring, Auditing and Resource Team (SMART), portion of the PCC budget.

Should you have any questions or need additional information, contact me at (505) 248-3200.

Sincerely yours,

CINDY L. COLLING, R.Ph., M.S.
Chief, Regulatory and Clinical Compliance

Enclosure(s)

CLC/mbg

Executive Summary/Abstract

Posttraumatic stress disorder (PTSD) affects more than 600,000 US Veterans and is the most common psychiatric condition for which Veterans seek VA disability benefits, making up a substantial proportion of the $23 billion pensions and disability annual budget. Although many Veterans with PTSD are college educated, few have jobs, almost 40% are impoverished, and most report work, role and social functioning scores below those of persons with serious mental illness. Veterans returning from the Gulf War-era II conflicts, defined as having served in the military since Sept 2001, often experience PTSD and confront unemployment upon their military discharge. The current methods used by the VA Compensated Work Therapy (CWT) programs do not sufficiently meet the employment rehabilitation needs of Veterans with PTSD. In a VA Northeast Program Evaluation Center (NEPEC) study evaluating administrative data of 5,862 Veterans from 122 CWT programs, Veterans with PTSD were 19% less likely to be employed at discharge from the VA CWT program compared to those without a diagnosis of PTSD. The rate of competitive employment at discharge was only 30% for Veterans with PTSD. Similarly, another VA study found that Veterans with PTSD involved in CWT were no more likely to be employed at 4 months follow-up compared to those who participated in a specialized PTSD treatment program.

Over the past two decades of studies, the Individual Placement and Support (IPS) model of Supported Employment has yielded remarkably robust and consistent employment outcomes for individuals with serious mental illness (defined as schizophrenia, schizoaffective disorder, bipolar disorder, and major depression with psychotic features). Overall, approximately two-thirds of participants in clinical trials with serious mental illness who received IPS achieved competitive employment. However, Veterans with PTSD have very different clinical characteristics and employment challenges compared to Veterans with SMI. Serving as the first study in a PTSD population, a recent single site pilot study found superior outcomes from IPS compared to the conventional VA vocational rehabilitation program (VRP) in unemployed Veterans with PTSD (n=85).[1] During the 12-month study follow-up period, 76% of the Veterans with PTSD randomized to IPS gained competitive employment, compared to 28% of those randomized to VRP. Together with the evidence base accumulated in the serious mentally

ill population, the positive results of the pilot study in PTSD support a VA Cooperative Study to definitively test the effectiveness of IPS in Veterans with PTSD.

The proposed study will randomize 540 participants at 12 to 15 VA sites over 1 year and follow each participant for 1.5 years. The objectives of this multi-site CSP study are to test the effectiveness of IPS compared to VA Transitional Work Programs (TWP) in the recovery of Veterans with PTSD and to learn more about IPS impact on PTSD symptoms, self esteem, quality of life, PTSD-related functional outcomes, and health outcomes in a large geographic and urban-rural diverse Veteran population. This study is a multisite, prospective, randomized controlled clinical trial comparing Individual Placement and Support (IPS) Employment to Transitional Work Programs (TWP) in unemployed Veterans with PTSD.

As the primary outcome, the two groups will be compared in terms of the proportion of study participants who meet the definition of steady worker, i.e. hold competitive employment for at least 50% of the 18-month follow-up period. Competitive employment is defined as a job receiving regular wages in a setting that is not set aside, sheltered, or enclaved, that is, the same job could be held by people without a mental illness or disability and is not a set-aside job in the TWP program. Secondary outcomes will include change in other occupational outcomes, PTSD symptoms, self esteem, quality of life, and PTSD-related functioning. We will explore the differences between groups in terms of occurrences of negative health outcomes.

These findings would provide generalizable evidence of the effectiveness of differing employment support to the VHA stakeholders who inform policy and service delivery for Veterans with PTSD. Given the number of Veterans with PTSD, it is of critical importance for the VA to offer employment service programs based on the best evidence-based recovery-orientated model for this group. Conducting a large multisite study is the next logical step in confirming IPS as an evidence-based employment service program for Veterans with PTSD.

Planning Committee

Lori L. Davis, M.D. – Study Chair
VA Medical Center
3701 Loop Road East
Tuscaloosa, AL 35213
Lori.Davis@va.gov

Robert E. Drake, Ph.D., M.D.
Psychiatric Research Center
2 Whipple Place
Lebanon, NH 03766
Robert.E.Drake@Dartmouth.edu

Charles E. Drebing, Ph.D.
Edith Nourse Rogers VA Medical Center
200 Springs Road
Bedford, Massachusetts 01730
Charles.Drebing@va.gov

Lisa A. Ottomanelli, Ph.D.
HSR&D/RR&D Center of Excellence
James A Haley Veterans Hospital
8900 Grand Oak Circle (118M)
Tampa, FL 33637
Lisa.Ottomanelli@va.gov

Richard Toscano, M.Ed.
Rehabilitation Program Specialist / VACO
National Program Evaluation on Evidence-based Employment Services
Washington, DC
Richard.Toscano@va.gov

Sandra G. Resnick, Ph.D.
VA Connecticut Healthcare System
NEPEC (182)
950 Campbell Avenue
West Haven, CT 06516
Sandy.Resnick@yale.edu

The late **Andrew C. Leon, Ph.D.**
Weill Cornell Medical College
525 East 68th Street
New York, New York 10065

Peter Guarino, M.P.H., Ph.D.
Director, CSPCC (151A)
VA Connecticut Healthcare System
950 Campbell Ave
West Haven, CT 06516
203-932-5711 x3780
Peter.Guarino@va.gov

Tassos Kyriakides, Ph.D.
Biostatistician, CSPCC (151A)
VA Conneticut Healthcare System
950 Campbell Ave
West Haven, CT 06516
Tassos.Kyriakides@va.gov

Robert Wallace, M.P.H., Sc.D.
Biostatistician, CSPCC (151A)
VA Conneticut Healthcare System
950 Campbell Ave
West Haven, CT 06516
Robert.Wallace3@va.gov

Scott Barnett, Ph.D.
HSR&D/RR&D Center of Excellence
James A Haley Veterans Hospital
8900 Grand Oak Circle (118M)
Tampa, FL 33637
Scott.Barnett2@va.gov

List of Abbreviations

Abbreviation	Description
ACOS/R&D	Associate Chief of Staff for Research
AE	Adverse Event
ANOVA	Analysis of Variance – Statistical Analysis
CAPS	Clinician-Administered PTSD Scale
CFR	Code of Federal Regulations
CIRS	Cumulative Illness Rating Scale
CPOC	Central Primary Outcome Coordinator
CRC	Clinical Research Coordinator
CRF	Case Report Form
CSP	Cooperative Studies Program
CSSEC	Cooperative Studies Scientific Evaluation Committee
CSPCC	Cooperative Studies Program Coordinating Center
CSPCRPCC	CSP Clinical Research Pharmacy Coordinating Center
CWT	VA Compensated Work Therapy
DCF	Data Clarification Form
DD214	Form Verifying Military Service
DMC	Data Monitoring Committee
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, 4th Edition
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, 5th Edition
DASS-21	Depression, Anxiety, and Stress scales
e-PDF	Electronic Portable Document Format Form, Scanner-Readable
FIPS 140-2	Federal Information Processing Standard, Publication 140-2
FTEE	Full Time Equivalent Employee
GCP	Good Clinical Practice
HCPHI	Highly Confidential Protected Health Information (SS#, name, address, phone numbers)
HIPAA	Health Information Portability and Accountability Act – VA Privacy Policy
HRC	Human Rights Committee
ICF	Informed Consent Form
IPS	Individual Placement and Support Intervention
IPS Specialist	Individual Placement and Support Specialist
IRB	Institutional Review Board
IPS-FM	National IPS Fidelity Monitor
IPS Supervisor	National Individual Placement and Support Supervisor
IVIP	Indianapolis Vocational Intervention Program
IRB	Institutional Review Board
LOC	Loss of Consciousness
LSI	Local Site Investigator
MedDRA	Medical Dictionary for Regulatory Activities
MINI	Mini-International Neuropsychiatry Inventory

Abbreviation	Description
MS	Microsoft Software
N/A	Not Applicable
NEPEC	VA Northeast Program Evaluation Center
NSC	National Study Coordinator
OEF-OIF	Operation Iraqi Freedom-Operation Enduring Freedom
OSU TBI-ID	Ohio State University Traumatic Brain Injury Identification Method
PCC	Albuquerque Clinical Research Pharmacy Coordinating Center
PCL	PTSD Checklist
PHI	Protected Health Information
PMCs	Participating Medical Centers
PTSD	Posttraumatic Stress Disorder
QOLI	Quality of Life Inventory
R&D	Research and Development
RSES	Rosenberg Self-Esteem Scale
SAEs	Serious Adverse Events
SD	Standard Deviation
SMART	Site Monitoring, Auditing, and Resource Team
SMI	Serious Mental Illness
SOPs	Standard Operating Procedures
SAS	Statistical Analysis Software
SSTS	Sheehan Suicidality Tracking Scale
TBI	Traumatic Brain Injury
TWP	Transitional Work Program
UPS	Traceable Mail System
VA	Veterans Administration
VA CSR&D	Veteran Affairs Clinical Studies Research and Development
VAMC	Veteran Affairs Medical Center
VHA	Veteran Health Administration
VIP-STAR	Veterans Individual Placement and Support Towards Advancing Recovery
VRP	Vocational Rehabilitation Program
WH-CSPCC	West Haven Cooperative Studies Coordination Center

I. Introduction and Background

A. Introduction

"Work is not part of my recovery; work is my recovery." IPS Consumer (2008)

The VA spends approximately $23 billion each year on pensions and disability, and posttraumatic stress disorder (PTSD) is the most common psychiatric condition for which Veterans seek VA disability benefits. According to the VA Fiscal Year 2009 "Long Journey Home" Report, 61% of Veterans entering specialized outpatient PTSD programs were not working, either due to inability to find work (27%), not looking for work (25%), retirement (26%), or 100% disability (22%).[2] Given the increased number of returning Gulf War-era II Veterans (defined as those serving in the military since 2001, which includes Iraq, Afghanistan, and all other southwest Asia conditions), whom often experience PTSD and confront unemployment upon their military discharge, an evidenced-based vocational rehabilitation program for Veterans with PTSD in VHA is sorely needed. This study addresses this urgent need.

Over the past two decades of studies involving individuals with a serious mental illness (SMI), defined as schizophrenia, schizoaffective disorder, bipolar disorder, and major depression with psychotic features, the Individual Placement and Support (IPS) model of supported employment has yielded remarkably robust and consistent outcomes. Overall, approximately two-thirds of participants with SMI in clinical trials who receive IPS achieve competitive employment. Most people with SMI who participate in IPS find satisfying employment and become steady workers. Convinced of the evidence in 2005, the VA implemented IPS as an alternative and best practice vocational rehabilitation treatment for Veterans with a SMI. Each VA medical center was provided with funding for an IPS specialist. However, Veterans with diagnoses that were not categorized as SMI, such as PTSD, were essentially excluded from the VA IPS rollout. The exclusion of Veterans with PTSD was the impetus for the single-site pilot study funded by VA Rehabilitation Research and Development to test the efficacy of IPS in unemployed Veterans with PTSD. As described in the Preliminary Research section below, 76% of the participants

randomized to IPS gained competitive employment, compared to 28% of those randomized to VRP during a 12-month follow-up period.[1] Together with the evidence base accumulated in the SMI population, these significantly positive results of the pilot study support a VA CSP multicenter trial to definitively test the effectiveness of IPS in Veterans with PTSD.

B. Study Rationale

Mental Health Disability, Recovery, and Choice of Primary Outcome of Study

Mental health disability is complicated because the illnesses that lead to disability are "invisible" to others, are highly stigmatized, have a fluctuating course, and may not always have a direct relationship to functional status.[3,4] Mental health disability causes personal suffering and has a substantial negative impact on the person's ability to work and earn an income. Disability and unemployment leads to demoralization, passivity, depression, social isolation, low self-esteem, substance use, and a general decline in mental health.[5] Societal costs of mental health disability encompass the costs of health care and social services, as well as the loss of economic and consumer productivity of the mentally ill individuals who becomes socially and economically marginalized when unemployed.

Recovery is the goal of mental health treatment and involves a multi-faceted process in which people with illnesses or disabilities move beyond preoccupation with illness, become hopeful about the future, and pursue their own journeys and goals.[6] Recovery involves not only clinical and physical recovery, but also functional and social recovery which involves obtaining and maintaining valued societal roles and responsibilities, including employment, education, stable housing, and meaningful relationships with family, friends and the community. These domains of recovery contribute to an existential recovery, which is having the sense of hope, empowerment, agency, and spiritual well-being needed for a high quality of life.[7] The essential concepts of recovery are reflected clearly in the Americans with Disabilities Act, which states that people with disabling conditions have civil rights and protections in employment and other public settings.[8] Individuals with a serious mental illness who gain steady employment report increased self-esteem, decreased psychiatric symptoms, reduced social disability, and overall greater quality of life.[9,10,11,12] For those who become steady workers, mental health treatment costs decline dramatically over the long term after adjusting for morbidity/needs.[13] In essence,

employment helps people to escape from the disabled patient role, to experience a sense of purpose and accomplishment, and to establish a new identity as a working, contributing citizen.

Whereas ***reduced or total loss of employability*** is the ultimate threshold that defines a disabling medical or mental illness, ***achieving and maintaining employment*** is one of the most significant goals in defining recovery. On this basis, this VA Cooperative Study #589 targets this critical health outcome, i.e. steady competitive employment, as its primary outcome of the interventions to be compared. Rather than selecting a PTSD symptom outcome, our primary functional outcome of steady employment is more relevant to the life and recovery of the person with PTSD. Functional recovery in the area of work sets forth a trajectory which improves psychological outcomes and reduces negative health outcomes over time.

Models of Vocational Rehabilitation and the Choice of Study Intervention

Transitional Work Programs: The long-standing approach to vocational rehabilitation in VHA and state programs is the ***"train-place" or "stepwise" model*** that is founded on the assumption that the patient or client benefits from some form of pre-vocational training, instruction, or practice in a protected, but artificial, work setting prior to entering or being placed in a competitive work role. These programs include pre-employment training, skills training, sheltered workshops, transitional employment, and set-aside or enclave jobs.

The rationale for these conventional transitional work programs is that clients with a mental illness or disability are assumed to need a gradual introduction into regaining work capacity, because of their lack of skills, limited experience, and/or their sensitivity to stress in the competitive work environment. These programs further assume that after gaining experience in a protected work or vocational training setting, clients are more capable of succeeding in competitive employment. Serving as the control intervention in this VA Cooperative Study, this usual care "train-place" vocational rehabilitation model in VHA is called Transitional Work Program (TWP) and is described in more detail in the Methods section below.

Supported Employment Programs: In the early 1980s, Wehman and colleagues first described supported employment as a ***"place-train" model*** of vocational rehabilitation,[14,15] and demonstrated that the approach of seeking rapid placement into competitive employment,

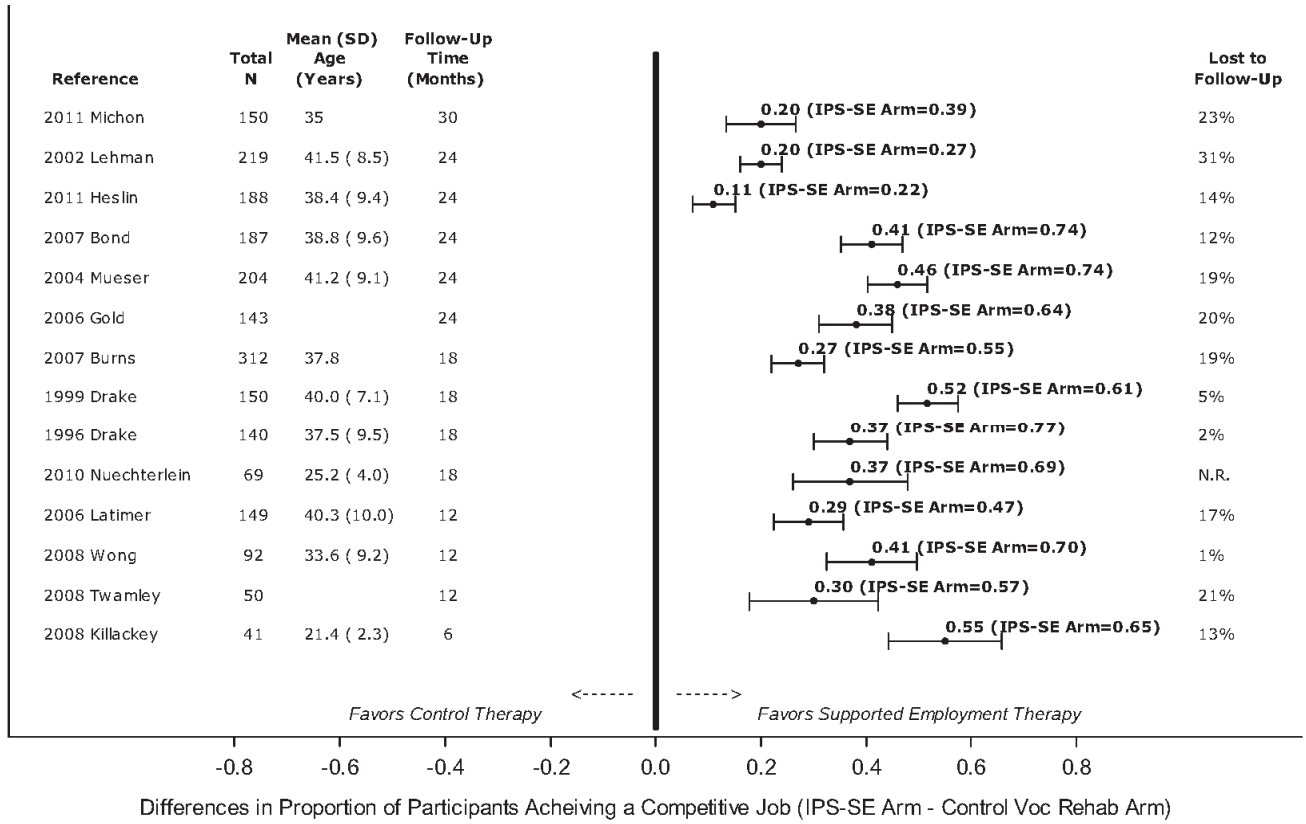
followed by specifically targeted job training and support, was superior to pre-employment "train-place" approaches. The supported employment approach was rapidly adopted by other leaders in the psychiatric rehabilitation movement.[16,17,18,19,20,21] As a result, the Rehabilitation Act Amendment of 1986 codified supported employment in law, specifying competitive employment, follow-along supports, and emphasis on the most severely disabled clients, without requiring a place-train approach. However, it is important to emphasize that over the past two decades supported employment has targeted persons with serious mental illness defined as severe psychotic disorders, e.g. schizophrenia, schizoaffective disorder, bipolar I disorder, or major depression with psychotic features. Except for one recent single-site study described in the Preliminary Research section below,[1] supported employment for anxiety disorders, such as PTSD, has not been studied or broadly implemented.

The rationale for a place-train supported employment model includes several important concepts.[22,23] First, without knowing ahead of time what type of job an individual will obtain, training the person for specific job skills is inefficient and often inaccurate. The "train-place" models assume that skills learned in the transitional job will transfer to different situations and different tasks, but this is often not the case. For example, practicing food preparation skills may give little benefit to an individual who obtains a gardening job. Instead, the supported employment approach serves to determine the needed supports and work skills in the context of an intact competitive job. Secondly, the supported employment approach searches for a competitive job that is in keeping with the interests and desires of the individual. Thus, supported employment is very client-centered, especially when compared to the Transitional Work Program, in which the transitional work tasks rarely match the client's skills or long-term work interests.[24,25,26] Third, supported employment is integrated within the mental health treatment team, which is not a defining factor of the Transitional Work Programs. The supported employment specialist attends the mental health treatment team meetings and provides feedback to the providers on the patient's work status and how their symptoms may be interfering with work function. This invaluable information can be used by the provider in making treatment decisions so that the symptoms or side effects of treatment can be stabilized before they become a problem and jeopardize employment. The supported employment specialist also encourages the patient to maintain adherence to treatment plans so that they maintain their ability to work and stay on the trajectory of recovery and community integration.

The specific supported employment model named in VA Cooperative Study #589 is called Individual Placement and Support (IPS). IPS is an advanced and manualized supported employment model that was originally developed in response to a statewide need for vocational services within the New Hampshire public mental health system.[27,28,29] IPS uses an integrated "place-train" approach, as described above, to help people obtain and maintain community-based competitive employment in their chosen occupation. The IPS model was first shown to be effective when IPS replaced a day treatment program for the seriously mentally ill.[30,31] Replication day treatment conversion studies and randomized controlled studies conducted in community mental health centers also demonstrated that IPS was effective in seriously mentally ill populations.[32]

As shown in the Figure 1 below, compared to the traditional vocational rehabilitation models, IPS has been proven to be efficacious in patients with a SMI in over a dozen randomized controlled studies.[33,34] In 14 studies involving individuals with a SMI, IPS achieved approximately 3 times the rate of competitive employment, significantly outpacing the comparison groups. In addition, the enhanced employment rates from implementation of IPS is durable over extended periods of time, as shown by studies tracking work outcomes over a 10-year follow-up period.[35] One can also see by Figure 1 that the attrition rates during long-term follow-up in IPS clinical trials are very low, especially when compared to the 40-50% attrition rates in pharmacologic trials for SMI populations. Also described in more detail below, IPS has other positive effects on secondary outcomes. VA Cooperative Study #589 has selected IPS as the best vocational rehabilitation intervention to compare to the VA treatment-as-usual, Transitional Work Program, in Veterans with PTSD.

Figure 1. Differences in Proportion of Participants Achieving Competitive Employment (IPS-SE Arm – Control Arm) with 95% Confidence Interval in 14 Randomized Controlled Trials



Durability and Secondary Outcomes Associated with IPS Supported Employment

The long-term vocational and nonvocational trajectories of participants with a SMI in IPS programs appear to be positive.[36] Of 38 participants with SMI who participated in IPS, 82% had held a competitive job and 71% had become steady workers, defined as having worked for more than half of the 8 to 12 year follow-up period. Participants reported enhanced self esteem, relationships, social activity and illness management.

Longitudinal studies of the course of schizophrenia have often found modest correlations between employment and symptoms.[37,38,39, 40,41] The direction of association is unclear. Secondary analyses of four IPS controlled trials in SMI groups have examined the longitudinal impact of competitive employment on non-vocational outcomes by comparing those who work against those that did not work or worked very little.[11, 12, 13,14] All four studies found some improvements in symptom control over time for working clients compared to nonworking clients. The improvement was a combination of worsening of symptoms for the non-working group and improvement in symptoms for the working group. Improvements were not consistent across all symptom subscales. Two studies found that working clients were less likely to be hospitalized and two did not. In the Bond et al. (2001) study, the Steady Worker group was contrasted to the combined group of clients who did not work at all and those who worked minimally; those who worked in sheltered employment were excluded. In the Kukla and Bond (in press) study, the Steady Worker group was compared to the group who did not work at all, with those who worked minimally or who worked in noncompetitive paid employment (e.g., agency-run businesses) excluded. Both studies examining self-esteem found an advantage for working clients over nonworking clients.

In general, these studies suggest that a meaningful period of competitive employment is associated with improvement over time in symptom control, quality of life, self-esteem, and social functioning as compared to not working. In summary, the findings from these studies suggest a modest effect over an 18-24 month follow-up period of employment on psychological and illness management outcomes.

Why do we need to test the effectiveness of IPS in Veterans with PTSD?

PTSD Impairs Occupational Functioning

Veterans' ability to maintain gainful employment is essential to successful reintegration into civilian life. Having a mental illness can substantially impede reintegration. The unemployment rate for persons with PTSD is consistently much higher than the general population rates.[42] Despite that the majority of Veterans with PTSD have some college education, few have jobs, almost 40% are impoverished, and most report work, role and social functioning scores below those of persons with serious mental illnesses. Also, unfortunately, 42% of Veterans who apply for VA disability compensation due to PTSD report poverty-level income (≤ $20,000/yr).[43] As evidenced by the findings of studies listed below, PTSD has a negative impact on employment, wages, and work performance.

Among 2,863 soldiers assessed 1 year after their return from Iraq combat duty, 16.6% screened positive for PTSD, and the presence of PTSD was significantly associated with more missed workdays, even after controlling for being wounded or injured.[44] In a cross-sectional self-report survey of National Guard soldiers (n=4,034), higher rates of both depression and PTSD were associated with financial difficulties, job loss, unfavorable effects of their deployment on co-workers, and/or non-support of their military affiliation by employers. The rates of PTSD were doubled in those who had lost jobs compared to those who had not (27.8% compared with 13.3% at 3 months and 47.7% *v.* 22.2% at 12 months). [45] While employment status did not differ in 262 National Guard/Reserve service members within 1 year of returning from a 16-month Operation Iraqi Freedom combat deployment, those with PTSD reported lower levels of work role functioning and greater rates of deterioration in work role functioning over time.[46]

The National Survey of the Vietnam Generation found that compared to Veterans without a lifetime diagnosis of PTSD, those with PTSD were significantly less likely to be working, and among those who were employed, Veterans with PTSD earned significantly lower hourly wage.[47] In an analysis of the Vietnam Era Twin Registry study (n=2,210 twins), those with PTSD were less likely to be currently employed or to achieve high status in income, education or occupation. Adjusting for pre-military and military service factors, only unemployment

remained significant in the identical twins discordant for PTSD.[48] Vietnam Veterans with PTSD (n=325) were more likely to work part-time or not at all than Vietnam veterans without PTSD. [49]

A recent cross-sectional study investigated the relationship between psychiatric diagnosis and impaired work functioning among 797 returning Operation Iraqi Freedom-Operation Enduring Freedom (OEF-OIF) service members, of whom 473 were employed.[50] A diagnosis of major depressive disorder, PTSD, generalized anxiety disorder, and panic disorder were all significantly associated with impairments in mental-interpersonal demands, time management, and output. These losses in productivity were on average four times higher than non-Veteran employees with no psychiatric disorder. In a different study, all three PTSD symptom clusters (reexperiencing, avoidance/emotional numbing, and hyperarousal) had significant independent associations with occupational impairment in a study of female Veterans with PTSD (n=253). While none of the symptom clusters were associated with employment status, the reexperiencing and hyperarousal clusters were significantly associated with lower occupational satisfaction.[51]

In a study of victims of violence (n=226) who had held a full-time job at time of victimization and had filed a disability claim, a diagnosis of PTSD and higher PTSD severity was positively associated to higher unemployment rates. These associations were not due to the level of disability compensation.[52] Compared to Veterans with PTSD who were denied VA PTSD disability benefits for PTSD, Veterans with PTSD who were receiving VA PTSD disability benefits had more severe PTSD symptoms. Both groups had meaningful improvements of similar magnitude in work, role, and social functioning, but functioning remained poor nonetheless. Comparing awardees with denied claimants, 13.2% vs. 19.0% were employed ($P = 0.11$); 15.2% vs. 44.8% reported poverty ($P < 0.001$); and 12.0% vs. 20.0% had been homeless ($P = 0.02$) during the 10-year outcome period. In summary, receiving PTSD benefits was associated with clinically meaningful reductions in PTSD symptoms and less poverty and homelessness.[53]

In summary, PTSD in Veterans is associated with significantly greater unemployment rates, number of lost jobs, absenteeism, financial difficulties, unfavorable effects of their deployment on co-workers, deterioration in work role functioning, and losses in productivity, and significantly lower hourly wage, income, occupational status, and occupational satisfaction.

VA Vocational Rehabilitation Programs are not Meeting the Needs of Veterans with PTSD

The current methods used by the VA Compensated Work Therapy (CWT) programs, which includes TWP, do not sufficiently meet the employment rehabilitation needs of Veterans with PTSD. In a VA study evaluating data of 5,862 Veterans from 122 CWT programs,[54] after controlling for independent variables, Veterans with PTSD were 19% less likely to be employed at discharge from the VA CWT program compared to those without a diagnosis of PTSD (odds ratio = 0.81, confidence interval = 0.69-0.96). The rate of competitive employment at discharge was low for both groups: only 30% for Veterans with PTSD and 36% for those without PTSD. PTSD had a significantly greater adverse effect on employment among veterans of the post-Vietnam era, highlighting the vulnerability of the Veterans who served in recent Gulf War II conflicts since 2001. Similarly, another VA study found that Veterans with PTSD involved in CWT were no more likely to be employed at 4 months follow-up compared to those who participated in a specialized PTSD treatment program.[55]

PTSD Differs from Serious Mental Illness

The clinical characteristics of Veterans with PTSD differ greatly from those with SMI, so one cannot automatically assume that IPS will yield the same results that have been replicated in SMI samples. PTSD is an anxiety disorder, whereas schizophrenia and schizoaffective disorders are psychotic disorders and bipolar disorder and major depression with psychotic symptoms are severe mood disorders with psychotic features. The major differences between these categories of illness involve thought content, thought process, and negative symptoms.

Thought Content: Although there some risk of developing comorbid psychotic symptoms, individuals with PTSD typically do not experience a break with reality (i.e. delusions or hallucinations). A PTSD flashback causes transient disorientation and perceptual disturbances; however, the person with PTSD is aware that the flashback was not a reality. Serious mental illnesses generally involve a course of illness that includes delusions or hallucinations (i.e. prolonged breaks with reality). Persons with SMI respond to internal stimuli (e.g. hallucinations

and delusions) and persons with PTSD are overly sensitive to external stimuli (e.g. loud, unexpected sounds).

Thought Process: Although interrupted by distractibility and hypervigilence, the thought processing of a person with PTSD is held intact, i.e. linear and coherent. A person with SMI typically has disrupted thought processes, in which the train of thought or verbal communication becomes rapid, disjointed, loose, or incoherent.

Negative Symptoms: Negative symptoms include flat facial affect, profound anhedonia, apathy, and alogia. PTSD involves a profound concern for safety that results in highly reactive fear mediated behaviors, such as physiologic arousal, hypervigilence and increased startle response, and maladaptive avoidant behaviors, such as social isolation and reduction in activities. The heightened vigilance and avoidant behaviors in persons with SMI are provoked by the delusions and psychotic symptoms rather than fears of life threatening event. In contrast to those with PTSD, persons with SMI suffer from profound negative symptoms that include flat affect, significant anhedonia/inactivity, alogia, and apathy.

From the point of view of a nonclinical employer, the Veteran with PTSD may seem tense, on edge, and nervous; whereas, the Veteran with an SMI may seem peculiar and slightly autistic. As a result of the different types of symptoms, the occupational difficulties and employment challenges also differ between these groups of patients. Those with PTSD may have difficulties maintaining concentration, feeling safe and secure, and working in large groups of people. A person with PTSD often misperceives routine activities as potentially threatening, for example, anticipating or interpreting a discussion with a supervisor as being a confrontation rather than a conversation. Persons with an SMI develop problems at work during periods of psychosis due to misinterpretation of the reality of their surroundings and due to disturbances in thought processing. In conclusion, the characteristics of PTSD versus SMI, while there is some overlap, are distinct, and these differences may have an impact, whether it is positive or negative, on the effectiveness of IPS in a real world setting.

The integration of IPS within a PTSD treatment team, as described in the Preliminary Research section below, is quite different than integration with a mental health treatment team for those

with a SMI. A better understanding of IPS integration within the PTSD treatment team is an important knowledge gap that will be filled by the experiences of CSP #589 VIP-STAR.

C. Preliminary Research

A Randomized Controlled Trial of Supported Employment Among Veterans With PTSD

The Study Chair and her collaborators completed the first single-site pilot study to examine whether IPS would be beneficial for Veterans with PTSD. Unemployed Veterans with PTSD were randomly assigned to either individual placement and support (IPS) supported employment (n=42) or a Veterans Health Administration Vocational Rehabilitation Program (VRP) treatment as usual (n=43) at the VA Medical Center in Tuscaloosa, AL. Transitional Work Program was the predominant VRP modality in the study. Employment rates and occupational outcomes were followed for 12 months post-randomization. A total of 71 (84%) participants completed the one-year of follow-up. Reasons for the 16% early exit included withdrawn consent (n=1 @ mo 3), relocation (n=3 @ mo 2, 8, 8), and incarceration (n=2 @ mo 4, 8) for the IPS group and loss to follow-up (n=2 @ mo 1, 2), relocation (n=5 @ mo 3,4,6,9,10), and incarceration (n=1 @ mo 6) for the VRP group.

During the 12-month study, 76% of the IPS participants gained competitive employment, compared with 28% of the VRP participants ($p<0.001$: number needed to treat=2.07). Veterans assigned to IPS also worked substantially more weeks than those assigned to VRP (42% versus 16% of the eligible weeks, respectively; $p<0.001$) and earned higher 12-month income during the 12-mo period (see Table 1). These findings are consistent with those of 8 IPS studies that show the mean number of annualized weeks worked in competitive jobs is 13 weeks for IPS and 5 weeks for the control group.[56]

Table 1. Occupational outcomes of Veterans with PTSD who received Individual Placement and Support (IPS) or VA Vocational Rehabilitation Program (VRP)

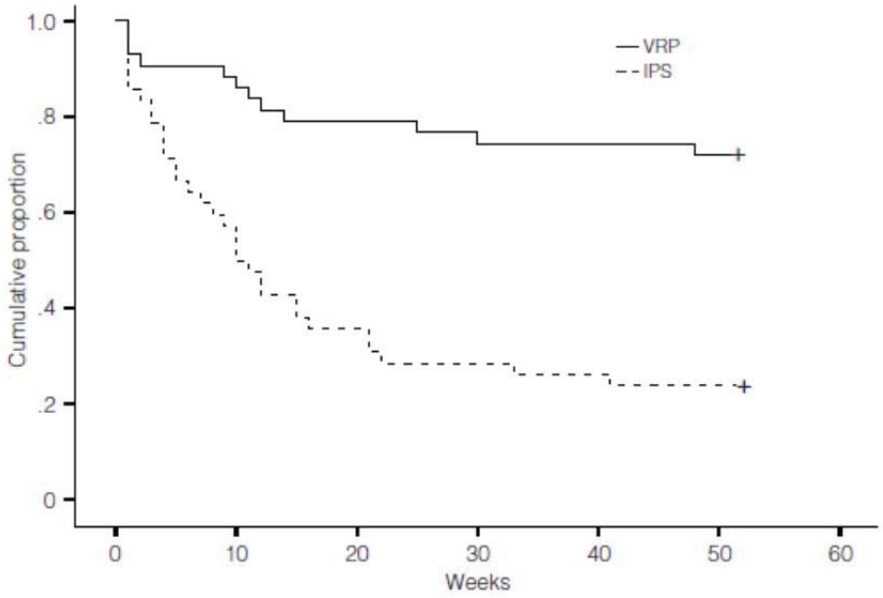
	IPS (N=42)		VRP (N=43)				
Outcome at 1 year	**M**	**SD**	**M**	**SD**	**p[a]**	**Cohen's d**	**95% CI**
Weeks competitively employed[b]	21.6	17.7	6.8	13.8	<.001	.93	.50–1.36
Days competitively employed	83.8	80.6	29.3	61.9	<.001	.76	.32–1.19
Hours competitively employed	656	661	236	494	<.001	.72	.29–1.15
Total gross 12-mo income, competitive ($)	9,264	13,294	2,601	6,009	<.001	.65	.21–1.28
Total gross 12-mo income, all sources ($)	9,308	13,449	3,909	6,212	.05	.52	.08–.95

[a] Mann-Whitney Z; [b]Competitive employment = a job for regular wages in a setting that was not set aside, sheltered, or enclaved, that is, the same job could be held by people without a mental illness or disability and was not a set-aside job in the VRP. Day labor (that is, pick-up cash-based day jobs for yard work, babysitting, and so forth) and military drill were not counted as competitive employment.

The specific outcome of whether or not the participant achieves competitive employment status was an excellent proxy for other occupational outcomes (e.g. percent of eligible weeks worked; number of weeks, days, hours worked; and income earned) as demonstrated by correlations ranging from 0.53 to 0.79 between occupational outcomes. Additional analysis revealed that 40% (17 of 42) of IPS participants became steady workers, defined as holding a competitive job for $\geq$ 50% of the 52-week follow-up, compared to 16% (7 of 43) of the VRP participants (p=0.01). When using a modified steady worker definition, i.e. worked in a competitive job for $\geq$ 20 weeks of the week 13-52 period, the pilot study found that 52.4% (22 of 42) randomized to IPS met the steady worker definition compared to 18.6% (8 of 43) randomized to the control met steady worker definition (p=0.0015).

The Kaplan-Meier survival curve in Figure 2 illustrates the time until first competitive job for each group. The participant is dropped from the curve as he/she obtains competitive employment. The IPS group achieved competitive employment significantly more quickly than the VRP group (log-rank p<0.001). Most job acquisition occurred within the first 20 weeks. These findings are consistent with those of 9 IPS studies that show the mean number of days to first competitive job is 136 day for IPS and 205 days for the control.[63]

Figure 2: Time from randomization until first competitive employment among Veterans with PTSD receiving Individual Placement and Support (IPS) or the Vocational Rehabilitation Program (VRP)



In an exploratory analysis of possible moderators of treatment, the employment rates of IPS to VRP were compared for the four psychosocial domains shown in Table 2. As shown by the differences in number needed to treat (NNT; i.e. lower is better), there was a greater IPS supportive employment benefit in those with inadequate transportation, inadequate housing, and for those without a family care burden (Table 2). These results support the inclusion of Veterans who lack housing and transportation, which is common among unemployed Veterans. The sample size of the pilot study was not large enough to analyze moderator by treatment interaction, which may be possible in the larger CSP study sample.

Table 2. Exploratory moderators of competitive employment in Veterans with PTSD who received IPS or the VA VRP

Exploratory Moderator	Vocational Rehabilitation		IPS Supported Employment		Statistic		
	N	Competitively Employed	N	Competitively Employed	Chi Square	P-value	NNT
Inadequate Transportation							
Yes	12	16.7%	11	81.8%	9.88	0.002	1.5
No	31	32.3%	31	74.2%	11.18	0.001	2.4
Inadequate Housing							
Yes	9	11.1%	14	78.6%	9.76	0.002	1.5
No	34	32.4%	28	75.0%	10.95	0.001	2.4
Inadequate Financial Means							
Yes	18	27.8%	19	73.7%	19.40	<0.001	2.2
No	25	28.0%	22	77.3%	4.61	0.032	2.0
Family Care Burden							
Yes	24	33.3%	25	64.0%	11.37	0.001	3.3
No	19	21.1%	17	94.1%	7.80	0.005	1.4

Another purpose of the pilot study was to see if integration of IPS within a PTSD treatment team was feasible and how the model needed to be tailored to be implemented in a VA PTSD treatment setting. The study demonstrated that IPS integration within a PTSD treatment team is feasible, however integration of IPS within a PTSD treatment team is very different than integration within a Mental Health Intensive Case Management team serving patients with SMI. PTSD treatment teams have much larger case loads, have less frequent contact with the patient, and have less frequent interdisciplinary treatment plan reviews of specific patients. PTSD providers are very busy with appointments and have limited time to meet with the IPS specialist. Thus, the IPS specialist had to be creative, assertive, and persistent in communicating and collaborating with the treatment provider in the care of a Veteran with PTSD. Strategies used by the IPS specialist included writing informative notes in the medical records and flagging the provider as co-signer, making direct request to the clerk for an extra appointment(s) in which the IPS specialist could attend with the Veteran to focus on symptoms and occupational function, directly bringing up a Veteran in the treatment team meeting when needed, and communicating with the nurse instead of the medication provider so that clinical issues could be addressed in a timely manner. Similar to a SMI treatment team, the PTSD treatment team providers had misunderstandings about recovery and paternalistic views about the need to protect the Veteran

with PTSD from work that might be stressful. However, with examples of successful outcomes and education from medical center leadership and the IPS specialists, these views and barriers to providers making referrals were able to be overcome, and IPS was embraced with enthusiasm.

D. Summary of Study Goals and Justification

Given the number of Veterans with PTSD and the disproportional unemployment rates, it is of critical importance for the VA to offer vocational rehabilitation programs based on the best evidence-based recover-orientated model. The goals of this multi-site study are to test the effectiveness of Individual Placement and Support (IPS) compared to VA Transitional Work Programs (TWP) in a large number of unemployed Veterans with PTSD, in a VA setting, and in a geographic and urban-rural diverse study population. The study is designed to evaluate the effectiveness of IPS on occupational functioning, PTSD symptoms, self esteem, quality of life, PTSD-related functional outcome, and health outcomes, compared to VA TWP treatment-as-usual. The primary hypothesis is that IPS would be significantly better than TWP for Veterans with PTSD in terms of the proportion of study participants who become steady workers, defined as holding a competitive job for at least 50% of the follow-up period. The secondary hypothesis is that IPS employment will result in better occupational outcomes, PTSD symptom improvement, self-esteem, quality of life, and PTSD-related functional outcome compared to TWP. We also plan to explore the differences between groups in terms of occurrences of negative health outcomes, such as emergency room visits, psychiatric inpatient hospitalizations, homelessness, weeks of substance misuse, encounters with law enforcement, and suicide behaviors. Conducting a large multisite study is the next logical step in assessing IPS as an evidence-based vocational rehabilitation program for Veterans with PTSD. These findings would provide generalizable evidence to clinicians and VHA stakeholders who inform policy and service delivery for Veterans with PTSD. In conclusion, a large multicenter randomized study comparing IPS with TWP for PTSD in Veterans is important, timely and necessary to provide evidence on the most effective way to improve employment in Veterans with PTSD.

In summary, the justifications for this study are:

1. Veterans with PTSD represent a substantial proportion of the VHA patient population, consume a great deal of VHA health care resources and disability payments, and are disproportionally unemployed.
2. The current vocational rehabilitation treatments are not adequately meeting the needs of Veterans with PTSD. Thus, new approaches need to be rigorously studied.
3. The clinical characteristics and occupational challenges of Veterans with PTSD differ greatly from Veterans with SMI, and thus, one cannot automatically assume that a rehabilitation approach that works best for SMI groups is going to have the same effectiveness for persons with PTSD.
4. IPS treatment integration differs between a PTSD Clinical Treatment and SMI treatment team, so further study of IPS within a PTSD treatment team is warranted.
5. There are no published multisite studies of IPS compared to TWP in a VA setting. Other than the published single site pilot study and several studies that have only recently been initiated in spinal cord injury and traumatic brain injury, a multisite comparison study of IPS and TWP in a VA setting has not been published. One cannot assume that findings from studies of IPS in a non-VA setting against non-VA comparison groups automatically translate to the VA healthcare setting.
6. Although a small single-site pilot study has been conducted and published (see Preliminary Research Section below), a large multisite randomized controlled study of IPS for PTSD has not been conducted. A larger study in more geographically and demographically diverse population is needed in order to show effectiveness and generalizability.

II. Importance to Veterans Health Administration

Separation from active service presents a critical question for Veterans with PTSD. Will they be reintegrated into mainstream civilian life or will they be socially excluded and marginalized? Reintegration requires finding mainstream competitive employment that provides the Veteran with identity, structure, income, daily activity, meaning, friends, and other benefits. Without mainstream competitive employment, many Veterans become enveloped by the negative sequelae of PTSD: preoccupation with symptoms, social isolation, economic instability, familial disintegration, substance abuse, legal problems, homelessness, and wayward lifestyles. Tragic stories of Veterans with PTSD pervade the post-Vietnam literature, the popular media, and everyday American life. The need for reintegration is paramount; without it, many Veterans will be traumatized again and again.

Medical treatment alone is not the answer. Many Veterans with PTSD try medications and/or psychotherapies without reconnecting with mainstream civilian life. Medical treatment and symptoms correlate minimally with competitive employment. Veterans with PTSD need and want services that specifically target reintegration. The VHA is one of the largest providers of vocational rehabilitation services in the United States, serving almost 60,000 Veterans per year through programming staffed by more than 680 FTEE, at a cost of more than $57 million dollars per year. Supported employment has enabled people with psychotic disorders to succeed in competitive employment and thereby become a part of mainstream society. In 2005, the VA chose to add IPS to the traditional model of services, specifically targeting IPS for the 20% of CWT participants who have a serious mental illness. This is now reflected in the current VHA Uniform Mental Health Service Handbook, which requires that every VHA Compensated Work Therapy (CWT) program offer both TWP and IPS, but IPS is prescribed for Veterans with a SMI psychotic disorder only. However, the 20-30% of Veterans who participate in VHA CWT and who have PTSD, do not qualify for IPS and so are routinely provided traditional TWP services. Supported employment is potentially the most effective service, but it has not been fully evaluated in a rigorous study and thus, is currently unavailable to these Veterans with PTSD.

Preliminary data suggest that Veterans with PTSD might benefit similarly. Our pilot study suggests that IPS may be more effective than TWP at helping Veterans with PTSD to achieve

stable employment in the community. If this early evidence could be confirmed in a larger multisite effectiveness study, the VHA would have the needed evidence to expand IPS to the thousands of Veterans with PTSD entering VHA CWT every year. This study provides the requisite data to guide VHA decisions as to whether to expand the target population for IPS to Veterans with PTSD. This expansion would require a major adaptation to CWT programming and personnel, and so clear substantial evidence is needed to support such a dramatic change. These modifications in VHA practice could substantially improve Veteran rehabilitation outcomes, moving a significantly greater number of disabled Veterans back to full and productive lives in the community.

The proposed project provides a critical test: Can evidence-based supported employment help Veteran's with PTSD to participate in competitive employment and reintegrate into mainstream society? Given the large influx of Gulf War-era II Veterans seeking services for PTSD, and the potential chronic course that is predicted for many of them, an improved employment and reintegration success rate will have a dramatic effect on the future functioning of this large cohort of young Veterans. An intervention, such as IPS, that directly addresses the occupational recovery of Veterans with PTSD has the potential to improve Veterans' personal income, clinical outcome, and quality of life, while offsetting VA disability costs and increasing the US income tax revenue. The outcomes of this study may lead to a shift in rehabilitation services within the VHA and improve the lives of thousands of Veterans who would otherwise have difficulty with reintegration and be pushed to the unhealthy and dangerous margins of society.

III. Study Hypotheses and Objectives

A. Primary Objective and Hypothesis

The primary objective of CSP #589 VIP-STAR is to evaluate the effectiveness of Individual Placement & Support (IPS) in unemployed Veterans with PTSD. The primary hypothesis is that, compared to those treated with transitional work program (TWP), unemployed Veterans with PTSD treated with IPS will be significantly more likely to become a steady worker. A steady worker is defined as holding a competitive job for ≥ 50% of the 18-month study follow-up period (i.e. ≥39 of the 78 weeks). All participants will be followed for 18 months post randomization.

B. Secondary Objectives and Hypotheses

The secondary objectives are to evaluate the effectiveness of IPS in regards to gross income, PTSD symptoms, self esteem, quality of life, and PTSD-related functional outcome. The secondary hypotheses are as follows. Over an 18-month (i.e. 78-week) follow-up period, compared to those treated with TWP, unemployed Veterans with PTSD treated with IPS will be significantly more likely to:

1) Earn greater cumulative gross income,
2) Experience a greater reduction in PTSD symptoms, as measured by the change in PTSD Checklist,
3) Experience a greater improvement in self esteem, a measured by the change in Rosenberg Self Esteem Scale,
4) Experience a greater improvement in quality of life, as measured by the change in Quality of Life Inventory.
5) Experience an improvement in PTSD related functioning, as measured by the change in PTSD Related Functional Inventory.

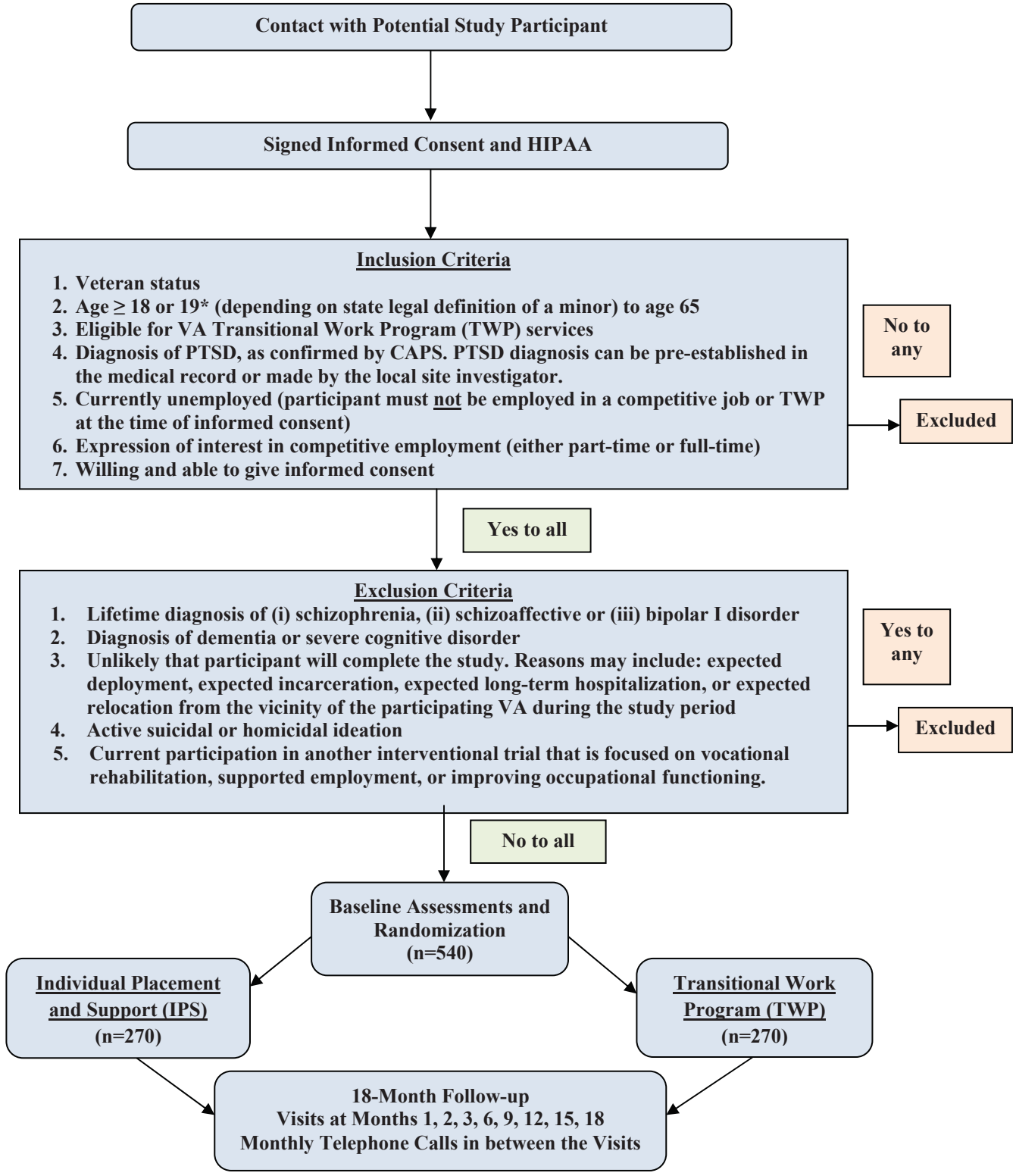
C. Exploratory Objectives and Hypotheses

The exploratory objective is to evaluate IPS in regards to of the number of selected crisis

events. The exploratory hypothesis is that over an 18-month follow-up period, compared to those treated with TWP, unemployed Veterans with PTSD treated with IPS will have significantly fewer negative health outcomes or crisis events that include emergency room visits, contacts with the legal system, homelessness, psychiatric inpatient utilization, weeks of substance misuse, and suicidal behaviors.

IV. Study Design

Figure 3. CSP #589 VIP-STAR



A. Study Population and Rationale

The target study population for CSP #589 VIP-STAR is Veterans with PTSD who are currently unemployed, i.e. the Veteran is not working in a competitive job as defined in Section C below. Veterans with PTSD suffer from high rates of unemployment, which, in turn, can contribute to poorer self esteem, community integration, quality of life, and more frequent crisis events. The inclusion criteria are broad in order to provide for a high level of generalizability of the study results. The study has very few exclusionary criteria since, based on an exploratory moderator analysis of the published pilot study, there is little justification to exclude subgroups of Veterans. In the exploratory moderator analysis several baseline variables were evaluated in terms of the magnitude of effects between groups. As shown in Table 2 in the Preliminary Research section, there was a greater IPS benefit in those with inadequate transportation, inadequate housing, chronic unemployment (≥2 years), and greater PTSD symptoms severity (≥70 on CAPS). Therefore, these disenfranchised and symptomatic Veterans are not excluded from the study since they are the very ones likely to benefit most from the intervention. The specific list of Inclusion/Exclusion criteria is presented in Section V. Study Population.

B. Treatment Regimens and Rationale

The Individual Placement and Support model of Supported Employment (IPS; intervention) will be compared to VA Transitional Work Program (TWP; control). When compared to "train-place" vocational rehabilitation models similar to VA TWP, IPS has been proven efficacious in over a dozen trials in seriously mentally ill populations (i.e. schizophrenia, schizoaffective disorders, bipolar I disorder, and severe major depression with psychotic features) and one single-site pilot study in Veterans with PTSD. A definitive multisite randomized controlled study in a larger, more geographically diverse PTSD population and in a VA setting is needed to evaluate IPS as an evidenced-based intervention for unemployed Veterans with PTSD.

C. Outcome Measures and Rationale

The primary outcome will be achievement of a 'steady worker' status, defined as obtaining and maintaining competitive employment for at least 50% of the active follow-up period (i.e. ≥39 weeks). The length of study follow-up is 18 months. Each participant is assessed

monthly, undergoes a final protocol assessment at 18 months post-randomization and is exited from the study at that time.

Participants may choose to exit the intervention but continue in study assessments for the 18-month follow-up. Participants may also choose to exit the intervention and study assessments but continue in research outcomes collection through their medical record or other remote data collection process (i.e. telephone contact or secure email/web access).

A steady worker is defined as holding a competitive job for ≥ 50% of the study follow-up period (i.e. ≥39 weeks). A week worked is defined as working for any period of time (i.e. part time or full time) during a Sunday to Saturday 7-day window. Competitive employment is defined as a job for regular wages, salary, or commission, in a setting that was not set aside, sheltered, or enclaved, that is, the same job could be held by people without a mental illness or disability and was not a set-aside job in the TWP program. Day labor (that is, pick-up cash-based odd jobs for yard work, babysitting, etc.) and military drill are not counted as competitive employment.

The primary outcome will be recorded by the participant on an at least weekly basis in a daily Employment Calendar Diary that is formatted and provided by the CSP study, or the IVR/Web system. On at least a monthly basis, the Clinical Research Coordinator (CRC) calls the participant or sees the participant during a research visit in order to collect summary employment information recorded on the calendar [whether or not the participant worked for pay (Y/N), number of days worked for each past referenced week, etc]. The rationale for the primary outcome is that competitive employment is the goal of vocational rehabilitation and one of the most important goals in the clinical recovery of a person with PTSD. One can think of the steady worker primary outcome in terms of a clinical goal of "remission" rather than only meeting the criteria of "response" (i.e. the pilot study's outcome of simply gaining competitive employment). The study length of 18 months is required in order to allow for the 3-6 month start-up time involved in each intervention prior to establishing competitive work and to allow enough time for an individual to establish steady work and achieve the secondary outcome goals. In comparison to other studies of IPS, an 18-month follow-up is a more typical, or even brief, follow-up period. In summary, achieving our primary outcome, the status of steady worker, is very clinically meaningful and sets the path for a trajectory of recovery and reintegration.

D. Sample Size and Rationale

The target sample size of 540 participants (270 per treatment arm) will provide 90% power to detect a 12.5% absolute difference in the percent of participants achieving 'steady worker' status between treatment arms (27.5% in the IPS arm vs. 15% in the TWP arm; Odds Ratio = 2.15), assuming about 13% overall loss to follow-up for assessment of the primary outcome. The recruitment period will be 12 months and the follow-up period for each randomized participant will be 18 months (i.e. 78 weeks). Regardless of adherence to or continuation in the assigned vocational rehabilitation, all randomized participants will be included in the analysis, based on an intent to treat design. Details of the sample size/power calculations are provided in Section XV.

E. Data Collection and Assessments

For individual participants, this study involves a baseline assessment period and an 18-month post-randomization follow-up assessment period. Primary outcome data collection occurs at least monthly and follow-up assessments with rating scales are collected every 3 months for 18 months. The study duration is 2.5 years excluding start-up and close-out periods. Table 3 below summarizes the data collected, assessments completed, and time intervals during this study.

F. Alternative Study Design Consideration

Primary Outcome: The alternative primary outcome of a simple "yes/no" gained competitive employment without a duration threshold, as defined in the pilot study, was considered. However, it was decided that the definition of steady worker provides a primary outcome that was achievable and more relevant to the trajectory of clinical recovery for Veterans with PTSD.

Duration of Follow-up: A shorter 12-month and longer 24-month follow-up period were considered. Instead of a 12-month follow-up, an 18-month follow-up period was selected to allow for the primary outcome of "steady worker" to have a fair opportunity of being demonstrated and for the secondary outcomes to be achievable since symptomatic recovery and quality of life changes take some time after employment is established in order to be realized. Timelines and budgetary considerations prevented a design with the 24-month follow-up period.

Secondary Outcomes: Numerous secondary outcomes that included alternative rating scales for the domains selected and alternative secondary outcome domains were considered. The number of secondary outcomes was narrowed to the most essential domains of recovery (gross income, PTSD symptoms, self esteem, quality of life, and PTSD-related functioning) in order to reduce issues of multiplicity bias. Justification for each secondary rating scale is provided in Section VI. Study Outcome Measures.

Health Economics/Utilization Analysis: Conducting a cost analysis within a randomized controlled trial is fraught with inflation due to the higher costs of study implementation when extra training is required, fidelity monitoring and data collection are ongoing, and first year start-up delays in achieving IPS specialist full capacity and efficiency are occurring. The combination of budgetary concerns and the issues of artificially inflated costs during the launch of a randomized controlled trial led to the decision to not pursue a full scale Health Economics/Utilization analysis. Instead, the study will gather the use of high costs crisis intervention services, as described in the exploratory outcome, as a reflection on the service impact of IPS, i.e. reducing costly high intensity services that reflect instability in health. In regard to the existing knowledge about costs, several economists and policy experts have recently reviewed the economic research on IPS.[57,58,59,60] Although costs vary from site to site and economies of scale may occur in larger agencies, the costs of IPS services for an individual client during the first and most intensive year of IPS service are estimated to be approximately $4,000 in 2006 dollars.[61,62] Studies comparing costs when a program shifts from facility-based services, such as rehabilitative day treatment, to IPS show that IPS reduces costs and improves vocational outcomes and is therefore highly cost-effective.[63] Studies in which IPS costs and outcomes are compared to those of another model of vocational services show that costs tend to be similar across the models, but vocational outcomes are two to three times greater for IPS participants.[64]

Table 3. Schedule of Data Collection/Assessments

Data Item	Completed By	Approx. Completion Time (Min)	STUDY TIMEPOINT				
			Screening/ Baseline Visit	Weekly Activity	Monthly Phone Contact	Month 1, 2 Visits	Month 3, 6, 9, 12, 15, 18 Visits
Informed Consent and HIPAA Authorization	Participant and CRC	20	X				
Form 00 Participant Contact	CRC	5	X				
Form 01 Screening – Randomization Status	CRC	10	X				
Form A Informed Consent Questionnaire	CRC	10	X				
Form 02 Demographics and Military Service History	CRC	5	X				
Form 03 Life Status	CRC	5	X				
Form 04 Medical History (CIRS)	CRC	5	X				
Form 05 Work History	CRC	10	X				
Form 06 Clinical Administered PTSD Scale (CAPS)	CRC	30	X				
Form 07 Mini-International Neuropsychiatry Inventory (MINI)	CRC	30	X				
Form 08 Ohio State University TBI Identification Method	CRC	10	X				
Form 09 PTSD Checklist (PCL-5)	Participant	5	X				X
Form 10 Rosenberg Self-Esteem Scale (RSES)	Participant	5	X				X
Form 11 Quality of Life Inventory (QOLI)	Participant	10	X				X**
Form 12 Post Traumatic Stress Related Functional Inventory (PRFI)	Participant	10	X				X
Form 13 Sheehan Suicidality Tracking Scale (SSTS)	Participant and CRC	10	X				X
Form 14 Inventory of Crisis Events	CRC	15	X			X	X
Form 15 Employment Inventory	CRC/Participant/CPOC	15			X	X	X
Form 16 Employment Reconciliation	CRC	20				X	X
Source Document: Employment Calendar	Participant	15	X (Orientation)	X		X (Review)	X (Review)
Form 17 Adverse Event	CRC	5				X	X
Form 18 Serious Adverse Event	CRC and LSI	5				X	X
Form 19 Follow-up Assessments Checklist	CRC	5				X	X
Form 20 Participant Study Status	CRC	5			X*	X*	X*
Form 21 Protocol Deviation – Unanticipated Problem V1.0	CRC				X***	X***	X***
Form 28 Supplementary Participant Study Exit Form	CRC						X****
Form 29 Customer Satisfaction Survey	CRC						X****
Supported Employment Fidelity Scale Form	Fidelity Monitor	-					
TOTAL TIME NEEDED FOR ASSESSMENT(S) (approximate hours):			3.0	<0.5	0.5	1.5	2.0

Note: N/A = Not Applicable; CRC = Clinical Research Coordinator; CPOC = Centralized Primary Outcome Coordinator; LSI = Local Site Investigator.
***Form 20** (Participant Study Status) is completed at any time during the study that the participant's status in the study changes, eg., participant withdraws consent, participant is lost to follow-up, etc.
****Form 11** (QOLI) is collected at baseline, month 6,12, and 18 only.

V. Study Population

A. Eligibility Criteria

The eligibility criteria are intentionally broad in order to yield a result that is generalizable to VHA clinical populations and settings. In addition, the eligibility criteria avoid unnecessary barriers to recruitment in order to ensure that the enrollment period is maintained on time.

Inclusion Criteria:

1. Veteran status;
2. Age ≥ 18 or 19 (depending on state legal definition of a minor) to age 65;
3. Eligible for VA Transitional Work Program (TWP) services;
4. Diagnosis of PTSD, as confirmed by Clinician Administered PTSD Scale. PTSD diagnosis can be pre-established in the medical record or made by the local site investigator;
5. Currently unemployed (participant must not be employed in a competitive job or TWP assignment at the time of informed consent);
6. Expression of interest in competitive employment (either part-time or full-time);
7. Willing and able to give informed consent.

Exclusion Criteria:

1. Lifetime diagnosis of (i) schizophrenia, (ii) schizoaffective or (iii) bipolar I disorder;
2. Diagnosis of dementia or severe cognitive disorder (evidenced in the medical record);
3. Unlikely that participant can complete the study. Reasons may include: expected deployment, expected incarceration, expected long-term hospitalization, and/or expected relocation from the vicinity of the participating VA during the study period, or other;
4. Active suicidal or homicidal ideation;
5. Current participation in another interventional trial that focuses on vocational rehabilitation, supported employment, or improving occupational functioning. Participants may not dually enroll in more than 2 VA sponsored intervention trials.

B. Inclusion of Women and Minorities

The investigators acknowledge and uphold the VA policy to include women and minorities in this multisite clinical research study. Women and minorities are included in order to ensure that the findings and benefits can be generalized and extended to women and minority Veterans. No Veteran is excluded on the basis of gender, race, or ethnicity. Demographics, including race, ethnicity, and gender, are recorded for randomized as well as non-randomized individuals. Participating VA medical centers will be requested to make a special effort to recruit female Veterans, such as working closely with VA women's clinics to obtain referrals of female Veterans. Since minorities are overrepresented in the population of unemployed Veterans with PTSD, we do not anticipate the need for special recruitment efforts for minorities.

C. Recruitment and Screening

Participants are recruited from the community, VA outpatient clinics, VA vocational rehabilitation programs, and VA domiciliary or residential programs, as they naturalistically present for treatment, are referred to the study, or make personal inquiry into the study. A HIPAA waiver for purposes of recruitment and pre-screening will be requested from the local VA or VA-affiliate IRB , so that the local site investigator and CRC may obtain personal identifying information, such as a list of names, social security numbers, and addresses of Veterans with the diagnosis of PTSD (excluding those over the age of 65 and with an exclusionary diagnosis or date of death) who have had contact with the local VA within the past two years. The clinical research coordinator will use this list to mail an IRB-approved letter or flyer to Veterans who live within a reasonable distance from the VA medical center that makes participation feasible, and to look in the VA medical record to pre-screen Veterans for the study (i.e. review the VA electronic medical record to determine if there are any obvious exclusionary criteria) prior to the Veteran signing informed consent. IRB-approved advertisements and flyers are also used as part of the recruitment strategy.

HIPAA Waiver and Contact Information:

The West Haven Coordinating Center requires the collection of the following data on a monthly basis: (a) the number of Veterans who were approached or referred for participation in the study and (b) the reasons why the Veterans did not sign or were not offered informed consent (reasons are determined based on the clinical research coordinator's ability to ascertain via either pre-existing

information in the clinical record, volunteered by the Veteran or offered by the Veteran after a gentle question). CSP #589 does NOT need any personal identifiable information or personal health information to be collected as part of this effort. CSP #589 does NOT need de-identified data (i.e., individualized line item de-identified data). We only need aggregate information reported on a monthly basis during the enrollment period (approximately 12 months). This request should fall under the local site HIPAA waiver for purposes of screening and recruitment.

A CSP form of the aggregate information has been sent to sites for use in compiling this monthly report, but sites can choose to send the aggregate information using another method. **It is entirely up to the local site to decide how this information is tracked**, however, an excel spreadsheet was provided for use or modification. The local site is not required to maintain a log of personal identifiers; however, some HIPAA waivers allow a local site to temporarily maintain a list of Veterans who refuse consent in order to have a way to not contact the Veteran in the future. **Under no circumstances is the local site to transmit personal identifiers of persons who did not sign informed consent to the West Haven CSP Coordinating Center**. The clinical research coordinator may keep a tally of Veterans who do not sign informed consent and reasons for no consent without recording the name, Date of Birth, SSN or any of the other 18 HIPAA identifiers. In other words, the local site can use numbers (1,2,3,4,…), letters (a,b,c,d,…) or any other strategy to keep a count of Veterans who are offered informed consent but do not sign consent.

The purpose of this aggregate information is to track screening and recruitment activities and use this information to understand barriers to recruitment and effect modifications to the screening and recruitment approach and/or inclusion/exclusion criteria, in the event the Study Leadership deems that necessary.

VI. Study Outcome Measures

A. Primary Outcome

The primary outcome is whether or not the participant holds a competitive job for 50% of the 18-month follow-up time, i.e., ≥39 of the 78 weeks, thereby meeting the definition of steady worker. Competitive employment is defined as a job for regular wages, salary, or commission, in a setting that was not set aside, sheltered, or enclaved, that is, the same job could be held by people without mental illness or disability and was not a set-aside job in the TWP program. Day labor (that is, pick-up cash-based odd jobs for yard work, babysitting, etc.) and military drill does

not count as competitive employment. For analysis purposes, a week of maintained employment is defined as working in a competitive job for at least one hour on one or more days from Sunday through Saturday 7-day window. For study purposes, Week #1 begins the Sunday after randomization. Weeks are counted consecutively from Week #1 through Week #78 (i.e. the end of the 18-month follow-up). The participant does not have to hold the same job during consecutive weeks to be counted towards meeting the primary outcome threshold. Adhering to the principal of intent-to-treat, a participant may discontinue the IPS or TWP intervention or be discharged from TWP, but he/she is encouraged to remain in the study for purposes of outcomes assessments for the entire 18-month follow-up period.

Every effort is made to collect employment data for the entire duration of the 18-month follow-up period in which the participant is in the study. The primary outcome is collected, retained and managed by a Calendar Method, in the following ways:

Employment Calendar Diary (source document): The local site CRC orients the participant to the Employment Calendar Diary or Interactive Voice Recognition/Web-based (IVR/Web) methods at baseline and reinforces his/her understanding and adherence at each monthly phone contact and every face-to-face research assessment visit. On at least a weekly basis, the participant records his/her employment information in a daily Employment Calendar Diary that is formatted and provided by the CSP study or enters the information in the IVR/Web system. If the preferred format is paper diary, the Employment Calendar Diary is submitted by the participant to the local site clinical research coordinator (CRC) at the research assessment visits or returned by mail. For each week in the Employment Calendar Diary or IVR/Web system, the participant indicates employment status (whether or not they worked for pay), number of days worked, number of hours worked, income earned (weekly), and reasons for missed work. The Participant also keeps a log of his/her jobs held during that interval (job name, employer, start date, end date, expected wage, etc) in the diary or IVR/Web. In addition, the diary has a section for the participant to record any adverse life events (emergency room visits, psychiatric inpatient hospitalizations, contacts with the legal system, homelessness,weeks of substance misuse).

Employment Inventory (Form 15). On at least a monthly basis and using the Employment Calendar Diary or IVR/Web as a reference, the participant provides summary employment

information through telephone contact or face-to-face visit with the local Clinical Research Coordinator (CRC). This summary employment information includes whether or not the participant worked for pay (Y/N), type of work (TWP, competitive, or other), type of job(s) (Hollingshead code), number of days worked, number of hours worked, gross income from work, and whether or not the job is new for each past referenced week.

The type of job is based on the Hollingshead Categories from the Addictions Severity Index [Hollingshead Categories: 1) Higher executives, major professionals, owners of large businesses. 2) Business managers if medium sized businesses, lesser professions, i.e., nurses, opticians, pharmacists, social workers, teachers. 3) Administrative personnel, managers, minor professionals, owners/proprietors of small businesses, i.e., bakery, car dealership, engraving business, plumbing business, florist, decorator, actor, reporter, travel agent. 4) Clerical and sales, technicians, small businesses (bank teller, bookkeeper, clerk, draftsperson, timekeeper, secretary). 5) Skilled manual - usually having had training (baker, barber, brakeperson, chef, electrician, fireman, machinist, mechanic, paperhanger, painter, repairperson, tailor, welder, police, plumber). 6)Semi-skilled (hospital aide, painter, bartender, bus driver, cutter, cook, drill press, garage guard, checker, waiter, spot welder, machine operator). 7) Unskilled (attendant, janitor, construction helper, unspecified labor, porter, including unemployed)].

The Central Primary Outcome Coordinator (CPOC) is available to the local site research teams to discuss the collection of the primary outcome and to guide the research team (mainly the CRC) is strategies to minimize missing data and how to evaluate the type of work activity (i.e. whether or not the work is TWP, competitive, or other). The West Haven CSP Coordinating Center tracks the collection of the Employment Inventory to ensure that all participants and CRCs from all sites are keeping up with the Employment Inventory data collection. If a site is missing Employment Inventory information, West Haven CSP Coordinating Center or the CPOC contacts the local CRC and/or the participant to inquire about the missing information and facilitate data entry. This oversight is a way to ensure timely data entry in as close to real time as possible, to minimize recall error and missing data.

Employment Reconciliation (Form 16). The CRC meets face-to-face (or by telephone if face-to-face visits are not feasible) with the participant on a monthly basis for the first 3 months, and

then on an every three month basis, to record whether or not they have worked, to answer any questions about the Employment Inventory, and to remind them to keep account of jobs on their Employment Calendar. At these follow-up study visits, the local site CRC examines the Employment Calendar or IVR/Web system with the participant, examines the Employment Inventory, reviews the VA medical record, and interviews the participant. If discrepancies in Employment data are found, the CRC completes an Employment reconciliation case report form to correct the information as needed. The Employment reconciliation case report form indicates all variables collected on the Employment Inventory case report form. There is also a space on the form to insert other details or comments to clarify the correction, and notes any discrepancy and how it was corrected. The CRC may refer to the VA medical records to confirm participation in TWP (if applicable), or other employment information named in the IPS employment specialist notes and use this information to resolve any discrepancies in the participant's self-report.

The local site CRC communicates to the WH-CSPCC of any errors that need to be corrected in the Employment Inventory. Missing weekly employment data will be counted as unemployed in the primary analysis to reduce type-I error and protect the study from bias.

B. Secondary Outcomes

Secondary outcome measures are described in more detail in Section VIII. Baseline Assessments and Procedures.

1. Cumulative gross income is collected using the Employment Calendar or IVR/Web source document and Employment reconciliation case report form used for the primary outcome correction as needed. When possible, the CRC verifies income earned by reviewing paycheck stubs that the participant is instructed to maintain with the Employment Calendar.

2. PTSD symptoms are assessed every three months during the follow-up period using the self-report PTSD Checklist (PCL) that the participant completes during the follow-up visits.

3. Self Esteem is assessed every three months during follow-up by the self-report Rosenberg Self Esteem Scale (RSES) that the participant completes during the follow-up visits.

4. Quality of Life is assessed every six months during the follow-up period using the self-report Quality of Life Inventory (QOLI) that the participant completes during the follow-up visits.

5. PTSD related functioning is assessed every three months during the follow-up period using the self-reported Post Traumatic Stress Related Functional Inventory (PRFI).

C. Exploratory Outcomes

Inventory of Crisis Events: At the months 1, 2, and 3 and at each 3-month follow-up visit thereafter, the local site CRC reviews the medical record, interviews the participant, and records all participant occurrences of crisis events for the previous months on a case report form inventory. The participant makes note of these events in the Employment Calendar Diary on a regular basis, which is reviewed by the CRC at the face-to-face or telephone assessment visits. Crisis events, defined in section VIII, include emergency room visits, contacts with the legal system, homelessness, psychiatric inpatient utilization, and weeks of substance misuse. Crisis events are tracked on the Inventory of Crisis Events (Form 14). Suicidal behaviors are tracked by the Sheehan Suicidality Tracking Scale (Form 13).

VII. Human Rights Issues and Informed Consent

A. Risks and Benefits

Potential Psychological Risks: There are minimal psychological risks associated with this study due to the fact that participants remain under treatment for their underlying Axis I condition(s). Participants may experience transient anxiety or embarrassment during the clinical interviews when answering questions about their work, PTSD symptoms, self-esteem, or quality of life. Participants may feel that participation in the study is an invasion of their privacy. The study team minimizes these potential psychological risks by maintaining a pleasant and professional demeanor, conducting the interviews and physical assessments in a private clinical office, and allowing the participant to discuss these reactions and feelings if they occur. Participants are allowed to take breaks during the interviews and assessments, if needed, to avoid or minimize discomfort.

Potential Social and Economic Risks: Participation in a study may involve risk of feeling "labeled" or "stigmatized." Confidentiality safeguards will be strictly maintained to prevent such risks. A HIPAA authorization page informs the patient of the use of identifiable personal health information. The informed consent and HIPAA authorization details the provisions for protecting the confidentiality of research data. The methods used to obtain information about the participants include direct query and medical record review. Participation in the study may involve economic risk of missing work or having to pay for transportation. The study team works with the participant to minimize these inconveniences by seeing the participants outside their work hours and by minimizing clinical appointments to those necessary to adhere to the protocol. Also participants are seen in a timely fashion upon arrival and appointments are kept as short as possible to minimize inconvenience of attending appointments. In addition to enhancing retention in the study, participants are paid per research visit and per completed monthly phone call to offset the economic burden of attending the study appointments and to reinforce submission of employment data through the phone. In order to avoid reinforcing dropout or compliance with financial incentives, all subjects who attend these follow-up visits and/or complete phone calls receive payment, regardless of whether they continued in the TWP/IPS programs. This modest payment adds incentive for subjects to follow-up and

secondarily covers the transportation cost. The payment is not viewed as coercive given the minimal risks involved in the psychological assessments by means of interview and self-reports; i.e. no invasive procedures, physical demands, or medications interventions are required to receive payment. Participants are paid for each visit that he/she attends and for completed monthly phone calls.

B. Informed Consent Procedure

Prior to admittance into the study, potential participants who meet eligibility criteria are provided and asked to sign a written informed consent form (ICF) by an authorized member of the study team. The ICF includes detailed information regarding the study's sponsor, purpose, procedures, potential risks and benefits, alternative treatments, compensation, and other required elements. Potential participants are given ample time to consider and ask questions regarding what is written in the informed consent document, and they may involve family members, significant others and his /her primary treatment team in making their decision. Potential participants are informed that refusal to participate in this research protocol does not penalize them or change their eligibility for non-study VA services, treatment, or disability payments. Participants are required to read and sign the Institutional Review Board (IRB)-approved ICF, along with a Privacy Officer-approved HIPAA form, prior to randomization and baseline assessment.

In regard to vulnerable patient populations, persons who require surrogate consent, persons with dementia or severe cognitive disorder, minors, prisoners and the terminally ill are excluded. Therefore, surrogate consent and consent by legally authorized representatives is not permitted.

In regard to protection of patient privacy, a Certificate of Confidentiality is acquired by the CSP study and statement of this protection is included in the ICF. The participant signs a VA release of information form (as often as needed) prior to the IPS or TWP specialist discussing the Veteran's individual health information with any prospective or current employer.

C. Capacity to Consent

Assessing capacity to consent is an important ethical responsibility on the part of the research team during the informed consent process in any research study. This research protocol will

require a checklist (Form A) to be filled out in order to document that capacity to consent was adequately assessed.

VIII. Baseline Assessments and Procedures

Once written informed consent and HIPAA Authorization have been obtained, study procedures, including data collection and randomization, can begin. See Table 3 in Section IV – Summary of Study Design for a tabular summary of the data collection schedule. Baseline assessments and procedures are performed in order to characterize the study population at baseline and for use in "change-from-baseline" analyses.

1. **Participant Contact (Form 00):** The local CRC collects participant SSN for safety-related monitoring activities and participant contact information on this form for use during follow-up.

2. **Screening (Form 01):** The local CRC confirms that all inclusion criteria are met and no exclusion criteria are present.

3. **Demographics and Military Service History (Form 02):** The local CRC collects baseline demographics and characteristics, including age, gender, race, ethnicity, marital status, highest education level achieved, and military history including branch of service, length of time served, period of service, combat exposure,.

4. **Life Status (Form 03):** The local CRC collects baseline housing status, household status, transportation status, family care burden status, VA and non-VA disability status, including claims/appeals pending, and PTSD history including category of trauma and current and past treatment for PTSD.

5. **Medical History (Form 04): The Cumulative Illness Rating Scale (CIRS):**[65,66] The CIRS is used to assess general medical conditions at baseline and provides a summary score that gives an index of baseline medical burden.

6. **Work History (Form 05):** The CRC collects variables related to prior work history, including length of current unemployment, number of competitive jobs and longest duration of competitive work.

7. **The Clinician Administered PTSD Scale (CAPS) (Form 06):**[67] A trained local CRC or CAPS-assessor assesses the participant at baseline with the CAPS to confirm that the participant has PTSD. The CAPS is a structured clinician-administered interview used to assess frequency and intensity of symptoms of PTSD over the past one month. The CAPS allows the assessor to confirm the DSM diagnosis of PTSD. The frequency and intensity of each symptom on the CAPS is rated on separate 5-point scales, yielding both dichotomous (yes/no scoring algorithm for the diagnosis of PTSD) and continuous scores for each symptom and for the disorder as a whole. The CAPS rating for index trauma is implemented in the following manner: Military service is verified by the DD214 form at the time the individual is enrolled at the VAMC for services. Trauma exposure is established based on the participants' verbal history, supplemented by the CAPS Life Events form and can include combat, noncombat, and sexual trauma. The type of trauma is recorded at baseline. This research protocol does not require military documentation of the trauma since this is often not available at the time that the person is seeking treatment. PTSD is complicated by the fact that the Veteran has often been exposed to multiple severe traumas. The CRC or CAPS assessor adheres to the instructions for the CAPS in the training manual as much as possible, in that the assessor asks the participant to describe and focus on the worse incident of trauma that is most likely causing the PTSD symptoms and rate the CAPS for that trauma. Many experts in the field recognize that in regard to combat trauma, an index trauma can involve more than one incident. The CAPS total score and sub-scores capture PTSD symptoms. The CRC or CAPS assessor completes the scoring algorithm to confirm the diagnosis of PTSD (i.e. "rule of fours" whereby an item score must be rated a $\geq$4 to count towards a symptom that confirms to DSM-IV diagnosis). The CAPS is public domain and Dr. Davis will train the CRCs to administer the CAPS. CSP#589 will use the current CAPS for DSM-IV.

8. **The MINI International Neuropsychiatric Interview (M.I.N.I.) (Form 07):**[68] The trained CRC conducts the baseline Mini-International Neuropsychiatric Inventory (M.I.N.I.), which is a structured clinician-administered interview that assesses current and lifetime Axis I disorders, including substance abuse and dependence. The M.I.N.I. has good reliability and validity and is selected for its reduced burden on the research participant (i.e. ~30 min to administer M.I.N.I. compared to 45-60 min for the Structured Clinical Interview). The M.I.N.I. includes items that assess the hallmark symptoms of the exclusionary psychotic disorders and bipolar disorder. Hence, the M.I.N.I. captures comorbid psychiatric diagnoses that are needed to describe the study cohort. The MINI for DSM-5 is in development. CSP#589 will use the current MINI for DSM-.

9. **Ohio State University Traumatic Brain Injury Identification Method – Short Form (OSU TBI-IM) (Form 08)**:[69,70,71] The OSU TBI-ID is an interviewer-administered questionnaire that captures the lifetime history of traumatic brain injury. The OSU TBI-ID gives a summary score that reflects the likelihood that consequences have resulted from lifetime exposure to traumatic brain injury. The OSU TBI-ID has high interrater reliability and established reliability and predictive validity. Questions 1-5 are about past head injuries. If answered "no," question 6 is not answered. If responses to #1-5 are "no" the participant is classified as 1 "improbable TBI". If in response to #6 reports never having loss of consciousness (LOC), being dazed or having memory lapses, the participant is classified as 1"improbable TBI". If in response to #6 reports being dazed or having a memory lapse, the participant is classified as 2 "possible TBI". If in response to #6 LOC does not exceed 30 minutes for any injury, the participant is classified as 3 "mild TBI". If in response to #6 LOC for any one injury is between 30 minutes and 24 hours, the participant is classified as 4 "moderate TBI". If in response to #6 LOC for any one injury exceeds 24 hours, the participant is classified as 5 "severe TBI". The OSU TBI-IM is used to classify TBI status of the study participant at baseline. Dr. Corrigan has granted permission for CSP#589 to use the OSU TBI-IM at no cost.

10. **PTSD Checklist (PCL) (Form 09):**[72, 73] The PCL is a self-report inventory of the 20 PTSD symptoms that define the disorder. Symptoms are rated on 5-point Likert scales, yielding a score ranging from 17 to 100. The PCL has been shown to be a reliable and valid measure of trauma-related PTSD symptoms in a variety of special populations. The PCL is useful as a continuous measure of PTSD symptom distress. Evidence suggests that a 5-10 point change represents reliable change (i.e., change not due to chance) and a 10-20 point change represents clinically significant change. In the VA CSP#420 (n= 360) comparing trauma-focused and present-centered group therapies, and the 2nd trial compared cognitive processing theory and a waitlist control condition (n=60) revealed significant longitudinal associations between clinician rated CAPS and the self-report PCL in total and symptom clusters of PTSD. The amount of change on the CAPS ranged from .75 to .82 standard deviations for every 1 standard deviation change on the PCL.[74] These analyses support the notion that veterans with PTSD can reliability report their symptoms and the degree of change over time on a self-report PTSD Checklist. The PCL score is used to capture change in self-reported PTSD symptoms over the 18- month study. The PCL is public domain, and the PCL for DSM-5 is currently available and will be used in CSP#589.

11. **Rosenberg Self-Esteem Scale (RSES) (Form 10):**[75] The RSES is one of the most widely used self-report measures for assessing global self-esteem. The RSES is a 10-item self-report Likert-type questionnaire that asks participants to indicate the degree of their agreement or disagreement with statements about their self-esteem and self-deprecation. Five of the items are phrased in a positive view of oneself and five are phrased in a negative view of oneself. Items are rated on a 4-point Likert scale (1=strongly disagree, 2= Disagree, 3=Agree, 4=strongly agree). Item ratings are summed to yield a total score that ranges from 10 to 40 (or 0-30 in some studies that use a 0 to 3 range for the items); higher scores indicate greater self-esteem. The RSES has high reliability with adolescent boys and young adult samples with Cronbach's α values of 0.88 for the English version. The Reliability coefficients from previous studies of clients with severe mental illness found internal consistency coefficients exceeding 0.80 and test-retest reliability of 0.87. It is available for use in the public domain. More information can be found at:

http://www.bsos.umd.edu/socy/Research/rosenberg.htm. Based on the Sinclair et al study[76] of the psychometric properties of the RSES across demographic groups living in the U.S., **unemployed persons scored 17.68 ± 7.70 (mean ± SD) and employed persons scored 23.35 ±5.36 using 0-30 point scoring.** A distribution frequency shows that a score of 22 falls in the 47.2 percentile and a score of 23 falls in the 52.2 percentile. Pearson correlations were evaluated between RSES and the Depression, Anxiety, and Stress scales (DASS-21). All correlations were statistically significant at $p < .001$.

Use of RSES in Clinical Populations and Vocational Rehabilitation Studies: Based on the RSES, self esteem has been shown to be low in unemployed persons compared to those who are employed[77] and in persons with PTSD compared to those without PTSD. Compared to Veterans without PTSD, Veterans with PTSD have more self esteem instability based on a shortened RSES, as well as greater negative affect and gratitude instability which were significant predictors of lower global wellbeing.[78] In a clinical trial of 143 participants with a SMI comparing two vocational rehabilitation programs, scores on the RSES did not vary with work status or other functional outcomes; however, improvement in RSES was strongly related to measures of life satisfaction and affective symptoms.[79] The hypothesis that working leads to improved self-esteem for people with SMI was not substantiated in this small study, but rather it appears that self esteem reflects general life satisfaction and affective symptoms rather than objective functional status. Clients with SMI participating in the Indianapolis Vocational Intervention Program (IVIP) showed sustained levels of hope (Beck Hopelessness Scale) and self-esteem (RSES) from baseline to the 5-month endpoint, while those receiving the standard support service experienced declines in hope and self-esteem. The IVIP group worked significantly more weeks and had better average work performance than the standard support group.[80] Finally, in a study of 149 vocational rehabilitation clients with a SMI who were unemployed at baseline, the self-esteem, as rated by the RSES, the group that worked in a competitive job for $\geq$ 20 weeks (n=31) improved significantly from baseline to the 18-month endpoint ($t=2.07$, $df= 40$, $p<.05$) compared to the group

combining those who worked minimally (n=50) or none (n=44).[11] Specifically, for those that were competitively employed ≥ 20 weeks (n=31), the mean ±SD RSES scores was 20.5 ±5.9 at baseline and improved to 17.3 ± 5.3 at 18-months (*note: this study used inverse scoring, so lower score reflects better self esteem*). There were no significant differences over time in the RSES from baseline (19.6 ± 5.6) to 18 months (18.1±6.1) for the group that had no competitive work (n=44). This study indicates that reaching the goal of a steady worker may also have an important bearing on improvements in self esteem.

12. **Quality of Life Inventory (QOLI) (Form 11):[81]** The QOLI developed by Frisch[82] is a 32-item self-report measure of life satisfaction that takes approximately 5 minutes to complete. Many quality of life scales that have been used in studies of SMI samples overemphasize location (i.e. how much time spent outside the home) and function (i.e. making independent purchases or meals) and fail to capture social dimensions of community and social integration. The Frisch QOLI seems more advanced in its recognition of social integration, which takes into account a persons' capacity to exercise connectedness and citizenship.[83] The QOLI 16 areas of life are health, self-esteem, goals and values, money, work, play, learning, creativity, helping, love, friends, children, relatives, home, neighborhood, and community. Each area is rated in terms of importance (0 = not important to 2 = extremely important) and satisfaction (-3 = very dissatisfied to +3 = very satisfied). Importance ratings are multiplied by satisfaction ratings to compute a weighted satisfaction score for each item and overall quality of life is obtained by averaging all the weighted scores that are nonzero. In the QOLI manual, overall QOLI scores of 1.6 to 3.5 are classified as "average," 0.9 to 1.5 as "low," and <0.8 as "very low." Normative data was based on 798 nonclinical adults sampled from 12 states from the Northeast, the South, the Midwest, and the West. Test–retest coefficients for the QOLI ranged from .80 to .91, and internal consistency coefficients ranged from .77 to .89 across 3 clinical and 3 nonclinical samples. The QOLI had significant negative correlations between the QOLI and measures of general psychopathology and depression. Clinical and nonclinical criterion groups differed significantly in mean QOLI scores.

Use of QOLI in Clinical Populations and VA CSP Studies: In a meta-analytic review of 23 separate studies (N=2892),[84] the effect size was large across all anxiety disorders, indicating poorer quality of life among anxiety disorder patients vs. nonclinical controls, with no anxiety disorder diagnosis associated with significantly poorer overall quality of life than any other. Patients with PTSD showed particularly prominent impairments in quality of life compared to controls (effect size 1.46; $p<.001$; 95% CI 1.32–1.60). A recent review indicates that OEF/OIF veterans with PTSD experience low quality of life comparable to findings obtained from other war cohorts and from nonveterans as well.[85]

The QOLI has been used in previous VA CSP studies of PTSD interventions, including a controlled study of trauma-focused group therapy[86] and an ongoing placebo-controlled study of prazosin. Although there were no overall improvements in quality of life among participants in the CSP group therapy study, the analysis[87] of the QOLI data from the 325 male Vietnam veterans with chronic PTSD who participated, demonstrated that PTSD symptoms were associated with reduced quality of life before treatment and there was a significant amount of change within individual participants that was related to PTSD symptom change. The QOLI mean (SD) scores at baseline, 7-month, and 12-month were -0.18 (2.07), -0.06 (1.93), and -0.12 (1.93), respectively.

Using data from two randomized clinical trials of veterans treated in Department of Veterans Affairs settings that included 358 male Vietnam veterans who received group therapy and 203 female veterans who received individual psychotherapy, a study[88] evaluating the QOLI found that overall quality of life was poor in men and women Veterans with PTSD, and in general, there were no gender differences in QOLI or in how PTSD was associated with quality of life. For both men and women, emotional numbing was uniquely associated with reduced quality of life. The unadjusted mean and standard error values for the QOLI were 0.02 ±2.0 in women and -0.22 ±2.03 in men with PTSD. Clinically significant improvement in PTSD

symptoms was associated with improvement in all quality-of-life domains; however these data were not presented.

13. **Posttraumatic Stress Related Functioning Inventory (PRFI) (Form 12):** The 30-item PRFI will be used to assess PTSD Related Functioning. This tool was found to have very good psychometrics in an OEF/OIF veteran population and will be used at Baseline and every 3 months during the 18-month follow-up period (personal communication with Dr. Shannon E McCaslin; manuscript under preparation).

14. **Sheehan Suicidality Tracking Scale (SSTS) (Form 13):**[89] The SSTS is an 8-item self-report scale that tracks treatment-emergent suicidal ideation (items 2, 3, 4 plus score from item 5 if <1) and behaviors (items 6, 7a, 8, plus item 5 if >1); This instrument is used because it is sensitive to change in frequency or intensity of suicidal thoughts or behaviors over time, and it maps directly to the suicidality classification coding system used by the FDA. The SSTS is reviewed by the CRC and positive endorsements are evaluated and handled by the Local Site Investigator.
15. **Inventory of Crisis Events (Form 14):** At baseline, months 1, 2, and 3 and at each 3-month follow-up visit thereafter, the local site CRC reviews the medical record and Employment Calendar Diary, interviews the participant while referring to the Employment Calendar Diary (using the Employment Calendar Diary in a similar manner as a Time-Line Follow Back method), and records the number crisis events for the previous months. Crisis events include VA and non-VA emergency room visits, contacts with the legal system, number of nights considered homelessness (i.e. defined as number of nights residing on the street, in a shelter, or in a domiciliary), psychiatric inpatient admission days(s), and weeks of substance misuse (i.e. number of weeks where at least one episode of heavy drinking, use of illicit substances, and/or use of controlled substances without a prescription occurred). The utilization of health services are tracked by self-report and VA service utilization are confirmed at the end of the study by gathering utilization data from the VA Administrative databases. Suicidal behaviors are tracked by the Sheehan Suicidality Tracking Scale (separate form).

16. **<u>Supplementary Participant Study Exit Form (Form 28).</u>** Case Report Form 28 was developed to facilitate the collection of certain additional data that include some re-assessment of baseline data (service connection and housing information) and some data that have not thus far been captured as part of either (a) the baseline data or (b) the current study close-out process. This information is relevant to further understanding the impact of the intervention and facilitators or barriers in the engagement of the intervention or the pursuit of competitive employment. This form does not replace or amend any existing study case report forms and should be used in the context of and during the study close-out process, as participants exit the study.

Form 28 is to be completed by the clinical research coordinator (CRC) ***ONCE*** *for all active participants during the last assessment/study exit visit.*

17. **Customer Satisfaction Survey (Form 29):** Case Report Form 29 is optional and will be administered ***ONCE*** (during the last assessment/study exit visit) to those participants who agree to complete it. The CRC should indicate on Form 28 as to whether the participant has agreed to fill out Form 29, in order for the CSP Coordinating Center to track whether the form is to be expected or not (i.e. not list as a missing form for those who opt out).

Note: For participants who have already completed their last assessment/study exit visit, an attempt should still be made to have these forms completed either via chart review and/or study participant contact (conditional on local IRB approval).

IX. Stratification and Randomization

Participants who meet eligibility criteria are randomized in a 1:1 ratio to receive either IPS or TWP. Randomization will be stratified by site and use a permuted block design of randomly varying block sizes. Randomization scheme will be generated by the WH-CSPCC using SAS. Local Site personnel will be able to access the randomization scheme by logging into a randomization website set up within the VA firewall by the CSPCRPCC Albuquerque Informatics group. Once assignment is made, the participant will be analyzed in that group regardless of future events or information, in accordance with the intent-to-treat principle.

PTSD severity and length of unemployment were considered as possible baseline variables upon which to stratify. However, in exploratory moderator analysis of data from the pilot study of IPS for Veterans with PTSD, these baseline characteristics did not have any differential impact on the primary outcome. In addition, randomization will render these variables well balanced between groups.

X. Treatment Regimens

A. Overview of Treatment Regimens

Although the approaches of vocational rehabilitation between the two groups are different, the goal of both IPS and TWP inventions is the same, i.e. to obtain Competitive Employment and become a steady worker. Competitive employment is defined as a job that pays at least minimum wage and the wage that others receive performing the same work, is based in community settings alongside others without disabilities, and is not reserved for people with disabilities.

As described above, the IPS intervention assists participants to directly enter into competitive jobs. IPS employment specialists do not encourage clients to obtain noncompetitive jobs, which include volunteer jobs, unpaid internships, sheltered work, and set-aside jobs. The focus on direct "place-and-train" entry into competitive employment is different than the stepwise "train-and-place" approach to employment involved in the TWP control intervention. The participants who are randomized to IPS will not engage in VA TWP set aside jobs. The TWP intervention places the participant in a time-limited set-aside job before seeking a competitive job.

B. Individual Placement and Support (IPS Intervention)

The IPS model is described in detail in a manual that is provided by CSP to all IPS specialists involved in the study, entitled Supported Employment: Applying the Individual Placement and Support (IPS) Model to Help Clients Compete in the Workforce by Swanson and Becker (2011).[90]

IPS Fidelity Ratings will use two scales, the well published scale and a new version that has recently been developed:

The individual placement and support (IPS) model of supported employment for people with severe mental illness is an evidence-based practice. The 15-item IPS Fidelity Scale (IPS-15) was developed to measure program fidelity and has been shown to have good psychometric properties, including predictive validity. On the basis of field experience and research updates, the authors developed an expanded and revised version of this scale, the IPS-25, also known as

the Supported Employment Fidelity Scale. Internal consistency reliability for the IPS-25 was .88. Predictive validity, measured as the correlation between the IPS-25 and site-level employment rate, was .34. Eight of the IPS-25 items were significantly positively correlated with employment rate. Items related to the vocational generalist role, disclosure, follow-along support, and vocational unit were the most strongly correlated with employment. Program longevity was positively associated with employment, whereas the unemployment rate was not.

The IPS-25 has promising psychometric properties, with greater precision and content coverage than the IPS-15. However, it has not demonstrated an advantage over the IPS-15 in predictive validity.

VIP-STAR will be monitoring the study sites using the IPS-15 (original scale) as the primary monitor of site performance. The IPS intervention must achieve a rating of >66 of a possible 75 points on this Supported Employment Fidelity Scale (see Appendix E). The Fidelity Monitor will also rate the sites using the IPS-25 (revised scale) as a secondary tool with more descriptive language useful to the local site's understanding of the core principles and functional implementation. The dual rating will add data to the field for future comparisons of effectiveness. There is no additional burden on the participant or local site research team to add this fidelity scale. The second fidelity scale is rated using the same information that was gathered during the on-site fidelity monitoring visit.

The fidelity ratings are conducted by the National IPS Fidelity Monitor at biannual on-site monitoring visits. All IPS specialists receive training prior to the initiation of the study taught by CSP #589 IPS National Fidelity Monitor and CSP #589 national IPS supervisors. The training is comprehensive and covers the evidence-based IPS practices and well as issues specific to management and care of Veterans with PTSD. The IPS specialist participates in face-to-face group supervision with local IPS team and biweekly group teleconference supervision with a national IPS supervisor. There will be two national IPS experts on the CSP study who will train and supervise the local site IPS specialists via biannual site visits and biweekly conference calls. The IPS specialist is an integral member of the interdisciplinary PTSD treatment team, and thereby has access to and is able to utilize the treatment team's resource to enhance the Veteran's recovery.

Based on qualitative and quantitative research, a successful IPS specialist needs to have these attributes: (1) initiative; (2) outreach; (3) persistence; (4) hardiness; (5) empathy; (6) passion; (7) team orientation (8) professionalism. He/she needs to have a recovery-oriented approach in knowing that participants want to and are able to work and that stigma is not an insurmountable barrier. The successful IPS specialist spends most of his/her time in the community, makes frequent contact with employers, manages time efficiently, develops egalitarian relationships with Veterans, and collaborates well with other professionals. The IPS specialist must be knowledgeable about IPS principles and how to apply them.

The IPS model involves the following important domains:

1. Competitive Employment: As stated above, the IPS intervention assists participants to directly enter into competitive jobs. IPS employment specialists do not encourage clients to obtain noncompetitive jobs, which include volunteer jobs, unpaid internships, sheltered work, and set-aside jobs. The IPS specialist carries out all phases of the vocational services and provides predominantly community-based services.

2. Eligibility Based on Client Choice: IPS embraces the notion of "zero exclusion." Other than the study entrance inclusion and exclusion criteria, participants are not excluded by IPS on the basis of readiness, diagnoses, symptoms, substance use history, psychiatric hospitalizations, level of disability, or legal system involvement. In an IPS program the only requirement for admission is a desire to work in a competitive job, either part-time or fulltime.

3. Integration of IPS and PTSD Services: IPS programs are closely integrated with PTSD or mental health treatment teams. The IPS specialist participates regularly in treatment team meetings and may ideally have an office in the PTSD clinic. Through treatment team meetings and frequent communication outside of meetings, IPS specialists and treatment providers share information and develop ideas to help Veterans with PTSD improve their functional recoveries. This principle was drawn from the multidisciplinary team approach.

4. Attention to Veteran Preferences: IPS services are based on clients' preferences and choices, rather than providers' judgments. Stemming from a motivational interview based evaluation by the IPS specialist, the IPS specialist and the Veteran conduct an individualized job

search, based on the Veteran's preferences, strengths, and work experiences. With encouragement from the IPS specialist, Veterans make choices about job types, work settings and environments, wages and hours, and level of IPS specialist involvement. For example, the Veteran discusses with their IPS specialists the advantages/disadvantages of disclosing to an employer that they have a disability and the Veteran determines whether the IPS worker will have direct contact with employers on their behalf.

5. Personalized Benefits Counseling: IPS specialists help Veterans obtain personalized, understandable, and accurate information about their VA, Social Security, Medicaid, and other government entitlements. The IPS specialist and Veteran may consult with the Veteran benefits counselors who are often available through the local VA medical center or Veteran service officers in the community. The fear of losing benefits is a common barrier to seeking employment, and Veterans are often misinformed about their benefits and their ability to work with a known disability. As stated in VHA Directive 2007-05 dated Jan 18, 2007 and entitled Compensated Work Therapy Supported Employment Services Implementation Plan: **t**he enactment of Pub. L. 108-170, the Veterans Health Care, Capital Asset, and Business Improvement Act of 2003, amended the authority for CWT programs under 38 U.S.C. 1718 to permit the provision of skills training, job placement, and support services. IPS is covered under this authority and Veterans who participate in IPS services are given the same protections as all other CWT programs. Participation in CWT transitional or supported employment cannot be used to reduce, deny, or discontinue VA compensation or pension. Pursuant to 38 U.S.C. 1718(g), a Veteran's participation in or receipt of a distribution as a result of participation in an activity carried out under 38 U.S.C .1718 may not be considered as a basis for denial or discontinuance of a rating of total disability for the purposes of compensation or pension based on the Veteran's inability to secure or follow a substantially gainful occupation as a result of disability. Pursuant to Title 38 Code of Federal Regulations (CFR) 3.343(c)(1), and 38 CFR 3.342(b)(4)(ii), neither participation in, nor the receipt of remuneration as a result of participation in, a therapeutic or rehabilitation activity under 38 U.S.C. 1718 shall be considered evidence of employability. For the purposes of 38 U.S.C. Chapter 15, Pension For Non-Service-Connected Disability, a distribution of funds and a payment made to a Veteran under a program of rehabilitative services authorized by 38 U.S.C. 1718, are considered to be a donation from a

public or private relief or welfare organization, and are not included in determining annual income.

6. Rapid Job Search: IPS specialists use a rapid job search approach to help Veterans obtain jobs directly, rather than providing lengthy pre-employment assessment, training, and counseling. In the first couple of sessions, the IPS specialist and Veteran build a career profile of the client's preferences, skills, strengths, and previous employment and education, which helps provide direction for the job search and job support. The IPS specialist, Veteran, or both start making face-to-face contacts with employers within 30 days of starting the IPS intervention. If the Veteran is uncertain of the type of work he or she wants, the search may begin by directly exploring different types of jobs. The rapid job search principle has sometimes been incorrectly understood to mean, *rapid placement*. But this principle focuses on the process of looking for a job, not the end result. Agencies that establish rapid placement as their goal run the risk of compromising client preferences in the type of job obtained.

7. Systematic Job Development: IPS specialists build an employer network based on Veterans' interests, developing relationships with local employers by making systematic contacts. Job development is more than contacting employers for job availability, it involves cultivating a relationship with prospective employers. People who are new to the position of employment specialist often have not developed skills in making face-to-face employer contacts (i.e. instead, they try to find job leads on the Internet or make cold calls to employers and ask directly about job openings). The trained IPS specialist provides assertive engagement and outreach to prospective employers in the community.

8. Time-Unlimited and Individualized Support: IPS follow-along vocational supports are individualized and continued for as long as the Veteran wants and needs the support. IPS specialists provide ongoing support and remain committed to the support of Veterans long after they have achieved employment. IPS follow-along support aids in job retention or facilitates a change to a better suited job. If a Veteran loses or ends a job, the IPS specialist assists in finding subsequent jobs if needed with the view that all jobs are positive learning experiences.

C. VA Transitional Work Program (TWP; control)

The Veterans Health Administration (VHA) Compensated Work Therapy (CWT) program provides diverse vocational approaches, with transitional work experience (TWE) or transitional work programs (TWP) representing the predominant vocational activity in CWT. The TWP programs across VHA vary in structure; however, our selected study sites' TWP programs will have common elements described below. TWP will adhere to a lower rating ($\leq$55 of a possible 75 points) on the Supported Employment Fidelity Scale rated by the national Fidelity Monitor. The TWP specialist participates in face-to-face supervision with the local CWT team according to the CWT manager's schedule.

1. Time-limited Set-Aside Employment: TWP is a step-wise approach to job placement with initial short-term (i.e. up to 6 months) transitional work experiences in a brokered or set-aside work setting. In the TWP programs, employers contract with the CWT program to fill job openings or to perform identified tasks. Work opportunities arranged by the CWT Program through agreements with local companies or Federal agencies including VA, for a time-limited, transitional basis. The Veteran-workers are "hired" by CWT, and although vocational staff may provide job coaching or other types of support, they are typically also supervised directly by the employer. The employee's wages, which are usually at the minimum wage but below market values for comparable jobs, are paid by CWT, and participating companies pay a small surcharge to support program operations. Some TWP positions are located in community businesses, but the majority of contracts for TWPs are between CWT and their parent VA medical center, such that Veterans work in such positions as environmental care, print shops, engineering service, laundry and food services, and groundskeepers for the facility. Veterans in transitional work receive their earnings through the VA fiscal payment process from the CWT Account 36X0160X4, and are not considered employees of participating companies or agencies. The Transitional Work is considered a pre-employment vocational assessment program that operates in the VA medical center and local community businesses. TWP participants are screened by vocational rehabilitation staff, assessed and placed in a work assignment for a limited time as deemed clinically appropriate. TWP work assignments are supervised by work site staff, and impose the same job expectations as are experienced by non-CWT workers in the organization or company. Every TWP participant has an Individual Treatment or Service Plan and is vocationally case managed by a VA Vocational Specialist. Veterans participating in TW are not considered employees of the VA or participating company, and receive no traditional employee

benefits. Payments received by participating TWP Veterans are tax exempt. There are no direct government entitlements that subsidize the Veteran's earnings in TWP programs. Although the intent of TWP is to have the Veteran participate in a time-limited TWP position, there is no guarantee for this provision due to various reasons such as Veteran preferences, availability of TWP assignments prior to Veteran gaining a competitive job or losing interest in a TWP assignment, or discharge from the TWP program without having attended the TWP assignment. Every effort will be made to ensure that all Veterans randomized to TWP participate in a TWP assignment at the local participating medical center. If the Veteran does not participate in a TWP assignment within the 18-month follow-up period, a reason for this will be noted at the end of or exit from the study.

2. Eligibility Criteria: The eligibility criteria for VA TWP programs vary; however, there is usually pre-employment readiness that has to be established prior to entering into the TWP program.

3. Limited Integration of TWP and PTSD Services: The TWP specialist obtains clinical information from the provider upon referral; however, the TWP specialist has very little contact with the PTSD providers after initial referral is made. The TWP specialist does not attend PTSD treatment team meetings. The TWP specialist's office is located within a separate vocational rehabilitation program area at some distance from the PTSD clinic.

4. Attention to Veteran Preferences: While the TWP specialist treats all Veterans with respect and professionalism, the types of jobs provided by the TWP are pre-arranged and thus, except for situations of happen stance, the set-aside jobs are less likely to have a meaningful relationship to the Veterans' preferences or career goals.

5. Personalized Benefits Counseling: As with IPS, the TWP specialists help Veterans obtain personalized, understandable, and accurate information about their VA, Social Security, Medicaid, and other government entitlements. The TWP specialist and Veteran may consult with the Veteran benefits counselors who are often available through the local VA medical center or Veteran service officers in the community. As stated in VHA Directive 2007-05 dated

Jan 18, 2007 and entitled Compensated Work Therapy Supported Employment Services Implementation Plan: **t**he enactment of Pub. L. 108-170, the Veterans Health Care, Capital Asset, and Business Improvement Act of 2003, amended the authority for CWT programs under 38 U.S.C. 1718 to permit the provision of skills training, job placement, and support services. TWP is covered under this authority and Veterans who participate in TWP services are given the same protections as all other CWT programs. Participation in CWT transitional work experiences cannot be used to reduce, deny, or discontinue VA compensation or pension. Pursuant to 38 U.S.C. 1718(g), a Veteran's participation in or receipt of a distribution as a result of participation in an activity carried out under 38 U.S.C .1718 may not be considered as a basis for denial or discontinuance of a rating of total disability for the purposes of compensation or pension based on the Veteran's inability to secure or follow a substantially gainful occupation as a result of disability. Pursuant to Title 38 Code of Federal Regulations (CFR) 3.343(c)(1), and 38 CFR 3.342(b)(4)(ii), neither participation in, nor the receipt of remuneration as a result of participation in, a therapeutic or rehabilitation activity under 38 U.S.C. 1718 shall be considered evidence of employability. For the purposes of 38 U.S.C. Chapter 15, Pension For Non-Service-Connected Disability, a distribution of funds and a payment made to a Veteran under a program of rehabilitative services authorized by 38 U.S.C. 1718, are considered to be a donation from a public or private relief or welfare organization, and are not included in determining annual income.

6. Job Search: The TWP specialists provide variable and limited guidance for competitive job search, but these are typically conducted within the facility using internet resources. In addition, job search for placement in a potentially permanent competitive job is often delayed until after the transitional work experience is nearly completed. The TWP specialist provides time-limited job search assistance (i.e. during the TWP placement period only or until the first job is found).

7. Systematic Job Development: The TWP specialists do not engage in community based job development for a specific Veteran.

8. Time Limited Support: The TWP specialist does not provide long-term follow-up vocational assistance after the first job is obtained and most often the time-limited follow-along supports are provided only during the time-limited transitional work experience.

Based on the IPS Fidelity Scale, IPS and TWP can be compared as shown in Table 4 below.

Table 4: Comparison of the VA Transition Work Program (TWP) and Individual Placement and Support (IPS)[a]

Domain	TWP	IPS
Staffing		
Caseload per specialist	30 or more clients	25 or fewer clients
Vocational services provided	Traditional "train-and place" vocational services (set-aside temporary jobs)	"place and train" IPS services (obtaining and maintaining a competitive job)
Vocational functions	Specialist maintains caseload but refers clients to other programs for vocational services	Specialist carries out all phases of vocational service (job search, placement, and follow-up).
Organization		
Integration with PTSD treatment team	Specialist is separate and has little or no regular direct contact with the PTSD team	Specialist is attached and integrated with one or more members of the PTSD treatment team
Vocational unit	Specialists may or may not be part of a unit; specialists may or may not meet as a group	Specialists form a vocational unit with group supervision at least weekly
Exclusion criteria	Clients are screened out on the basis of job readiness, limited functioning, or other reason	All clients are encouraged to participate, and there are no exclusion criteria
Ongoing, work-based assessment	Vocational evaluation is conducted before job placement with emphasis on office-based tests	Vocational assessment is ongoing and occurs in community jobs
Competitive job search	First contact with employer about competitive job is delayed several months after entry	First contact with employer about competitive job is typically within one month after entry
Individualized job search	Decisions are usually driven by the nature of the availability of set-aside jobs	Employer contacts are based on job choices that reflect clients' preferences and strengths
Diversity of jobs	There is little diversity, and set-aside jobs are usually entry level	There is broad diversity; jobs are varied entry level and community based
Permanence of jobs developed	Specialists usually do not provide options for permanent, competitive jobs	Virtually all of the competitive jobs offered by specialists are permanent
Jobs as transitions	Specialists prepare clients for one job and, if it ends, they do not necessarily help clients find another	Specialists help clients end jobs when appropriate and offer to help clients find other jobs
Follow-along supports	Nonexistent or time limited	Flexible, individualized and ongoing
Community-based	Specialists spend less 10% of their time in the community	Specialists spend 70% or more of their time in the community
Assertive engagement and outreach	Specialists do not provide outreach to clients as part of initial engagement or to those who stop attending the vocational service	Specialists provide outreach as part of initial engagement and at least monthly on a time-unlimited basis when clients

[a] The domains for comparison are from the Supported Employment Fidelity Scale (Appendix F).

XI. Follow-up Assessments and Procedures

Selected Outcome Measures

See Table 3 in Section VI. Study Outcomes Measures for a tabular summary of the follow-up assessments and time points of collection.

1. **Employment (Primary Outcome) Assessments:**

   On at least a weekly basis, the participant completes an **Employment Calendar Diary or IVR/Web,** in which he/she records following information for each week:

   a. worked in a job for pay (yes/no)
   b. job name
   c. number of days worked
   d. number of hours worked
   e. amount of wages earned
   f. reasons for missed work

   On a monthly basis, the Clinical Research Coordinator telephones the participant or sees the participant during a research assessment visit to collect the following information (**Employment Inventory Form 15)** for each week:

   a. worked in a job for pay (yes/no)
   b. was the job TWP, competitive, or other
   c. Hollingshead code
   d. number of days worked
   e. number of hours worked
   f. gross income earned
   g. whether the job is new or not

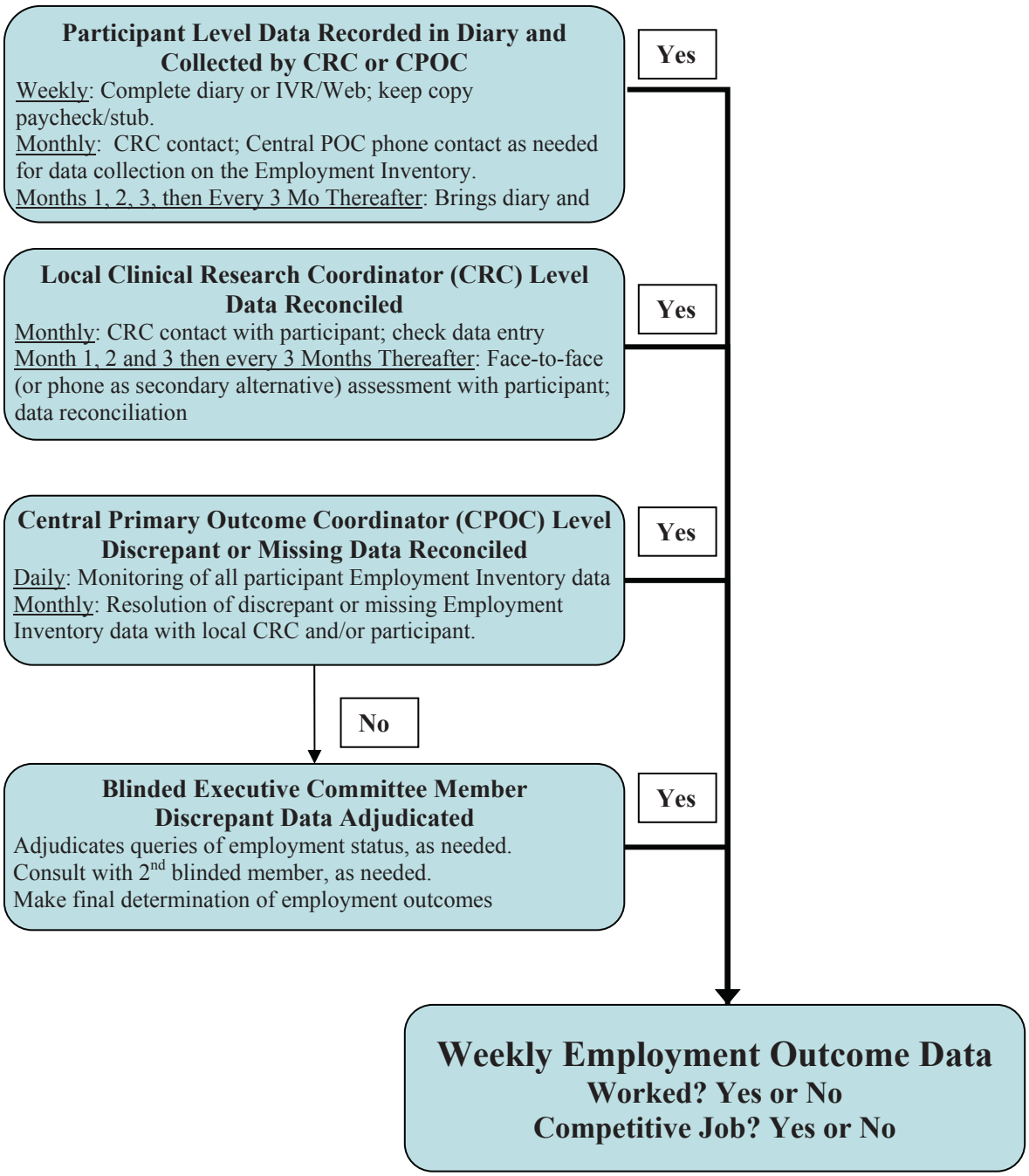
   At each research visit, if discrepancies are found in the information collected during a phone or previous visit, the local site CRC completes an **Employment Reconciliation (Form 16)** to make correction in the Employment Inventory and make sure all data are consistent with the participant's self-report Employment Calendar Diary or IVR/Web and VA medical record notes of the IPS or TWP specialists, e.g., the CRC will make sure that

a TWP set-aside job is not listed as a competitive job. The CRC records the correct information on an Employment reconciliation data form as needed.

Primary outcome collection, verification, validation, and adjudication process

The Employment Calendar Diary is used in a manner that is similar to the Time-Line Follow Back method (TLFB) for the primary outcome collection. This is a well-established assessment method that has been tested and used in obtaining estimates of daily alcohol or drug consumption. The TLFB has been evaluated with clinical and nonclinical populations, and has been shown to have good psychometric characteristics. Using a Employment Calendar Diary at the telephone and face-to-face assessments, the participant will provide retrospective estimates of the employment variables in question and also tertiary outcome data.

*The flow chart below illustrates this verification process***.** This process will be uniformly applied to ensure the maximum level of validation. Although other data points are important, the two key questions for determining the primary outcome are: 1) "Did the participant work in a job?" and 2) "Was the work performed in a competitive job?" for each week of each participant's follow-up period. The majority of the participants' employment record will be straightforward and will not need to be elevated to a higher level; and most discrepant or missing data will be resolved at the level of the local site CRC and the National Primary Outcome Coordinator. However, for a small sample, members of the Executive Committee (blinded to the participant's assignment) will be consulted and have final authority on determining if the week(s) in question are deemed as "worked" in a "competitive job" or not (i.e. Adjudication Process).


Participant Level Data Recorded in Diary and Collected by CRC or CPOC
Weekly: Complete diary or IVR/Web; keep copy paycheck/stub.
Monthly: CRC contact; Central POC phone contact as needed for data collection on the Employment Inventory.
Months 1, 2, 3, then Every 3 Mo Thereafter: Brings diary and
Yes
Local Clinical Research Coordinator (CRC) Level Data Reconciled
Monthly: CRC contact with participant; check data entry
Month 1, 2 and 3 then every 3 Months Thereafter: Face-to-face (or phone as secondary alternative) assessment with participant; data reconciliation
Yes
Central Primary Outcome Coordinator (CPOC) Level Discrepant or Missing Data Reconciled
Daily: Monitoring of all participant Employment Inventory data
Monthly: Resolution of discrepant or missing Employment Inventory data with local CRC and/or participant.
Yes
No
Blinded Executive Committee Member Discrepant Data Adjudicated
Adjudicates queries of employment status, as needed.
Consult with 2nd blinded member, as needed.
Make final determination of employment outcomes
Yes
Weekly Employment Outcome Data
Worked? Yes or No
Competitive Job? Yes or No

Participant Level Assessment: In order to reduce recall bias, the participant will use a diary method (paper or IVR/Web) to record employment activities on a weekly basis. The participant will also be instructed to record any events such as homelessness, legal encounters, weeks of substance misuse, emergency room visits, and inpatient psychiatric hospitalizations in their diary. The participant is instructed to keep a copy of paychecks or paystubs and bring them to the research assessment visits. When the participant is not being seen at these research visits, Clinical Research Coordinator will call the participant on a monthly basis to obtain employment summary information on the Employment Inveotry.

Local Site Clinical Research Coordinator Level Assessment: The participant will meet with (preferably face-to-face, but phone contact is optional) the local site CRC at month 1, 2, 3 and then every 3 months thereafter to complete the assessment of primary and exploratory outcomes (using the Employment Calendar Diary or IVR/Web as reference in a similar manner as a Time Line Follow Back method). Source documents will be used to validate and/or reconcile the employment data, and these include pay stubs or copy of pay checks, CPRS notes from providers and employment specialists, participant diary, and the participant's self-report. The local site CRC will be responsible for ensuring that the source documents and data entry is consistent and that discrepancies are reconciled.

Central Primary Outcome Coordinator Level Assessment: The Central Primary Outcome Coordinator (CPOC) is available to the local site research teams to discuss the collection of the primary outcome and to guide the research team (mainly the CRC) is strategies to minimize missing data and how to evaluate the type of work activity (i.e. whether or not the work is TWP, competitive, or other). Monitoring of primary outcome completeness will be implemented immediately so that the study team can act quickly to address issues at a local level that might hinder the collection of data.

Executive Committee Level Adjudication: A formal adjudication process will be implemented and coordinated by the Central Primary Outcome Coordinator and WH-CSPCC. Two members of the study's executive committee, blinded to the treatment

assignment, will review all queries that cannot be resolved by the central primary outcome coordinator, local site clinical research coordinator, and local site investigator. A query will be reviewed and adjudicated by one of the two trained members of the Executive Committee (depending on availability). However, if needed, both members may consult with each other to make the final determination. The executive committee adjudicator will make a final determination as to whether the participant worked in a competitive job during the week(s) in question.

2. **Self-Report Clinical Assessments:** The participant meets with the CRC every three months (months 3, 6, 9, 12, 15, and 18). At these research assessment visits or by mail, the participant completes the same self-report assessments that were done at baseline, i.e., PTSD Checklist (PCL), Rosenberg Self-Esteem Scale, Sheehan Suicidality Tracking Scale (SSTS), and Posttraumatic Stress Related Functioning Inventory (PRFI). The QOLI is collected at six-month interval research visits (in person or by mail), i.e., baseline and months 6, 12, and 18.

3. **Safety Assessments:** The participant meets (preferably in person, or alternatively by telephone) with the CRC every three months (months 3, 6, 9, 12, 15, and 18) and is assessed for the occurrence of adverse events (Form 17) or serious adverse events (Form 18) (See XII. Study Monitoring and Quality Control Procedures, section G and H).

4. **Inventory of Crisis Events (Form 14):** The participant meets (preferably in person, or alternatively by telephone) with the CRC at months 1, 2 and every three months thereafter (months 3, 6, 9, 12, 15, and 18). At these research assessment visits, the local CRC completes the same inventory that was done at baseline.

5. **Close-out procedures:** It is important that CRCs ensure that all procedures are completed:

    - All outcome data are collected,
    - Form 20 - Participant Status is completed,

- When Participant is exited from the study they are referred to the appropriate treatment service for continued treatment.

The following case report forms have been developed for use during study exit:

Form 28: Supplementary Participant Study Exit Form

Case Report Form 28 was developed to facilitate the collection of certain data variables that include some re-assessment of baseline data (service connection and housing information) and also new variables that were not thus far captured as part of either (a) the baseline data or (b) the current study close-out process. This information is relevant to further understanding the impact of the intervention and facilitators or barriers in the engagement of the intervention or the pursuit of competitive employment. This form does not replace or amend any existing study case report form and should be used in the context of and during the study close-out process, as participants exit the study.

Form 28 is to be completed by the clinical research coordinator (CRC) ***ONCE*** for all active participants during the last assessment/study exit visit.

Form 29: Customer Satisfaction Survey

A Satisfaction Survey (Form 29; enclosed) has been developed to allow for study participants to indicate their level of satisfaction with the CSP#589 (VIP-STAR) in terms of study participation and study interventions, as well as provide their suggestions for future research topics. This form collects qualitative information that reflects the voice of the Veteran who is a participant in a VA research study. Including the Veteran in a survey of satisfaction and suggestions for future research meets an important part of the VA research mission. This ***optional*** form will collect qualitative data that will be analyzed by the Study Chair's site.

Form 29 will be administered ***ONCE*** (during the last assessment/study exit visit) to

any participants who opts to complete it. The CRC should indicate on Form 28 as to whether the participant has agreed to fill out Form 29, in order for the CSP Coordinating Center to track whether the form is to be expected or not (i.e. not list as a missing form for those who opt out).

Note: For participants who have already completed their last assessment/study exit visit, an attempt should still be made to have these forms completed either via chart review and/or study participant contact (conditional on local IRB approval).

IPS Close-out Procedures: This process is designed to allow for minimal disruption in the Veterans' recovery and treatment. As the caseload decreases, the IPS Specialist should focus their full-time efforts on the remaining active study participants.

Guidance can be offered on a case-by-case basis by the National IPS trainers. The IPS specialist should also work with the local site investigator(s) to develop the most appropriate transition plan for each Veteran.

At the end of the 18-month follow-up, the IPS Specialist should take the following steps:

- Keep the participant abreast of the study 18-month timeline and closeout date
- Communicate with other clinical providers so they can be aware and/or can assist with the transition process.
- Clearly communicate with the participant that there will be a 30-day transition period for Veteran to engage in appropriate and available therapeutic services, such as mental health or PTSD treatment team follow-up or usual care vocational rehabilitation services.
- Work with the Veteran over the 30-day transition period to reinforce community, family, and VA support systems.

XII. Study Monitoring and Quality Control Procedures

The Cooperative Studies Program (VA Central Office) establishes overall policies and procedures which are applied to all VA cooperative studies through the Study Chair's office, and the West Haven Cooperative Studies Coordinating Center (WH-CSPCC). The Cooperative Studies Scientific Evaluation Committee (CSSEC) reviews the scientific merit of all new cooperative study proposals. The CSSEC is composed of both VA and non-VA clinical research scientists, most of whom have had experience in managing their own cooperative studies. The organizational and administrative structure of this cooperative study is similar to others in the Cooperative Studies Program and includes the components described below.

A. Monitoring Bodies and CSP Monitoring

The Executive Committee is chaired by the Study Chair and consists of the study Biostatistician, study Project Manager, selected participating investigators, and outside expert consultants. The Executive Committee is concerned with the overall management of the study and is the decision-making body for the operational aspects of the study. The Executive Committee monitors the performance of participating medical centers and quality of data collected, plans the publications, and oversees the publication and presentation of all data from the study. The Executive Committee must grant permission before any study data may be used for presentation or publication. This committee meets by conference call typically on a monthly basis to review the study progress and meets every 12 months to review blinded data (not broken down by treatment group), decide upon changes in the study, determine the fate of hospitals whose performance is substandard, initiate any sub-protocols, and discuss publication of the study results.

The West Haven Cooperative Studies Coordinating Center and the Study Chair administer the trial, oversee its organization, and perform the day-to-day scientific and administrative coordination of the study. These duties include developing the study protocol, operations manual, and case report forms; ensuring the appropriate support for the participating centers; scheduling meetings and conference calls; responding to site queries about the protocol; conducting site visits; publishing newsletters; preparing interim and final progress reports; and archiving study data. Participant accrual and data quality are monitored closely to ensure that the study is progressing satisfactorily.

Local VA or the VA-affiliate IRB (IRB) serves as the oversight body for the protection of human subjects. The study is reviewed and approved by the IRB of record at the initiation and continuing review. Each site's local R&D must also review and approve the local site's involvement in the study.

The CSP Clinical Research Pharmacy Coordinating Center (CSPCRPCC) is responsible for monitoring and reporting the safety of trial participants through the review, assessment, and communication of adverse events and serious adverse events reported by study personnel. The CSPCRPCC's responsibilities occur through ongoing communication with the Study Chairman, Executive Committee, West Haven CSPCC, and CSP Central Office. The reporting activities include the filing of regulatory documents involving adverse events to meet applicable federal regulations and CSP policies. In conjunction with the West Haven CSPCC, the CSPCRPCC prepares reports safety data for various committees including the Data Monitoring Committee (DMC), the IRB, Executive Committee, and the study group.

The Data Monitoring Committee (DMC) provides interim, independent, and unbiased reviews of the study's ongoing progress. The DMC is composed of clinical and statistical members who have expertise in the subject area(s) of the study. These experts are not participants in the trial and have not participated in the planning of the protocol. The Study Chair Study Chair, study Biostatistician, Clinical Research Pharmacist, and the Director of the CSPCC are *ex officio* (liaison, non-voting) members of the DMC. The DMC meets at least annually to review the progress of the study and monitor participant intake, outcomes, adverse events, serious adverse events, and other issues related to participant safety. At its meetings, the DMC reviews the randomization rates and assess the difference between the actual and the projected rates, as well as the impact of these assessments on overall trial size. If the study enrollment is inadequate, the reasons for exclusion may be scrutinized and actions may be suggested. The DMC's primary responsibilities are to review safety and the progress of the study and to decide whether or not the study should continue. To help them make their assessment, the Study Chair and Study Biostatistician will provide the DMC with appropriate monitoring data before each meeting. The DMC makes recommendations to the Director, VA CSR&D about whether the study should continue or be stopped.

A member of the Human Rights Committee (HRC) at the Coordinating Center conducts a site visit to at least one participating center during the course of the study to determine if participants' rights and safety are being properly protected. The HRC member may interview study participants during the site visit.

The Local Site Investigator (LSI) at each participating VA medical center is responsible administratively and scientifically for the conduct of the study at the center. The LSI is expected to attend all annual Study Group meetings, as well as to hire and supervise personnel. By agreeing to participate in the study, the medical center Director delegates responsibility for global monitoring of the ongoing study to the DMC, the CSPCC Human Rights Committee, the IRB of record, and CSSEC. However, the Research and Development Committee (R&D) of the medical center may require the participating investigator to submit annual reports concerning the status of the study at the medical center for local monitoring purposes.

The Study Group consists of the Study Chair, the CSP staff (Biostatistician, Project Manager, Clinical Research Pharmacist, and others), all participating local site investigators, and clinical research coordinators (CRCs). The Study Chair leads the Study Group, which typically meets monthly by teleconference and once per year in face-to-face meeting to discuss the progress of the study, any problems that the investigators have encountered, and any suggestions for improving the study. No endpoint data are presented to this group.

The Site Monitoring, Auditing and Resource Team (SMART), located at the CSP Clinical Research Pharmacy Coordinating Center (CSPCRPCC) in Albuquerque will conduct monitoring visits at all sites. A SMART member visits participating sites shortly after enrollment is initiated to monitor investigator regulatory compliance, protocol adherence, and overall research practices. In addition to the regularly scheduled GCP review visits, an independent comprehensive GCP site audit may be conducted at any time at the request of CSP study management.

B. GCP Monitoring Visits

A member of the Site Monitoring And Resource Team (SMART) conducts at least one site visit to each site during the enrollment period for monitoring GCP and study protocol adherence (see Section XIV). The purpose of these visits is to assess and promote compliance with GCP requirements. Additional monitoring visits may be conducted as deemed necessary by study leadership or SMART as described below. The investigator is contacted prior to the visit to arrange a mutually agreeable time for the visit. The SMART reviewer is on site for approximately two days to review study records and discuss the conduct of the trial. The SMART reviewer examines participant study files, including source documents held electronically, in clinic files and participants' official medical records and reviews regulatory and essential documents, such as IRB correspondence. Areas of particular concern are informed consent issues, protocol adherence, safety monitoring, IRB reviews and approvals, regulatory documents, participant records, site operations, and investigator involvement. The Executive Committee will consider recommending additional SMART site visits for any participating centers with repeated protocol violations to evaluate a sites' need for additional training to remedy compliance concerns. Additional site-specific monitoring may be conducted if triggered by study performance metrics. In addition to monitoring visits, for-cause audits may be conducted at any time if requested by the study leadership or CSP Central Office. For-cause audits can be announced or unannounced. In addition to SMART visits, WH-CSPCC, the Executive Committee, and DMC will monitor protocol adherence centrally through periodic reports, data queries and coordinator/PI conference calls.

C. Monitoring Participant Intake and Probation or Termination of Participating Sites

The Study's Executive Committee, Study Chair and the Study Biostatisticians will monitor the intake rate and operational aspects of the study. The Executive Committee may take action leading to the discontinuation of enrollment at a center with the concurrence of the Director, VA CSR&D. Participating medical centers may continue in the study only if adequate participant intake is maintained.

If recruitment is not proceeding at an appropriate rate, the Study Chair and the Study Biostatisticians scrutinize the reasons for participant exclusions and other barriers to recruitment.

Based on this information, the Executive Committee may choose, with the approval of the DMC and the Director, VA CSR&D, to drop centers or add additional centers, to make minor modifications to the inclusion/exclusion criteria, or with the concurrence of the DMC, and the Director CSR&D to extend the recruitment period in some or all centers and/or to extend the total length of the study.

Medical centers will only be allowed to continue in the study if adequate participant intake is maintained. Although 12 sites are initially selected and launched, there is a high likely that at least 3 sites will be high enrollers and will be augmented by additional staff to sustain a higher enrollment. Should all study sites recruit equally, each site would randomize 45 participants within 12 months (~4 per month). The minimum number of randomized participants to maintain funding for 1FTE CRC and 1FTE IPS specialist is 40 participants (90%). IPS staffing ratio is calculated at 25 participants assigned to IPS to every 1 IPS specialist. Because there is usually a ramp-up in recruitment early on, participating sites that do not enroll at least three participants during their first three months, or nine participants within six months, will be considered for probation or reduction in funding. If a medical center is placed on probation, the Study Chair and Study Biostatistician confer with the site personnel and, if necessary, visit the site to help improve the rate of recruitment. If there is no improvement in accrual after the probation period, the site may be subject to reduced funding or possible termination as a study site. The Executive Committee only takes actions leading to discontinuation of a center with the concurrence of the Director, VA CSR&D. If a center is terminated from the trial, resources are reallocated to other centers or used to start up a backup site.

D. Monitoring Medical Center Performance

Strict adherence to the protocol is expected of every participating center and monitored by the DMC, the Executive Committee and the Study Group. Data quality and the completeness of data retrieval are closely monitored on an ongoing basis by the WH-CSPCC. The Study Biostatistician presents interim monitoring reports, overall and by site, to the Executive Committee and DMC that include the following types of information: recruitment of participants, characteristics of the population, completeness of data retrieval, and data quality. If a site is identified as an outlier in terms of data quality, a site conference call or site visit is

initiated to assess the reasons that problems are occurring and how they can be corrected. If the problems continue, the site may be placed on probation or terminated from the study if the problems cannot be corrected.

E. Monitoring Participant Safety

The local site investigator is responsible for following adverse event reporting requirements as outlined below in the protocol. These responsibilities include: 1) reviewing the accuracy and completeness of all adverse events reported, 2) compliance with IRB policies for reporting adverse events and/or serious adverse events, and 3) closely monitoring research participants at each follow-up visit for any new Adverse Events (AEs) or Serious Adverse Events (SAEs). Study participants are monitored at each research visit for AEs and SAEs. All AEs and SAEs are recorded on the appropriate event form(s). Active monitoring of AEs and SAEs begin as soon as the study participant is randomized and to 30 days post-study follow-up.

F. Adverse Event Definition and Monitoring

All adverse events that are related to the PTSD, the occupation, or the study intervention or procedures are recorded at each research assessment visit (description, severity, relationship to study intervention, date onset, date resolution). Adverse Events (AEs) are collected using the CSP Global SOP 3.6 definitions. An adverse event is "any untoward physical or psychological occurrence in a human subject participating in research. An AE can be any unfavorable and unintended event, including an abnormal laboratory finding, symptom, or disease associated with the research or the use of a medical investigational test article. An AE does not necessarily have to have a causal relationship with the research. **All adverse events related to PTSD, an occupation will be collected, or study intervention or procedures will also be collected.** Relatedness involves an assessment of the degree of causality (attributability) between the PTSD, occupation, and/or study intervention and the adverse event. Site investigators are asked to provide an assessment of relatedness or attribution to PTSD, occupation, and/or the study intervention or procedures. All adverse events with a reasonable causal relationship to PTSD, occupation, and/or the study intervention should be considered respectively "related". A definite relationship does not need to be established.

G. Serious Adverse Event Definition and Reporting

Serious Adverse Events (SAEs) are a subset of adverse events and are those defined by the CSP Global SOP 3.6., as an event that results in any of the following outcomes:

a. Death;
b. A life-threatening adverse event;
c. Inpatient hospitalization or prolongation of existing hospitalization;
d. A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
e. A congenital anomaly/birth defect.
f. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based on appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

All serious adverse events are collected, including those related to and not related to the study intervention or procedure. Any suspected adverse events that are both serious and unexpected will be reported to the Sponsor and CSP Central Office. All SAEs require prompt notification by the local research team to the CSP CSPCC within three (3) working days of the site investigator being made aware of the event. Prompt notification of the SAE should be made by the local research team by faxing the SAE form to the CSPCC. The CSPCC arranges to have all faxes sent automatically to the CSPCRPCC and Study Chair. The CSPCRPCC will be responsible for evaluating all serious adverse events for participant safety concerns.

All SAEs will be followed up at each study visit until the event is resolved or no further progress is expected.

Serious adverse events that are **unexpected/unanticipated and possibly related/related to the study intervention** are expeditiously reported to the CSPCRPCC Director, CSPCC, IRB, and DMC.

The Clinical Research Pharmacist and Study Biostatistician generate tabulations of adverse events and present a summary of all PTSD-related, occupation-related, and study-related AEs, all

unanticipated adverse events, and all SAEs to the DMC on a schedule set by the DMC. The DMC also determines when they should be unblinded to treatment assignment in reviewing adverse event data. The Study Biostatisticians provide the appropriate data to the DMC at specified intervals for this purpose. Serious adverse events are reported on a regular basis to the DMC for their review. Unexpected/unanticipated serious adverse events are reported to the DMC as soon as they become known based upon the consensus of the Study Chair, the Study Biostatisticians, the Director of the West Haven CSPCC, and the Study Pharmacist.

H. Monitoring of Suicidal Behaviors

Subjects are evaluated at baseline and follow-up visits by the clinical research coordinator in collaboration with the LSI using an established rating form for suicidal thoughts, behaviors and intent (SSTS). The LSI explores all positive endorsements with the subject and judges the clinical state and risk of suicide. At baseline, the LSI and participant agree on a suicide prevention plan, such as 24 hr. access to the VAMC emergency room and one of the investigators (paging) in the event of suicidal thoughts, plans or behaviors, knowing the VA suicide prevention crisis and VA suicide prevention coordinators' phone numbers (cards and flyers are given to subjects), identifying a significant other who can assist during a crisis, removal of all lethal weapons from the immediate access of the participant (if applicable), and participant's agreement to abstain from drugs and alcohol. The suicide prevention plan should be complimentary or consistent with the participant's PTSD treatment provider(s) suicide prevention plan. At follow-up, if positive endorsements are made on the SSTS, the investigator reviews and modifies the suicide prevention plan with the participant. Should the investigator deem the participant to be at heightened risk of suicide, the participant is treated in the most clinically appropriate setting (outpatient, residential or inpatient).

I. Participant Assessments and Compensation

Participants meet with their Clinical Research Coordinator at regular intervals either face-to-face or through telephone calls. While it is stressed that scheduled face-to-face visits should remain face-to-face, and scheduled telephone visits should remain telephone visits, circumstances can arise when flexibility is required. The needs of participants should be taken into consideration. In these cases, the Clinical Research Coordinator is allowed to travel to a location in the community

in order to make more convenient contact with the participant for assessments. They may also complete face-to-face assessments via the telephone (mailing the self-assessments prior to the telephone call, if possible) and telephone assessments can be done face-to-face. However, the payment schedule for each assessment period will continue as stated below.

To contend with the challenge of getting participants to return for follow-up assessments, we plan to provide compensation to help overcome any transportation cost barriers or loss of wage due to missed work. All participants are paid per follow-up visit. In order to avoid reinforcing dropout or compliance with financial incentives, all participants who attend these follow-up visits receive payment, regardless of whether they continued in the treatment or were an early exit for any reason. This modest payment adds incentive for participants to follow-up and secondarily covers the transportation cost in rural areas. The amounts are not coercive given the relatively modest payment and the fact that there are minimal risks involved in the assessments by means of interview and self-report (i.e. no invasive procedures, physical demands, or medications interventions are required in order to receive payment).

The CSP #589 protocol payment schedule is set up such that participants receive $50.00 for the baseline study assessment visit, $40.00 for follow-up visits that occur at month 1, 2, 3 and every 3 months thereafter (months 6, 9, 12, 15 and 18), and $5 for the telephone calls made during the months in between the face-to-face visits (at month 4, 5, 7, 8, 10, 11, 13, 14, 16, and 17). (*Note: The maximum amount that a participant can currently be paid for participating in this study is $420.)*

Non-Adherence to Schedule

Non-adherence to the follow-up schedule **due to a participant's unwillingness or inability to come in for a visit or complete a visit in-person or by telephone call when asked** does not need to be reported to the WH-CSPCC as a protocol deviation. In this case, a Note-To-File should be made; Non-adherence to the follow-up schedule **due to a study team member's lapse in diligence in scheduling or seeing/calling a participant** needs to be reported to the WH-CSPCC as a protocol deviation.

Participant Retention:

A goal of CSP #589 is to complete, 100% of follow-up assessment of all randomized study participants for primary outcome data, even if this can only be achieved through looking up employment information in VA clinical and/or national databases. **Consequently, participant retention is paramount to the success of the VIP-STAR trial.**

CSP #589 Study Leadership would like to emphasize that that non-compliance to the protocol visit schedule is **not** a reason for initiating a participant's withdrawal of consent. Some study participants may no longer be able or willing to attend the study visits and/or telephone appointments and/or fill out all study questionnaires, yet would not object to remaining in the study for the continuation of collection of study-related data. In this case, the participant should not be withdrawn and collection of study-related data (through both follow-up with the participant (to the extent possible) and/or through VA clinical and/or national databases) should not cease. The participant's change in study status (i.e., indication that he/she no longer wants to attend VIP-STAR visits and/or complete questionnaires but still wishes to remain in the study) should be recorded in the progress notes.

J. CAPS Rater Reliability, Training, and Monitoring

Our procedures for training the local CRC or CAPS-assessor to conduct the CAPS include specific guidelines for establishing and preserving inter-rater reliability. The Study Chair, Dr. Davis, has received training on the CAPS from the authors of the CAPS, Dudley Blake, Ph.D. and Frank Weathers, Ph.D. She has subsequently trained other investigators and clinical research coordinators. Prior to study initiation, training for the CAPS is conducted using the training materials provided on the VA National Center for PTSD website.

K. IPS Invention Fidelity Monitoring

Each site is monitored by an IPS fidelity monitor on at least a biannual basis, with the first fidelity monitoring visit occurring within 3 months of the first participant randomization at each site. IPS fidelity monitoring is an important component of this protocol. The study will budget for one FTE trained IPS fidelity monitor based at the Study Chair's office. An IPS fidelity monitor will spend two days at a site during each monitoring visit. The fidelity monitor observes the IPS specialist in the field during job development and interaction with participants, interviews participants, interviews clinical treatment providers, interviews leadership, and reviews the VA electronic medical record. The IPS fidelity monitor evaluates the site using the

Supported Employment Fidelity Scale, the IPS-15 (included in Appendix E), and the new version of the Supported Employment Fidelity Scale, the IPS-25. On the IPS-15 scale, 66–75 is regarded as good IPS implementation, 56–65 as fair implementation, and ≤55 as "not supported employment." The IPS intervention needs to adhere to a rating ≥66 of a possible 75 points on the Supported Employment Fidelity Scale. The IPS fidelity monitor provides feedback on the fidelity rating to the local site investigator and national IPS supervisor(s) to aid in working with the sites' IPS specialists to ensure high quality of IPS services. The IPS fidelity monitor also evaluates the TWP treatment arm using the same methods to ensure that the TWP treatment arm is rated ≤55 on the Supported Employment Fidelity Scale (not supported employment). The IPS fidelity monitor evaluates 1-2 sites per month. Cumulative reports of fidelity ratings and written comments are forwarded to the Study Chair and Executive Committee on a quarterly basis.

The Supported Employment Fidelity Scale is comprehensive, detailed, and research-based. Although the methodological details varied, 10 studies assessed the correlation between program fidelity and concurrent site-level employment rates for evaluation of the predictive validity of the 15-item IPS Fidelity Scale.[9192] Six of the 10 studies reported statistically significant measures of association between fidelity and employment outcome, and two others had results approaching statistical significance. More recently, the relationship between IPS fidelity and employment outcome using the 25-item IPS fidelity scale[93] has been shown to have predictive validity is similar for the original and revised scales. The research has found that the scale as a whole is a dependable tool for guiding effective IPS practice.[94]

XIII. Data Management and Quality Control

A. Data Collection Methods

The WH-CSPCC will collect and manage the trial data for CSP #589 using Teleform® processing system and eProHealth® IVR-IWR system (IVR/Web).

In order to ensure complete primary outcome ascertainment while minimizing the potential for participant recall bias, the participants will be contacted by phone by the local Clinical Research Coordinator on a monthly basis during the months when participants are not being seen face-to-

face for research assessment visits. The deployment of a national central primary outcome coordinator will ensure completeness of the monthly primary outcome assessment.

B. Teleform System

The paper CRF will be readable by Teleform's optical character recognition software. Electronic scanner-readable e-PDF versions of the data collection forms are sent to the sites. These e-PDF versions may be completed on a personal computer at the study site. If a form is completed on a personal computer or terminal, a completed copy of the form must be printed. The printed copy is faxed to the WH-CSPCC fax data server. The printed copy kept at the site is filed in the patient study folder. Once the forms are received at WH-CSPCC, they are processed through the Teleform form reader and verifier software where a research assistant at the WH-CSPCC reviews the forms for consistency and completeness. Forms that have major deficiencies or are not accepted by the reader are reconciled with the site personnel by telephone calls or e-mails, usually by requesting a resubmission of the completed form with corrections annotated. CRF processed by the Teleform Verifier are exported as an image file folder and the extracted data items are exported to a comma-delimited file in a data capture folder, both on a secure WH-CSPCC file server. All changes or corrections to data entered on paper CRF forms are dated and initialed by site personnel, on the original CRF and the associated data edit sheet, if applicable.

C. eProHealth® IVR-IWR System

The research participants will have the option to track their outcomes via an automated self-reporting Interactive Voice Recognition/Web-based (IVR/Web) system as described below.
The research participants will have the option to track their outcomes via an automated self-reporting Interactive Voice Recognition/Web-based (IVR/Web) system as described below.

The ePROHealth Platform, developed and owned by Interactive Performance Technologies, LLC (IPT) will be used. ePROHealth is an existing, proven, highly-scalable technology architecture for clinician-facing and patient-facing tools for implementing and sustaining electronic patient self-reporting, easily and efficiently. The ePROHealth Platform enables both web-enabled and voice communication channels in a single integrated application architecture and will be used by study participants to self-report the study's primary outcome data on the telephone or on the web.

This platform has already been used successfully by VA clinicians and patients. It has been tested in rigorous trials among patients in urban and rural areas. Applications based on the Platform are extensible to a wide range of research and patient care applications where patient engagement and especially regular self-reporting, are prerequisites for success, including applications in care planning and coordination, quality improvement, patient safety, and accreditation.

To enroll in this system each newly enrolled and randomized participant, in addition to signing the study Informed Consent Form, will also sign an Informed Consent Form Addendum for the use of the IVR/Web system, and VA Form 3203, Consent for Use of Picture and/or Voice. Local Site personnel, the Central Primary Outcome Coordinator and the West Haven Coordinating center personnel will enroll participants opting to use the automated self-reporting system, and maintain and support the system throughout the participants' use of the system throughout the duration of the study. This platform will provide an accessible, convenient, easy to use, and reliable system for both study personnel and study participants to use that will help ensure timely, accurate collection of the critical data required for the successful completion of the study.
Platform Roles

The platform allows for two user roles for study personnel:

a. *Central Study User (CSU) Role With Cross-Site/All-Site Access Permission*: The Central Primary Outcome Coordinator at Study Chair's office and CSPCC West Haven study team members will be designated as Central Study Users (CSUs). CSUs will function as study monitors and managers and will be given access and views of all study data from all sites.
b. *Site-Only User (SOU) Role:* All other CSP Study #589 study site personnel users will be assigned to be Site Only Users (SOUs). SOUs are responsible for managing the study at a single site location, including the responsibility for recruiting consenting, and managing subject participants in the study. SOUs will only (i) be able to enroll study participants recruited at their local site; (ii) have access only to participants recruited and enrolled at their local site and their data.

Only study personnel (at local sites, Chair's office and Cooperative Studies Program (CSP) Coordinating Center) who have received and are up to date with all required and appropriate VHA Privacy Policy training and VA Privacy and Information Security and Rules of Behavior training will be permitted to use the IVR/Web system. IVR/Web-specific training will be provided to ensure familiarity and ability to work through the system.

Under this system, all study participants who enroll in (opt to use) the automated self-reporting system have already been randomized to one of two study intervention arms (IPS or TWP) and the randomized arm of the subject is known prior to enrollment in this platform. At enrollment, each participant will be permanently assigned to use the IPS or the TWP version of the question set for the duration of their participation in the study.

Since the study is on-going, this automated self-report option will be offered as an option to both the newly enrolled and randomized participants. Any participants randomized prior to deployment of the platform, would be given the option of enrolling into this system and have their 'prior-to-enrollment' pertinent data transferred to a secure, common storage place. Participants randomized prior to deployment of this system will sign an Informed Consent Form

Addendum for the Use of the IVR/Web system, and fill out VA Form 3203, Consent for Use of Picture and/or Voice to activate their enrollment in this system.

A platform list will be constructed using the following variables:

i. Participant IVR/Web ID
ii. Participant First and Last name
iii. Randomization assignment to IPS or TWP arm
iv. Participant contact phone number
v. Participant email address
vi. Participant Study Status

The platform participant list provides direct access for CSUs and SOUs to all data pertaining to a single selected participant. Using Participant List filters, the CSU or SOU can search for and select a single participant for the purpose of accessing and viewing all data pertaining to the selected participant.

In the platform's Main Menu, the CSU or SOU can search for a participant using one or more filter fields provided in the List. Once a participant is found, the user can press a "select participant"

link in the Select/Lock column to open a Participant-Specific Forms menu with the following form/view options listed:

i. Participant Enrollment Form
ii. Event Scheduler
iii. Schedule Snapshot
iv. Detailed Participant-Reported Data
v. Cumulative Study Staff Notes on the Participant including messages from participants
vi. Event Log

vii. Event History

The system allows for participants to use both phone and web for self-reporting, thus making primary outcome self-reporting easier and more convenient for CSP Study #589 participants, potentially enhancing data completeness for the remainder of the study.

Data Flow and Data Access

The system has the capability to allow local (SOUs) and central (CSU) research staff to see 'missing data' on the primary outcome (e.g. via the number of times a participant call was not completed or incomplete web-based data collection). Centralized users (CSUs) will be able to download data and/or run reports, in real time.

The system has been designed and will be implemented and executed in compliance with all VA IT regulations and requirements. It will be able to integrate full telephony and interactive voice response

(IVR) functional capabilities. In addition, it will have the capability to interface into the VA Mobile Framework (VAMF) and will reside behind the VA firewall.

Electronic data records will be stored on servers that will be residing behind the VA firewall. Data collected on this system will be downloaded using technology and software that is VA IT Security-compliant (FIPS 140-2 validated encryption methods) on the West Haven Cooperative Studies Program Coordinating Center (CSPCC) servers for use in data and report generation. In addition, the system will generate individualized site reports to assist in the local coordinators efforts to complete follow-up/clarify data entered by the participant through use of the system. At the coordinating center, only authorized study personnel (on an as-needed basis) will be given access to the data derived from the system.

Data from this system will be merged with data received through other study data collection methods already in place, and the combined database will reside on WH-CSPCC servers; this database will be securely stored and backed-up on a daily basis and will be used to (a) generate queries related to the study's primary outcome; (b) reports for the Central Study Coordinator and local site coordinators; and, ultimately, (c) employment data reports.

Data collected through this system is property of VACSP and will remain on VACSPCC servers for 5 years after the study's primary manuscript has been published. These data will be archived after this period of time according to VACSPCC policy.

Local Site Coordinator access to the system and its data will be terminated following study close-out. However, the National Study Coordinator and the West Haven CSPCC study team will continue to have access to this data past close-out, in order to facilitate additional reports and analyses.

In accordance with VA policy, any incidents (e.g. loss of or unauthorized access to the data, theft of data, non-compliance with security controls) related to the storage, management and security of this data will be reported to either the local site ISO or the CSP Coordinating Center,.

Participant enrollment in the platform

After deployment of the platform, participants randomized to CSP#589 will be able to select use of this system (IVR and/or Web) to report the primary outcome. Participants may choose to use either or both interfaces-phone or web. Should participants also continue using current paper forms, the system will allow study personnel the ability to enter paper form data into the electronic system. Participants already randomized and in follow-up would be provided with the option of selecting to use the platform for the remainder of their follow-up.

Participants enrolled in the system will receive an automated reminder e-mail at a scheduled time (and date) they prefer. Additional reminders will be sent over a span of 3 days. The follow up schedule is configurable and adaptable to the participant's requests and choices. The reminder e-mail is outbound only i.e. the system does not accept reply e-mails from the participant; the body of the email (see sample below) will include a clear indication "Do Not Reply – Not Monitored".

This is a reminder that your VIP-STAR report is scheduled for completion today.

Your Study ID #: XXXXX

Scheduled Reporting Time: yyyy-mm-dd hh:mm:ss

To do your report now, click on this LINK to go directly to the VIP-STAR login page.

Remember, you can also report by phone anytime you want. Sometimes calling in is more convenient and saves you time.

To report by phone, call in to the following toll-free number: 1-XXX-XXX-XXX

We look forward to receiving your report – your reports help us help you!

Need Help? Do You Have Questions?

If You Have Questions or Need Help Using the automated system, please call the staff below:

[Name of Site Coordinator]

VIP-STAR Clinical Research Coordinator

at the following VA [Site Name] VAMC phone number: XXX-XXX-XXX

Always Remember: The VIP-STAR automated support system is NOT a substitute for seeking medical care from your regular sources. If you feel you need immediate medical attention, or this is emergency, contact your regular doctor or your local emergency services.

Do Not Reply to this email message-This email address is Not Monitored.

Appropriate language is included in the Informed Consent Form (ICF) and HIPAA document; this will allow for participants randomized after deployment of the platform to utilize the IVR

and/or IWR components of the system. For participants, who, at the time of system deployment, are randomized to the trial and who decide to use this platform for the remainder of their participation in the study, an addendum to their existing ICF and HIPAA documents indicating this decision must be signed.

Participants who consent to the use of the platform could, at any given time during their participation in the trial, revoke their consent and HIPAA authorization and opt out of the system.

D. Central Primary Outcome Coordinator

The Central Primary Outcome Coordinator will be provided with information on the completeness of the Employment Inventory. As needed, he/she will contact the local CRC regarding participants who have incomplete Employment Inventories. Employment information collected by the Central Primary Outcome Coordinator is submitted through a paper Teleform.

E. Data Quality Control

The progress of data collection is monitored and the status of forms expected and received for each participant is reported to the WH-CSPCC research coordinators for review and follow-up with study sites or the Chairs' offices as needed. Interim progress reports of cumulative errors and overall data quality and completeness is sent to the investigators, the Executive Committee, and the DMC. Unresolved data queries are included in the data file that is analyzed. Every effort is made to resolve all outstanding queries prior to a DMC report.

Data quality is monitored on an ongoing basis by the WH-CSPCC. The Study Biostatistician, Tassos Kyriakides, Ph.D., presents interim monitoring reports to the Executive Committee at least monthly and to the DMC quarterly or as specified in the current standard reporting guidelines or as decided by the DMC at its first meeting. Interim reports include recruitment of participants, characteristics of the population, completeness of data retrieval, and data quality. Prototype tables are given in Appendix D and serve as an example of the statistical reports that are generated for study monitoring by the Executive Committee and the DMC.

Most of the operational aspects of the study are managed using the study SharePoint web site. On the study web site, participating medical centers are able to access the Study Protocol, Operations Manual, CRFs, and other study related documentation, as well as meeting announcements, conference call notices and study newsletters.

F. Quality Control of the Process

After the study is approved, the Study Chairperson, the WH-CSPCC and the CSPCRPCC will prepare an Operations Manual that is provided to the investigators and the site study coordinators as a guide to the operation and management of the study as well as a technical reference manual. A training session is held for all study personnel in order to: (1) assure uniformity in participant management and data collection procedures, and (2) train the personnel in study procedures and criteria. Study procedures are reinforced by the use of regular conference calls, particularly in the first few months of the study and by the periodic distribution of a study newsletter. All study personnel will attend annual meetings during the enrollment period when study procedures again are discussed in detail. The Study Chair's Office and the WH-CSPCC study personnel are available to clarify study procedures by telephone, fax and e-mail.

If the Executive Committee determines that a study procedure must be changed, the participating sites are informed by conference call and/or newsletter and an updated section of the Operations Manual pertinent to the changed procedure are provided to all sites. The trial is conducted in compliance with Good Clinical Practices (see Section XIV).

G. Data Security

CSP is committed to maintaining data security and patient privacy. CSP Center Directors are responsible for ensuring that all CSP Data Security Policies are enforced within their Centers. All study data collected are handled, maintained and stored according to CSP standard practices and policies. This includes:

1. Protected Health Information (PHI) as defined by HIPAA is not used for any purpose that is not related to the activities of this study.

2. Except for the informed consent, HIPAA, and the participant contact information form (Form 00), case report forms are identified only by a patient identification number and date of report.
    a. Patient identification numbers are not derived from or related to information about an individual.
    b. All electronic PHI are stored on secure servers and may not be moved to a PC or other external device.
    c. Paper CRFs, if any, are stored in locked file cabinets and rooms.
3. Highly confidential protected health information (HCPHI: names, Social Security Number, address and phone numbers) collected by the study are defined in the informed consent or privacy authorization document, and are stored in the central study database separate from other study data (except for the IVR/Web system as described above).
4. When necessary, PHI may be transported between secure servers. PHI must be encrypted and password protected while being transferred using a FIPS 140-2 certified program to a removable storage device. Hard-copy printouts, data tapes, encrypted CDs and other removable media should either be destroyed after transfer is complete, given to the Data Security Administrator to be secured in a secure, fireproof safe, or erased using a triple pass Department of Defense specification approved data erasure software. A traceable mail system (e.g., UPS), must be used for the physical data transfers.
5. Data from studies are utilized at WH-CSPCC and are not removed from the Center without written authorization from the WH-CSPCC Director.
6. PHI may only be sent via MS Outlook or Exchange if the message is secured utilizing encryption and VA authorized security protocol and with the approval of the Center Director.
7. Documents sent for medical evaluation purposes, such as endpoint adjudication, are sent via a traceable mail system (e.g., UPS). Personal information is redacted by the participating VAMC or by WH-CSPCC if not determined to be necessary for completing the evaluation.
8. Only VA-owned equipment or equipment configured to VA security standards is permitted to connect to the VA network and CSP servers in accordance with VA Directive 6504.

9. Training, reminders and signed data security statements are used to ensure CSP personnel understand VA policies.
10. Sharing of CSP study data outside of CSP requires the approval of the Director, CSR&D and signed data use agreements.

Consent forms and completed Teleform data collection forms are sent via secure fax server located in the secure West Haven VA server room. All hard copy data sent to WH-CSPCC are secured in locked file cabinets at the WH-CSPCC.

Backup copies of the database are transferred and stored across secure connections according to VA regulations and CSP global operating procedures. Periodic off-site back-ups are made as part of a comprehensive disaster recovery plan in compliance with current VA policy. As the policy changes, the level of security in this study meets or exceeds whatever the current policies are over the life of the study.

XIV. Good Clinical Practices

A. Role of Good Clinical Practices

This trial is conducted in compliance with the Good Clinical Practice (GCP) regulations. All investigators and clinical research coordinators will be trained in Good Clinical Practices and the Protection of Human Subjects in Research. The Site Monitoring, Auditing and Resource Team (SMART) is responsible for assessing and promoting compliance with Good Clinical Practices at participating sites throughout the trial. An overview of GCP is provided at study start-up by the CSP SMART team. During the start-up phase, SMART develops study specific GCP guidance and tools for the sites, and provides training in the use of these materials and in the principles of GCP during site visits. Monitoring of sites participating in the trial is executed according to the VA Cooperative Studies Program Guidelines.

B. Summary of Monitoring and Auditing Plans

- Monitoring Visits
    1) Initiation visits at each site soon after study start-up.

2) Additional monitoring visits may be conducted as deemed necessary by study leadership or SMART.

- Audits
  1) Routine audits – independent site visits to one or more sites per year during the first three years of the trial (site selection as determined by SMART).
  2) For-Cause audits – an independent audit of any participating site as requested by study leadership or CSP Central Office. For-cause audits may be announced or unannounced.

XV. Biostatistical Considerations

A. Hypothesized event rate and treatment effect

Investigations of the efficacy of IPS have mostly been studied in the severely mentally ill (SMI) population, as demonstrated in the forest plot of SMI population studies in Figure 1 (see Section III – Importance to the VA). With respect to investigations in the PTSD population, a 2008 analysis of VA administrative data (see Resnick, S.G., 2008 in Table 5 below) demonstrated the limited ability to obtain competitive employment at discharge amongst Veterans with PTSD who participated in the conventional VA vocational rehabilitation program (VRP). One recent single-site pilot clinical trial in a group of unemployed Veterans with PTSD found a superior effect of IPS compared to VRP (Davis, L.L., 2012) in terms of percent of those achieving competitive employment by 12 months.

Table 5. Studies of TWP and IPS in Veterans with PTSD

Primary Author, Pub. Date	Years of Study Entry	Population Description	Sample Size, N	Endpoint	Results	
					Standard VA VRP	Supported Employment Program
Resnick, S.G., 2008	Administrative Data Collection from FY 2006 to the first half of FY 2007.	Veterans with PTSD who: • Served in the post-Vietnam era; • Completed episodes of care with the VA Compensated Work Therapy Program.	925	% with Competitive Employment at Discharge	30%	N/A
Davis, L.L., 2012	Randomization into clinical trial occurred from 2006 to 2010.	Veterans with PTSD at the Tuscaloosa VA Medical Center who: • Were age 19 to 60 • Currently unemployed and interested in competitive employment • Did not have SMI diagnosis	85 (IPS: 42, VRP: 43)	% Gained Competitive Employment by 12 Months	28%	76%

The primary outcome, ability to become a "steady worker", is not directly comparable to previous clinical trials in the SMI population and the PTSD pilot study. However, amongst all occupational outcomes studied in the pilot study, ability to become a "steady worker" is thought to be most clinically meaningful in that, those participants who are able to obtain and hold a steady competitive job benefit the most in terms of gaining wages and may be able to do so in large part due to better control over PTSD symptoms and other aspects of their life. In the pilot

study, 40 % of participants in the supported employment arm were able to be employed 50% of the 12-month follow-up time versus 16% in the control arm.

Table 6 below shows power calculations under different scenarios for the primary outcome: Assumptions used in sample size estimation

- Participant Recruitment: 1 year
- Participant Follow-up (maximum): 18 months
- Attrition/Loss to follow-up (for primary outcome assessment): 13%* (both groups)
- alpha-level = 0.05
- Power = 90%

* The attrition/loss to follow-up rate is assumed to be lower than that detected in a previous study[1] of 16% since, in addition to the scheduled protocol visits, a system of central primary outcome ascertainment in conjunction with different technology tools, would minimize the loss of primary outcome data.

Table 6. CSP #589 Sample Size Calculation

IPS Arm Rate of "Steady Worker"	TWP (Control) Arm Rate of "Steady Worker"		
	10%	**15%**	**20%**
25.0%	321	779	3,309
27.5%	251	**540**	1,542
30.0%	202	383	906
32.5%	167	295	605
35.0%	143	235	436

Adhering to the principle of intention to treat, the primary and all secondary analyses will include all randomized participants, i.e., irrespective of employment status or early exit from the study.

B. Power and Sample Size Calculations

Power for the Primary Hypothesis:

The primary hypothesis is that compared to those participants who are treated with TWP, those participants treated with IPS are more likely to become a steady worker, i.e., hold competitive employment for at least 50% of the 18-month follow-up period.

A sample size of 540 will have 90% power to detect a 12.5% absolute difference in the percent of participants achieving competitive employment between arms (27.5% in the SE arm vs. 15% in the TWP arm; Odds Ratio = 2.15). This difference in event rates is very conservative compared to what has already been detected and reported in the Study Chair's pilot study.

Power for the Secondary Hypotheses:

To provide control for multiple treatment comparisons, a Type I error of 0.0125 (two-sided) was used for the power calculations for the secondary outcomes. The Bonferroni adjustment is used for power estimates of the secondary outcomes for conservatism. In the analysis, the sequentially rejective procedure of Hochberg[95] will be used to control for multiple comparisons with an overall Type I error of 5% (two-sided).

The following are the assumptions and power calculations for the secondary hypotheses:

1. **Cumulative Gross Income**: It is hypothesized that participants in the IPS arm will earn greater cumulative gross income. In the pilot study, participants in the IPS arm earned a mean amount of $9,264 (SD = 13,294) versus $2,601 (SD = 6,009) in the control arm. Assuming a pooled standard deviation of $10,153 for CSP #589 and using non-parametric methods to compare cumulative gross income between the two groups, this study will have >95% power to detect a similar difference between arms.

2. **PTSD Symptoms**: It is hypothesized that participants in the IPS arm will experience a greater reduction in PTSD symptoms, as measured by change from baseline in the total PTSD checklist (PCL) score. Change from baseline for this outcome will be analyzed using a mixed effects model with time as a repeated measures covariate. A prospective study of 41 participants with chronic PTSD randomized to nefazodone (n=26) versus

placebo (n=15) for the treatment of PTSD showed a 4.1 point difference between arms in mean change from baseline in PCL at 12 weeks [mean ±SD changes were -7.0 ±24 for the nefazodone arm and -2.9 ±8 for the placebo arm].[96] Assuming a pooled standard deviation of 14 in CSP #589, the study will have 80% power to detect a similar 4.1 overall mean difference in change from baseline between treatment arms over the course of the study.

3. **Self Esteem**: It is hypothesized that participants in the IPS arm will experience a greater improvement in self-esteem, as measured by Rosenberg Self Esteem Scale. The Rosenberg self-esteem scale ranges from 0 to 30, with higher scores indicating higher self-esteem.

   One study of 143 participants with severe mental disorders in two New Hampshire cities reported a significant difference in change from baseline after 12 months of vocational rehabilitation [mean ±SD at baseline: 22.8 ± 5.6; mean ± SD at 12 months: 21.8 ± 6; t-value for change from baseline: 2.24, df = 128, $p<0.05$).[87] From this study's reported test statistic values, a standard deviation of 5 is obtained for change from baseline in Rosenberg self-esteem.

   For the expected treatment difference, a subgroup analysis of a randomized study of IPS in participants with serious mental illness conducted in Washington, DC showed a mean difference of 2.7 at 18 months in the Rosenberg Self-Esteem scale between two subgroups.[11] The subgroups in this analysis were defined by cumulative earnings. Namely, one subgroup was composed of persons who worked in competitive work and whose cumulative earnings reached or exceeded the median for competitive earnings (n = 31, mean change from baseline in the Rosenberg Self-Esteem scale = -3.2). The other subgroup was persons who worked in either competitive or sheltered work but whose cumulative earnings did not reach the median for either (n = 50, mean change from baseline = -0.5).

   Assuming a pooled standard deviation of 6, the study will have >95% power to detect a similar 2.7 overall mean difference in change from baseline between treatment arms over the course of the study.

4. **Quality of Life**: It is hypothesized that participants in the IPS will experience a greater improvement in quality of life, as measured by the Quality of Life Inventory (QOLI). The overall QOLI score ranges from 0 to 77, with higher scores indicating better satisfaction with life.

   A literature search on QOLI did not turn up any reported findings that could be used to obtain assumptions for the standard deviation for change in QOLI score. However, the investigators of CSP #420, a randomized study of Vietnam veterans taking part in group psychotherapy for PTSD, reported QOLI scores (mean ± SD) of 0.02 ±2.0 for 203 female participants and -0.22 ±2.03 for 358 male participants.[97] Therefore, a pooled standard deviation of 2.0 is assumed in CSP #589.

   Assuming a pooled standard deviation of 2.0 and using a similar mixed effects model as stated above, this study will have >80% power to detect an 0.6 difference between treatment arms at the end of the study.

5. **Post Traumatic Stress Related Functional Inventory:** The hypothesis is that, compared to the TWE group, the IPS group will show a greater improvement in the Posttraumatic Stress Related Functional Inventory over the 18-month follow-up period. The effect of treatment on the Posttraumatic Stress Related Functional Inventory will be analyzed the same as the other secondary outcome measures.

   Unpublished analysis of a study of 211 veterans who had served in Operations Iraqi Freedom (OIF) or Enduring Freedom (OEF) showed a mean score of 56.4 (SD = 13.3) for the PRFI at baseline. Assuming a pooled standard deviation of 13 and using a similar mixed effects model as stated above, this study will have >80% power to detect a 4 point mean difference between treatment arms at the end of the study.

C. Interim Monitoring and Analysis

Interim monitoring will be performed by the West Haven CSP Coordinating Center (WH-CSPCC) and will focus on:

- Recruitment (overall and by enrolling site)

- Baseline comparability of treatment groups
- Protocol adherence
- Safety
- Completeness of data

Recruitment and completeness of data will also be monitored for purposes of daily trial operations and quality assurance. The WH-CSPCC monitoring provides the basis for reporting to the Data Monitoring Committee (DMC). A prototype set of tables and figures for presentation to the DMC is provided in Appendix D.

Monitoring Recruitment

The WH-CSPCC will monitor all steps in the recruitment process to assure early recognition of inadequate performance and to identify reasons for inadequate performance at each recruitment site and for the trial overall. To assist in this process, the WH-CSPCC will produce weekly data monitoring reports. These reports will include number of screening forms completed, reasons for ineligibility at screening, number of informed consent documents signed, and number of randomizations. The same reports will be made available to the DMC at each of its meetings. The data gives the DMC a regular opportunity to compare the trial assumptions with the observed data to make early judgments about the merits of continuing the study.

Baseline Comparability

In order to assess the adequacy of randomization, the distribution of baseline characteristics among the treatment groups will be compared: demographic information, medical history, clinical characteristics. The distribution of baseline patient characteristics among the two groups will be evaluated using descriptive summary statistics (means, medians, quartiles, etc. for continuous variables; frequency distributions for categorical variables).

Protocol Adherence

Protocol adherence will be monitored to assure early identification of poor performance at individual sites and in the trial overall. Periodic reports will be provided to the Executive Committee and to the DMC at each of its meetings. Specific parameters to be monitored include:

- Randomization of ineligible participants
- Treatment allocation errors
- Failure to complete required follow-up assessments on time
- Loss and withdrawal rates
- Adherence to the assigned employment intervention

Monitoring for Efficacy and Futility

No interim "looks" for efficacy or futility are planned. The overall duration of the study will not allow for enough information to be accumulated in time prior to the end of participant follow-up to make an informed decision related to efficacy or futility. Even if one were to consider an interim look when a smaller amount of information is obtained (e.g. 20-30%), the confidence intervals for stopping boundaries will be rather wide to reach definitive conclusions.

Analysis of Adverse Events

Trial safety will be monitored throughout the study by WH-CSPCC, the CSPCRPCC and the Study Chair's Offices. Safety reports will be submitted for review to the DMC at its scheduled meetings or sooner as deemed appropriate. The closed session reports generated for the DMC meetings will include a summary of serious adverse events (SAEs) by type and MedDRA coding by treatment group. The incidence of SAEs and of other adverse events including suicidal behaviors and ideation will be calculated and compared among the treatment groups using statistics appropriate for discrete or count data. Initially, due to the presence of small counts of serious and non-serious adverse events before data collection completion, the Fisher's exact test will be used for comparing proportions of adverse events between treatment groups. Where possible and if requested by the DMC, benchmarks will be established for key serious adverse event rates on published data to aid the Committee in the evaluation of safety. If the established benchmarks are exceeded, the DMC may consider recommending that the trial be stopped or revised because of safety concerns.

D. Final Statistical Analysis of the Data

All primary analyses for efficacy and safety will be performed according to the intent-to-treat principle. That is, participants will be analyzed according to their original treatment assignment regardless of adherence. Exploratory secondary on-treatment analyses will also be performed.

Baseline Characteristics by Treatment

Because of the size of this study, we expect that the randomization process will produce reasonably comparable groups of patients. However, the adequacy of the randomization will be assessed by comparing the distribution of baseline demographics, medical history, clinical characteristics and PTSD symptoms among the treatment groups. Comparability for continuous variables will be examined graphically and by summary statistics (means, medians, quartiles, etc.). Categorical variables will be examined by calculating frequency distributions. No adjustment for treatment imbalances in baseline covariates will be performed since this approach can be biased introduce.[97,98]

Analysis of the Primary Outcome

The primary outcome of steady worker, i.e., holding competitive employment for at least 50% of the 18-month follow-up period (i.e., 39/78 weeks), will be compared by treatment group using a logistic regression model in order to adjust for each participating medical center at a two-tailed alpha-level of 0.05. Weekly employment data values (binary outcome of success/failure; 0/1) will be summed over the total follow-up period to provide a score for each patient over the follow-up period. Participants with cumulative scores of ≥50% or higher (≥ 39 out of the 78 weeks of follow-up) will be considered as 'steady workers' (primary outcome success) and those with cumulative scores <50% (< 39 weeks) will be considered as primary outcome failures. Participants who are lost to follow-up and have no primary outcome assessment will be counted as failures in the primary analysis. Missing weekly employment data will be counted as unemployed (failure; 0) in the primary analysis to reduce type-I error and protect the study from bias.

Secondary sensitivity analyses of the primary outcome will also be conducted. Total time worked (days or weeks) as well as proportions of participants with competitive employment of pre-specified durations (i.e., worked at all, 26 and 52 weeks) will be compared between the two

groups. Total mean time worked between the groups will be compared using an analysis of variance (ANOVA) adjusted for site or the Kruskal–Wallis test if the data are not normally distributed. The proportions of participants with competitive employment of pre-specified durations will be tested using a logistic regression model in the same manner as the primary analysis.

Additional sensitivity analysis will be carried out using a variation of the primary outcome where a steady worker is defined as holding a competitive job for 50% of the weeks during months 4 through 18 of the follow-up period, i.e., ≥33 weeks of week 13-78 post randomization. Weeks worked during the first 12 weeks post-randomization will not count for purposes of this sensitivity analysis.

A sensitivity analysis on the number of days of unemployment and number of days of job-seeking prior to baseline assessment will be conducted. Logistic regression modeling will be considered.

Unemployment rates for each clinical site location will be collected at study initiation and every six months during active study period. These rates will be analyzed to determine if local unemployment rates affected study outcomes for a particular site.

Analysis of Secondary Outcomes

To control for multiplicity, the sequentially rejective procedure of Hochberg will be used to determine statistical significance for the treatment comparisons for secondary outcomes using an overall Type I error of 5% (two-sided).[99]

Cumulative Gross Income

The cumulative gross income of the two groups will be compared using ANOVA adjusted for site or the non-parametric test if income data are not normally distributed.

PTSD, Self Esteem and Quality of Life

PTSD symptoms, Self Esteem, and PTSD Function will be assessed every three months and the Quality of Life will be assessed every six months over the 18 month follow-up visit period.

PTSD will be assessed using the PTSD Checklist (PCL), self esteem using the Rosenberg Self Esteem Scale, quality of life using the Quality of Life Inventory, and PTSD related functioning using the Post Traumatic Stress Disease Related Functional Inventory (PRFI). The effect of treatment on each of these outcome measures will be analyzed by a longitudinal repeated measures mixed effects model, adjusted for the study design (randomization by site as a random effect in the model) and for the baseline outcome score.[100,101] The outcome variable in the model will be the change in the outcome score at each follow-up time point relative to baseline. Each follow-up visit (+/- 1 month visit window) will be categorized by a visit number. Any follow-up outcome data collected outside of a study window will be assigned the nearest uncompleted visit number by the coordinating center. Any unscheduled visit that cannot be assigned a unique visit number will be excluded from the repeated measures analyses.

Model building methods will be used to first determine the best mean structure of the outcome (e.g., time as linear or categorical, and treatment by time interactions) and then to determine the best fitting and most parsimonious covariance structure for the data. A likelihood ratio test will be conducted between models with time as categorical and time as continuous to determine if a linear trend is consistent with the data. If a linear trend is not consistent with the data, a treatment by time interaction will be examined to determine if a two-way analysis of covariance model that allows the treatment effect to vary from one time point to another is more appropriate than analyzing the effect of treatment as constant over time. The model will be fitted by maximum likelihood methods using all available data. Once the mean structure is determined, a likelihood ratio test will be conducted to determine if a more parsimonious covariance structure than an unstructured covariance matrix can be estimated including compound symmetry and autoregressive-1.

Analysis of Exploratory Outcomes

The exploratory outcome of crisis events will include VA and non-VA emergency room visits, contacts with the legal system, number of nights considered homelessness (i.e. defined as number of nights residing on the street, in a shelter, or in a domiciliary), psychiatric inpatient admission days(s), and weeks of substance misuse (i.e. number of weeks where at least one episode of heavy drinking, use of illicit substances, and/or use of controlled substances without a

prescription occurred). Suicidal behaviors are tracked by the Sheehan Suicidality Tracking Scale. Crisis events will be compared by treatment group using counts of total interventions, and the proportion of participants who experience at least one intervention using statistics appropriate for discrete or count data. If there are few crisis events, the Fisher's exact test will be used for comparing proportion of between treatment groups.

Other Exploratory Analyses

Although we expect the randomization process will produce comparable groups of participants given the size of the study, sensitivity analyses will be conducted to determine the relationship of pre-specified covariates on outcomes and their influence on the treatment effect using appropriate analytical techniques as described above. The pre-specified baseline covariates that will be examined include PTSD severity, TBI, overall medical burden (CIRS score), homelessness and Fidelity score. In addition, exploratory analyses will examined these covariates using tests of interaction to determine the effect of treatment in subgroups. Appropriate adjustments for multiple testing will be considered.

Missing Data

Every effort will be made to assess each outcome for all participants, and the completeness of data retrieval will be closely monitored by CSPCC. Because of this effort and the fact that most measured can be assessed over the phone if needed, we anticipate only a small amount of missing data. Nevertheless, because missing observations have the potential to alter the results of analyses, we will examine whether the pattern of missing data and dropouts is different between the two treatment arms. We will also examine the distribution of baseline covariates between those with and without missing outcome data. If there are no systematic differences between those with and without missing data, the data can be considered to be observed at random. The secondary outcome repeated measures models are also unbiased if missing data are unrelated to outcomes, i.e., if the data are considered missing at random or missing completely at random.

If there are significant differences in dropout and missing data patterns between treatment arms, we will conduct sensitivity analyses to determine the impact of missing information on the treatment comparisons. Multiple imputation methods will be considered to impute values[102] for missing employment data for the primary outcome and missing secondary outcomes in the

repeated measures analyses. In addition, for the primary outcome, the proportion of weeks worked will compared between the group ignoring missing weeks.

XVI. Feasibility

Under the leadership of experienced investigators and the VA Cooperative Studies Program, the VA is an excellent setting to conduct this study which has been designed to ensure feasibility within the VA system. Feasibility, acceptability, and preliminary efficacy have already been determined in the single-site study (Davis et al 2012). The lessons learned from the pilot study are being leveraged to improve the feasibility, efficiency, and success of this VA Cooperative Study.

A. Estimates of Patient Availability

Estimates of potentially eligible patients were derived from VA databases and surveys that were sent to investigators at potential participating sites. In April 2012, a Survey of Interested Sites was sent to all Research Services at VA Medical Centers that are authorized to conduct research. Over 40 VA Medical Centers responded immediately. A VA database query was requested for the number of unique veterans in FY11 who were seen in within the past 2 years, were under the age of 65, and who had a diagnosis of PTSD, did not have an exclusionary diagnosis, and did not have a date of death. Based on this query for the 38 potential participating sites that met initial site selection criteria, there were an average of 1186 potential participants/site (Table 7); these estimates were also supported by site survey responses. If one assumes that approximately 50% are unemployed (based on VA FY09 Long Journey Home report), each site would have an average of 593 potential participants. With the target enrollment for CSP#589 at 540, the study sites would need to enroll 6% of the potential participant pool, representing a target enrollment number that is achievable. In addition, a rate of randomization of 3 to 4 participants per month during the 12 month enrollment period is feasible and ensures that the enrollment goal is met within the timeline.

Table 7. Number of PTSD Participants at Interested Clinical Sites that Responded to April 2012 Survey of Site Interest.

Site	Number of Veterans with PTSD*
1. Albuquerque (501)	1,392
2. Atlanta (508)	2,284
3. Birmingham (521)	1,448
4. Bronx (526)	530
5. Charleston (534)	1,669
6. Chicago (537)	760
7. Cleveland (541)	1,476
8. Coatesville (542)	683
9. Columbia (544)	2,085
10. Dallas (549)	3,000
11. Detroit (553)	566
12. Durham (558)	1,291
13. Hines (578)	1,171
14. Honolulu (459)	824
15. Houston (580)	2,233
16. Indianapolis (583)	1,070
17. Jackson (586)	689
18. Kansas City, MO (589)	853
19. Leavenworth (589)	1,223
20. Los Angeles (691)	2,170
21. Northampton (631)	420
22. Madison (607)	609
23. Martinsburg (613)	683
24. Miami (546)	1,263
25. Minneapolis (618)	1,053
26. New Orleans (629)	1,073
27. Phoenix (644)	2,276
28. Providence (650)	599
29. Reno (654)	406
30. Richmond (652)	1,154
31. Salt Lake City (660)	1,445
32. San Francisco (662)	729
33. St Louis (657)	991
34. Tucson (678)	1,005
35. Tuscaloosa (679)	751
36. Washington, DC (688)	1,295
37. West Haven (689)	1,273
38. White River Junction (405)	630
Average	*1186*

*Number of Veterans with PTSD in FY11 who were seen in within the past 2 years, were under the age of 65, and who had a diagnosis of PTSD, did not have an exclusionary diagnosis, and did not have a date of death. Data extracted from Austin VA database.

B. Study Site Selection

Clinical sites were selected based on criteria that include (a) an experienced and qualified local site investigator; (b) a PTSD clinical treatment team that is motivated to participate in this study and allow IPS to be integrated within the treatment program, (c) presence of an operational TWP service that agrees to meet the demand of new Veterans with PTSD entering into the existing TWP service, (d) a high level of support from the medical center leadership, and (e) adequate space and resources. Preferred sites also should have past experience conducting VA clinical trials, past good performance on enrollment rates for clinical trials (especially in the area of PTSD), ability to work with IRBs, good research compliance program, and adequate number of potential participants. In addition, distribution of clinical sites aims for adequate geographic and rural/urban diversity. The composition of study sites will include large and small sites with the larger sites having a greater monthly recruitment goal. The budget for the large sites will include additional research staff, for example, an additional IPS specialist, Clinical Research Coordinator, and/or Research Assistant (full time or part-time depending on level of enrollment and performance).

The clinical research sites include the following:

Raymond G. Murphy VAMC (501)	1501 San Pedro SE Albuquerque, NM 87108
Birmingham VAMC (521)	700 South 17th St Birmingham, AL 35233
James J. Peters VAMC (526)	130 West Kingsbridge Rd Bronx, NY 10468
Ralph H. Johnson VAMC (534)	109 Bee St Charleston, SC 29401
VA North Texas Healthcare System (549)	4500 South Lancaster Rd Dallas, TX 75216
Durham VAMC (558)	508 Fulton St Durham, NC 27705
Edward Hines Jr. VA Hospital (578)	5000 South 5th Ave Hines, IL 60141
Michael E. DeBakey VAMC (580)	2002 Holcombe Blvd Houston, TX 77030
William S. Middleton Memorial Veterans Hospital (607)	2500 Overlook Terrace Madison, WI 53705
Miami VA Healthcare System (546)	1201 NW 16th St Miami, FL 33125
VA Minneapolis Health Care System (618)	One Veterans Dr Minneapolis, MN 55417

San Francisco VAMC (662)	4150 Clement St San Francisco, CA 94121

XVII. Publications

The policy of the Cooperative Studies Program is that outcome data will not be revealed to the participating investigators until the data collection phase of the study is completed. This policy safeguards against possible biases affecting the data collection. All presentations and publications from this study will follow CSPCC policy as stated in the CSP Guidelines. The presentation or publication of any or all data collected by participating investigators on participants entered into this VA Cooperative Study is under the direct control of the study's Executive Committee. This is true whether the publication or presentation is concerned with the results of the principal undertaking or is associated with the study in some other way. No investigator may perform analyses or interpretations or make public presentations or seek publication of any data unless approved by the Executive Committee. The Executive Committee has the authority to establish one or more publication committees, usually comprised of subgroups of participating investigators and some members of the Executive Committee, for the purpose of producing manuscripts for presentation and publication. Any presentation or publication, when formulated by the Executive Committee or its authorized representatives, should be circulated to all participating investigators for review, comments, and suggestions, at least four weeks prior to submission of the manuscript to the presenting or publishing body. All publications must give proper recognition to the study's funding source, and should list all participants in the study. If an investigator's major salary support and/or commitment is from the VA, it is obligatory that investigators list the VA as his/her primary institutional affiliation. Submission of manuscripts or abstracts must follow the usual VA policy; ideally, a subtitle states, "A Department of Veterans Affairs Cooperative Study." A copy of the letter to the editor and the manuscript/abstract submitted for publication or presentation should be sent to the Director, CSR&D. The CSP also requires that every manuscript be reviewed and approved by the Director, CSPCC prior to submission as a final quality control step. Participation in Department of Veterans Affairs Cooperative Studies is voluntary. Any investigator who cannot accept these operational guidelines regarding publication policy should not volunteer to participate in the study.

A. Anticipated Publications

The results of IPS vs. TWP on the prospectively designated primary and secondary outcome measures will be presented in a major manuscript entitled "Veterans Individual Placement and Support Towards Advancing Recovery (VIP-STAR) in the Treatment of Posttraumatic Stress Disorder." The manuscript will be submitted for consideration for publication in a broadly read high quality journal such as the *New England Journal of Medicine* or the *Journal of the American Medical Association*. Authors will consist of the CSP #589 Study chair and members of the planning committee and other individuals who have made intellectual contributions to study design, conduct of the study, and/or preparation of the manuscript. An appendix will contain the names of the organizational units, their Principal Investigators and Co-Investigators. Organizational units will include the Clinical Sites, the Data Monitoring Committee, the Central Research Pharmacy, the Coordinating Center, Center Laboratory, and the Study chairs' office.

Other aspects of the study results likely will warrant publication. These manuscripts include secondary outcomes, exploratory analysis of moderators of treatment outcomes, methods of IPS delivery in the PTSD population, and economic analysis. Proposals for such analyses and publications can arise from multiple sources, including the Study chairs, site investigators, or other investigators including pharmacy support, statistical support, etc. Such proposals will be presented for approval to a publications committee consisting of all willing members of the current planning committee.

XVIII. References

[1] Davis LL, Leon AC, Toscano R, Drebing CE, Ward LC, Parker PE, Kashner TM, Drake RE. A randomized controlled trial of supported employment among veterans with posttraumatic stress disorder. *Psychiatr Serv*. 2012 May 1:63(5):464-70.

[2] Desia, R., Spencer, H. *The Long Journey Home XVIII Treatment of Posttraumatic Stress Disorder in the Department of Veterans Affairs: Fiscal Year 2009 Service Delivery and Performance*. http://vaww.nepec.mentalhealth.med.va.gov/PTSD/ptsLJHAI.pdf . Accessed March 7, 2013.

[3] Institute of Medicine. *The dynamics of disability: Measuring and monitoring disability programs for Social Security Programs.* Washington, DC: National Academy Press. 2002.

[4] World Health Organization. *World Health Organization International Classification of Functioning, Disability and Health (ICF)*. Geneva: World Health Organization. 2001a.

[5] Warr, P. *Work, unemployment, and mental health*. Oxford: Oxford University Press. 1987.

[6] Deegan, P. E. Recovery: The lived experience of rehabilitation. *Psychiatric Rehabilitation Journal.* 1988;11(4):11-19.

[7] Whitley, R. E., & Drake, R. E. Dimensions of recovery. *Psychiatric Services*. 2010;61:1248-1250.

[8] Americans with Disabilities Act of 1990. Pub. L. No. 101-336, Stat. 328.1990.

[9] Bond, G. R., Resnick, S. G., Drake, R. E., et al. Does competitive employment improve nonvocational outcomes for people with severe mental illness? *Journal of Consulting and Clinical Psychology*. 2001;69:489-501.

[10] Burns, T., Catty, J., White, S., et al. The impact of supported employment and working on clinical and social functioning: Results of an international study of Individual Placement and Support. *Schizophrenia Bulletin.* 2009;35: 949-958.

[11] Kukla, M., Bond, G. R., & Xie, H. A prospective investigation of work and nonvocational outcomes in adults with severe mental illness. *Journal of Nervous and Mental Disease*. 2012 Mar;200(3):214-22.

[12] Mueser, K. T., Becker, D. R., Torrey, W. C., et al. Work and nonvocational domains of functioning in persons with severe mental illness: A longitudinal analysis. *Journal of Nervous and Mental Disease.* 1997;185:419-426.

[13] Bush, P. W., Drake, R. E., Xie, H., McHugo, G. J., Haslett, W. R. The long-term impact of employment on mental health service use and costs. *Psychiatric Services.* 2009;60:1024-1031

[14] Wehman, P. Supported competitive employment for persons with severe disabilities. *Journal of Applied Rehabilitation Counseling. 1986;17:*24-29.

[15] Wehman, P. Supported employment: Toward zero exclusion of persons with severe disabilities. In P. Wehman & M. S. Moon (Eds.), *Vocational rehabilitation and supported employment*. Baltimore: Paul Brookes. 1988:3-14.

[16] Anthony, W. A., Blanch, A. Supported employment for persons who are psychiatrically disabled: An historical and conceptual perspective. *Psychosocial Rehabilitation Journal. 1987:11*(2):5-23.

[17] Danley, K. S., Anthony, W. A. The Choose-Get-Keep Model: Serving severely psychiatrically disabled people. *American Rehabilitation.* 1987;13(4):6-9, 27-29.

[18] Fabian, E. S. Supported employment for severely psychiatrically disabled persons: A descriptive study. *Psychosocial Rehabilitation Journal.* 1989a;13(2):53-60.

[19] Mellen, V., & Danley, K. Special issue: Supported employment for persons with severe mental illness. *Psychosocial Rehabilitation Journal.* 1987*;9*(2).

[20] Noble, J. H., Conley, R. W., Banerjee, S., & Goodman, S. Supported employment in New York State: A comparison of benefits and costs. *Journal of Disability Policy Studies.* 1991*;2*:39-73.

[21] Trotter, S., Minkoff, K., Harrison, K., & Hoops, J. Supported work: An innovative approach to the vocational rehabilitation of persons who are psychiatrically disabled. Rehabilitation *Psychology*. 1998;33*:*27-36.

[22] Bond, G. R. Principles of the Individual Placement and Support model: Empirical support. *Psychiatric Rehabilitation Journal. 1998;22*(1):11-23.

[23] Bond, G. R. Vocational rehabilitation. In R. P. Liberman (Ed.), *Handbook of psychiatric rehabilitation*. New York: Macmillan. 1992:244-275.

[24] Estroff, S. E. *Making It Crazy*. Berkeley, CA: University of California Press. 1981.

[25] Quimby, E., Drake, R. E., & Becker, D. R. Ethnographic findings from the Washington, DC, Vocational Services Study. *Psychiatric Rehabilitation Journal, 2001;24:*368-374.

[26] Schultheis, A. M., & Bond, G. R. Situational assessment ratings of work behaviors: Changes across time and between settings. *Psychosocial Rehabilitation Journal, 1993;17*(2):107-119.

[27] Becker D.R. & Drake R.E. *A Working Life for People with Severe Mental Illness*. Oxford Univ Press, NY. 2003.

[28] Becker, D. R., & Drake, R. E. *A working life: The Individual Placement and Support (IPS) Program.* Concord, NH: New Hampshire-Dartmouth Psychiatric Research Center. 1993.

[29] NIMH. *Bridging science and service:* A report by the National Advisory Mental Health Council's Clinical Treatment and Services Research Workgroup. Rockville, MD: National Institute of Mental Health. 1999.

[30] Torrey, W. C., Becker, D. R., & Drake, R. E. Rehabilitative day treatment versus supported employment: II. Consumer, family and staff reactions to a program change. *Psychosocial Rehabilitation Journal*, 1995;18(3):67-75.

[31] Drake, R. E., Becker, D. R., & Anthony, W. A. The use of a research induction group in mental health services research. *Hospital and Community Psychiatry,* 1994;45*:*487-489.

[32] Drake, R. E., McHugo, G. J., Becker, D. R., Anthony, W. A., & Clark, R. E. The New Hampshire study of supported employment for people with severe mental illness: Vocational outcomes. *Journal of Consulting and Clinical Psychology,* 1996;64:391-399.

[33] Drake, R. E., Becker, D. R., & Bond, G. R. Recent research on vocational rehabilitation for persons with severe mental illness. *Current Opinion in Psychiatry*, 2003;16:451-455.

[34] Crowther MM, Almaraz-Serrano A, Creed F, et al. Systematic reviews of the effectiveness of day care for people with severe mental disorders: (1) acute day hospital versus admission; (2) vocational rehabilitation; (3) day hospital versus outpatient care. *Health Technol Assess* 2001;5(21):1-75.

[35] Salyer MP, Becker, Drake. A ten-year follow-up of a supported employment program. *Psych Services*. 2004;55:302-308.

[36] Becker D, Whitley R, Bailey EL, Drake RE. Long-term employment trajectories among participants with severe mental illness in supported employment. *Psych Services*. 2007:922-928.

[37] Cook, J. A., & Razzano, L. Vocational rehabilitation for persons with schizophrenia: Recent research and implications for practice. *Schizophrenia Bulletin*. *2000;26*, 87-103.

[38] Gaebel, W., & Pietzcker, A. Prospective study of course of illness in schizophrenia: Part II. Prediction of outcome. *Schizophrenia Bulletin*, *1987;13*, 299-306.

[39] Strauss, J. S., & Carpenter, W. T. Prediction of outcome in schizophrenia. III. Five-year outcomes and its predictors. *Archives of General Psychiatry, 197734*. 1977;159-163.

[40] Möller, H.-J., von Zerssen, D., & Wüschner-Stockheim, M. Outcome in schizophrenic and similar paranoid psychoses. *Schizophrenia Bulletin*, 1982;*8:*99-108.

[41] McGlashan, T. H. A selective review of recent North American long-term follow-up studies of schizophrenia. *Schizophrenia Bulletin, 1988;14*, 515-542.

[42] Kimerling R, Alvarez J, Pavao J, et al. Unemployment among women: examining the relationship of physical and psychological intimate partner violence and posttraumatic stress disorder. *J Interpers Violence.* 2009;24(3):450-63.

[43] Murdoch M, van Ryn M, Hodges J, et al. Mitigating effect of Department of Veterans Affairs disability benefits for posttraumatic stress disorder on low income. *Military Medicine*. 2005;120:137-140.

[44] Hoge CW, Terhakopian A, Castro CA, et al. Association of posttraumatic stress disorder with somatic symptoms, health care visits, and absenteeism among Iraq war Veterans. *Am J Psychiatry.* 2007 Jan;164(1):150-3.

[45] Riviere LA, Kendall-Robbins A, McGurk D, et al. Coming home may hurt: risk factors for mental ill health in US reservists after deployment in Iraq. *Br J Psychiatry.* 2011 Feb;198(2):136-42.

[46] Erbes CR, Kaler ME, Schult T, Polusny MA, Arbisi PA. Mental health diagnosis and occupational functioning in National Guard/Reserve Veterans returning from Iraq. *J Rehabil Res Dev*. 2011;48(10):1159-70.

[47] Savoca E, Rosenheck R. The civilian labor market experiences of Vietnam-era Veterans: the influence of psychiatric disorders. *J Ment Health Policy Econ*. 2000 Dec 1;3(4):199-207.

[48] McCarren M, Janes GR, Goldberg J, et al. A twin study of the association of post-traumatic stress disorder and combat exposure with long-term socioeconomic status in Vietnam Veterans. *J Trauma Stress*. 1995 Jan;8(1):111-24.

[49] Smith MW, Schnurr PP, Rosenheck RA. Employment outcomes and PTSD symptom severity. *Ment Health Serv Res.* 2005 Jun;7(2):89-101.

[50] Adler DA, Possemato K, Mavandadi S, et al. Psychiatric status and work performance of Veterans of Operations Enduring Freedom and Iraqi Freedom. *Psychiatr Serv*. 2011 Jan;62(1):39-46.

[51] Schnurr PP, Lunney CA. Work-related quality of life and posttraumatic stress disorder symptoms among female Veterans. *Womens Health Issue*s. 2011 Jul-Aug;21(4 Suppl):S169-75.

[52]Maarten J. J. Kunst. Employment Status and Posttraumatic Stress Disorder Following Compensation Seeking in Victims of Violence. *J Interpers Violence*, 2011 Jan;26:377-393.

[53] Murdoch M, Sayer NA, Spoont MR, Rosenheck R, et.al.. Long-term outcomes of disability benefits in US Veterans with posttraumatic stress disorder. *Arch Gen Psychiatry*. 2011 Oct;68(10):1072-80.

[54] Resnick SG, Rosenheck RA. Posttraumatic stress disorder and employment in Veterans participating in Veterans Health Administration compensated work therapy. *J Rehab Res Dev*. 2008. 45:427-436.

[55] Rosenheck R, Stolar M, Fontanta A. Outcomes monitoring and testing of new psychiatric treatments: Work therapy in the treatment of chronic post-traumatic stress disorder. *Health Serv Res*. 2000;35:133-51.

[56] Bond, G. R., Drake, R. E., & Becker, D. R. Generalizability of the Individual Placement and Support model of supported employment outside the US. *World Psychiatry*, 2012 Feb; 11(1):32-9.

[57]Drake, R. E., Skinner, J. S., Bond, G. R., & Goldman, H. H. Social Security and mental illness: Reducing disability with supported employment. *Health Affairs. 209;28:*761-770.

[58] Karakus, M., Frey, W., Goldman, H., Fields, S., & Drake, R. *Federal financing of supported employment and customized employment for people with mental illnesses*. Rockville, MD: Westat. 2011.

[59] Latimer, E. Economic considerations associated with assertive community treatment and supported employment for people with severe mental illness. *Journal of Psychiatry and Neuroscience. 2005;30:*355-359.

[60] Schneider, J. Is supported employment cost effective? A review. *International Journal of Psychosocial Rehabilitation. 2003;7:*145-156

[61]Salkever, D. S. *Toward a social cost-effectiveness analysis of programs to expand supported employment services: An interpretive review of the literature*. Rockville, MD: Westat. 2011.

[62] Latimer, E., Bush, P., Becker, D. R., Drake, R. E., & Bond, G. R. How much does supported employment for the severely mentally ill cost? An exploratory survey of high-fidelity programs. *Psychiatric Services. 2004;55:*401-406.

[63]Clark, R. E., Bush, P. W., Becker, D. R., & Drake, R. E. A cost-effectiveness comparison of supported employment and rehabilitative day treatment. *Administration and Policy in Mental Health. 1996;24:*63-77.

[64]Clark, R. E., Xie, H., Becker, D. R., & Drake, R. E. Benefits and costs of supported employment from three perspectives. *Journal of Behavioral Health Services and Research. 1998;25:*22-34.

[65] Linn BS, Linn MW, Gurel L: Cumulative Illness Rating Scale. *J Am Geriatr Soc.* 1968;16:622–626

[66] Miller MD, Paradis CF, Houck PR, et al: Rating chronic medical illness burden in geropsychiatric practice and research: application of the Cumulative Illness Rating Scale. *Psychiatry Res.* 1992;41:237–248.

[67] Blake DD, Weathers FW, Nagy LM, et.al. The development of a clinician-administered PTSD scale. *Jr Traumatic Stress.* 1995;8:75-90.

[68] Sheehan DV, Lecrubeir Y, Harnett-Sheehan K, Janavs J et al. Reliability and validity of the MINI International Neuropsychiatric Interview (M.I.N.I.): according to SCID-P. *European Psychiatry.* 1997;12:232-241.

[69] Corrigan JD, Bogner J. Initial Reliability and Validity of the Ohio State University TBI Identification Method. *J Head Trauma Rehabil.* 2007;22(6):318–329.

[70] Corrigan JD, Bogner J, Holloman C. Lifetime history of traumatic brain injury among persons with substance use disorders. *Brain Injury.* 2012; 26(2):139–150.

[71] Bogner J, Corrigan JD. Reliability and Predictive Validity of the Ohio State University TBI Identification Method With Prisoners. *J Head Trauma Rehabil.* 2009;24(4):279–291.

[72] Weathers, F., Litz, B., Herman, D., et al. The PTSD Checklist (PCL): Reliability, validity, and diagnostic utility. Paper presented at the Annual Convention of the International Society for Traumatic Stress Studies, San Antonio, TX. 1993 October.

[73] Blanchard, E. B., Jones-Alexander, J., Buckley, T. C, et al. Psychometric properties of the PTSD checklist (PCL). *Behavioral Research & Therapy. 1996;*34, 669-673.

[74] Monson, C. M., Gradus, J. L., Young-Xu, Y., et.al. Change in posttraumatic stress disorder symptoms: Do clinicians and patients agree? *Psychological Assessment.* 2008;20*(2):*131-138.

[75] Rosenberg M. *Society and the Adolescent Self-Image*. Princeton, NJ: Princeton University Press; 1965.

[76] Sinclair SJ, Blais MA, Gansler DA, Sandberg E, Bistis K, LoCicero A. Psychometric properties of the Rosenberg Self-Esteem Scale: overall and across demographic groups living within the United States. *Eval Health Prof.* 2010;33:56–80.

[77] Perfetti, Lawrence J.; Bingham, William C. Unemployment and self-esteem in metal refinery workers. *Vocational Guidance Quarterly.* 1983 Mar;31(3):195-202.

[78] Kashdan TB, Uswatte G, Steger MF, Julian T. Fragile self-esteem and affective instability in posttraumatic stress disorder. *Behaviour Research and Therapy*. 2006;44:1609–1619

[79] Torrey WC, Mueser KT, McHugo GH, Drake RE. Self-esteem as an outcome measure in studies of vocational rehabilitation for adults with severe mental illness. *Psychiatr Serv*. 2000;51(2):229-33.

[80] Lysaker PH, Bond G, Davis LW, Bryson GJ, Bell MD. Enhanced cognitive-behavioral therapy for vocational rehabilitation in schizophrenia: Effects on hope and work. *J Rehabil Res Dev*. 2005 Sep-Oct;42(5):673-82.

[81] Frisch MB. *QOLI or Quality of Life Inventory*. Minneapolis (MN): Pearson Assessments; 1994.

[82]Frisch MB, Cornell J, Villanueva M, Retzlaff PJ. Clinical validation of the Quality of Life Inventory: a measure of life satisfaction for use in treatment planning and outcome assessment. *Psychol Assess*. 1992;492- 101

[83] Ware NC, Hoope K, Tugenberg T, Dickey B, Fisher D. Connectedness and citizenship: redefining social integration. *Psych Services*. 2007;58:469-474.

[84] Olatunji BO, Cisler JM, Tolin DF. Quality of life in the anxiety disorders: A meta-analytic review. *Clinical Psychology Review*. 2007;27:572–581.

[85] Schnurr PP, Lunney CA, Bovin MJ, Marx BP. Posttraumatic stress disorder and quality of life: Extension of findings to veterans of the wars in Iraq and Afghanistan. *Clinical Psychology Review.* 2009 Dec;29(8):727-73.

[86] Schnurr PP, Friedman MJ, Foy DW, et al. Randomized trial of trauma-focused group therapy for posttraumatic stress disorder: results from a Department of Veterans Affairs Cooperative Study. *Arch Gen Psychiatry*. 2003;60(5):481-489.

[87] Schnurr PP, Hayes AF, Lunney CA, McFall M, Uddo M. Longitudinal analysis of the relationship between symptoms and quality of life in veterans treated for posttraumatic stress disorder. *Journal of Consulting and Clinical Psychology*, 2006 Aug;74(4):707-713.

[88] Schnurr PP, Lunney CA. Exploration of gender differences in how quality of life relates to posttraumatic stress disorder in male and female veterans. *J Rehabilitation Research and Development*. 2008;45(3):383-394.

[89] Coric V, Stock EG, Pultz J, Marcus R, Sheehan DV. Sheehan Suicidality Tracking Scale (Sheehan-STS): Preliminary Results from a Multicenter Clinical Trial in Generalized Anxiety Disorder. *Psychiatry* (Edgmont). 2009 Jan;6(1):26-31.

[90] Swanson SJ and Becker DR. *Supported Employment: Applying the Individual Placement and Support (IPS) Model to Help Clients Compete in the Workforce*. Hazelden Foundation. 2011.

[91] Becker, D. R., Smith, J., Tanzman, B., Drake, R. E., & Tremblay, T. Fidelity of supported employment programs and employment outcomes. *Psychiatric Services, 2001;52:*834-836.

[92] McGrew, J. H., & Griss, M. Concurrent and predictive validity of two scales to assess the fidelity of implementation of supported employment. *Psychiatric Rehabilitation Journal*, *2005;29:*41-47.

[93] Bond, G. R., Peterson, A. E., Becker, D. R., & Drake, R. E. *Validating the Individual Placement and Support Fidelity Scale*. Psychiatr Serv. 2012 Aug;63(8): 758-63.

[94] Bond, G. R., Becker, D. R., & Drake, R. E. Measurement of fidelity of implementation of evidence-based practices: Case example of the IPS Fidelity Scale. *Clinical Psychology: Science and Practice, 2011;18:*126-141.

[95] Hochberg, Y. A sharper Bonferroni procedure for multiple significance testing," *Biometrika. 198;*75:800–803.

[96] Davis, L.L., Jewell, M.E., Ambrose, S. et al. A placebo-controlled study of nefazodone for the treatment of chronic posttraumatic stress disorder: a preliminary study. J Clin Psychopharmacol. 2004;24(3):291-7.

[97] Sen, P. K. Incomplete multiresponse designs and surrogate endpoints in clinical trials. *Journal of Statistical Planning and Inference.* 1994;42:161-186.

[98] Senn SJ. Covariate imbalance and random allocation in clinical trials. *Stat Med*. 1989 Apr;8(4):467-75.

[99] Hochberg, Y. A sharper bonferroni procedure for multiple significance testing," *Biometrika*. 1988;75:800–803.

[100] Laird, N.M. and Ware, J.H. Random-effects models for longitudinal data. *Biometrics.*1982*;*38:963–974.

[101] Diggle P, Heagerty P, Liang KY, Zeger S. *Analysis of Longitudinal Data*. Oxford University Press, USA; 2 edition, 2002.

[102] Rubin D.B. *Multiple Imputation for Nonresponse in Surveys*. John Wiley and Sons; New York: 1987.