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TITLE: Development of a PTSD Population Registry

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14. ABSTRACT

Project VALOR (Veterans' After-discharge Longitudinal Registry) is an observational patient registry design for conducting a prospective, observation (i.e., clinical, non-interventional study) of PTSD trajectories among combat-exposed Veterans who served in the recent military operations in Iraq and Afghanistan. The objective of the VALOR registry is to provide longitudinal data on the natural history and outcomes associated with PTSD in Veterans who have utilized the Department of Veteran Affairs (VA) health care system. A secondary objective of our study is to determine predictors of a PTSD diagnosis by comparing diagnosed cases without a diagnosis of PTSD in a case-control design. Project VALOR will provide essential data on the natural history and outcomes associated with PTSD in military service men and women who have utilized the Department of Veterans Affairs (VA) health care system. An additional goal of this project is to evaluate risk factors for PTSD among combat-exposed service men and women. Since the start of this study, data were collected on 1650 participants. Among the 1597 included in the analysis sample, 799 were men and 798 were women, and, 73.4% of the sample had received a diagnosis of PTSD at enrollment.

15. SUBJECT TERMS
Risk factors for PTSD; PTSD diagnosis and symptoms; PTSD trajectories; VA healthcare utilization.

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INTRODUCTION

Project VALOR (Veterans' After-discharge Longitudinal Registry) is an observational patient registry design for conducting a prospective, observation (i.e., clinical, non-interventional study) of PTSD trajectories among combat-exposed Veterans who served in the recent military operations in Iraq and Afghanistan. The objective of the VALOR registry is to provide longitudinal data on the natural history and outcomes associated with PTSD in Veterans who have utilized the Department of Veteran Affairs (VA) health care system. A secondary objective of our study is to determine predictors of a PTSD diagnosis by comparing diagnosed cases without a diagnosis of PTSD in a case-control design.

The study represents an ongoing collaboration between investigators at the National Center for PTSD and Boston VA Healthcare System and New England Research Institutes. Key personnel include PI Dr. Terence Keane and co-investigators Dr. Jennifer Vasterling, Dr. Brian Marx, and Dr. Darren Holowka from the VA Boston Healthcare System, and Dr. Raymond Rosen (partnering PI), Dr. Shona Fong (epidemiologist), Julia Dixon (project manager) and Dr. Heather Litman (biostatistician) from NERI. Key advisors include Matthew Friedman (MD), Evelyn Bromet, Ph.D., Javier Escobar, M.D., David Barlow, (Ph.D), Harvey Levin, M.D., Ph.D., Bruce Dohrenwend (Ph.D), and Karen Seal (MD). Despite administrative delays in initiating the project which resulted in a one-year, no-cost extension, we succeeded in recruiting the complete sample, with slight over-recruitment. In order to ensure enrollment of our full target cohort for the study, we continued recruitment until September, 2012. A total of 1650 subjects met all of the eligibility criteria for the study and were enrolled. This exceeded slightly our original target for recruitment (N=1600). As shown in Tables 1 and 2, our sample characteristics closely matched our study design in that half of the sample (50.0%) are combat-exposed female veterans and include a balanced age range and race-ethnic composition. By design, one quarter of the sample participants (26.6%) had no prior diagnosis of PTSD.

We met all the study goals in the design and implementation of the study protocol (See Appendix B), collection of study data (See Appendix D, E), and timely analysis of study data and presentations and publications (See Appendix F). Based on our record of productivity, track record of achievements to date and rationale for continuation of the study, we have been awarded an additional CDMRP funding for Project VALOR for the period of 2012-2016. This additional grant funding will be used to collect longitudinal data on our current sample, including suicide, military sexual trauma (MST), traumatic brain injury (TBI), and their combined effects on PTSD-related outcomes in our highly diverse sample of combat-exposed male and female veterans. Most importantly, we will examine trajectories of change in these outcomes and the role of health utilization in our cohort. These findings will be used in turn to guide future policy and resources allocation for combat-exposed male and female veterans with symptoms of PTSD.

BODY

Phase I - Study Initiation

1. IRB Approvals/Finalize Protocol
   A large portion of the first study year was spent on an extensive review and revision of the study protocol and study aims. The Project VALOR Scientific Advisory Board met in person with the investigators shortly after initiation of the grant to provide advice on the study protocol and measures. The feedback received at the SAB meeting and from the initial OHRP review served at the basis for the revisions to the study protocol and aims. As minor revisions were made to the study protocol, changes were submitted to the

Institutional Review Boards of the New England Research Institute (NERI), VA Boston Healthcare System, and The Washington DC VA Medical Center, for approval. All of these approvals were received prior to the start of data collection. Waivers of HIPAA authorization and documentation of informed consent were obtained at the VA Boston Health Care System and Washington DC VA Medical Center, in addition to a certificate of confidentiality from NIH. The final versions of the study protocol, manual of operations, study materials, and all study site IRB approvals were submitted to OHRP and final OHRP approval was obtained at the end of year 1. These materials are included in Appendix B and C.

2. Program and Test De-Identification

   Programs were created to de-identify the VA in/outpatient electronic records database and were tested in sample data. Statistical analysis plans were also developed and finalized.

<u>Phase II – Data Collection</u>

3. Prepare Data for Abstraction

   Data on potential study participants were merged from electronic databases and de-identified prior to being transferred to NERI. No difficulties were encountered with this phase of the process.

4. Resolve Queries

   Study statisticians generated query reports related to the quality of the database based on pre-determined values and cleaned and tracked the data. Again, no difficulties were encountered with this phase.

5. Telephone Interview Instrument

   The telephone interview was extensively pre-tested by research staff and determined to be of sufficient duration and participant burden. The final interview was pre-tested to allow completion in a 40-50 minute telephone call. Since the interview consisted of previously validated scales and measures (e.g., SCID PTSD, Suicidality Modules), no additional validation was necessary prior to initiation of the study. A detailed manual of operations was developed as a guide to the conduct of the interview and all other study-related procedures.

6. Identify Target Sample for Interview
   a. The level 1 roster of potential participants was obtained from the DC VA Medical Center early in Y02. The initial opt-out letter was mailed to the 3,000 participants on the level 1 roster. A second opt-out letter was later mailed to the 2,169 potential participants on the level 1 roster who did not respond to the initial opt-out letter. Approximately 900 letters were returned because of a bad addresses or forwarding address. A third cycle of opt-out letters was mailed to these participants after a correct address was located in CPRS. In total, 772 positive responses and 160 refusals were received. Of the original level 1 roster there were a total 1,232 of non-responders. Research technicians then contacted all remaining non-responders by phone, as outlined in the project protocol. In month 25 of the project, a new level 1 roster of 6,000 potential participants was received. In months 25 through 34 initial opt out letters were sent to all 6,000 participants on the roster. Of the 6,000 letters mailed, 1,959 were returned. A second round of opt-out letters was then sent to the 4,041 participants who did not respond to the initial mailing. Of the 6,000 participants who have been

contacted, 1,372 returned letters agreeing to be contacted about the study, and 222 returned letters declining to be contacted further. Five hundred and fifty-eight (558) recruitment letters have been returned for bad addresses. A second opt-out letter was sent to these participants using the secondary address that was provided with the second level 1 roster. A total of 1650 phase 2 participants completed the project.

7. Conduct Interim Analyses

   Interim analyses were conducted using updated PTSD Registry data. These analyses were used throughout the study to ensure adequate completion of interviews and study questionnaires and to assess initial trends in the data.

8. Conduct Interviews

   Interviewers were extensively trained and monitored for quality assurance. Biweekly rating meetings were held to calibrate ratings and achieve consensus regarding problem ratings. These meetings were designed to prevent rater drift. Patients were contacted by telephone and informed consent was obtained verbally. Patients were provided with a URL in order to access the online questionnaire along with a unique random participant identification number. Following completion of the online questionnaires participants were interviewed by doctoral level interviewers. In the event that participants indicated high suicide risk, their mental health providers were contacted and asked for clearance to proceed. If this was not obtained the participant was dropped from the study and provided appropriate referrals at their nearest VAMC.

9. Interview Data Entry De-Identification and Transfer

   Data entry and quality control measures were conducted on an ongoing basis throughout the study at the VA through the complete Data Collection Phase. The study data was de-identified at regular intervals and transferred to the Data Center at NERI.

Phase III – Data Analysis and Reports

10. Conduct Data Analysis
    a. Multiple statistical analyses were conducted during the final phase of the project to address the Specific Aims of the Registry (see presentations and publications list below). Three papers have been published or accepted for publication, and more than 15 abstracts have been submitted for presentation at professional meetings.

11. Continued Abstraction
    a. Abstraction of VA in/outpatient electronic medical records for PTSD registrants who have return in/outpatient visits to VA medical centers has been performed periodically and is ongoing.

12. Prepare PTSD Database for Future Use
    a. The PTSD Registry database is being prepared for future use by other investigators. We anticipate this being made available in 2013.

Sample Characteristics

As shown in Tables 1 and 2 below, the sample was evenly divided between male (50%) and female (50%), combat-exposed veterans from OIF/OEF. Three quarters of the sample (73.4%) had a medical record diagnosis at the time of their enrollment into the study, by protocol design. Combat-exposure occurred for the majority of participants either during their service in the army (90.5%) or marine (9.5%) branches of the service, as expected. Moreover, as described in our recent presentations (See Appendix F), adjustment problems and psychiatric comorbidities, including prior suicide attempts and suicidal thoughts, substance abuse and depression, and military sexual trauma (MST) are all highly prevalent in our sample. The Project VALOR cohort has similar demographic characteristics and comorbidities compared to other recent reports of larger cohorts of male and female veterans with PTSD (e.g., Seal et al.,2009; Seal et al., 2012).

Table 1. Demographic characteristics of VALOR participants stratified by gender (n=1597)*.

Covariate	Overall (n=1597)	Men (n=799)	Women (n=798)
	Mean (SD) or n (%)	Mean (SD) or n (%)	Mean (SD) or n (%)
Age (SD)	37.4 (9.9)	38.1 (10.2)	36.8 (9.6)
PTSD Diagnosis			
Yes (%)	1172 (73.4)	584 (73.1)	588 (73.7)
No (%)	425 (26.6)	215 (26.9)	210 (26.3)
Race/ethnicity			
Black (%)	179 (11.2)	59 (7.4)	120 (15.0)
Hispanic (%)	153 (9.6)	69 (8.6)	84 (10.5)
White (%)	900 (56.4)	496 (62.1)	404 (50.6)
Other/unknown (%)	365 (22.9)	175 (21.9)	190 (23.8)
Military branch			
Army (%)	1446 (90.5)	684 (85.6)	762 (95.5)
Marines (%)	151 (9.5)	115 (14.4)	36 (4.5)
Married or living with partner (%)	929 (58.2)	535 (67.0)	394 (49.4)

Table 2. Demographic characteristics of VALOR participants stratified by PTSD diagnosis (n=1597)*.

Covariate	Overall (n=1597)	PTSD (n=1172)	No PTSD (n=425)
	Mean (SD) or n (%)	Mean (SD) or n (%)	Mean (SD) or n (%)
Age (SD)	37.4 (9.9)	37.8 (9.9)	36.4 (9.8)
Gender			
Male (%)	799 (50.0)	584 (49.8)	215 (50.6)
Female (%)	798 (50.0)	588 (50.2)	210 (49.4)
Race/ethnicity			
Black (%)	179 (11.2)	129 (11.0)	50 (11.8)
Hispanic (%)	153 (9.6)	121 (10.3)	32 (7.5)
White (%)	900 (56.4)	650 (55.5)	250 (58.8)
Other/unknown (%)	365 (22.9)	272 (23.2)	93 (21.9)
Military branch			
Army (%)	1446 (90.5)	1057 (90.2)	389 (91.5)
Marines (%)	151 (9.5)	115 (9.8)	36 (8.5)
Married or living with partner (%)	929 (58.2)	676 (57.7)	253 (59.5)

*These tables were developed based on results for the first 1597 participants enrolled in the registry. Results for the additional participants beyond (N=53) will be available following verification of the database and transfer to NERI. Additional data from these participants will not affect the composition of the study sample in regards to key socio-demographic and diagnostic characteristics as shown.

KEY RESEARCH ACCOMPLISHMENTS

- Prepared and finalized research protocol
- Obtained all relevant approvals for revised protocol
- Finalized Statistical Analysis Plan
- Registry database programmed
- Online data collection platform programmed and tested for QC
- Pilot testing was completed
- Recruited 1650 participants
- Presented study at numerous professional society and research meetings (See Reportable Outcomes below)
- Published 3 papers in relevant peer-reviewed journals. (See Reportable Outcomes below)

REPORTABLE OUTCOMES

Publications

Rosen, R.C., Marx, B.P., Maserejian, N.N., Holowka, D.W., Gates, M.A., Sleeper, L.A., Vasterling, J.J., Kang, H.K., Keane, T.M. (2011). Project VALOR: design and methods of a longitudinal registry of post-traumatic stress disorder (PTSD) in combat-exposed veterans in the Afghanistan and Iraqi military theaters of operations. *Int J Methods Psychiatr Res*; 2012;21(1)5-16.

Gates, M.A., Holowka, D.W., Vasterling, J.J., Keane, T.M., Marx, B.P., Rosen, R.C. (2012). Posttraumatic stress disorder in veterans and military personnel: epidemiology, screening & case recognition. *Psychol Serv* (Epub ahead of print).

Miller, M.W., Wolf, E.J., Kilpatrick, D., Resnick, H., Marx, B.P., Holowka, D.W., Keane, T.M., Rosen, R.C. and Friedman, M.J. The prevalence and latent structure of proposed DSM-5 posttraumatic stress disorder symptoms in US national and veteran samples. *Psychological Trauma: Theory, Research, Practice and Policy*. 2012; Online first publication, Sep 3. Doi: 10.1037/a0029730.

Scientific Meeting and Conference Presentations

Keane, T.M., Rosen, R.C., Maserejian, N.N., Holowka, D.W., Rodriguez, P., Marx, B.P., Kang, H., Vasterling, J.J., Wunderle, K.B., Rodier, N.A., Sloan D.S., Friedman, M.J., Sleeper, L.A. (2009). Creation of a PTSD Registry for Veterans: Project VALOR. Poster presented at the annual meeting of the Association for Behavioral and Cognitive Therapies, New York, NY.

Keane, T.M., Rosen, R.C., Maserejian, N.N., Holowka, D.W., Rodriguez, P., Marx, B.P., Kang, H., Vasterling, J.J., Wunderle, K.B., Rodier, N.A., Sloan D.S., Friedman, M.J., Sleeper, L.A.

(2009). Creation of a PTSD Registry for Veterans: Project VALOR. Poster and oral presentation at the Department of Defense (DOD) Military Health Research Forum (MHRF), Kansas City, MO.

Rosen, R.C., Keane, T.M., Marx, B.P., Maserejian, N.N., Holowka, D.W., Kang, H.K., Vasterling, J.J., Rodier, N.A., Sleeper, L.A. (2010). The natural history of combat-related posttraumatic stress disorder: Project VALOR. Poster presented at the World Congress of Behavioural and Cognitive Therapies, Boston, MA.

Holowka, D.W., Marx, B.P., Rodriguez, P., Gates, M.A., Rosen, R.C., Keane, T.M. (2011). Medical chart PTSD diagnostic accuracy among OEF/OIF veterans: preliminary results. Poster presented at the 31st annual meeting of the Anxiety Disorders Association of America, New Orleans, LA.

Gates, M.A., Holowka, D.W., Rodriguez, P., Keane, T.M., Marx, B.P., Rosen R.C. (2011). A longitudinal registry of post-traumatic stress disorder in OEF/OIF veterans: the early recruitment experience. Poster presented at the 3rd North American Congress of Epidemiology, Montreal, Canada.

Holowka, D.W., Marx, B.P., Gates, M.A., Guey, L. Rosen, R.C., Vasterling, J.J., Keane, T.M. (2011). Posttraumatic stress disorder, mild traumatic brain injury, & psychosocial functioning among Iraq and Afghanistan veterans. Poster presented at the annual meeting of the International Society for Traumatic Stress Studies, Baltimore, MD.

Miller, M.W., Wolf, E., Marx, B., Holowka, D., Resnick, H., Kilpatrick, D., Gates, M., Rosen, R., Guey, L., Keane, T., Friedman, M. (2011). Pilot study of a DSM-V internet survey instrument in a U.S. Department of Veterans Affairs PTSD sample. Presented as part of a symposium entitled *Internet Surveys on Proposed DSM-5 Criteria for PTSD* (M. Friedman, Chair) at the 27th annual meeting of the International Society for Traumatic Stress Studies, Baltimore, MD.

Bovin, M.J., Wisco, B.E., Holowka, D.W., Marx, B.P., Gates, M.A., Guey, L.T., Rosen, R.C., Keane, T.M. (2012). Peritraumatic response, PTSD and functional impairment among OEF/OIF veterans. Presented as part of a symposium entitled *On trauma: A theoretical and clinical perspective on how traumatic experiences shape subsequent PTSD* (M.G. Fetzner, Chair) at the 32nd annual meeting of the Anxiety Disorders Association of America, Arlington, VA.

Fink, H.L., Han, S.C., Franz, M.R., Chen, M.S., Holowka, D.W., Marx, B.M., Gates, M.A., Rosen, R.C. & Keane, T. M. (2012). Post-deployment social support as a mediator between military sexual trauma and PTSD among OIF/OEF veterans. Poster presented at the 32nd annual meeting of the Anxiety Disorders Association of America, Arlington, VA.

Lachowicz, M., Gorman, K., Holowka, D., Gates, M., Rosen, R., Marx, B., Keane, T. Posttraumatic stress and depressive symptoms in a sample of returning OIF/OEF veterans. Poster presented at the 32nd annual meeting of the Anxiety Disorders Association of America, Arlington, VA.

Marx, B.P., Holowka, D.W., Gates, M.A., Guey, L.T., Rosen, R.C., Vasterling, J.J., Keane, T.M. (2012). PTSD, mTBI and psychosocial function among Iraq and Afghanistan veterans. Presented as part of a symposium entitled *Impact of mTBI on Cognition, Emotion and the Neurobiology of PTSD in OEF/OIF Veterans* (R.E. McGlinchey and W.P. Milberg, Chairs) at the 120th Annual Convention of the American Psychological Association, Orlando, FL.

Rosen, R.C., Gates, M.A., Holowka, D.W., Marx, B.P., Vasterling, J.J., Keane, T.M. (2012). Psychosocial Outcomes in OEF/OIF Veterans with PTSD. Poster presented to the 2012 Military Health System Research Symposium, Fort Lauderdale, FL.

Chen, M.S., Holowka, D.W., Marx, B.P., Gates, M.A., Rosen, R.C., Keane, T.M. (2012). Anger mediates the relationship between combat exposure and functioning. To be presented at the 28th annual meeting of the International Society for Traumatic Stress Studies, Los Angeles, CA.

Chen, M.S., Han, S.C., Holowka, D.W., Marx, B.P., Gates, M.A., Rosen, R.C., Keane, T.M. (2012). Problem drinking moderates the effect of social support on PTSD and suicide risk. To be presented at the 28th annual meeting of the International Society for Traumatic Stress Studies, Los Angeles, CA.

Han, S.C., Chen, M.S., Fink, H.L., Holowka, D.W., Marx, B.P., Gates, M.A., Rosen, R.C., Keane, T.M. (2012). PTSD symptoms and parental functioning among male and female OEF/OIF Veterans. To be presented at the 28th annual meeting of the International Society for Traumatic Stress Studies, Los Angeles, CA.

Lachowicz, M.J., Franz, M.R., Gorman, K.R., Holowka, D.W., Marx, B.P., Gates, M.A., Rosen, R.C., Keane, T.M. (2012). Deployment and post-deployment experiences in Iraq-deployed soldiers: comparison of soldiers deployed during the Iraq invasion, insurgency, and surge. To be presented at the 46th annual convention of the Association for Behavioral and Cognitive Therapies, National Harbor, MD.

Submitted: ADAA Symposium Proposal (T. M. Keane, R. C. Rosen; Co-Chairs):
The Impact and Outcomes of Post-Traumatic Stress Disorder on Combat-Exposed Veterans: Findings from Project VALOR (under review)

Personnel Receiving Pay from this Research Effort

Personnel receiving salary from this research effort are Raymond C. Rosen, Ph.D. (Partnering PI), Margaret A. Gates, Sc.D. (Co-I), Lin Guey, Ph.D. (hired to replace Lynn Sleeper as Project Statistician and Co-I), Julia Dixon, MPH (Project Manager), Heather Litman, Ph.D. (Senior Statistician), Gayatri Rangathian, MS (Statistician) and Blandyna Williams (Research Assistant).

Project VALOR Continuation Funding:

The project was recently approved by CDMRP for 4 additional years of data collection on the full VALOR cohort (2012-2016). Project VALOR is positioned to provide new understanding of PTSD and comorbid conditions by 1) examining trajectories of PTSD diagnostic status and symptom severity, and the relationship of these trajectories to gender, comorbid disorders and service connection and treatment utilization; 2) assessing how trajectories of PTSD symptoms and diagnoses, comorbid conditions, and functioning covary over time; 3) evaluating gender differences in trajectory patterns and related clinical and psychosocial outcomes; 4) identifying both static and dynamic predictors of PTSD trajectory patterns by means of latent class analysis; and 5) examining factors which moderate trajectory patterns in male and female veterans with and without PTSD.

CONCLUSION

The VALOR PTSD registry will provide critical information to assist researchers, military leaders, and treatment providers to better understand the etiology and course of PTSD, how it can be identified at early stages, and the responsiveness of recent returnees to various treatment options. This knowledge will be of benefit to policy makers and current service members as well as victims of trauma in the broader community. It will include:

- Evaluation of the natural history and long-term outcomes of PTSD across treatments, treatment settings, and practitioners, using cost-efficient methods and economies of scale;
- A more accurate assessment of current theoretical models of symptom development, and
- Documentation of health resource utilization and development of a database that is an ideal resource for health services planning and policy.

Furthermore, this study will contribute:

- The formation of a potential cohort of subjects for ancillary studies, ranging from genomic influences to quality of life and psychosocial outcomes, as well as future clinical trials;
- The creation of a representative sample of PTSD OEF/OIF Veterans who use the VA medical system, available for use in epidemiologic studies, particularly for comparisons with active duty and other Veteran or civilian populations;
- Utility to clinicians, patient advocacy groups, and health policy planners;
- Publications and dissemination of the registry results to provide a representative perspective of what is achieved in actual current care settings, thereby augmenting outcomes data from clinical trials.

References

Trends and risk factors for mental health diagnoses among Iraq and Afghanistan veterans using Department of Veterans Affairs health care, 2002-2008. Seal KH, Metzler TJ, Gima KS, Bertenthal D, Maguen S, Marmar CR. Am J Public Health. 2009 Sep;99(9):1651-8.

Association of mental health disorders with prescription opioids and high-risk opioid use in US veterans of Iraq and Afghanistan. Seal KH, Shi Y, Cohen G, Cohen BE, Maguen S, Krebs EE, Neylan TC. JAMA. 2012 Mar 7;307(9):940-7.

APPENDIX A

AMENDED STATEMENT OF WORK – MAY 12, 2011

12-MONTH NO-COST EXTENSION START DATE- September 1, 2011

VA Boston Healthcare System (BVARI)
Research Service (151)
150 South Huntington Avenue
Boston, MA 02130
PI: Terence M. Keane, Ph.D.

New England Research Institutes, Inc. (NERI)
9 Galen Street
Watertown MA 02472
Partnering PI: Raymond Rosen, Ph.D.

This project requires human subject participation.

Major Task (Milestone)	Timeline (Months)	BVARI	NERI
PHASE I – STUDY INITIATION			
IRB Approvals/Finalize Protocol			
Finalize Protocol; NERI/VHA IRB approvals and USAMRMC HRPO human subject protocol approval	Completed	TK/BM	RR
Program and Test De-Identification			
Programs to de-identify VA in/outpatient electronic records database will be created	33-36	TK/BM	RR
De-identification programs will be tested on sample data	33-36	TK/BM	RR
Design statistical analysis programs	33-45	TK/BM	RR
PHASE II – DATA COLLECTION			
Prepare Data for Abstraction			
Data on potential subjects will be merged from electronic databases	Completed	TK/BM	
Data will be de-identified	Completed	TK/BM	
Transfer data to NERI	33-45	TK/BM	RR
Resolve Queries			
Generate query reports that relate to the quality of the database based on pre-determined values	33-45		RR
Data cleaning and tracking	33-45		RR
Pretest telephone Interview Instrument			
The interview will be tested in a sample of 20 veterans who will not be enrolled in the study to assess burden, ease of comprehension and time to completion	Completed	TK/BM	
Make modifications based on pre-testing	Completed	TK/BM	RR
Final interview tested to allow completion in a 40-50 minute telephone call	Completed	TK/BM	
Develop manual of operations	Completed	TK/BM	RR

Identify Target Sample for Interview			
Identify 1,200 OIF/OEF veterans with diagnosis of PTSD and 400 OIF/OEF veterans without diagnosis of PTSD and one or more visits during post-deployment years in the VA medical records database	Completed	TK/BM	
Conduct Interim Analyses			
Conduct interim analyses using existing PTSD Registry data	33-39		RR
Conduct Interviews			
Interviewers will be extensively trained and monitored for quality assurance	10-45	TK/BM	RR
Patients will be contacted by telephone and informed consent will be obtained verbally	21-45	TK/BM	
Patients provide verbal consent and interviews are scheduled	21-45	TK/BM	
Interview Data Entry De-Identification and Transfer			
Data entry and quality control measures will be ongoing at the VA	21-45	TK/BM	
Data will be de-identified	33-45	TK/BM	
Data will be transferred to NERI	33-45		RR
PHASE III – DATA ANALYSIS & REPORTS			
Conduct Data Analysis			
Analyses will be conducted to address the Specific Aims of the Registry	36-48		RR
Reports and Publication	36-48	TK/BM	RR
Continued Abstraction of Medical Records			
Perform abstraction periodically of VA in/outpatient electronic medical records for PTSD registrants who have return in/outpatient visits to VA medical centers	24-48	TK/BM	RR
Prepare PTSD Database for Future Use			
PTSD Registry database of 1,200 OIF/OEF veterans will be prepared for potential sharing as a public dataset	46-48	TK/BM	RR

TK = Terence Keane; BM = Brian Marx; RR = Raymond Rosen

APPENDIX B: STUDY PROTOCOL

Project VALOR
Veterans' After-Discharge Longitudinal Registry

Principal Investigators:

Terence M. Keane, Ph.D.
Associate Chief of Staff for Research & Development
VA Boston Healthcare System
Director: Behavioral Science Division
National Center for Posttraumatic Stress Disorder

Raymond C. Rosen, Ph.D.
Chief Scientist and Institute Co-Director
New England Research Institutes
Watertown, Massachusetts

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REGISTRY PROTOCOL SYNOPSIS

The Veterans' After-Discharge Longitudinal Registry (Project VALOR) is a 3-year project resulting from a joint effort by researchers at the National Center for PTSD at the Department of Veterans Affairs (VA) Boston Healthcare System (clinical center) and New England Research Institutes, Inc. (NERI) (statistical center). The objective is to develop the first longitudinal registry of combat-exposed men and women with post-traumatic stress disorder (PTSD) and to provide data on the natural history and outcomes associated with PTSD in military service men and women who have utilized the VA health care system. The source population of participants is combat-exposed army or marine veterans from Operation for Enduring Freedom (OEF) or Operation Iraqi Freedom (OIF) who are in the VA health care system database. From this source population, 1200 men and women with PTSD and 400 men and women without PTSD will be invited to participate. Analyses will include longitudinal analyses within the group of 1200 veterans with PTSD, as well as case-control analyses comparing these PTSD-diagnosed veterans to the 400 veterans without PTSD. Identification of the registry sample pool and abstraction of existing military deployment and medical data from existing databases will be conducted under direction of Dr. Han Kang, Senior Scientist of the Environmental Epidemiology Service at the VA. Existing background and service utilization data will be merged with additional data from electronic medical records, a mailed questionnaire, and a structured telephone interview. The questionnaire and interview assess relevant risk factors and comorbidities, quality of life and other clinically-relevant outcomes. The role of NERI as an independent statistical center will ensure scientific integrity of the statistical analyses. The current project (a) builds on existing knowledge of PTSD causes and consequences; (b) will provide an independent, longitudinal registry design to further investigate the natural history and outcomes associated with PTSD; (c) will not only create the registry but also gather data on a comparison group of veterans and conduct case-control analyses; (d) assembles an exceptional group of senior advisors for the scientific advisory committee for the registry; and (e) has at its base a strong partnership between the clinical center (National Center for PTSD at VA Boston) and the statistical center (NERI) for conduct of the registry, dissemination of key findings, and development of potential ancillary studies in the future.

1. INTRODUCTION

1.1. POSTTRAUMATIC STRESS DISORDER (PTSD) DEFINITION & PREVALENCE

Posttraumatic stress disorder (PTSD) is a psychiatric disorder with potentially devastating emotional and interpersonal consequences.[1] PTSD may result from combat exposure or non-combat traumas such as sexual or physical abuse, and exposure to life-threatening risks or disasters. The mechanisms and etiology of PTSD are addressed in a recent review by Keane and Barlow.[2] Common symptoms of PTSD include re-experiencing of traumatic events, avoidance, numbing and hyperarousal reactions, such as insomnia, nightmares and other sleep difficulties. In addition, PTSD sufferers experience "flashback" episodes wherein recurrence of at least a portion of the traumatic event occurs. Extreme distress and avoidance of cues or reminders of the event also occur.

The lifetime prevalence of PTSD is 3-4% in the general population, and the trauma most commonly associated with PTSD in men is combat exposure.[3, 4] Recent evidence from returning Iraqi veterans [5] indicates that the prevalence of PTSD is approximately 10% immediately upon return.[6] The risk of PTSD is elevated more than three-fold for service members exposed to a combat situation.[6-8] Prevalence rates are even higher in some cohorts and may increase over time. For example, in a longitudinal study of Gulf War veterans, the prevalence of PTSD more than doubled between the initial assessment immediately upon return from combat and a follow-up assessment conducted two years later.[9] Despite accumulating evidence of the prevalence and impact of PTSD on active duty soldiers and veterans, major limitations exist in the information available. The creation of a longitudinal registry of a diverse sample of veterans will be of enormous value in addressing current gaps in our understanding of PTSD and associated outcomes.

1.2. VIETNAM VETERANS READJUSTMENT STUDY (NVVRS)

The largest body of epidemiologic data on PTSD is the National Vietnam Veterans Readjustment Study (NVVRS), [10] a congressionally mandated study of post-Vietnam veterans. Interviews were performed using a two stage methodology [11] in which lay interviewers evaluated a representative sample of Vietnam Theater Veterans (VTV; n=1632), Vietnam Era Veterans (VEV; n=716), and a group of civilian controls (n=668). To make the diagnosis of PTSD these investigators relied upon a triangulation approach that utilized information from the diagnostic interviews as well as self-report questionnaires. [12]

More than 15% of VTV males met criteria for current PTSD and 30% met criteria for lifetime PTSD. There were different rates for current PTSD among the various ethnic and racial groups: 13.7% for the white/other group, 20.6% for African Americans, and 27.9% for Hispanics. The differences were largely due to higher levels of combat exposure among the minorities. For women, 9% met criteria for current PTSD and 27% met criteria for lifetime PTSD, likely due to the different roles that women had in the military at that time (primarily nursing and clerical), the different types of stressors to which they were exposed, and to their higher educational levels. In a study of PTSD among female Vietnam veterans who served as nurses, war trauma and sexual trauma contributed about equally to the development of PTSD. [13] Other studies have documented high rates of family violence and social adjustment problems in veterans with PTSD. [1, 14] Sleep disturbances, including frequent nightmares and sleep onset insomnia, were

more prevalent in Vietnam theater veterans; frequent nightmares occurred almost exclusively in veterans with PTSD, and combat exposure was highly associated with nightmares. [15] Hispanic Vietnam veterans, especially those who are Puerto Rican, had a higher probability of experiencing PTSD and significantly more severe PTSD symptoms than non-minority veterans. [16] In each of these studies, VTV prevalence rates were five to ten times higher than those found for the VEV and the civilians. These findings suggested that there were approximately 479,000 cases of current PTSD and nearly 1 million cases of lifetime PTSD in America stemming from the Vietnam War. Controversy about the accuracy and implications of these PTSD rates in the NVVRS continues to the present. [8, 17-20] Despite the controversy, public and professional awareness of the problem of PTSD was greatly increased by the publication of results from the NVVRS.

1.3. OIF/OEF STUDIES

More recently, studies by several investigators [6, 21, 22] have reported on the effects of combat exposure on PTSD and related problems in veterans in Operation for Enduring Freedom (OEF) in Afghanistan, and Operation Iraqi Freedom (OIF) in Iraq. In the first study, [21] anonymous surveys were administered to four groups of US. Infantry units (3 Army, 1 Marine Corps Unit), with a total of 2530 soldiers completing the questionnaire prior to deployment, and 3671 completers at 3-4 months post return from combat duty. The rates of PTSD were about 18.0% for Army participants following service in Iraq, 11.5% after service in Afghanistan, and 9.4% prior to deployment to Iraq. [21] Among the post-Iraq deployment group, 16.6% met criteria for PTSD and there were markedly increased rates of disability and health service utilization. [22] Hoge et al.[6] administered the Post-Deployment Health Assessment (PDHA) Questionnaire to all post-deployment service members. [6] A total of 222,620 individuals completed the PDHA survey after deployment from Iraq, along with 16,318 from Enduring Freedom in Afghanistan. Almost 10% of OIF combatants scored positive for 2 or more responses on the PTSD screener, compared to 4.7% for OEF, and 2.1% for soldiers in other locations.

Vasterling et al. [23] gave neuropsychological tests to 654 soldiers prior to and following deployment to Iraq. Results demonstrated that Iraq deployment was associated with neuropsychological alterations on tasks of sustained attention, verbal learning, reaction time, and visual-spatial memory, and with increased negative state affect on measures of confusion and tension. A screening-based estimate of PTSD also suggested that about 12% of the deployed soldiers experienced clinically significant levels of PTSD symptoms upon their return from Iraq. The findings could not be explained by head injury or other medical diagnoses, but instead pointed to a specific pattern of neuropsychological sequelae consistent with an acute stress response.

Other studies of OIF/OEF soldiers have been reported by Grieger et al.[24] and Seal. [25] Although overall rates of PTSD were not as high in battle-injured soldiers, PTSD with comorbid depression was observed in approximately 10% of battle-injured soldiers in the study by Grieger et al. [24] Seal et al., [25] have recently reported on a large database (103,788 veterans) of OEF/IEF seen at VA health care facilities. A quarter of these individuals received a psychiatric diagnosis; among those with psychiatric diagnoses, more than half received multiple diagnoses, including PTSD. [25] Overall, these studies confirm the high rates of PTSD and PTSD-related symptoms in

post-deployment OIF/OEF soldiers. However, these studies provide little information regarding outcomes or progression over time in these individuals. Thus far, the trajectories of change and specific predictors of relapse or recovery have not been investigated.

1.4. CURRENT MODELS OF ETIOLOGY AND DISEASE PROGRESSION

Current conceptual models emphasize three classes of variables as major risk factors for PTSD: 1) pre-existing factors in the individual, such as family psychopathology and socio-demographic factors; 2) the severity of the traumatic event and surrounding circumstances, and 3) events that took place after the trauma, such as social and occupational support. [26, 27] Although post-trauma factors are not "causal", they may increase understanding of the delayed onset of PTSD in some individuals. An analysis of the relationships between pre-war factors, war zone stress and PTSD symptomatology in NVVRS revealed that for men, a previous history of trauma directly predicted PTSD, and also interacted with war-zone stressors to worsen PTSD symptoms in veterans exposed to high level of combat.[27] War zone factors were of primary importance for men, while women were more affected by post-trauma resilience and recovery factors. The term recovery is used to describe a trajectory in which an individual's normal functioning gives way to symptoms of depression or PTSD for at least several months, followed by gradual return to pre-trauma function; resilience is defined as the ability to maintain stability in the face of disruptive or traumatic events. [28] A model using both recovery and resilience variables to mediate the relationship between trauma and PTSD has been shown to have the highest predictive value for both male and female Vietnam veterans. [28,29]

Evidence suggests that PTSD evolves over time, although the course of progression, natural history and consequences of the disorder are not well understood. Although treatments for PTSD may offer symptomatic relief in the short-term, symptoms of PTSD frequently persist and become chronic, particularly in those patients lacking adequate long-term emotional or social support.[30] Longitudinal research in diverse populations is urgently needed to assess long-term outcomes associated with PTSD and the impact of the disorder on veterans, their families and the mental health care system.

1.5. INTERVENTIONS AND OUTCOMES: LIMITATIONS OF CLINICAL TRIALS

Interventions for PTSD include pharmacological treatment (e.g., benzodiazepines, serotonin reuptake inhibitors), and cognitive behavioral therapies. Randomized clinical trials (RCTs) have been conducted to assess the efficacy of available treatment approaches, including cognitive-behavioral therapy (e.g., prolonged exposure, present-centered therapy), eye movement desensitization reprocessing, acupuncture and various psychotropic medications (e.g., sertraline, paroxetine, fluoxetine).[31-38] Although RCTs remain the cornerstone for treatment efficacy and safety evaluation, their generalizability and relevance beyond the trial setting is a source of increasing concern.[39] These trials may not provide reliable outcomes data in a broad population of patients in non-research settings; most trials are of relatively short duration, and most studies discontinue follow-up at 24 weeks. Furthermore, RCTs are limited by the patient population selected and highly controlled environment of the clinical trial.[31, 33] Combination treatments and treatment sequencing are virtually untested, although in reality, patients are likely to undergo multiple treatment regimens. Moreover, treatment acceptability and satisfaction data are lacking, in addition to data on long-term outcomes and costs of treatment.

1.6. KNOWLEDGE GAPS AND POTENTIAL BENEFITS OF A REGISTRY

These knowledge gaps in the current system present a major challenge to effective planning and service delivery efforts. In addressing these needs, a registry can provide a complementary perspective to results obtained from RCTs and current observational studies, particularly in regard to service utilization and psychosocial outcomes. The registry facilitates planning by providing long-term data on these outcomes, and is a major resource for ancillary studies on specific topics of interest. An additional advantage of a registry is that the duration of the study and sample size may be increased over time, as resources and needs determine.

1.7. RATIONALE FOR A REGISTRY

A well-designed registry is a major source of knowledge regarding disease progression and the natural history of common physical and mental health disorders. The AHRQ Guide for registries,[40] a recent government publication, notes that when properly designed and implemented, registries offer unique information regarding disease impact and outcomes not addressed by randomized trials or retrospective surveys. As described by the AHRQ guide,[40] a patient registry provides "a real-world view of clinical practice, patient outcomes, safety and comparative effectiveness, and serves a number of evidence development and decision-making purposes." Major benefits of the PTSD registry include:

MULTIPLE ADVANTAGES OF REGISTRIES

- Natural History – (progression and remission)
- Health Services Utilization – (costs and benefits)
- Safety Considerations – (monitoring adverse events)
- Ancillary Observational Studies – (case-control)
- Assembled Population for Clinical Trials – (rapid start-up)
- Overall Cost Efficiency – (multiple endpoints)
- Real World Results – (external validity)
- Complementary Outcomes to Clinical Trials

- Evaluation of natural history and long-term outcomes of PTSD across treatments, treatment settings and practitioners, using cost-efficient methods and economies of scale
- Documentation of health resource utilization and development of a database that is an ideal resource for health services planning and policy
- Formation of a potential cohort of participants for ancillary studies, ranging from genomic influences to quality of life and psychosocial outcomes, as well as future clinical trials
- Creation of a representative sample of PTSD patients who use the VA medical system, available for use in epidemiologic studies, particularly for comparisons with active duty, and other veteran or civilian populations (a comparison study is embedded in the current project)
- Utility to major stakeholders, including clinicians, patient advocacy groups and health policy planners.
- Publications and dissemination of the registry results to provide a representative perspective of what is achieved in actual current care settings, thereby augmenting outcomes data from clinical trials

2. REGISTRY OBJECTIVES

The overall objective of this project is to develop the first longitudinal registry of combat-exposed men and women with PTSD. This registry will provide essential data on the natural history and outcomes associated with PTSD in military service men and women who have utilized the Department of Veterans Affairs (VA) health care system. An additional goal of this project is to determine risk factors for PTSD among combat-exposed service men and women (by incorporating a combat-exposed non-PTSD group of veterans into analyses). Thus, the registry will allow an evaluation of current theoretical models of symptom development in a large sample of service men and women who utilize the VA medical system.

3. SPECIFIC AIMS

This project is designed to address a range of research questions within the registry itself, as well as in comparisons with a non-registry study group. The theoretical model underlying this research is presented in Figure 2.0. Specific aims of this project can be divided into the following two research areas:

3.1. EPIDEMIOLOGY OF PTSD

Aim 1. To describe the natural history of PTSD using the long-term psychosocial, medical and quality of life outcomes associated with the disorder, and to evaluate disparities by sociodemographic, military and post-deployment factors.

Aim 2. To identify risk factors (e.g., demographic, social support, socioeconomic resources) and comorbidities (e.g., other mental health disorders, neurological conditions) of PTSD, by comparing PTSD patients to a "control" group of veterans without PTSD.

3.2. PTSD HEALTH SERVICES

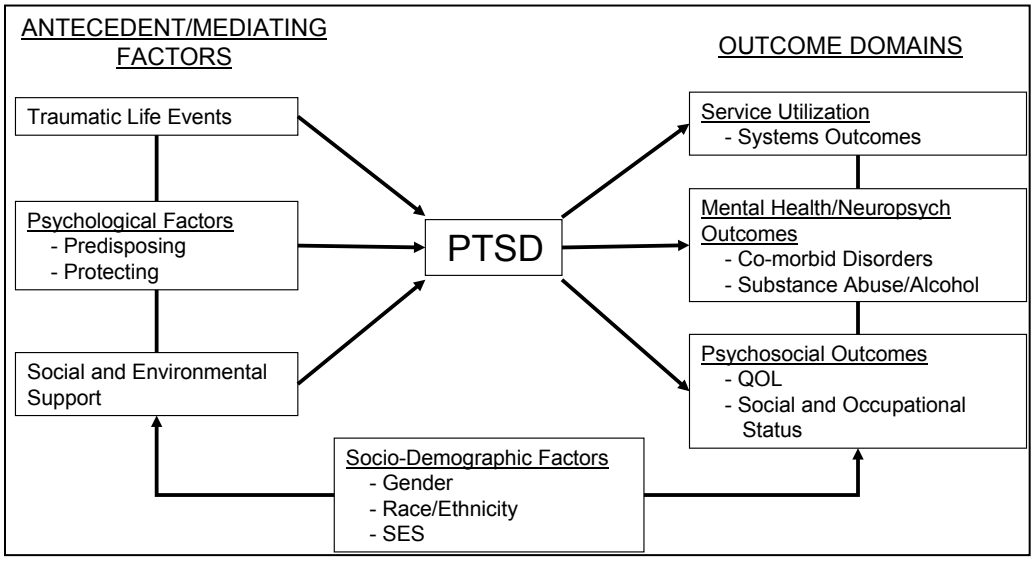
Aim 3. To identify treatment approaches through time.

Aim 4. To establish the prevalence of PTSD in a comparison group of service men and women who did not have the PTSD diagnosis in the medical record, and to identify risk factors for a missed PTSD diagnosis.

Aim 5. To assess current referral and health care utilization patterns among patients with PTSD, and also to compare their health care utilization to a group of veterans without PTSD.

Aim 6. To develop a large database of servicemen and women with PTSD and network of treatment sites that are potentially available for further observational and interventional studies, as well as concurrent ancillary studies.

Figure 2.0 PTSD Research Model



4. RESEARCH STRATEGY

4.1. OVERVIEW

This project designs and implements a VA system-wide patient registry to obtain a registry database of combat veterans from recent military operations in Iraq and Afghanistan who have utilized the VA medical system and have received a diagnosis of PTSD. As defined by the AHRQ and World Health Organization,[40] "a patient registry is an organized system that uses observational study methods to collect uniform data (clinical and other) to evaluate a specific outcome for a population defined by a particular disease, condition, or exposure, and that serves one or more predetermined scientific, clinical, or policy purposes." The patient registry *database* is defined as a file (or files) derived from the registry. A patient-based database is necessary to allow direct access to information on diagnoses of interest and treatment outcomes, as well as to longitudinally track follow-up visits, progress, and treatment courses.

In contrast to these criteria, the database of utilizers of the VA healthcare system is structured by chronological in-patient and out-patient visits, rather than unique patient identifiers or diagnoses. Thus, with the existing database, there is no readily accessible way to identify unique patients with PTSD or to assess their longitudinal outcomes and utilization of VA healthcare. Therefore, a fundamental objective of this project is to establish a registry of patients with PTSD from the existing VA utilization database. Electronic medical records such as those in the VA database are increasingly important sources of data, but data must be extracted, transformed into registry format, and loaded into the registry, where they will reside in the registry database, together with registry-specific data that is imported from other sources.[40] The other sources of data for the PTSD registry will be the OIF/OEF veteran roster (particularly for military specific data, e.g., branch, rank, deployment dates, etc.) and, in Phase III, the self-administered questionnaire and telephone interview (described in Section 4.5.1).

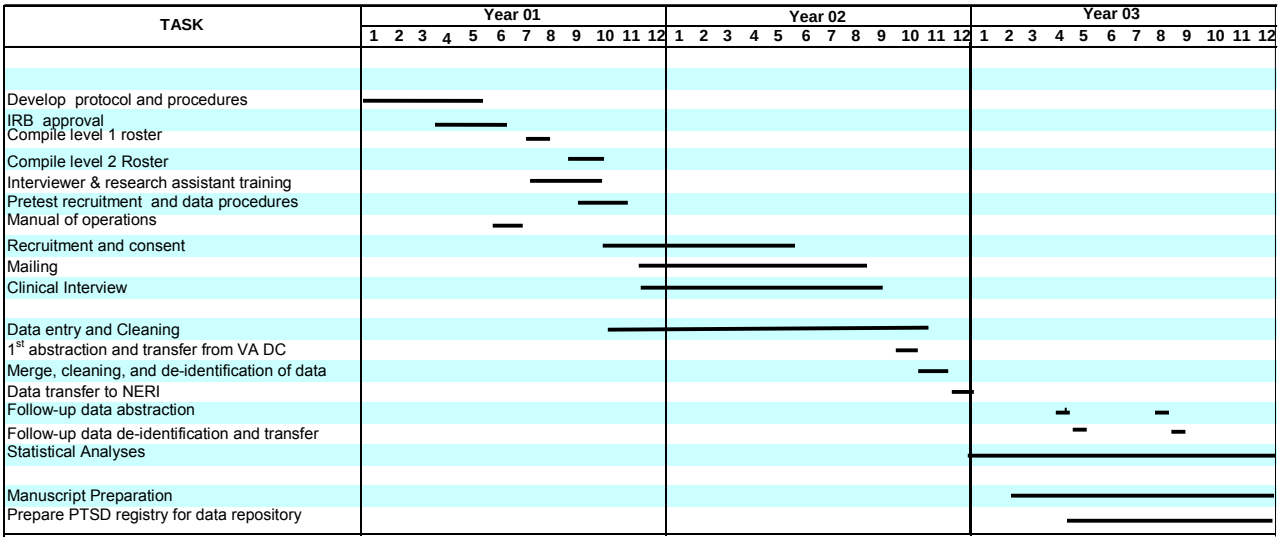
In addition to the PTSD registry, we will collect information on a comparison group of OIF/OEF-era veterans to conduct nested case control studies within the general VA health care utilization database. The comparison group will include combat veterans who have not received a diagnosis of PTSD (as detailed in Section 4.3.2). This group will be used in analyses to identify risk factors for PTSD (Aim 3). Thus, Project VALOR will create a PTSD registry from the VA database to assess the natural history of PTSD in combat veterans from OIF/OEF and also conduct case-control studies nested within the VA database. The case-control comparisons will be used to evaluate key hypotheses related to the specific aims of the overall project.

4.2. PROJECT TIMELINE

The project is to be conducted over a 3-year period (**Figure 4.2**). The study uses both existing data abstracted from the VA military and medical record database and prospectively collected data, collected by two additional data transfers, a mailed questionnaire, and a structured telephone interview. During Year 01 (Y01), upon obtaining all IRB approvals, a manual of operations will be created (months 6-7), and the rosters of potential participants will be compiled (Level 1 roster: months 7-8, Level 2 roster, months 9-10). Meanwhile, training of interviewer and research assistant staff will occur. Also in Y01 (months 9-11), the procedures for contacting participants for recruitment and study assessments, the data abstraction procedures, the de-identification program and the data transfer for statistical analyses, will be pre-tested. Full

recruitment and contacting of participants will begin in Y01 (month 10) and continue through Y02 (month 9). Data entry will occur concurrently. The first abstraction of data from military and medical records will occur upon completion of the study mailing and interview for all participants (Y02, months 9-10). The data will be merged, cleaned, and de-identified at the Boston VA (Y02 months 10-11), in preparation for transfer to NERI (Y02 month 12) for statistical analyses and manuscript preparation (Y03 months 1-12). The PTSD registry database will be updated up to two times as new VA electronic medical records for registry participants appear in Y03 (tentatively scheduled for months 4 and 8), thereby capturing the trajectory of PTSD patients.

Figure 4.2. Registry Timeline



4.3. PARTICIPANTS AND SAMPLING STRATEGY

The source population of participants is combat-exposed OIF/OEF army or marine veterans who are in the VA health care system database. From this source population, 1200 men and women with PTSD (using the selection algorithm below) and 400 men and women without PTSD will undergo informed consent procedure to participate in the Registry study. The VA health administrative database rigorously records all in-patient and out-patient visits, and includes basic information regarding each visit, such as the patient name, date of birth, gender, and ICD-9 diagnostic codes to describe the purpose of the visit.

4.3.1. Inclusion Criteria for PTSD Registry Group

The following criteria must be met for potential veterans to be included in the PTSD group.

- OIF/OEF army or marine veteran (deployed to combat)
- In the VA health care system database
- Not currently participating in a clinical (intervention) trial
- Mental health evaluation/assessment conducted at least twice (on different days) in the past 12 months; these evaluations are coded in the electronic medical record as one or more of the following ("evaluation and management" services

are visits and consultations furnished by physicians and including medical management):

- 90801- mental health assessment
- 90804- 20-25 min therapy
- 90805- 20-25 min therapy with evaluation & management
- 90806- 45-50 min therapy
- 90807- 45-50 min therapy with evaluation & management
- 90808 - 75-80 min therapy
- 90809- 75-80 min therapy with evaluation & management
- 90853- group therapy

- PTSD diagnosis coded (ICD9-309.81) within the past 12 months in the electronic medical record
  - PTSD diagnosis code can be the primary or secondary diagnosis
  - PTSD diagnosis code appears at least once subsequent to the date and time of the mental health evaluation coding, in association with at least one of the later mental health evaluation codes.

4.3.2. Inclusion Criteria for Non-PTSD Study Group

The following criteria must be met for potential veterans to be included in the non-PTSD study group.

- OIF/OEF army or marine veteran (deployed to combat)
- In the VA health care system database
- Not currently participating in a clinical (intervention) research trial
- Mental health evaluation/assessment conducted in the past 12 months; this evaluation is coded in the electronic medical record as in the criteria in Section 4.3.1 for the PTSD Registry group
- No record of any PTSD diagnosis (ICD9-309.81) in the VA electronic medical record

4.3.3. Creation of the Registry Database: Selection and Contact of Eligible Participants

During Phase II, a roster of potential participants for the PTSD Registry and the non-PTSD study group will be created using the inclusion criteria specified in Sections 4.3.1 and 4.3.2 above. The DC VA project team will create the roster by matching unique OIF/OEF veterans who have been separated from active duty with VA inpatient and outpatient databases. This initial roster, referred to as the **Level 1 Roster**, will include approximately 3000 veterans. Veterans on the Level 1 Roster will be sent an initial ‘opt-out’ letter that introduces the study and asks the veteran to indicate if he/she would like to be contacted further about the study or not. Veterans respond using the prepaid response envelope enclosed with the letter. Those who opt out of any further contact with the initial opt-out letter will be removed from the list of potential participants. A second follow-up ‘opt-out’ letter will be mailed to Level 1 Roster participants who do not respond to the initial opt-out letter. The second letter will again ask the veteran to indicate if he/she would like to be contacted about the study or not using the prepaid response envelope. Those who opt-out of any further contact with the second letter will be dropped from the

potential participant list, and the resulting narrowed list is referred to as the **Level 2 Roster**. The Level 2 Roster lists veterans who may be contacted for informed consent (as described in Section 4.4) to be part of the final 1600 total participants. The procedures for selecting the rosters and final participants are outlined below. A second Level 1 Roster of 6000 veterans was created in November 2010, to increase the number of potential participants available for study. The contact procedures were the same as those described for the initial Level 1 Roster.

(1) The DC VA project team will create a data file of approximately 3000 veterans meeting initial eligibility criteria and share it with the Boston VA project staff using the secure VA network. This list will be properly encrypted and password protected as required by the VA data security and information protection policies, described in VHA handbook 1605.1, VA Directive 6500, and VHA Handbook 1200.5.

(2) The Boston VA project team will mail an 'opt-out' letter to the ~3000 Level I potential participants; the letter, which will be signed by project investigators Dr. Keane and Dr. Kang, will briefly describe the study and note that the recipient can choose to be contacted further about the study, or not be contacted further regarding the study by returning a pre-addressed and postage-paid response letter.

(3) Level I potential participants will have 30 days to mail back the opt-out letter to Boston VA project team for processing. The opt-out period will begin on the day the last recruitment letter is mailed out.

(4) After the initial 30 day wait period is over, the Boston VA project team will remove the potential participants who indicated they did not want to be contacted about the study from the Level 1 roster. Those potential participants who indicated interest in the study will become part of the Level 2 roster. The remaining potential participants who did not respond to the initial opt-out letter will be mailed a second, follow-up opt-out letter describing the study and asking the potential participant to indicate if he/she would like to be contacted further about the study, or not be contacted further regarding the study by returning the prepaid envelope enclosed with the letter.

(5) Potential participants will have 14 days to mail back the second opt-out letter to Boston VA for processing. The second opt-out period will begin on the day the last follow-up opt-out letter is mailed out. After the second wait period is over, Boston VA project staff will create the Level 2 Roster, which is a narrowed list of potential participants, excluding all those indicated on either of the 'opt-out' post letters that they did not want to be contacted further about the study.

(6) VA Boston study staff will contact Level 2 potential participants via phone to provide more details about the study, assess the inclusion requirement of not currently participating in a clinical (intervention) research trial, and begin the informed consent process (detailed in Section 4.3.4). Those who consent will be included as participants of the study. Contact information will be recorded for participants at this time. All calls will be recorded in a password protected contact log maintained by study staff.

4.3.4. Potential Risks and Benefits of Participation

As the Registry study has an observational design, with no interventions, there are minimal foreseeable risks or benefits for participants.

The primary risk for participants is the time and inconvenience that may result from participating in the study. Due to the sensitive nature of the subject matter and psychological symptoms discussed during the interview, participants may also experience some mild transient distress when answering questions about their traumatic experiences. Highly trained clinical psychologists who specialize in PTSD will conduct the interviews to minimize any such risks to participants. Additionally, participants will be provided with emergency contact information, as well as instructions about what to do should they experience distress during or after participation.

4.3.5. Compensation to Participants

Upon the completion of the online SAQ or return of the mailed forms (self-administered questionnaires) and the completion of the telephone interview, participants will be compensated $50. Participants who complete three additional questionnaires added as part of a DSM-V substudy – the PTSD Checklist (PCL), the National Stressful Events Survey, and a brief demographics questionnaire – will be reimbursed an additional $15. A check, issued by the Boston Veterans Affairs Research Institute (BVARI), will be mailed to them at the address of their choosing. If participants complete half of the SAQ they will be paid $10.

4.4. INFORMED CONSENT AND HIPAA PROCEDURES

VA Boston study staff will telephone Level 2 potential participants to follow-up on the information in the opt-out letter and formally invite the veteran to participate in the study. This study uses verbal, not written, informed consent and Health Insurance Portability and Accountability Act (HIPAA) release procedures. A trained research assistant will administer the call using the Project VALOR informed consent and HIPAA release script (Appendix B). If the potential participant is willing to enroll in the study, the research assistant will read the informed consent statement verbatim as directed in the informed consent script. If the potential participant has questions at any time during the reading of the consent statement, the research assistant will stop to answer the potential participant's questions. It is acceptable to depart from the exact consent statement language in order to facilitate the potential participant's understanding of the consent statement. Once verbal consent has been obtained for the study, the research assistant will read the HIPAA release statement to obtain authorization for records release. This will then be followed by the future contact consent statement. The research assistant will document all verbal consents and refusals on the participant's informed consent script form. The participant's informed consent script form will function as a record of the entire consent process, and it will be kept in the participant's file (details on file storage and security are in Section 4.9). A copy of the informed consent and authorization information that was agreed to over the phone will be emailed to the participant for his/her records. If the participant does not have access to the internet, a paper copy of the consent and HIPAA authorization will be mailed to the participant. The research assistant will then set up a time and date for the telephone interview. The research assistant will provide the participant with the name of the clinical psychologist who will be interviewing them. Lastly, the research assistant will confirm the address and contact information of the participant, as well as details on his/her deployment history (form available in Appendix E).

Those who provided informed consent will be told that the questionnaires will be administered using an internet based survey website (see section 4.5.2 for details). Once the participant has provided consent, and a date for the phone interview has been set, the participant will be given a username to use to login to the secure website. The password for the secure website and the URL will be emailed to the participant. Participants who do not have access to the internet or who don't feel comfortable using the internet will be mailed the paper self administered questionnaire (SAQ). Should the participant choose the paper option, the packet with the study questionnaire forms will be mailed to the participant, along with the informed consent and HIPAA authorization statements, and a self-addressed postage-paid envelope (details on study instruments are in Section 4.5). A list of the items enclosed in this packet appears in **Table 4.4**.

Those who provided informed consent will be told that the questionnaires will be administered using an internet based survey website (see section 4.5.2 for details). Once the participant has provided consent, and a date for the phone interview has been set, the participant will be given a username to use to login to the secure website. The password for the secure website and the URL will be emailed to the participant. Participants who do not have access to the internet or who don't feel comfortable using the internet will be mailed the paper self administered questionnaire (SAQ). Should the participant choose the paper option, the packet with the study questionnaire forms will be mailed to the participant, along with the informed consent and HIPAA authorization statements, and a self-addressed postage-paid envelope (details on study instruments are in Section 4.5). A list of the items enclosed in this packet appears in **Table 4.4**. If VA Boston does not show the participant as having completed the online questionnaires 7 days prior to the participant's scheduled phone interview, a trained research assistant will call to inquire if the participant still wishes to participate in the study and if so, remind the participant about the online survey and the upcoming phone interview (script available in appendix C). If the participant chose to use the paper option and VA Boston has not received the participant's completed questionnaires within 30 business days after its mailing, a trained research assistant will call to confirm their receipt of the packet and inquire as to whether the individual is planning to participate (script available in Appendix C). Up to 8 attempts will be made to contact consented individuals before deeming the individual administratively withdrawn from the study.

Table 4.4. Enclosures in the Mailing to Consented Participants (see Appendices for complete documents)

• **Instruction Letter**: This will include instructions for the participants on how to complete the measures as well as instructions for returning the packet. The letter will also contain investigator contact information for questions. *This letter will only go to participants who request the paper SAQ.
• **Consent and HIPAA Release Statement**: As informed consent and authorization of HIPAA release is obtained by telephone, this is a document for the participant to keep, containing all the information discussed on the informed consent phone call. (Appendix D)
• **Contact and Deployment Information Form**: Updates to name, address, and phone number of participant will be collected on this form. (Appendix E)

4.5. STUDY MEASURES AND INSTRUMENTS

4.5.1. Assessment Methods

The Registry uses an observational study design; thus no treatments are assigned to participants. Rather, details on participants' medical history and PTSD-related factors will be collected through medical records abstraction up to 3 times during the course of the two-year study, and additional information will be collected via a secure internet-based survey and a one-time telephone-administered interview. Participants who do not have access to the internet will be mailed the questionnaires. The questionnaires and interview will be used to fill gaps in the electronic medical record by assessing factors such as exposure to traumatic events, comorbid symptoms of anxiety or depression, probable substance abuse and alcoholism, social and occupational status, and overall quality of life, as well as confirming the presence or absence of PTSD. Recognizing the limitations of self-report data, each of these domains will be assessed by means of brief, validated scales and measure current symptoms and outcomes (**Table 4.5**; full contents of assessment measures are available in Appendix F and G). The assessment measures may be modified based on results of the pre-testing of the study instruments (described in Section 4.5.4). The specific assessment measures included are selected based on psychometric criteria (sensitivity, specificity), public health and policy relevance, and level of burden for the respondent.

Table 4.5. Project VALOR Study Domains and Assessment Methods

Domain	Assessment Measure(s)	Project VALOR Administration	References
Suicidal Ideation	Mini-International Neuropsychiatric Interview (M.I.N.I.) suicide module	Telephone Interview	[41]
PTSD	Structured Clinical Interview for DSM-IV (SCID-IV) PTSD module	Telephone Interview	[42, 43]
Self-Assessed Effects of Military Experiences on Post-discharge Life	Two new open-ended question (qualitative data): "How have your military experiences affected your [ability to do work] *or* [personal relationships] after you came home?"	Telephone Interview	-
Traumatic Brain Injury	Questionnaire	Telephone Interview	[44]
Combat Exposure	DRRI Section I (Combat Experiences) and Section J (Post-Battle Experiences)	Website survey/ mailed paper form	[45]
Quality of Life	SF-12v2	Website survey/ mailed paper form	[46]
Sleep	Jenkins Sleep Questionnaire	Website survey/ mailed paper form	[47]
Absenteeism	World Health Organization Health and Work Performance Questionnaire (HPQ)	Website survey/ mailed paper form	[48]
Life Stressors/Trauma	Life Events Checklist (LEC)	Website survey/ mailed paper form	[49]

Social Support	Deployment Risk and Resilience Inventory (DRRI) Section L (Post-deployment support)	Website survey/ mailed paper form	[45]
Mental Health Disorders and Stresses (including Depression, Anxiety, Panic, Somatoform Disorder)	▪ Prime-MD Patient Health Questionnaire (PHQ) ▪ New measure on PTSD-related psychosocial impairment	Website survey/ mailed paper form	[50]
Alcohol/Drug Use	▪ Alcohol Use Disorder Identification Test (AUDIT) ▪ Two-Item Conjoint Screen (TICS)	Website survey/ mailed paper form	▪ AUDIT [51, 52] ▪ TICS [53]
Anger/Hostility	Dimensions of Anger Reactions, revised short form (DAR-5)	Website survey/ mailed paper form	[54, 55]
Treatment Utilization	New Questions	Website survey/ mailed paper form	-
PTSD Related Functional Impairment	Multidimensional Impairment Scale (MIS)	Website survey/ mailed paper form	(currently in development at Boston VA)
PTSD assessment for DSM-V substudy	PTSD Checklist (PCL)	Website survey/ mailed paper form	[56, 57]
DSM-V substudy	National Stressful Events Survey	Website survey/ mailed paper form	[58]
DSM-V substudy	Brief demographics questionnaire	Website survey/ mailed paper form	-

4.5.2. Online Data Collection Procedure & Data Safety

Participants will complete the self administered questionnaire (SAQ) using a secure online survey hosted by psychdata.com. PsychData is a web-based company that specializes in internet-based social science research (see section 4.5.2B for information about PsychData and its security features***). No identifying information will be collected using the online SAQ. This includes removal of the subject's IP address. Participant responses will be identified only by the subject ID number provided to them as their username.*** All participants who complete a survey at PsychData are automatically assigned an internal number called the Respondent ID Number. This number will not be the same as the Participant's project VALOR study ID number. It will, however, be used to generate confirmation that the participant completed the online SAQ. Each participant's data from the online survey will be linked to his/her data in the VA database by the project valor study id number provided to the subject at the time of informed consent. Programming the online SAQ will be done by the doctoral level project manager at VA Boston. The online SAQ will be a replica of the paper SAQ (see appendix F). The project manager will be responsible for overseeing the online data collection including error testing, data monitoring, and data transfer to the SPSS database. The doctoral level project manager will then train the study research assistants how to use the site.

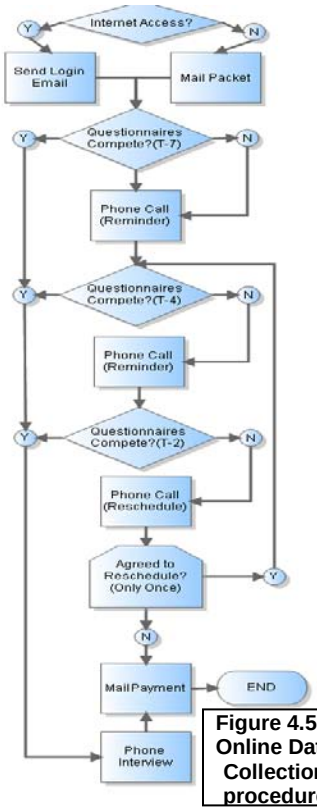


Figure 4.5.2 Online Data Collection procedure

A. Online SAQ administration procedure

1. After the participant has provided consent the interview date will be set for approximately two weeks from the date of the consent phone call. The trained research assistant will explain the online SAQ procedure to the participant and provide the participant with his or her study ID number. The study ID will be the participant's username for the website. The subject's study ID number will only be given to the participant over the phone.
2. The participant will be sent an email on the day of the consent phone call containing the link to the online SAQ at psychdata.com as well as the password for the website (see appendix H for details). The email will also contain a reminder about the date of the interview and instructions about how to login and what to expect while completing the survey. Additionally, the email will contain study staff contact information should the participant forget his or her username and an emergency number.
3. Once the participant has the password and the instruction email the participant will have approximately two weeks to complete the questionnaires before the phone interview.
4. Seven days prior to the participant's scheduled interview date the VA Boston research assistants will check the status of the participant's online SAQ. If the participant has not begun the online SAQ, or has not completed it, the research assistant will call the participant to check in, remind the participant that he/she needs to complete the online SAQ prior to the interview and ask the participant if he/she is still interested in completing the study (see **appendix C** for the check in call script).

   If the participant received the initial reminder call, the research assistant will check the status of the participant's online SAQ again 4 days prior to the participant's scheduled interview. If the online SAQ is not yet complete, the research assistant will call the participant with a second reminder call.
5. If the participant received the first and second reminder call, the research assistant will check the status of the participant's online SAQ 2 days prior to the scheduled interview date. If the online SAQ is not complete, the participant will be called and asked to reschedule the phone interview (see **appendix C** for script).
6. If the participant wants to reschedule the interview and complete the study, the interview will be scheduled approximately a week from the original interview date.
7. Once the subject completes the online SAQ the data will be downloaded to SPSS and a paper copy will be printed from PsychData for the participant's study file. After the participant's responses have been downloaded into the SPSS database and the paper survey has been retrieved, the participant's record will be erased from the PsychData server. The progress of participants will be closely monitored to ensure that each subject record is erased as quickly as possible.

B. Website Company Information & Data Safety

PsychData is a professionally developed and maintained web-based company specifically geared toward internet-based social science research. The company uses parent-level, centralized database architecture and strict security policies and procedures to meet and exceed industry standards for internet security.

1. Technology

PsychData uses a redundant, high bandwith, private transport network. This network has demonstrated 99.999% availability, which means that the network will be down no more than 5 minutes in one year. PsychData servers are housed in a secure data facility that is monitored 24 hours 7 days a week by network operations professionals for all aspects of operational security. Biometric/intrusion sensors, card readers, pin numbers, and environmental sensors are used to insure server integrity and safety. Redundant HVAC systems ensure an optimized operational environment.

2. Data Safety and Security

All surveys are accessed and completed in a Secure Survey Environment (SSE)

All survey pages are constructed such that a completed survey cannot be viewed by simply pressing the "Back" button (thus greatly reducing the chance that someone could "back up" to see previously entered data).

The SSE incorporates additional security measures to ensure that a participant's responses are not retrievable from their computer. First, all survey pages are entirely dynamic and database-generated (instead of static web pages that could be stored by the participant's computer). Second, all surveys have redundant server-side code to ensure that they always load directly from our server and not from a prior cached version. Finally, upon completion of the survey, the survey window itself automatically closes and disappears eliminating temporary history files associated with that survey.

Data security during Transmission

All surveys hosted with PsychData are encrypted using 128-bit SSL Technology (Secure Socket Layer) that is equivalent to the industry standard for securely transmitting credit card information over the Internet. This technology encrypts BOTH the questions displayed to the participants and their responses. Thus, all responses are instantly encrypted and remain so until they are received at the PsychData database. Interception of data when it is being transmitted between the Internet browser (i.e., Internet Explorer or Netscape Navigator) and the PsychData database is HIGHLY unlikely (consider the motivations of a person attempting to intercept research data over the internet vs. papers stored in an office vs. credit card information). However, should interception of encrypted data occur, that data could not be decoded without the unique encryption key that is held only by PsychData.

Safety and Control of Stored Data

Once research data is stored on a PsychData server, it is held in an isolated database ***that can only be accessed by a researcher with the correct username and password. PsychData employees do NOT examine customer data unless***

requested to do so by the account owner; additionally, those employees are trained in the ethics of research involving human subjects. The researcher has full control over their data including the ability to delete all data at the completion of their survey. All data stored at PsychData is backed up on a daily basis, held in a tightly secured facility and typically overwritten after seven days. Therefore, once a user has deleted their data, it will be permanently deleted from our backups in about one week.

IP Addresses

An IP address is a unique identifying number used to identify computers connected to the Internet. An IP address might be static (i.e., always refer to one institution's server), dynamic (assigned upon connection), or pooled (a group of servers share one or more IP addresses). IP addresses may also change multiple times during the same connection - for example, the IP address of AOL users may change multiple times per minute. An IP address generally will represent either an institution (i.e. a university or large company) or an Internet Service Provider (i.e. AOL or an ISP serving one or more communities). ***Project VALOR will EXCLUDE all participant IP addresses.***

Unique Respondent Number

All participants who complete a survey at PsychData are automatically assigned an internal number called the Respondent ID Number. This number will not be the same as the Participant's project VALOR study ID number. It will, however, be used to generate confirmation that the participant completed the online SAQ.

4.5.3. Assessment of Unstable/ Untreated Veterans and Safety Plan

In advance of each telephone interview, the assessor will be provided with a list of resources, including VA/DoD healthcare facilities and local police contact information for the area in which the participant lives. The assessor will thus be prepared to use any of these resources in the event that the participant demonstrates safety risk behaviors.

Assessors will administer and score the Mini-International Neuropsychiatric Interview (M.I.N.I.) suicide module prior to administering the Structured Clinical Interview for DSM-IV (SCID-IV) PTSD module during the telephone interview. Regardless of score on the MINI suicide module, for any participant thought to be at imminent risk, the assessor will contact local VA or DoD facility and inform the mental health provider on call or suicide prevention coordinator, as appropriate. The assessor will administer the further risk assessment measure as necessary to gain additional information regarding risk and protective factors and suicidal ideation risk level. Procedures for the MINI results are:

Low suicide risk (0-8 points on MINI suicide module) and no participant expression of suicidal ideation in other components of the interview:

- Assessor will follow judgment in whether to provide follow-up.
- If participant is mildly symptomatic or distressed, the assessor will:

1) Perform a "check out" with the participant at the conclusion of the interview.
2) Provide the participant with the VA Suicide Hotline number (1-800-273-TALK), number for local VA/DoD.

Moderate suicide risk (9-16 points on MINI suicide module)
The assessor will:

1) Provide the participant with the VA Suicide Hotline number (1-800-273-TALK)
2) Provide the participant with local VA/DOD contact information
3) Offer to provide local treatment referrals within the next 24 hours
4) Offer to contact participant's mental health provider (e.g., therapist, psychiatrist)
5) Take steps to reduce participant risk:

- Ask participant to remove weapons/medications from his/her access

4) Help participant identify important protective factors:

- Religious beliefs
- Dependent children
- Belief in treatment
- Future oriented goals
- Social supports
- The assessor will follow judgment in whether to continue with SCID.

High suicide risk without imminent risk (>= 17 points on MINI suicide module)
The assessor will:

1) Provide VA Suicide Hotline number (1-800-273-TALK)
2) Offer to provide the participant with information on VA/DOD facilities and/or contact the participant's treating clinician, within 24 hours. If the participant identifies barriers to using VA/DOD facilities, the participant will be provided with local/regional resources, including treatment referrals.
3) Follow up with the participant within 24 hours.
4) Mail letter to participant with referral information, including VA Suicide hotline phone number and VA/DOD phone number.

- DO NOT continue current protocol (i.e., do not administer SCID).
- Must follow-up with the participant's treatment provider to confirm that participant is stable before rescheduling the SCID and open-ended interview.

High suicide risk with imminent risk (>= 17 points on the MINI suicide module)
The assessor will:

1) Further assess current SI (plan, means, access, intent)
2) Provide VA Suicide Hotline number (1-800-273-TALK)
3) Contact the VA or DoD suicide prevention coordinator or mental health provider on call, as appropriate, in closest proximity to the participant.
4) If the VA/DoD is unresponsive, contact the local law enforcement and inform them of the participant's emergent psychiatric needs.
5) Follow up with the participant within 24 hours.
6) Follow up with the VA/DoD or local law enforcement within 24 hours to determine the disposition of the case.

- DO NOT continue current protocol (i.e., do not administer SCID).
- Must follow-up with the participant's treatment provider to confirm that participant is stable before rescheduling the SCID and open-ended interview.

An important aspect of the Registry is that it is as inclusive as possible of the entire range of PTSD experiences; thus, it includes high-risk cases when possible, although data on SCID may remain unavailable until high-risk cases are determined to be stable by contact with the treatment provider.

4.5.4. Pretesting the Assessment Methods and Study Instruments

The protocol for obtaining forms and data from potential participants will be tested in a sample of 20 OIF/OEF veterans for feasibility and time to completion over a 2-month period prior to launch of the full study recruitment:

- Month 1: The Boston VA will randomly select 20 veterans from the Level II sample of PTSD patients (described in Section 4.3.3) to contact for the consent phone call (script in Appendix B). Individuals who consent will be emailed a link to the online questionnaire along with an electronic copy of the consent and HIPAA statement or mailed the packet including the self-administered questionnaire and the consent and HIPAA statement, depending on participant preference (described in Sections 4.4 and 4.5, available in Appendix D-G). VA Boston staff will schedule the clinical interview with the participant during the consent phone call.
- Month 2: Consented individuals will have 10 days to complete the online questionnaire. Consented individuals who have not completed the online questionnaire after 7 days will be contacted by phone to confirm their participation in the study and inquire as to whether the individual is planning to complete the questionnaire and interview (script in Appendix C). Up to 8 attempts will be made to contact consented individuals before deeming the individual administratively withdrawn from the study. A trained psychologist from VA Boston will conduct the telephone interview. Once participants complete the interview, they will be compensated $65. Potential risks and benefits of participation in the testing phase are outlined in Section 4.3.4. Pilot participants will be provided with emergency information, contacts, and support per the standing protocol (see Appendix E: Informed Consent Statement).
- The 30-60 minute clinical interview will be administered by a trained clinical psychologist over the telephone within 2 to 4 weeks of the completion of the self administered questionnaire. Boston VA researchers will enter the data from the testing sample into the Boston VA data management system, to allow testing of the de-identification and transfer procedures, as described in Section 4.8.4.
- Results of the testing phase, including statistics on the success rates of contacting participants by phone, the length of time it took for participants to complete the online questionnaire, the number of forms completed, the length of phone interview, and completion rates, will be reported to the project team to assess the feasibility of the protocol. Should problems with any aspects of feasibility arise, the project team will discuss options to improve the process within the scope of the current protocol; any changes to the protocol will follow the approval procedures described in Section 6.4.

4.6. MILITARY AND MEDICAL RECORD DATA ABSTRACTION PROCEDURES

The Registry creation will involve a multi-step data abstraction process, including steps to identify all PTSD diagnoses, to identify unique patients within the PTSD diagnoses, and to identify each additional visit made by each PTSD patient; similar procedures will occur for the non-PTSD comparison group. Investigators at the D.C. VA will abstract military and medical

record data upon complete enrollment of all participants. Additional medical record data not available in the D.C. database will be extracted by research technicians at the Boston VA. To longitudinally follow participants, the medical record abstraction procedures will be repeated up to two more times during the course of the 2-year project.

4.6.1. Data Tables and Variables

Variables that will be abstracted from the existing military and medical record database include demographic factors (age, race/ethnicity, gender, marital status), military service factors (branch, rank, unit component, deployment dates), existence of comorbid conditions (psychiatric, musculoskeletal, traumatic brain injury, or other major medical conditions), utilization of health care (number of visits), comorbid diagnoses, and assigned treatments. All DoD military deployment data abstraction will be conducted by investigators at the D.C. VA. There are two sources of medical record data: (1) VHA Medical SAS Datasets (accessed by researchers at the D.C. VA), and the Veterans Health Information Systems and Technology Architecture (VistA) / Computerized Patient Record System (CPRS) (accessed by researchers at the Boston VA). NERI will not have access to any of these three databases. A list of specific data fields to be abstracted and the source database for each is provided in **Table 4.6**. This list may be modified according to input from the Scientific Advisory Panel and availability of relevant data. The list includes identifiable data in order to allow participant contact. All identifiable data will be removed from the compiled Registry database prior to its transfer for statistical analysis, as described in Section 4.8.

Table 4.6. Data Abstraction: Source Database and Data Fields (Working List)

Source Database	**DOD Defense Manpower Data Center Contingency Tracking System Deployment File**	**VHA Medical SAS Datasets**	**Veterans Health Information Systems and Technology Architecture (VistA), Computerized Patient Record System (CPRS)**
Accessed by	D.C. VA	D.C. VA	Boston VA
Data Fields	SURNAME FORENAME MIDDLE NAME DATE OF BIRTH SEX ETHNIC RACE MARITAL STATUS RANK SERVICE COMPONENT EVENT NAME COUNTRY UNIT IDENTIFICATION CODE EDUCATION LEVEL BASIC ACTIVE SERVICE DATE MAJOR COMMAND CODE	-Diagnoses (ICD-9 codes) • Primary diagnosis • Secondary diagnosis (up to 9) • Dates associated with each diagnosis -Number of appointments within VA medical system • Clinic visited • Diagnosis (up to 10) • Procedure code (indicates procedure and approximate length of appointment	-Positive Screens • Iraq/Afghanistan Screens • Mental Health • Alcohol Use • Tobacco Use • Military sexual trauma • Traumatic brain injury • Learning Needs Assessment • Pain Assessment -Global Assessment of Functioning -Medications (VA & non-VA) • Active • Inactive • Text fields for indication -Consults • Service of consult • Provisional diagnosis -Vital signs/anthropometrics at physical examinations

	HOME OF RECORD STATE PRIMARY MOS DUTY MOS BEGIN DATE END DATE ACTIVE DUTY LOSS DATE ISC TYPE UIC ADDRESS DEATH FLAG (FROM DEERS) HOME MAILING ADDRESS	-Service Connection • Total % • % per condition	• Height, weight, body mass index -Flags/Warning (e.g., Combat, OIF, Military sexual trauma, Suicide)

4.6.2. Pre-testing of Data Abstraction Procedures

The feasibility of the data abstraction will be pre-tested in the sample of up to 20 PTSD veterans described in Section 4.5.4. Upon receipt of a returned opt out letter or completion of the phone consent, the VA Boston staff will pre-test the manual abstraction of medical record data from the VistA CPRS. Should problems arise with abstracting specific data fields or any other aspects of feasibility, the project team will discuss options to solve issues within the scope of the current protocol; any changes to the protocol will follow the approval procedures described in Section 6.4.

4.7. FROM D.C. VA TO BOSTON VA: DATA TRANSFER AND MERGE PROCEDURES

The abstracted medical record data will be sent from the D.C. VA to the Boston VA using the secure file sharing mechanism of the VA. Investigators at the D.C. VA and at the Boston VA will create a file sharing account through the VA network, using the established secure methods. Only key study investigators will have access to this account. Abstracted medical record data will be merged with data from the self-administered questionnaires and interview using subject identifiers. The data merge will take place at the Boston VA.

Because a primary aim of the registry is to track patients longitudinally, medical record data abstraction and transfer from the D.C. VA to the Boston VA will be repeated up to 2 additional times during the study after the initial transfer, which occurs upon completion of recruitment.

4.7.1. Pre-Testing of Data Transfer and Merge Procedures

The feasibility of the data transfer mechanism will be pre-tested in the sample of up to 20 PTSD veterans described in Section 4.5.2. Upon completion of abstraction of their data (as described in Section 4.6.2), the D.C. VA will send the data file to the Boston VA investigators to pretest the transfer and merge procedures. Should problems arise with any aspects of the data transfer or merge, the project team will discuss options to solve the issues within the scope of the current protocol; any changes to the protocol will follow the approval procedures described in Section 6.4.

4.8. FROM BOSTON VA TO NERI: DE-IDENTIFICATION AND TRANSFER OF DATA

4.8.1. De-Identification of Data

As described in Section 4.7, the Boston VA will merge the data generated from the D.C. VA and the data collected from the Boston VA into one file for each participant. Each file will be given a participant identification number unrelated to any of that participant's personal identifying information. To prepare the merged data for transfer from the Boston VA to NERI, all

participant information will be de-identified in accordance with HIPAA regulations. The only institution with access to linkage data allowing linkage between participants' personal identifying information and participants' study identification numbers will be the VA Boston. This linkage and personal identifying information will be securely stored as described in Section 4.9.

The following identifying information about each participant and each participant's relatives, employers, or household members will be removed from the Registry study dataset in preparation for transfer to NERI for statistical analysis and eventual public use access:

a) Names
b) All geographic subdivisions smaller than a State, except for the initial three digits of a zip code if (i) the geographic unit formed by combining all zip codes with the same three initial digits contains more than 20,000 people, and (ii) the initial three digits of a zip code for all such geographic units containing 20,000 or fewer people is changed to 000
c) All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date and date of death and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older
d) Telephone numbers
e) Fax numbers
f) E-Mail addresses
g) Social security numbers
h) Medical record numbers
i) Health plan beneficiary numbers
j) Account numbers
k) Certificate/license numbers
l) Vehicle identifiers and serial numbers, including license plate numbers
m) Device identifiers and serial numbers
n) Web Universal Resource Locators (URLs)
o) Internet protocol (IP) address numbers
p) Biometric identifiers, including voice and finger prints
q) Full face photographic images and any comparable images
r) Any other unique identifying number, characteristic or code, except as permitted to re-identify information (i.e. the subject identification number)

4.8.2. Confidentiality and Privacy within the De-identification Program

All de-identification will be performed by research credentialed study personnel, and will be checked by doctoral level study personnel. The only list linking the names of the study participants to their subject numbers will be kept in a secure, password protected computer account accessible only to certain study staff. The servers used to store the personally identifiable information will be kept in a secure, locked environment in a separate location from the portal and website servers at the Boston VA campus. Only team members who need the information to perform a specific job will be granted access to personally identifiable information by the PI.

4.8.3. Transfer of De-Identified Data to NERI

In order to minimize a breach of confidentiality and privacy during transfer, all research staff involved in the transfer will follow policies as described in VHA Directive 1605.1 (Privacy and Release of Information). As the data will already be de-identified as described in VHA Handbook 1605.1 and Common Rule (38 CFR 16), its transfer presents a relatively low level of risk of breach of confidentiality and privacy. Still, data transferred from the Boston VA to NERI will utilize encryption techniques. The specific transfer mechanism will be determined in part by the final size of the data file; possible mechanisms include SFTP (secure file transfer program) connection or creation of a secure encrypted email connection. The VA Boston team will work closely with the on-site information security officer, Eileen Robillard, to ensure that the best practices for data security are used.

4.8.4. Pretesting the Data De-identification and Transfer Procedures

The program to de-identify the data and the transfer of de-identified data from Boston VA to NERI will be pretested over a 2-week period in Y01. The pre-testing will be done using data from the sample of up to 20 veterans used to pretest the recruitment and study assessment procedures, as described in Section 4.5.2. Upon completion of the interviews for these ~20 participants, researchers at the Boston VA will enter all the data from their questionnaire and interview forms and run the program developed by Boston VA study staff to de-identify the data. The resulting de-identified data set will be closely re-analyzed at Boston VA to ensure that no remaining identifiers (including those listed in Section 4.8.1) remain. The de-identified sample data will be transferred to NERI study staff using the decided secure transfer mechanism. Should problems with any aspects of feasibility arise, the project team will discuss options to improve the process within the scope of the current protocol; any changes to the protocol will follow the approval procedures described in Section 6.4.

4.9. DATA STORAGE PROCEDURES

4.9.1. Boston VA

All paper measures will be secured behind locked and alarmed doors and only credentialed research study personnel will have access to them. All consent documents will be stored in a locked file cabinet, separate from the data. Electronic data will be stored on password protected systems located on the Boston VA campus. Paper or electronic data linking participants to their study ID numbers will be stored separately from all other study materials, using these same secure mechanisms and restricting access to limited key study staff. All data storage devices, including computers and servers, will be VA issued and monitored by VA Boston information management services. Only study personnel authorized by the Principal Investigator (PI) or Project Director (PD) will have access to the data, and the file server is protected from the internet by a firewall. All paper files and electronic data will be stored for a minimum of 6 years. If and when the data is destroyed, all paper files will be shredded, and electronic files will undergo a shredding process that will permanently delete the file, such as with Simple File Shredded 3.2 by scar5 Software.

4.9.2. New England Research Institutes (Watertown, MA)

NERI will have access to and store only de-identified Registry study data to conduct statistical analysis. This electronic data will be stored for a minimum of 6 years. In order to

effectively protect all research data, NERI has established a comprehensive set of security procedures for its data management systems. NERI's multi-facetted approach to security assures that research data is obtained and maintained in the highest quality and most secure manner. NERI responds to the Automated Information System Security Policy (AISSP) requirements with the following security and quality assurance measures:

- Operating Systems Documentation
- User Names, Passwords and Authorization
- Data Confidentiality
- Threat Detection
- Internet Security
- Inventory
- Facility
- Computer Facility
- Employee Training
- Backups

Registry study data will be stored on a project drive clustered Microsoft Windows 2003 file server per existing SOPs. The file server is protected from the internet by a firewall; internal access to the project drive is restricted to authorized users only. Users are only authorized by the Principal Investigator (PI) or Project Director (PD). All project drives are backed up nightly to tape, regular hot backups occur during the day to capture daily changes. Tapes are routinely rotated and stored offsite.

A firewall limits the communications protocols allowed between NERI and the outside world to only those needed to support the operations of our data systems. A Microsoft Certified Systems Engineer is an integral part of NERI's network staff. This position specializes in Internet and Intranet web access, architecture and security, firewalls and routers and is constantly monitoring all of NERI's web sites using Web Internet tools to determine how NERI's Web site is being accessed, where access is originating and how often it is being used. For additional security checks, NERI employs a company that on a regular basis attempts to hack into NERI's computer systems. The company provides NERI with reports of any potential holes they find in our security, and suggestions to improve Internet safety.

NERI utilizes a system for desktop and server inventories. The automated electronic desktop system is designed to track all hardware and software on each computer attached to the NERI network. To complement this system, a physical inventory is done on a yearly basis and the electronic system is verified. Each NERI server has a physical file into which all maintenance and updates are logged.

Entrance into the building during non business hours is by access card only. All doors to NERI offices are locked at all times, with the exception of the reception area, which has a receptionist on duty during business hours and is locked during non-business hours. Visitors must sign in with the receptionist and are accompanied by an employee at all times. The access card to the building and the NERI issue key are returned at the end of an employee's term of employment.

4.10. ANALYSIS PLAN

4.10.1. Statistical Analysis

The full database created by the Registry includes abstracted military and medical record data merged with data collected from paper forms and the telephone interview. Descriptive analyses will be conducted to characterize the two enrolled samples in terms of demographics, diagnosis, symptomatology, quality of life, current therapies used, and clinical trajectories. The 1200 PTSD group participants will be considered as the "index group" in most of the analyses, as they are the targets for the majority of the Specific Aims, while the 400 non-PTSD participants will be considered the comparison group. The general analysis plan for each aim is briefly provided below. Most variables will be considered in categorical form to avoid assumptions of linearity in analyses; the operational definitions for selected outcomes of interest are listed in **Table 4.9**. Covariates (and interaction terms) will be retained in the models if they are found to be significant predictors of the outcome (at the 0.05 level of significance) or if they confound the effects of significant predictors, defined as changing the effect estimate by at least 20%. Analyses will be conducted in SAS 9.2 (SAS Institute, Cary, NC) or SUDAAN 9.0.1 (Research Triangle Institute International, Research Triangle Park, NC) as appropriate, considering stratification and matching factors. NERI's computer network and its information systems team support the use of these packages.

Table 4.9. Operational Definitions of Selected Outcomes of Interest

Outcome	Definition	Anticipated Variable Form
PTSD	Diagnosis of PTSD, by electronic medical record (ICD-9 code 309.81) or interview assessment	Dichotomous
Psychiatric comorbidities	Diagnoses of depression, anxiety, substance abuse or other DSM-IV diagnoses	Dichotomous
Treatment Utilization	Number of healthcare visits, pharmaceutical usage	Continuous
Productivity Loss	Self-reported absentee days, decreased accomplishments, decreased diligence	Continuous
Quality of Life	SF-12 scores	Continuous

4.10.1.1. Analysis Plans for Specific Aims

Specific aims and a brief analysis plan for each follows:

Aim 1: This aim focuses on the describing the natural history of the PTSD group, which includes estimation of comorbidities, disparities in these comorbidities by key subgroups, as well as longitudinal descriptive analyses of the PTSD group. Analyses will be conducted to describe existing and new medical and psychological comorbidities, overall and by sociodemographic, military and post-deployment factors. Confidence intervals for the observed co-morbidities will be constructed. Where there are multiple assessments of one outcome, longitudinal mixed models will be used to test for significant changes over time. If two time points only are available, then a paired t-test or nonparametric equivalent will be used to assess change for

continuous outcomes. If the outcome is categorical (presence vs. absence of a condition), a generalized mixed model (e.g., logit, multinomial links) will be utilized. In longitudinal analyses, as it is likely that the correlation of responses will decrease over time, an unstructured or autoregressive correlation will be assumed. Additionally, Cox proportional hazard models can be used to predict the time to event.

Aim 2: These analyses will be a comparison of the PTSD index group to utilizers of the VA medical care who served in OIF/OEF but have not received the PTSD diagnosis. The analyses will use multivariate conditional logistic regression to examine factors associated with the PTSD diagnosis while controlling for matching factors of gender and deployment country. The outcome of interest will be PTSD case status and potential predictors include race/ethnicity, level of social support, socioeconomic status, and military service record variables (e.g., rank, duration of service).

Aim 3: These analyses will describe in detail current treatment approaches and then consider the PTSD treatment(s) as the independent variable(s) and psychosocial and medical outcomes occurring after treatment as dependent variables.

Aim 4: These analyses will establish the prevalence of PTSD in the non-PTSD group. Risk factors for missed diagnoses will be explored by comparing those in this group to those in the index PTSD group, on factors such as age, military service factors, race/ethnicity, medical comorbidities, and health care utilization.

Aim 5: These analyses will obtain estimates of costs of PTSD and its associated treatment, in terms of health care utilization costs, health care staff resource needs, and lost productivity, in the PTSD Registry index group.

Aim 6: There are no statistical analyses for this aim, which is to prepare the database for future applications and research use.

4.10.1.2. Propensity Scores

Because a registry has by definition observational data that arise from a clinically indicated setting, it must be noted that assessment of causality and treatment effects with respect to remission of PTSD are subject to potentially important biases. The veterans who receive treatment for PTSD may have different characteristics than those who do not undergo treatment, and these differences can be related to gender, race/ethnicity, severity of PTSD, accessibility of health care services, and unmeasured factors. Therefore, propensity score analyses may be conducted, [59] in which the likelihood of receiving treatment is considered the outcome, and a multivariate model that identifies correlates of receiving treatment are established. This model is then used to obtain a model-based predicted probability of undergoing treatment, and all subsequent analyses of treatment effectiveness stratifies the analytic dataset according to propensity score quantile, therefore ensuring that at least to some degree, cases within a propensity quantile are most similar to each other, and treatment effect estimates are less biased than those that do not attempt to account for measured and unmeasured differences in the treated vs. untreated groups.

4.10.1.3. Missing Data

Although every effort will be made to achieve complete interviews and full abstraction of health care visits and treatment, there may be some missing outcome and predictor information

in the final database. Initial tasks to address the impact of missing data on statistical inferences include documenting the types of missing data, accounting for different sources of missing data, and assessing the implications of irretrievably missing information for potential biases. Because interview data may not be missing completely at random, statistical analyses must account for possible non-response bias, particularly if missing data are associated with severity of PTSD. Consequently, analyses should adjust in some way for characteristics associated with both non-response and the outcomes of interest. [60, 61] Multiple imputation will be used as appropriate.

4.11. Power Calculations

4.11.1. Primary Aims

The primary aim of the registry is to describe the natural history of PTSD, characterized by the long-term psychosocial, medical and quality of life outcomes associated with the disorder, and to assess whether these outcomes differ by subgroups defined by sociodemographic, military and post-deployment factors. In this section, we provide the estimated precision for 90% confidence intervals to describe the underlying annual incidence of co-morbidities, and the power to detect differences in the rate of co-morbidities amongst participants with PTSD by subgroup.

Table 4.11.1 indicates that with 1200 participants with PTSD, there is high precision to estimate co-morbidity rates. If the rate is as high as 40%, the relative precision (half-width) of the confidence interval is less than 6% (.023/.40). If the rate is only 10%, then the relative precision of the confidence interval is 14% (.014/.10).

Table 4.11.1. Precision of 90% Confidence Interval for A Range of Co-Morbidity Rates assuming 1200 Participants with PTSD, two-sided α=0.05.

Rate	Precision	90% CI	Estimated Number with Co-Morbidity
.05	.01	(.04, .06)	48 to 72
.10	.014	(.086, .114)	103 to 137
.20	.019	(.181, .219)	217 to 263
.30	.022	(.278, .322)	334 to 386
.40	.023	(.377, .423)	452 to 508

Table 4.11.2 displays power for hypothetical subgroup comparisons that might be conducted to assess whether comorbidity rates differ by subgroup in the PTSD cohort (e.g., males vs. females, high vs. low SES, etc.). The table shows that if the comorbidity rate of the lesser affected subgroup is relatively rare (10%), there is over 84% power to detect an odds ratio of 1.7 (0.10 vs. 0.16 rates). If the co-morbidity rate of the lesser affected subgroup is 20%, there is over 89% power to detect an odds ratio of 1.56 (0.20 vs. 0.28 rates). If the co-morbidity is quite prevalent (40%), there is 87% power to a smaller effect size (odds ratio of 1.44). Of note, if the subgroup sizes are more evenly split amongst the 1200 PTSD cases, power will be greater than shown in Table 4.11.2.

Table 4.11.2. Power to Detect Subgroup Differences for Co-Morbidity Rates of 0.10, 0.20, 0.40, assuming 1200 Participants with PTSD, Subgroup sizes of 840 vs. 360 (70%/30%), and two-sided α=0.05.

$p_0 = 0.10$				$p_0 = 0.20$				$p_0 = 0.40$		
p_1	Odds Ratio	Power		p_1	Odds Ratio	Power		p_1	Odds Ratio	Power
.13	1.35	.311		.24	1.26	.346		.45	1.23	.391
.14	1.47	.506		.26	1.41	.658		.47	1.33	.663
.15	1.59	.696		.28	1.56	.885		.49	1.44	.869
.16	1.71	.843		.30	1.71	.977		.51	1.56	.966
.17	1.85	.932		.32	1.88	1.00		.53	1.69	.994
.18	1.98	.976		.34	2.06	1.00		.55	1.83	1.00

4.11.2. Secondary Aims

Power calculations are provided in **Table 4.11.3** to address selected secondary aims related to the case-control study comparisons of study outcomes such as social support and quality of life, where it is hypothesized that the cases (1200 PTSD veterans) will have lower social support and quality of life than controls (400 non-PTSD veterans). Therefore, the case: control ratio is 3:1 and this has been incorporated into the power calculations. For simplicity, it is assumed here that the outcome is a dichotomous indicator of low social support/low quality of life defined by a pre-specified cutoff from the overall social support or QOL score derived from interview instruments. Therefore, these power estimates to detect associations are conservative, as continuous analyses of scores will also be conducted (see below). Two scenarios are provided: (a) 20% of controls have low social support or QOL and are compared against rates of low social support of 25% to 31%; and (b) 40% of controls have low social support or QOL and are compared against rates of 47% to 53%, resulting in similar effect sizes to detect in the two scenarios. Table 4.11.3 demonstrates that if the control rate of low social support is 20%, there is approximately 80% power to detect an odds ratio for low social support in cases vs. controls of 1.5, and if the control rate is 40%, there is approximately 80% power to detect odds ratios over 1.4 for low social support in cases vs. controls. If the low social support rate in controls is only 10%, then the current design (1200 cases and 400 controls) will have 85% power (not shown in table) to detect an odds ratio of 1.72, and 70% power to detect an odds ratio of 1.6.

Table 4.11.3. Power to Detect Differences in Rates of Low Social Support or Low Quality of Life for 1200 PTSD cases (p_1) vs. 400 non-PTSD controls (p_0) assuming a two-sided exact test with α=0.05

$p_0 = 0.20$				$p_0 = 0.40$		
p_1	Odds Ratio	Power		p_1	Odds Ratio	Power
.25	1.33	.503		.47	1.33	.663
.26	1.41	.658		.48	1.38	.779
.27	1.48	.790		.49	1.44	.869
.28	1.56	.885		.50	1.50	.929

.29	1.63	.945		.51	1.56	.966
.30	1.71	.977		.52	1.62	.985
.31	1.80	.991		.53	1.69	.994

It should be noted that outcomes will also be analyzed continuously, and only 503 cases (vs. 167 controls) are required to detect an effect size (defined as mean difference divided by sample standard deviation) of 0.25 standard deviations with 80% power, which is a minimum clinically significant difference. With 1200 cases and 400 controls, there is >99% power to detect a 0.25 effect size. Therefore, continuous analyses of case-control differences in functioning can support multivariate modeling as well as subgroup analyses defined by gender and race/ethnicity.

4.12. Participation Rate and Follow-Up

In the event of insufficient response rate to initial recruitment, we will increase the number of recruitment mailings and calls. We have estimated a response rate based on previous similar studies in VA. We estimate a high rate (>90%) of retention in the VA database.

5. RESOURCE SHARING PLAN

5.1. CREATION OF A PUBLIC USE PTSD REGISTRY DATABASE

Upon finalization of the PTSD registry database, NERI will create a public use dataset using the de-identified data. NERI has ample experience in the generation of public use datasets. A read-only CD-ROM is produced with the following: all files reformatted for public use and saved in SAS export format; a Microsoft Word document describing how each variable deemed unacceptable for public use was resolved; a codebook containing summary distributions of all variables; a Microsoft Word document called “readme.doc” containing a study overview that will include study background information, description of the study design, sampling, and primary and secondary outcomes; system requirements for using the SAS datasets; data collection forms; and a list of study publications. This CD-ROM will be transferred to the VA Boston for oversight and management of the public use database.

5.2. OVERSIGHT AND MAINTENANCE OF THE PUBLIC USE REGISTRY DATABASE

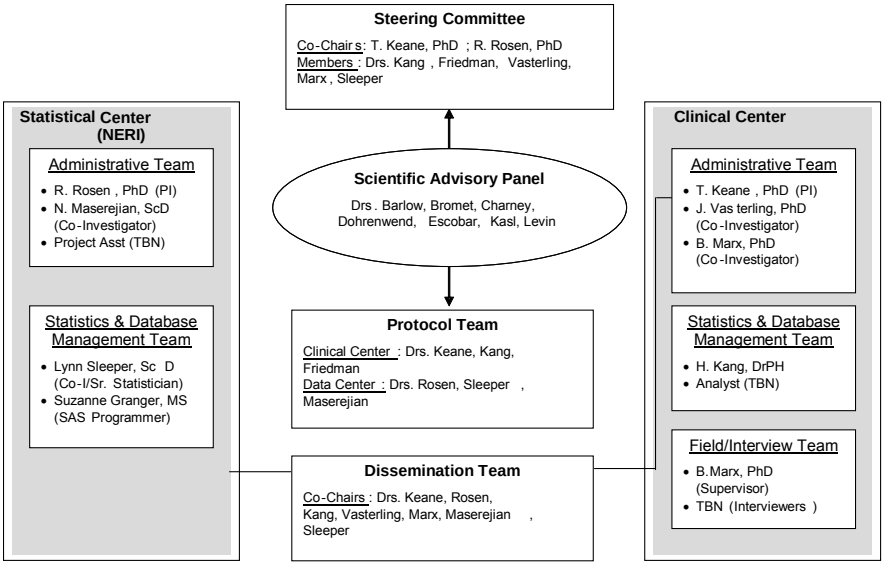
The VA Boston will maintain the public use database under the supervision of the PI. The VA is currently developing guidelines on data repository and access; all procedures to store and supervise the PTSD Registry database will follow these guidelines. Under the supervision of the PI, the database will be stored in a VA repository protected by a firewall in the VA Boston research server. Support and supervision of public access to the data will occur in accordance with the VA guidelines.

6. PROJECT ORGANIZATION

6.1 OVERVIEW

As shown in the organizational chart (Figure 6.1), a Registry Steering Committee will have responsibility for scientific and budgetary oversight of the project. The protocol team will have responsibility for development of the study protocol and interview, with consultation from the Scientific Advisory Panel (SAP). The Statistical Center (NERI) will have responsibility for administrative coordination of the project and statistical analyses. The Clinical Center (NCPTSD –BSD/ VA Boston HCS) and the grant administration center (BVARI) will be supervised by Dr. Keane (Project PI), who will also serve as the overall PI for the project. The VA statistics and database management for the project will be directed by Dr. Han Kang. The dissemination team will comprise investigators from both the Clinical Center (NCPTSD-BSD/VA Boston HCS) and Statistical Center (NERI).

Figure 6.1. Organizational Chart



6.2. ROLES OF EACH INSTITUTION

6.2.1. Boston VA Research Institute (BVARI)

A non-profit, tax-exempt institution, BVARI holds the grant for Project VALOR. BVARI oversees the budget and other business aspects of the grant. BVARI will be engaged in research activities using identifiable participant information to reimburse participants for their time by mailing personal checks. BVARI works closely with the researchers at the Behavioral Sciences Division of the National Center for PTSD in the VA Boston Healthcare System.

6.2.2. National Center for PTSD, Behavioral Sciences Division/ VA Healthcare System Boston

National Center for PTSD, Behavioral Sciences Division at the Boston VAMC will be engaged in research activities using identifiable participant information. In particular NCPTSD-BSD/ VAMC Boston staff will make telephone and postal contact with participants during the course of the study. This team will also be responsible for conducting clinical interviews. NCPTSD-BSD/VAMC Boston will work closely with BVARI on business aspects of the project.

6.2.3. New England Research Institutes, Inc. (NERI)

NERI will be responsible for the administrative coordination of the project and the statistical analyses, with access limited to deidentified data sets. NERI project staff will not contact participants and will not have access to identifiable data; thus, NERI is not engaged in direct research with participants or their identifiable information.

6.2.4. DC VA

The DC VA will be responsible for identifying eligible veterans through existing databases, creating the initial level 1 roster, and abstracting data from electronic medical records to send to the Boston VA. The VA DC staff will be engaged in research activities with identifiable participant information, but will have no interaction with participants.

6.3. PERSONNEL

6.3.1. Clinical Team

Terence M. Keane, PhD is the project PI and PI for the clinical center (VA) for the study. Dr. Keane is the Associate Chief of Staff for Research and Development at VA Boston, Director of the Behavioral Science Division of the National Center for PTSD, and Professor and Vice Chair in the Division of Psychiatry at BUSM. His home institution is the VA Boston Healthcare System, which encompasses the Behavioral Sciences Division of the National Center for PTSD. He has an extensive record of scientific achievement including numerous publications and grant awards. Dr. Keane was a leader in the development of the multi-site National Center for PTSD, he served as the Department of Veterans Affairs administrative head of the NVVRS study, and he is Past President of the International Society for Traumatic Stress Studies. His work in this area was recognized recently with two career awards: the Lifetime Achievement Award from the International Society for Traumatic Stress Studies and the Outstanding Researcher Award in Behavior Therapy from the Association of Behavioral and Cognitive Therapies (formerly AABT).

Han K. Kang, DPH is a Co-Investigator for the clinical center (VA) and Chief of the VA Statistics and Database Management Team for the project. Dr. Kang is Senior Scientist of the Environmental Epidemiology Service, US Department of Veterans Affairs. In addition to epidemiological studies in the VA, Dr. Kang performs large health surveillance studies on veterans using various health registries that his office maintains, such as the Ionizing Radiation Registry, Agent Orange Registry, and Gulf War Health Registry. He also monitors health care utilization among 750,000 OIF/OEF veterans who became eligible for VA healthcare using VA's electronic medical records. Dr. Kang is a fellow of the American College of Epidemiology and faculty member of George Washington University and the Uniformed Services University of the Health Sciences.

Matthew J. Friedman, MD, PhD is Co-Investigator and Ex Officio member of the Registry Steering Committee. Dr. Friedman is the Executive Director of the National Center for Post-Traumatic Stress Disorder and Professor of Psychiatry, Pharmacology and Toxicology at Dartmouth Medical School. Dr. Friedman is the Past President of the International Society for Traumatic Stress Studies and has published extensively on the neurobiological basis of traumatic stress and on ethnocultural aspects of PTSD. He has served on many NIMH and VA national committees, and is currently a member of the NIMH Violence and Traumatic Stress Study Section and the VA's Persian Gulf Expert Scientific Committee.

Jennifer Vasterling, PhD is a Co-Investigator for the clinical center (VA) and will coordinate the neuropsychological component of the study. Her home institution, where she is

Chief of Psychology, is the VA Boston Healthcare System, which encompasses the Behavioral Science Division of the National Center for PTSD. Dr. Vasterling is a Professor at Boston University School of Medicine. Trained as a clinical neuropsychologist, Dr. Vasterling's research career has centered on neuropsychological abnormalities associated with PTSD and war-zone deployment. She edited the only existing volume on this topic and has been the lead investigator of a DoD-VA collaborative effort that includes prospective examination of neuropsychological and emotional outcomes of Iraq deployment.

Brian P. Marx, PhD is a Co-Investigator for the clinical center (VA) and will coordinate the structured interviews for the study. Dr. Marx is a staff psychologist at the Behavioral Science Division of the National Center for PTSD in the VA Boston Healthcare System, which is his home institution. He is also an Associate Professor of Psychiatry at Boston University School of Medicine. Dr. Marx is an expert in behavior therapy, PTSD assessment, and the effects of trauma. Currently, he is site PI on a VA HSR&D Research study (SDR 06-331) examining the efficacy and effectiveness of standardized assessment instruments in PTSD compensation and pension examinations.

Denise M. Sloan, PhD is a Co-Investigator for the clinical center (VA) and will oversee the Project Coordinator and Research Technicians in the scheduling and coordination of the structured interviews for the study. Dr. Sloan is a staff psychologist at the Behavioral Science Division of the National Center for PTSD in the VA Boston Healthcare System, which is her home institution. She is also an Associate Professor of Psychiatry at Boston University School of Medicine. Dr. Sloan is an expert in written disclosure and the effects of trauma.

6.3.2. Statistical Center

Raymond C. Rosen, PhD (Partnering PI) is Chief Scientist at NERI. Dr. Rosen is a fellow of the American Academy of Sleep Medicine and the Institute for Health and Health Policy at Rutgers University. He has extensive experience in quality of life assessment in medical and psychiatric populations, and is the recipient of several NIH grants in this area. Dr. Rosen serves as principal investigator and steering committee chair for a large, multi-national registry of androgen deficiency in men, and has served as an investigator and steering committee member for other large national and international registries. Dr. Rosen has extensive experience in design of clinical trials and observational studies, and has published more than 200 articles in peer-review journals. He has served on multiple NIH and NIMH review committees, and is the former Study Section Chair on Criminal and Violent Behavior.

Lynn Sleeper, ScD (Co-Investigator/Sr. Statistician). Dr. Sleeper has more than 15 years of experience as a biostatistician for multi-center clinical trials, registries and observational studies. Dr. Sleeper received her doctorate in biostatistics from the Harvard School of Public Health and joined NERI in 1990. She has been the Principal Investigator of the NHLBI Pediatric Heart Network (PHN) DCC since its inception in 2001. As PI of the PHN DCC, which has executed seven studies to date, Dr. Sleeper has been a significant contributor to the development of all PHN protocols, procedures, and manuscripts, as well the Statistics Team Leader at the DCC. She is also currently the Principal Investigator of the Pediatric Cardiomyopathy Registry (PCMR) Data Coordinating Center. From 2000-2004, Dr. Sleeper was PI of the DCC for the NHLBI SHOCK Trial and Registry. She has been an author/coauthor of

over 80 publications describing the design and results of multi-center clinical trials, registries, and observational studies.

Nancy Maserejian, ScD (Co-Investigator) is a Research Scientist at NERI with experience in registry design and management. She received her doctorate in Epidemiology from the Harvard School of Public Health, where she has also served as a consultant in biostatistics and epidemiological methods. At the Columbia University Presbyterian Medical Center, she developed protocol and questionnaires for the Metropolitan New York Breast Cancer Registry, as part of the National Cancer Institute's Cooperative Family Registry for Breast Cancer Studies, and she also coordinated the efforts of investigators at various sites. Particular highlights of her recent work include studies of nutrition, oral health, and disparities in health care access and utilization

Suzanne Granger, MS (Statistician) is a statistician with advanced training and interests in survival analysis, categorical data analysis, regression, and non-parametrics. Ms. Granger is currently working for both the Virology Quality Assessment Project (VQA) and the Transfusions Medicine/Hemostasis Clinical Trials Network (TMH CTN). She is currently responsible for data analysis, statistical programming, and report and manuscript generation. In addition to her experience on the VQA Program and the TMH CTN, Ms. Granger was the statistical programmer for two clinical trials of stroke prevention in sickle cell disease.

6.3.3. Scientific Advisory Panel

A scientific advisory panel has been developed for the project (Table 6.3.3). These individuals were selected as prominent researchers and clinicians in PTSD and related areas of research, who will advise the protocol team on all aspects of the study design, data collection instruments, and interpretation and dissemination of the study findings. Several of the advisors have been leading authors or investigators on other large-scale epidemiological studies in the area. As indicated by the attached letters of support, scientific advisors were uniformly positive about the potential significance of the project for long-term planning and service delivery in this area.

Table 6.3.3. Scientific Advisory Panel

SCIENTIST	AFFILIATION	AREA(S) OF EXPERTISE
Bruce Dohrenwend, PhD	Professor of Epidemiology, Columbia University	Psychiatric Epidemiology; Post Traumatic Stress Disorder
David Barlow, PhD	Professor of Psychology, Boston University	Anxiety Disorders; Cognitive behavior therapy
Dennis Charney, MD	Dean and Chair of Psychiatry, Mt. Sinai Medical Center	Psychiatric diagnosis, anxiety disorder, PTSD
Javier Escobar, MD	Associate Dean for Global Health and Professor of Psychiatry and Family Medicine, Robert Wood Johnson Medical School	Psychiatric diagnosis, cross-cultural psychiatry
Stanislav Kasl, PhD	Professor of Epidemiology, Yale University	Psychiatric epidemiology; post traumatic stress disorder
Evelyn Bromet, PhD	Professor of Psychiatry, SUNY at Stony Brook	Psychiatric epidemiology; post traumatic stress disorder

Harvey Levin, PhD	Professor of Neuropsychology Baylor College of Medicine	Neuropsychological Assessment – Traumatic Brain Injury

6.4. REPORTING REQUIREMENTS AND RESPONSIBILITIES OF THE PI

6.4.1. The protocol will be conducted in accordance with the protocol submitted to and approved by the USAMRMC ORP HRPO and will not be initiated until written notification of approval of the research project is issued by the USAMRMC ORP HRPO.

6.4.2. Accurate and complete study records will be maintained and made available to representatives of the U.S. Army Medical Research and Materiel Command as a part of their responsibility to protect human subjects in research. Research records will be stored in a confidential manner so as to protect the confidentiality of subject information.

6.4.3. All unanticipated problems involving risk to subjects or others, serious adverse events related to participation in the study and subject deaths related to participation in the study will be promptly reported by phone (301-619-2165), by email (hsrrb@.amedd.army.mil), or by facsimile (301-619-7803) to the USAMRMC, Office of Research Protections, Human Research Protection Office. A complete written report will follow the initial notification. In addition to the methods above, the complete report will be sent to the U.S. Army Medical Research and Materiel Command, ATTN: MCMR-RP, 504 Scott Street, Fort Detrick, Maryland 21702-5012.

6.4.4. Suspensions, clinical holds (voluntary or involuntary), or terminations of this research by the IRB, the institution, the Sponsor, or regulatory agencies will be promptly reported to the USAMRMC ORP HRPO.

6.4.5. Any deviation to the protocol that may have an adverse effect on the safety or rights of the subject or the integrity of the study will be reported to the USAMRMC ORP HRPO as soon as the deviation is identified.

6.4.6. Major modifications to the research protocol and any modifications that could potentially increase risk to subjects will be submitted to the USAMRMC ORP HRPO for approval prior to implementation. All other amendments will be submitted with the continuing review report to the USAMRMC ORP HRPO for acceptance.

6.4.7. A copy of the approved continuing review report and the local IRB approval notification will be submitted to the USAMRMC ORP HRPO as soon as these documents become available. A copy of the approved final study report and local IRB approval notification will be submitted to the USAMRMC ORP HRPO as soon as these documents become available.

6.4.8. The knowledge of any pending compliance inspection/visit by the FDA, OHRP, or other government agency concerning this clinical investigation or research, the issuance of Inspection Reports, FDA Form 483, warning letters or actions taken by any Regulatory Agencies including legal or medical actions and any instances of serious or continuing noncompliance with the regulations or requirements that relate to this clinical investigation or research will be reported immediately to USAMRMC ORP HRPO.

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ACRONYMS AND DEFINITIONS

AABT	Association for the Advancement of Behavior Therapy
AHRQ	Agency for Healthcare Research and Quality
BVARI	Boston VA Research Institute, Inc.
CAGE-D	Cut Down, Annoyed, Guilty, and Eye Opener (alcohol use disorders screening test
CIDI	Composite International Diagnostic Interview
DCC	Data Coordinating Center
DMDC	Defense Manpower Data Center
DOB	Date of Birth
DOD	Department of Defense
DRRI	Defense Race Relations Institute
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders
EES	Environmental Epidemiology Service
FY	Fiscal Year
HADS	Hospital Anxiety and Depression Scale
HSR&D	VA's Health Services Research and Development Service
ICD-9	International Classification of Disease, 9th Edition
ID	Identification
LEC	Life Events Checklist
MIRECC	Mental Illness Research, Education & Clinical Center
NERI	New England Research Institutes, Inc.
NHLBI	National Heart, Lung, and Blood Institute
NIH	National Institute of Health
NIMH	National Institute of Mental Health
NVVRS	Vietnam Veterans Readjustment study
OEF	Operation for Enduring Freedom
OIF	Operation Iraqi Freedom
OPC	VA outpatient treatment services
PCMR	Pediatric Cardio-Myopathy Registry
PDHA	Post Deployment Health Assessment
PHN	Pediatric Heart Network
PI	Principal Investigator
PTF	VA inpatient treatment services
PTSD	Post-traumatic Stress Disorder
RADAR	Registry for Androgen Deficiency and Replacement
RCTs	Randomized Clinical Trials
SAP	Scientific Advisory Panel
SAS	Statistical Analyses Software
SDR	Service Directed Research
SF-12	Short Form-12 (Medical Outcomes Survey)
SHOCK	SHould we revascularize Occluded coronaries for cardiogenic shoCK?
SSN	Social Security Number
SSRI	Selective Serotonin Reuptake Inhibitor

SUDAAN	Proprietary Software for Epidemiology Studies
TBI	Traumatic Brain Injury
TMH CTN	Transfusions Medicine/Hemostasis Clinical Trials Network
VA	Veterans' Affairs
VALOR	Veterans' After-Discharge LOngitudinal Registry
VEV	Vietnam Era Veterans
VQA	Virology Quality Assessment
VTV	Vietnam Theater Veterans

APPENDIX C: STUDY MANUAL OF OPERATIONS

Project VALOR: Veterans' After-Discharge Longitudinal Registry

MANUAL OF OPERATIONS

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1. PROJECT OVERVIEW

1.1. SYNOPSIS

The Veterans' After-Discharge Longitudinal Registry (Project VALOR) is a 3-year project resulting from a joint effort by researchers at the National Center for PTSD at the Department of Veterans Affairs (VA) Boston

Healthcare System (clinical center) and New England Research Institutes, Inc. (NERI) (statistical center). The objective is to develop the first longitudinal registry of combat-exposed men and women with post-traumatic stress disorder (PTSD) and to provide data on the natural history and outcomes associated with PTSD in military service men and women who have utilized the VA health care system. The source population of participants is combat-exposed army or marine veterans from Operation for Enduring Freedom (OEF) or Operation Iraqi Freedom (OIF) who are in the VA health care system database. From this source population, 1200 men and women with PTSD and 400 men and women without PTSD will be invited to participate. Analyses will include longitudinal analyses within the group of 1200 veterans with PTSD, as well as case-control analyses comparing these PTSD-diagnosed veterans to the 400 veterans without PTSD. Identification of the registry sample pool and abstraction of existing military deployment and medical data from existing databases will be conducted under direction of Dr. Han Kang, Director of the Environmental Epidemiology Service at the VA. Existing background and service utilization data will be merged with additional data from electronic medical records, a mailed questionnaire, and a structured telephone interview. The questionnaire and interview assess relevant risk factors and comorbidities, quality of life and other clinically-relevant outcomes. The current project (a) builds on existing knowledge of PTSD causes and consequences; (b) will provide an independent, longitudinal registry design to further investigate the natural history and outcomes associated with PTSD; (c) will not only create the registry but also gather data on a comparison group of veterans and conduct case-control analyses; (d) assembles an exceptional group of senior advisors for the scientific advisory committee for the registry; and (e) has at its base a strong partnership between the clinical center (National Center for PTSD at VA Boston) and the statistical center (NERI) for conduct of the registry, dissemination of key findings, and development of potential ancillary studies in the future.

1.2. OBJECTIVES AND SPECIFIC AIMS

The overall objective of this project is to develop the first longitudinal registry of combat-exposed men and women with PTSD. This registry will provide essential data on the natural history and outcomes associated with PTSD in military service men and women who have utilized the Department of Veterans Affairs (VA) health care system. An additional goal of this project is to determine risk factors for PTSD among combat-exposed service men and women (by incorporating a combat-exposed non-PTSD group of veterans into analyses). Thus, the registry will allow an evaluation of current theoretical models of symptom development in a large sample of service men and women who utilize the VA medical system.

This project is designed to address a range of research questions within the registry itself, as well as in comparisons with a non-registry study group. The theoretical model underlying this research is presented in **Figure 1.2**. Specific aims of this project can be divided into the following two research areas:

EPIDEMIOLOGY OF PTSD

Aim 1. To describe the natural history of PTSD using the long-term psychosocial, medical and quality of life outcomes associated with the disorder, and to evaluate disparities by sociodemographic, military and post-deployment factors.

Aim 2. To identify risk factors (e.g., demographic, social support, socioeconomic resources) and comorbidities (e.g., other mental health disorders, neurological conditions) of PTSD, by comparing PTSD patients to a “control” group of veterans without PTSD.

PTSD HEALTH SERVICES

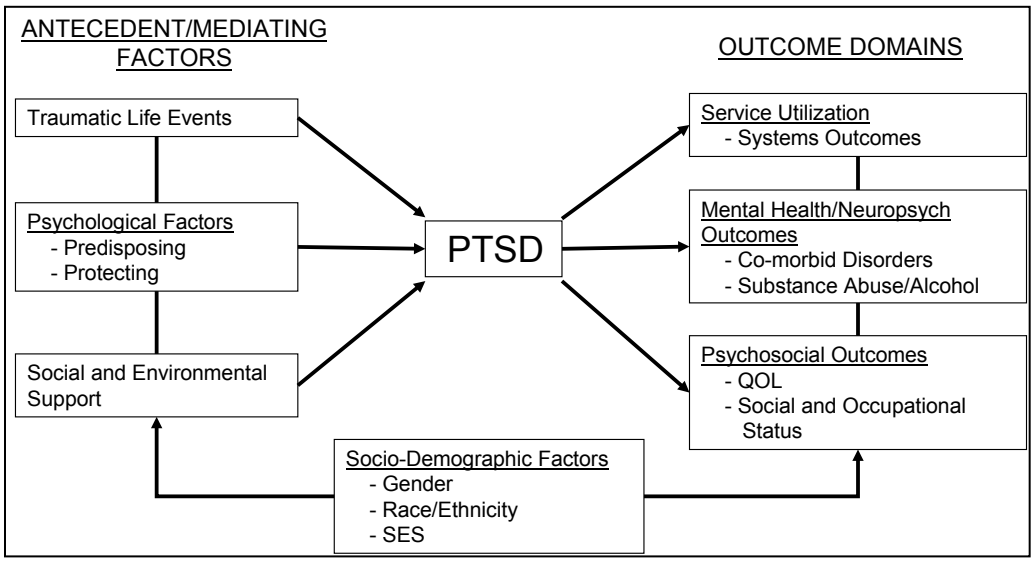
Aim 3. To identify treatment approaches through time.

Aim 4. To establish the prevalence of PTSD in a comparison group of service men and women who did not have the PTSD diagnosis in the medical record, and to identify risk factors for a missed PTSD diagnosis.

Aim 5. To assess current referral and health care utilization patterns among patients with PTSD, and also to compare their health care utilization to a group of veterans without PTSD.

Aim 6. To develop a large database of servicemen and women with PTSD and network of treatment sites that are potentially available for further observational and interventional studies, as well as concurrent ancillary studies.

Figure 1.2 PTSD Research Model



1.3. RESEARCH STRATEGY OVERVIEW

This project designs and implements a VA system-wide patient registry to obtain a registry database of combat veterans from recent military operations in Iraq and Afghanistan who have utilized the VA medical system and have received a diagnosis of PTSD. As defined by the AHRQ and World Health Organization, "a patient registry is an organized system that uses observational study methods to collect uniform data (clinical and other) to evaluate a specific outcome for a population defined by a particular disease, condition, or exposure, and that serves one or more predetermined scientific, clinical, or policy purposes." The patient registry *database* is defined as a file (or files) derived from the registry. A patient-based database is necessary to allow direct access to information on diagnoses of interest and treatment outcomes, as well as to longitudinally track follow-up visits, progress, and treatment courses.

In contrast to these criteria, the database of utilizers of the VA healthcare system is structured by chronological in-patient and out-patient visits, rather than unique patient identifiers or diagnoses. Thus, with the existing database, there is no readily accessible way to identify unique patients with PTSD or to assess their longitudinal outcomes and utilization of VA healthcare. Therefore, a fundamental objective of this project is to establish a registry of patients with PTSD from the existing VA utilization database. Electronic medical records such as those in the VA database are increasingly important sources of data, but data must be extracted, transformed into registry format, and loaded into the registry, where they will reside in the registry database, together with registry-specific data that is imported from other sources. The other sources of data for the PTSD registry will be the OIF/OEF veteran roster (particularly for military specific data, e.g., branch, rank, deployment dates, etc.) and, in Phase III, the self-administered questionnaire and telephone interview.

In addition to the PTSD registry, we will collect information on a comparison group of OIF/OEF-era veterans to conduct nested case control studies within the general VA health care utilization database. The comparison group will include combat veterans who have not received a diagnosis of PTSD. This group will be used in analyses to identify risk factors for PTSD (Aim 3). Thus, Project VALOR will create a PTSD registry from the VA database to assess the natural history of PTSD in combat veterans from OIF/OEF and also conduct case-control studies nested within the VA database. The case-control comparisons will be used to evaluate key hypotheses related to the specific aims of the overall project.

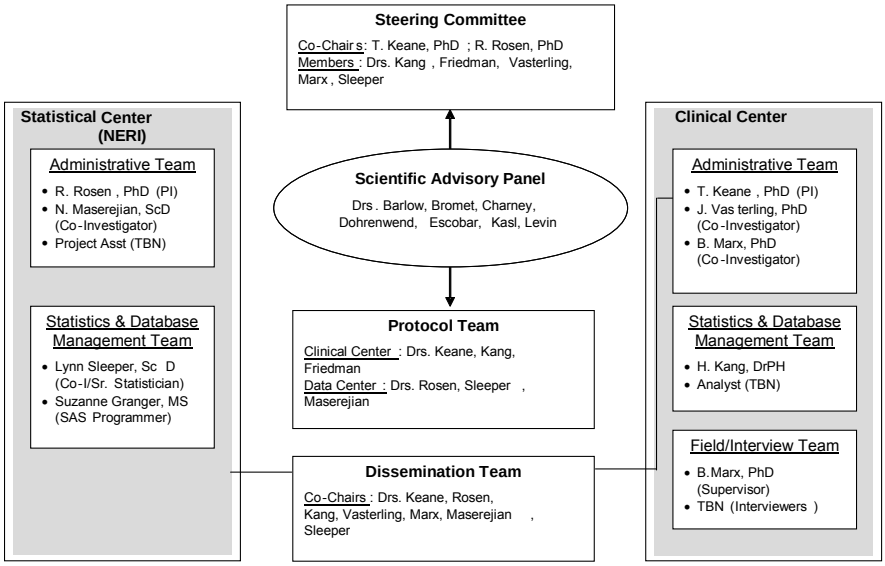
1.4. PROJECT TIMELINE

The project is to be conducted over a 3-year period. The study uses both existing data abstracted from the VA military and medical record database and prospectively collected data, collected by two additional data transfers, a mailed questionnaire, and a structured telephone interview. During Year 01 (Y01), upon obtaining all IRB approvals, a manual of operations will be created (months 6-7), and the rosters of potential participants will be compiled (Level 1 roster: months 7-8, Level 2 roster, months 9-10). Meanwhile, training of interviewer and research assistant staff will occur. Also in Y01 (months 9-11), the procedures for contacting participants for recruitment and study assessments, the data abstraction procedures, the de-identification program and the data transfer for statistical analyses, will be pre-tested. Full recruitment and contacting of participants will begin in Y01 (month 10) and continue through Y02 (month 9). Data entry will occur concurrently. The first abstraction of data from military and medical records will occur upon completion of the study mailing and interview for all participants (Y02, months 9-10). The data will be merged, cleaned, and de-identified at the Boston VA (Y02 months 10-11), in preparation for transfer to NERI (Y02 month 12) for statistical analyses and manuscript preparation (Y03 months 1-12). The PTSD registry database will be updated up to two times as new VA electronic medical records for registry participants appear in Y03 (tentatively scheduled for months 4 and 8), thereby capturing the trajectory of PTSD patients

1.5. ORGANIZATIONAL CHART AND INSTITUTIONAL ROLES

As shown in the organizational chart (**Figure 1.5**), a Registry Steering Committee will have responsibility for scientific and budgetary oversight of the project. The protocol team will have responsibility for development of the study protocol and interview, with consultation from the Scientific Advisory Panel (SAP). The Statistical Center (NERI) will have responsibility for administrative coordination of the project and statistical analyses. The Clinical Center (NCPTSD –BSD/ VA Boston HCS) and the grant administration center (BVARI) will be supervised by Dr. Keane (Project PI), who will also serve as the overall PI for the project. The VA statistics and database management for the project will be directed by Dr. Han Kang. The dissemination team will comprise investigators from both the Clinical Center (NCPTSD-BSD/VA Boston HCS) and Statistical Center (NERI).

Figure 1.5 Organizational Chart



1.5.1. Boston VA Research Institute (BVARI)

A non-profit, tax-exempt institution, BVARI holds the grant for Project VALOR. BVARI oversees the budget and other business aspects of the grant. BVARI will be engaged in research activities using identifiable participant information to reimburse participants for their time by mailing personal checks. BVARI works closely with the researchers at the Behavioral Sciences Division of the National Center for PTSD in the VA Boston Healthcare System.

1.5.2. National Center for PTSD, Behavioral Sciences Division/ VA Healthcare System Boston

National Center for PTSD, Behavioral Sciences Division at the Boston VAMC will be engaged in research activities using identifiable participant information. In particular NCPTSD-BSD/ VAMC Boston staff will make telephone and postal contact with participants during the course of the study. This team will also be responsible for conducting clinical interviews. NCPTSD-BSD/VAMC Boston will work closely with BVARI on business aspects of the project.

1.5.3. New England Research Institutes, Inc. (NERI)

NERI will be responsible for the administrative coordination of the project and the statistical analyses, with access limited to de-identified data sets. NERI project staff will not contact participants and will not have access to identifiable data; thus, NERI is not engaged in direct research with participants or their identifiable information.

1.5.4. DC VA

The DC VA will be responsible for identifying eligible veterans through existing databases, creating the initial level 1 roster, and abstracting data from electronic medical records to send to the Boston VA. The VA DC staff will be engaged in research activities with identifiable participant information, but will have no interaction with participants.

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2. BACKGROUND ON POSTTRAUMAMTIC STRESS DISORDER (PTSD) AND REGISTRY RATIONALE

2.1. POSTTRAUMATIC STRESS DISORDER (PTSD) DEFINITION & PREVALENCE

Posttraumatic stress disorder (PTSD) is a psychiatric disorder with potentially devastating emotional and interpersonal consequences.[1] PTSD may result from combat exposure or non-combat traumas such as sexual or physical abuse, and exposure to life-threatening risks or disasters. The mechanisms and etiology of PTSD are addressed in a recent review by Keane and Barlow.[2] Common symptoms of PTSD include re-experiencing of traumatic events, avoidance, numbing and hyperarousal reactions, such as insomnia, nightmares and other sleep difficulties. In addition, PTSD sufferers experience "flashback" episodes wherein recurrence of at least a portion of the traumatic event occurs. Extreme distress and avoidance of cues or reminders of the event also occur.

The lifetime prevalence of PTSD is 3-4% in the general population, and the trauma most commonly associated with PTSD in men is combat exposure.[3, 4] Recent evidence from returning Iraqi veterans [5] indicates that the prevalence of PTSD is approximately 10% immediately upon return.[6] The risk of PTSD is elevated more than three-fold for service members exposed to a combat situation.[6-8] Prevalence rates are even higher in some cohorts and may increase over time. For example, in a longitudinal study of Gulf War veterans, the prevalence of PTSD more than doubled between the initial assessment immediately upon return from combat and a follow-up assessment conducted two years later.[9] Despite accumulating evidence of the prevalence and impact of PTSD on active duty soldiers and veterans, major limitations exist in the information available. The creation of a longitudinal registry of a diverse sample of veterans will be of enormous value in addressing current gaps in our understanding of PTSD and associated outcomes.

2.2. VIETNAM VETERANS READJUSTMENT STUDY (NVVRS)

The largest body of epidemiologic data on PTSD is the National Vietnam Veterans Readjustment Study (NVVRS), [10] a congressionally mandated study of post-Vietnam veterans. Interviews were performed using a two stage methodology [11] in which lay interviewers evaluated a representative sample of Vietnam Theater Veterans (VTV; n=1632), Vietnam Era Veterans (VEV; n=716), and a group of civilian controls (n=668). To make the diagnosis of PTSD these investigators relied upon a triangulation approach that utilized information from the diagnostic interviews as well as self-report questionnaires. [12]

More than 15% of VTV males met criteria for current PTSD and 30% met criteria for lifetime PTSD. There were different rates for current PTSD among the various ethnic and racial groups: 13.7% for the white/other group, 20.6% for African Americans, and 27.9% for Hispanics. The differences were largely due to higher levels of combat exposure among the minorities. For women, 9% met criteria for current PTSD and 27% met criteria for lifetime PTSD, likely due to the different roles that women had in the military at that time (primarily nursing and clerical), the different types of stressors to which they were exposed, and to their higher educational levels. In a study of PTSD among female Vietnam veterans who served as nurses, war trauma and sexual trauma contributed about equally to the development of PTSD. [13] Other studies have documented high rates of family violence and social adjustment problems in veterans with PTSD. [1, 14] Sleep disturbances, including frequent nightmares and sleep onset insomnia, were more prevalent in Vietnam theater veterans; frequent nightmares occurred almost exclusively in veterans with PTSD, and combat exposure was highly associated with nightmares. [15] Hispanic Vietnam veterans, especially those who are Puerto Rican, had a higher probability of experiencing PTSD and significantly more severe PTSD symptoms than non-minority veterans. [16] In each of these studies, VTV prevalence rates were five to ten times higher than those found for the VEV and the civilians. These findings suggested that there were approximately 479,000 cases of current PTSD and nearly 1 million cases of lifetime PTSD in America stemming from the Vietnam War. Controversy about the accuracy and implications of these PTSD rates in the NVVRS continues to the present. [8, 17-20] Despite the controversy, public and professional awareness of the problem of PTSD was greatly increased by the publication of results from the NVVRS.

2.3. OIF/OEF STUDIES

More recently, studies by several investigators [6, 21, 22] have reported on the effects of combat exposure on PTSD and related problems in veterans in Operation for Enduring Freedom (OEF) in Afghanistan, and Operation Iraqi Freedom (OIF) in Iraq. In the first study, [21] anonymous surveys were administered to four groups of US. Infantry units (3 Army, 1 Marine Corps Unit), with a total of 2530 soldiers completing the questionnaire prior to deployment, and 3671 completers at 3-4 months post return from combat duty. The rates of PTSD were about

18.0% for Army subjects following service in Iraq, 11.5% after service in Afghanistan, and 9.4% prior to deployment to Iraq. [21] Among the post-Iraq deployment group, 16.6% met criteria for PTSD and there were markedly increased rates of disability and health service utilization. [22] Hoge et al.[6] administered the Post-Deployment Health Assessment (PDHA) Questionnaire to all post-deployment service members. [6] A total of 222,620 individuals completed the PDHA survey after deployment from Iraq, along with 16,318 from Enduring Freedom in Afghanistan. Almost 10% of OIF combatants scored positive for 2 or more responses on the PTSD screener, compared to 4.7% for OEF, and 2.1% for soldiers in other locations.

Vasterling et al. [23] gave neuropsychological tests to 654 soldiers prior to and following deployment to Iraq. Results demonstrated that Iraq deployment was associated with neuropsychological alterations on tasks of sustained attention, verbal learning, reaction time, and visual-spatial memory, and with increased negative state affect on measures of confusion and tension. A screening-based estimate of PTSD also suggested that about 12% of the deployed soldiers experienced clinically significant levels of PTSD symptoms upon their return from Iraq. The findings could not be explained by head injury or other medical diagnoses, but instead pointed to a specific pattern of neuropsychological sequelae consistent with an acute stress response.

Other studies of OIF/OEF soldiers have been reported by Grieger et al.[24] and Seal. [25] Although overall rates of PTSD were not as high in battle-injured soldiers, PTSD with comorbid depression was observed in approximately 10% of battle-injured soldiers in the study by Grieger et al. [24] Seal et al., [25] have recently reported on a large database (103,788 veterans) of OEF/IEF seen at VA health care facilities. A quarter of these individuals received a psychiatric diagnosis; among those with psychiatric diagnoses, more than half received multiple diagnoses, including PTSD. [25] Overall, these studies confirm the high rates of PTSD and PTSD-related symptoms in post-deployment OIF/OEF soldiers. However, these studies provide little information regarding outcomes or progression over time in these individuals. Thus far, the trajectories of change and specific predictors of relapse or recovery have not been investigated.

2.4. CURRENT MODELS OF ETIOLOGY AND DISEASE PROGRESSION

Current conceptual models emphasize three classes of variables as major risk factors for PTSD: 1) pre-existing factors in the individual, such as family psychopathology and socio-demographic factors; 2) the severity of the traumatic event and surrounding circumstances, and 3) events that took place after the trauma, such as social and occupational support. [26,27] Although post-trauma factors are not “causal”, they may increase understanding of the delayed onset of PTSD in some individuals. An analysis of the relationships between pre-war factors, war zone stress and PTSD symptomatology in NVVRS revealed that for men, a previous history of trauma directly predicted PTSD, and also interacted with war-zone stressors to worsen PTSD symptoms in veterans exposed to high level of combat.[27] War zone factors were of primary importance for men, while women were more affected by post-trauma resilience and recovery factors. The term recovery is used to describe a trajectory in which an individual’s normal functioning gives way to symptoms of depression or PTSD for at least several months, followed by gradual return to pre-trauma function; resilience is defined as the ability to maintain stability in the face of disruptive or traumatic events. [28] A model using both recovery and resilience variables to mediate the relationship between trauma and PTSD has been shown to have the highest predictive value for both male and female Vietnam veterans. [28, 29]

Evidence suggests that PTSD evolves over time, although the course of progression, natural history and consequences of the disorder are not well understood. Although treatments for PTSD may offer symptomatic relief in the short-term, symptoms of PTSD frequently persist and become chronic, particularly in those patients lacking adequate long-term emotional or social support.[30] Longitudinal research in diverse populations is urgently needed to assess long-term outcomes associated with PTSD and the impact of the disorder on veterans, their families and the mental health care system.

2.5. INTERVENTIONS AND OUTCOMES: LIMITATIONS OF CLINICAL TRIALS

Interventions for PTSD include pharmacological treatment (e.g., benzodiazepines, serotonin reuptake inhibitors), and cognitive behavioral therapies. Randomized clinical trials (RCTs) have been conducted to assess the efficacy of available treatment approaches, including cognitive-behavioral therapy (e.g., prolonged exposure, present-centered therapy), eye movement desensitization reprocessing, acupuncture and various psychotropic medications (e.g., sertraline, paroxetine, fluoxetine).[31-38] Although RCTs remain the cornerstone for treatment efficacy and safety evaluation, their generalizability and relevance beyond the trial setting is a source of increasing

concern.[39] These trials may not provide reliable outcomes data in a broad population of patients in non-research settings; most trials are of relatively short duration, and most studies discontinue follow-up at 24 weeks. Furthermore, RCTs are limited by the patient population selected and highly controlled environment of the clinical trial.[31, 33] Combination treatments and treatment sequencing are virtually untested, although in reality, patients are likely to undergo multiple treatment regimens. Moreover, treatment acceptability and satisfaction data are lacking, in addition to data on long-term outcomes and costs of treatment.

2.6. KNOWLEDGE GAPS AND POTENTIAL BENEFITS OF A REGISTRY

These knowledge gaps in the current system present a major challenge to effective planning and service delivery efforts. In addressing these needs, a registry can provide a complementary perspective to results obtained from RCTs and current observational studies, particularly in regard to service utilization and psychosocial outcomes. The registry facilitates planning by providing long-term data on these outcomes, and is a major resource for ancillary studies on specific topics of interest. An additional advantage of a registry is that the duration of the study and sample size may be increased over time, as resources and needs determine.

2.7. RATIONALE FOR A REGISTRY

A well-designed registry is a major source of knowledge regarding disease progression and the natural history of common physical and mental health disorders. The AHRQ Guide for registries,[40] a recent government publication, notes that when properly designed and implemented, registries offer unique information regarding disease impact and outcomes not addressed by randomized trials or retrospective surveys. As described by the AHRQ guide,[40] a patient registry provides "a real-world view of clinical practice, patient outcomes, safety and comparative effectiveness, and serves a number of evidence development and decision-making purposes." Major benefits of the PTSD registry include:

MULTIPLE ADVANTAGES OF REGISTRIES

- Natural History – (progression and remission)
- Health Services Utilization – (costs and benefits)
- Safety Considerations – (monitoring adverse events)
- Ancillary Observational Studies – (case-control)
- Assembled Population for Clinical Trials – (rapid start-up)
- Overall Cost Efficiency – (multiple endpoints)
- Real World Results – (external validity)
- Complementary Outcomes to Clinical Trials

- Evaluation of natural history and long-term outcomes of PTSD across treatments, treatment settings and practitioners, using cost-efficient methods and economies of scale
- Documentation of health resource utilization and development of a database that is an ideal resource for health services planning and policy
- Formation of a potential cohort of subjects for ancillary studies, ranging from genomic influences to quality of life and psychosocial outcomes, as well as future clinical trials
- Creation of a representative sample of PTSD patients who use the VA medical system, available for use in epidemiologic studies, particularly for comparisons with active duty, and other veteran or civilian populations (a comparison study is embedded in the current project)
- Utility to major stakeholders, including clinicians, patient advocacy groups and health policy planners.
- Publications and dissemination of the registry results to provide a representative perspective of what is achieved in actual current care settings, thereby augmenting outcomes data from clinical trials

2.8. REFERENCES

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3. Participants: Sampling Strategy and Eligibility Criteria

3.1. SOURCE POPULATION

The source population of participants is combat-exposed OIF/OEF army or marine veterans who are in the VA health care system database. From this source population, 1200 men and women with PTSD (using the selection algorithm in Section 3.2) and 400 men and women without PTSD (Section 3.3) will undergo informed consent procedure to participate in the Registry study.

3.2. ELIGIBILITY CRITERIA FOR PTSD REGISTRY GROUP

The following criteria must be met for potential veterans to be included in the PTSD Registry group. (n = 2,250 for sample, target goal of 1,200 for study)

- OIF/OEF army or marine veteran (deployed to combat)
- In the VA health care system database
- Not currently participating in a clinical (intervention) trial
- Mental health evaluation/assessment conducted; this evaluation is coded in the electronic medical record as one of the following ("evaluation and management" services are visits and consultations furnished by physicians and including medical management):
  - 90801- mental health assessment
  - 90804- 20-25 min therapy
  - 90805- 20-25 min therapy with evaluation & management
  - 90806- 45-50 min therapy
  - 90807- 45-50 min therapy with evaluation & management
  - 90808 - 75-80 min therapy
  - 90809- 75-80 min therapy with evaluation & management
  - 90853- group therapy
- PTSD diagnosis coded (ICD9-309.81) within the past 6 months in the electronic medical record
  - PTSD diagnosis code can be the primary or secondary diagnosis
  - PTSD diagnosis code appears at least once subsequent to the date and time of the mental health evaluation coding
- The earliest CPT code may be associated with any other mental health diagnosis (including ICD-9 CM 309-Adjustment reaction).

3.3. ELIGIBILITY CRITERIA FOR NON-PTSD STUDY GROUP

The following criteria must be met for potential veterans to be included in the non-PTSD study group. (n=750 for sample, target goal of 400 for study)

- OIF/OEF army or marine veteran (deployed to combat)
- In the VA health care system database
- Not currently participating in a clinical (intervention) trial
- Mental health evaluation/assessment conducted; this evaluation is coded in the electronic medical record as one of the following ("evaluation and management" services are visits and consultations furnished by physicians and including medical management):
    - 90801- mental health assessment
    - 90804- 20-25 min therapy
    - 90805- 20-25 min therapy with evaluation & management
    - 90806- 45-50 min therapy
    - 90807- 45-50 min therapy with evaluation & management
    - 90808 - 75-80 min therapy
    - 90809- 75-80 min therapy with evaluation & management
    - 90853- group therapy
- No record ever of any PTSD diagnosis (ICD9-309.81) or history in the electronic medical record
- The CPT code may be associated with any other mental health diagnosis (including ICD-9 CM 309- Adjustment reaction)

4. Recruitment Procedures

4.1 OPT-OUT LETTER AND RECRUITMENT PROCEDURE

A roster of potential participants for the PTSD Registry and the non-PTSD study group will be created using the inclusion criteria specified in Section 3 of this manual. The DC VA project team will create the roster by matching unique OIF/OEF veterans who have been separated from active duty with VA inpatient and outpatient databases. This initial roster, referred to as the **Level 1 Roster**, will include approximately 3000 veterans.

Veterans on the Level 1 Roster will be sent an initial 'opt-out' letter (see appendix) that introduces the study and asks the veteran to indicate if he/she would like to be contacted further about the study or not. Veterans respond using the prepaid response envelope enclosed with the letter. Those who opt out of any further contact with the initial opt-out letter will be removed from the list of potential participants. A second follow-up 'opt-out' letter will be mailed to Level 1 Roster participants who do not respond to the initial opt-out letter. The second letter will again ask the veteran to indicate if he/she would like to be contacted about the study or not using the prepaid response envelope. Those who opt-out of any further contact with the second letter will be dropped from the potential participant list, and the resulting narrowed list is referred to as the **Level 2 Roster**. The Level 2 Roster lists veterans who may be contacted for informed consent to be part of the final 1600 total participants. The procedures for selecting the rosters and final participants are outlined below.

(7) The DC VA project team will create a data file of approximately 3000 veterans meeting initial eligibility criteria and share it with the Boston VA project staff using the secure VA network. This list will be properly encrypted and password protected as required by the VA data security and information protection policies, described in VHA handbook 1605.1, VA Directive 6500, and VHA Handbook 1200.5.

(8) The Boston VA project team will mail an 'opt-out' letter to the ~3000 Level I potential participants; the letter, which will be signed by project investigators Dr. Keane and Dr. Kang, will briefly describe the study and note that the recipient can choose to be contacted further about the study, or not be contacted further regarding the study by returning a pre-addressed and postage-paid response letter.

(9) Level I potential participants will have 30 days to mail back the opt-out letter to Boston VA project team for processing. The opt-out period will begin on the day the last recruitment letter is mailed out.

(10) After the initial 30 day wait period is over, the Boston VA project team will remove the potential participants who indicated they did not want to be contacted about the study from the Level 1 roster. Those potential participants who indicated interest in the study will become part of the Level 2 roster. The remaining potential participants who did not respond to the initial opt-out letter will be mailed a second, follow-up opt-out letter describing the study and asking the potential participant to indicate if he/she would like to be contacted further about the study, or not be contacted further regarding the study by returning the prepaid envelope enclosed with the letter.

(11) Potential participants will have 14 days to mail back the second opt-out letter to Boston VA for processing. The second opt-out period will begin on the day the last follow-up opt-out letter is mailed out. After the second wait period is over, Boston VA project staff will create the Level 2 Roster, which is a narrowed list of potential participants, excluding all those indicated on either of the 'opt-out' post letters that they did not want to be contacted further about the study.

(12) VA Boston study staff will contact Level 2 potential participants via phone to provide more details about the study, assess the inclusion requirement of not currently participating in a clinical (intervention) research trial, and begin the informed consent process. Those who consent will be included as participants of the study. Contact information will be recorded for participants at this time. All calls will be recorded in a password protected contact log maintained by study staff (see appendix).

4.1.1 Letters returned to the VA by the Postal Service with no forwarding address

When a letter is returned to the VA by the US Postal Service with no forwarding address, study staff will first flag the participant as having an unknown address in the level 1 roster. Study staff will then look up the potential participant in the VA electronic medical record system, VISTA WEB, and attempt to identify the current address of the participant. If a new address is identified, study staff will re-send the opt-out letter to the potential participant using the new address. The new address will be recorded in a separate possible address list. Study staff will not change the participant's address in the level 1 roster when the opt-out letter is re-sent. The participant's address will only be changed in the level 1 roster if the participant returns the opt-out letter.

Participants flagged as having an unknown address in the first opt-out mailing will not be included in the second opt-out mailing.

Locating addresses in VISTA WEB:

To locate participant addresses in VISTA WEB, login to VISTA WEB and select the VA network for the participant's last known address. Type the first initial of the participant's last name followed by the last four digits of the participant's social security number. Click the search button. If the participant is located, record the new address in the possible address list and re-send the opt-out letter. If the participant is not listed in the VA network for the participant's last known address check all other VA networks for the participant. If the participant is not found in

any of the VA networks listed in Vista Web, flag the participant in the master list and put the participant's letter in the unknown address file. Follow the instructions in section 4.3. for administrative withdrawals.

4.1.2 Letters returned to the VA by the Postal Service with a forwarding address

When a letter is returned to the VA by the US Postal Service with a forwarding address, study staff will flag the participant as having a forwarding address in the level 1 roster and change the current address to the forwarding address. Study staff will then re-send the opt-out letter to the participant using the forwarding address provided by the Postal Service. The participant will remain flagged as having a forwarding address until the opt-out period is over or the participant returns the opt-out letter to VA Boston. If the participant does not provide a response during the opt-out period the participant will be sent the second opt-out letter at the forwarding address. Should the participant not respond to either opt-out letter, the participant will be called per the protocol described above.

4.1.3 Letters with Unknown Addresses

If a letter is returned to the VA by the US Postal Service without a forwarding address and study staff are unable to locate a new address for the participant using Vista Web, then the participant will be considered administratively withdrawn from the study.

4.2 TELEPHONE CONSENT AND HIPAA PROCEDURE

VA Boston study staff will telephone Level 2 potential participants to follow-up on the information in the opt-out letter and formally invite the veteran to participate in the study. This study uses verbal, not written, informed consent and Health Insurance Portability and Accountability Act (HIPAA) release procedures.

A trained research assistant will administer the call using the Project VALOR informed consent and HIPAA release script (see appendix). If the potential participant is willing to enroll in the study, the research assistant will read the informed consent statement verbatim as directed in the informed consent script. If the potential participant has questions at any time during the reading of the consent statement, the research assistant will stop to answer the potential participant's questions. It is acceptable to depart from the exact consent statement language in order to facilitate the potential participant's understanding of the consent statement.

Once verbal consent has been obtained for the study, the research assistant will read the HIPAA release statement to obtain authorization for records release. The research assistant will then request the participant's consent to be contacted for future studies. The research assistant will document all verbal consents and refusals on the participant's informed consent script form. The participant's informed consent script form will function as a record of the entire consent process, and it will be kept in the participant's file. A copy of the informed consent and authorization information will be emailed to the participant for his/her records. If the participant does not have access to the internet, a paper copy of the consent and HIPAA authorization will be mailed to the participant.

The research assistant will then set up a time and date for the telephone interview. The research assistant will provide the participant with the name of the interviewer who will be contacting them. Lastly, the research assistant will confirm the address and contact information of the participant, as well as details on his/her deployment history (see appendix for form). If the participant declines to participate in Project VALOR during the consent/recruitment call, the research assistant will follow the procedure outlined in section 4.3 below.

A reasonable attempt will be made to make telephone contact with all participants on the level 2 roster. Up to 8 attempts will be made to contact participants at which point the participant will be considered administratively withdrawn from the study. In order to maximize the possibility of reaching a participant, study staff will call at varying times of day and on different days. All recruitment call attempts will be recorded on the call log on the consent/HIPAA document (see appendix). The research assistant may use his/her judgment when trying to reach participants. For example, if the research assistant has made 4 or 5 attempts to contact a participant and received no return call the research assistant may cease attempts at communication and move on to more available participants.

If initial phone contact has been made with the participant, but the participant was unable to complete the consent process at the time of the initial call, then up to 8 attempts will be made to re-contact the participant. After 8 attempts have been made the participant will be considered administratively withdrawn from the study. Again, it is acceptable for the research assistant to use his/her judgment when trying to re-contact participants.

4.3. Tracking Participant Refusals/ Withdrawals

Information about participants who decline to participate in Project VALOR will be documented. Participant refusals will be tracked on a separate 'refusal' section of the subject tracking document (see appendix). In addition to noting the name and subject ID numbers of participants, the research assistant will record the following information from the Level 1 roster in the subject tracking document on participants who refuse participation in Project VALOR.

A. Race
B. Ethnicity
C. Gender
D. Date of Birth

4.3.1 Opt-out letter Refusals
As noted in section 4.1, participants who opt-out of the study by returning one of the recruitment letters will be tagged in the subject tracking document. If a participant declines participation using an opt-out letter, the research assistant will note this in the 'reason' column on the refusal tab of the subject tracking document by writing 'letter refusal'. If the participant also provides a comment on the letter explaining his/her reasons for declining participation, the research assistant will note the basic sentiment of the comment. For example, if a participant declines participation and writes that it is because he/she is too busy then the research assistant would write 'letter refusal- too busy' in the 'reason' column.

4.3.2 Verbal Refusals
If a participant chooses not to participate in the study during the consent/recruitment call, the research assistant will tag the participant as a refusal in the subject tracking document and the master level 2 roster. Before ending the recruitment call the research assistant will ask the participant if he/she would like to share his/her reasons for declining to participate in the study. The research assistant should record the basic sentiment of any reason provided for refusal in the 'reason' column in the refusal section of the subject tracking document. For example, if the participant declined participation because he is too busy then the research assistant would write, 'verbal refusal- too busy'. If the participant does not want to provide a reason for declining participation, the research assistant should write 'verbal refusal' in the 'reason' column in the refusal section of the subject tracking document.

4.3.3 Administrative Refusals/ Withdrawals
The category of administrative refusal encompasses participants who are withdrawn from the study as indicated by the protocol and not because of written or verbal refusal. Potential participants from the level 2 roster are considered administratively withdrawn from the study if they never respond to staff calls, or if they become unreachable after initial contact. Staff will make up to 8 attempts to reach participants. Additionally, participants can be administratively withdrawn from the study if they miss two scheduled interview appointments or if they have an unknown address. The research assistant will note administrative refusals/ withdrawals in the 'reason' column in the refusal section of the subject tracking document by writing 'admin refusal'.

5. SAQ Administration Procedures/ Participant Files

5.1. ONLINE DATA COLLECTION PROCEDURE

Participants will complete the self administered questionnaire (SAQ) using a secure online survey hosted by psychdata.com. PsychData is a web-based company that specializes in internet-based social science research ***. No identifying information will be collected using the online SAQ. This includes removal of the subject's IP address. Participant responses will be identified only by the subject ID number provided to them as their username.*** All participants who complete a survey at PsychData are automatically assigned an internal number called the Respondent ID Number. This number will not be the same as the Participant's project VALOR study ID number. It will, however, be used to generate confirmation that the participant completed the online SAQ. Each participant's data from the online survey will be linked to his/her data in the VA database by the Project VALOR study ID number provided to the subject at the time of informed consent. Programming the online SAQ will be done by the doctoral level project manager at VA Boston. The online SAQ will be a replica of the paper SAQ (see appendix). The project manager will be responsible for overseeing the online data collection including error testing, data monitoring, and data transfer to the SPSS database. The doctoral level project manager will then train the study research assistants how to use the site.
See section 5.2 for paper SAQ administration procedure.

5.1.1 Online SAQ administration procedure

8. After the participant has provided consent the interview date will be set for approximately two weeks from the date of the consent phone call. The trained research assistant will explain the online SAQ procedure to the participant and provide the participant with his or her study ID number. The study ID will be the participant's username for the website. The subject's study ID number will only be given to the participant over the phone.
9. The participant will be sent an email on the day of the consent phone call containing the link to the online SAQ at psychdata.com as well as the password for the website (see appendix for details). The email will also contain a reminder about the date of the interview and instructions about how to login and what to expect while completing the survey. Additionally, the email will contain study staff contact information should the participant forget his or her username and an emergency number.
10. Once the participant has the password and the instruction email the participant will have approximately two weeks to complete the questionnaires before the phone interview.
11. Seven days prior to the participant's scheduled interview date the VA Boston research assistants will check the status of the participant's online SAQ. If the participant has not begun the online SAQ, or has not completed it, the research assistant will call the participant to check in, remind the participant that he/she needs to complete the online SAQ prior to the interview and ask the participant if he/she is still interested in completing the study (see **appendix** for the check in call script). If the participant received the initial reminder call, the research assistant will check the status of the participant's online SAQ again 4 days prior to the participant's scheduled interview. If the online SAQ is not yet complete, the research assistant will call the participant with a second reminder call.
12. If the participant received the first and second reminder call, the research assistant will check the status of the participant's online SAQ 2 days prior to the scheduled interview date. If the online SAQ is not complete, the participant will be called and asked to reschedule the phone interview (see appendix for script).
13. If the participant wants to reschedule the interview and complete the study, the interview will be scheduled approximately one week from the original interview date.
14. Once the subject completes the online SAQ the data will be downloaded to SPSS and a paper copy will be printed from PsychData for the participant's study file. After the participant's responses have been downloaded into the SPSS database and the paper survey has been retrieved, the participant's record will be erased from the PsychData server. The progress of participants will be closely monitored to ensure that each subject record is erased as quickly as possible.

5.2. PAPER SAQ ADMINISTRATION

If a participant does not have access to the internet or does not feel comfortable using the internet to complete the SAQ, a paper copy of the SAQ will be mailed to the participant. The packet will include an instruction letter, a copy of the consent/HIPAA statement, and the paper SAQ. The participant will have approximately 4 weeks to fill out the paper SAQ. (See appendix for materials)

1. After the participant has provided consent, a packet will be mailed to the participant.
2. Approximately 2 weeks after the packet mailing date, a research assistant will call to make sure the participant received the materials and check on the status of the questionnaire. If the participant has received the materials, an interview will be scheduled approximately 2 weeks from the date of the first reminder call.
3. If the participant has not returned the paper SAQ 4 weeks after the mailing date/ by the interview date, the research assistant will make a second reminder call asking the participant if he/she still has the study materials and is still interested in participating in the study. If the participant is still interested in participating then he/she will have 2 weeks to return the questionnaire. An additional packet will be mailed to the participant if the participant requests one.

4. If the packet has not been returned by the second interview date, approximately 2 weeks from the second reminder call, the participant will be considered dropped from the study.
5. Once the SAQ is returned to VA Boston HCS a research assistant will login to psychdata and enter the participant's responses into the online SAQ. A copy of the online SAQ responses will be placed in the participant's folder in addition to the original paper SAQ.

5.3. DOWNLOADING QUESTIONNAIRES FROM PSYCHDATA INTO SPSS

Psychdata files will be downloaded and backed up on a daily basis using the following protocol:

1. Log in to Psychdata
2. Click the Data icon under Tools.
3. Click on "Download Survey Data" (at the bottom of the page).
4. Choose SPSS as your file format choice.
5. Wait for the file to load. It will be called an "EnZip Archive".
6. Save the file in the registry folder under DATA/Psychdata Survey Files.

5.4. WEBSITE COMPANY INFORMATION

PsychData is a professionally developed and maintained web-based company specifically geared toward internet-based social science research. The company uses parent-level, centralized database architecture and strict security policies and procedures to meet and exceed industry standards for internet security.

1. Technology

PsychData uses a redundant, high bandwith, private transport network. This network has demonstrated 99.999% availability, which means that the network will be down no more than 5 minutes in one year. PsychData servers are housed in a secure data facility that is monitored 24 hours 7 days a week by network operations professionals for all aspects of operational security. Biometric/intrusion sensors, card readers, pin numbers, and environmental sensors are used to insure server integrity and safety. Redundant HVAC systems ensure an optimized operational environment.

5.4.1. Data Safety and Security

<u>All surveys are accessed and completed in a Secure Survey Environment (SSE)</u>

All survey pages are constructed such that a completed survey cannot be viewed by simply pressing the "Back" button (thus greatly reducing the chance that someone could "back up" to see previously entered data).

The SSE incorporates additional security measures to ensure that a participant's responses are not retrievable from their computer. First, all survey pages are entirely dynamic and database-generated (instead of static web pages that could be stored by the participant's computer). Second, all surveys have redundant server-side code to ensure that they always load directly from our server and not from a prior cached version. Finally, upon completion of the survey, the survey window itself automatically closes and disappears eliminating temporary history files associated with that survey.

<u>Data security during Transmission</u>

All surveys hosted with PsychData are encrypted using 128-bit SSL Technology (Secure Socket Layer) that is equivalent to the industry standard for securely transmitting credit card information over the Internet. This technology encrypts BOTH the questions displayed to the participants and their responses. Thus, all responses are instantly encrypted and remain so until they are received at the PsychData database. Interception of data when it is being transmitted between the Internet browser (i.e., Internet Explorer or Netscape Navigator) and the PsychData database is HIGHLY unlikely (consider the motivations of a person attempting to intercept research data over the internet vs. papers stored in an office vs. credit card information). However, should interception of encrypted data occur, that data could not be decoded without the unique encryption key that is held only by PsychData.

<u>Safety and Control of Stored Data</u>

Once research data is stored on a PsychData server, it is held in an isolated database ***<u>that can only be accessed by a researcher with the correct username and password. PsychData employees do NOT examine customer data unless requested to do so by the account owner;</u>*** additionally, those employees are trained in the ethics of research involving human subjects. The researcher has full control over their data including the ability to delete all data at the completion of their survey. All data stored at PsychData is backed up on a daily basis, held in a tightly secured facility and typically overwritten after seven days. Therefore, once a user has deleted their data, it will be permanently deleted from our backups in about one week.

<u>IP Addresses</u>

An IP address is a unique identifying number used to identify computers connected to the Internet. An IP address might be static (i.e., always refer to one institution's server), dynamic (assigned upon connection), or pooled (a group of servers share one or more IP addresses). IP addresses may also change multiple times during the same connection - for example, the IP address of AOL users may change multiple times per minute. An IP address generally will represent either an

institution (i.e. a university or large company) or an Internet Service Provider (i.e. AOL or an ISP serving one or more communities). ***Project VALOR will EXCLUDE all participant IP addresses.***

Unique Respondent Number

All participants who complete a survey at PsychData are automatically assigned an internal number called the Respondent ID Number. This number will not be the same as the Participant's project VALOR study ID number. It will, however, be used to generate confirmation that the participant completed the online SAQ.

5.5. SAQ MEASURES

The self administered questionnaire (SAQ) is comprised of 13 measures that will be used to fill gaps in the electronic medical record by assessing factors such as exposure to traumatic events, comorbid symptoms of anxiety or depression, probable substance abuse and alcoholism, social and occupational status, and overall quality of life. Recognizing the limitations of self-report data, each of these domains will be assessed by means of brief, validated scales and measure current symptoms and outcomes. See figure 5.1 for a list of SAQ measures.

Table 5.1. Project VALOR SAQ Domains and Measures

Domain	Assessment Measure(s)	Project VALOR Administration
Combat Exposure	DRRI Section I (Combat Experiences) and Section J (Post-Battle Experiences)	Website survey/ mailed paper form
Quality of Life	SF-12v2	Website survey/ mailed paper form
Sleep	Jenkins Sleep Questionnaire	Website survey/ mailed paper form
Absenteeism	World Health Organization Health and Work Performance Questionnaire (HPQ)	Website survey/ mailed paper form
Life Stressors/Trauma	Life Events Checklist (LEC)	Website survey/ mailed paper form
Social Support	Deployment Risk and Resilience Inventory (DRRI) Section L (Post-deployment support)	Website survey/ mailed paper form
Mental Health Disorders and Stresses (including Depression, Anxiety, Panic, Somatoform Disorder)	▪ Prime-MD Patient Health Questionnaire (PHQ)	Website survey/ mailed paper form
Alcohol/Drug Use	▪ Alcohol Use Disorder Identification Test (AUDIT) ▪ Two-Item Conjoint Screen (TICS)	Website survey/ mailed paper form
Anger/Hostility	Dimensions of Anger Reactions, revised short form (DAR-5)	Website survey/ mailed paper form
Treatment Utilization	New Questions	Website survey/ mailed paper form
PTSD Related Functional Impairment	Inventory of Functional Impairment (IFI)	Website survey/ mailed paper form

Project VALOR staff will make every reasonable attempt to encourage participants to provide complete responses on all study measures. The following procedures should be followed if there is a significant amount of missing information:

5.6.1 Incomplete SAQ

If a participant's SAQ is missing large amounts of information, such as more than one section (defined as the questions covering a specific domain or existing scale) entirely missing, it is acceptable for the research assistant to contact the participant to clarify why the participant did not complete the questionnaire. If the participant indicates he/she had trouble understanding the questions or that the section was confusing, ask if the participant would like to go over the questions over the phone. If the participant agrees to go over the questions with the research assistant on the call, the research assistant will record the answers on a paper SAQ. The additional SAQ answers should be entered into the database and the paper SAQ used to record the missing data should be placed in the participant's data file.

If the participant completed a paper SAQ and is willing to go over the unanswered sections, the research assistant will use the original SAQ returned by the participant to record the responses. The research assistant will initial sections he/she completed and write "filled out with participant on phone" to note sections not originally completed by the participant.

If the participant indicates that he/she did not complete all the questions on the SAQ because he/she did not feel comfortable answering the questions or did not want to complete the questions, the research assistant will thank the participant and end the call. The research assistant will note this in the 'comments' area of the run sheet.

5.6.2 Incomplete Contact Information and Deployment Form

If the participant cannot remember the details of his/her deployment information at the time of the consent call, the research assistant should ask the participant if he/she could look for the information in his/her records and schedule a time to re-contact the participant. It is unlikely that the participant will not remember his/her contact information.

5.6.3 Incomplete Interview Measures

The clinician will use his/her judgment during the interview when participants do not want to complete a significant part of one or more measures.

5.7. PARTICIPANT FILES

Two participant files will be maintained for each subject. Subject files will be stored in separate, locked file cabinets at the Boston VA HCS. Only Project VALOR staff will have access to the participant files. Individual participant files will not be maintained for participants who decline participation using either of the opt-out letters. (See the appendix for copies of all materials)

5.7.1 Recruitment File

The recruitment file will contain all of the participant's identifiable recruitment materials. This subject file WILL contain PHI. The recruitment file will contain the following items:

- Opt-Out Letter – the opt-out letter will be kept in the file only if the participant provides a positive response. If a participant did not return either opt-out letter his/her recruitment file will not contain an opt-out letter
- Consent/ HIPAA script – Since Project VALOR does not have a written consent form the consent/HIPPAA script will be kept as documentation of consent. This document also serves as a paper call log for each participant. It is completed by the research assistant.
- Contact information/Deployment form – This form is completed by the research assistant during the consent/recruitment phone call. It documents the participant's current contact information, including email address, preferred VA medical center, as well as deployment information.
- SAE Form – Because the SAE form has the subject's name it will be maintained in the recruitment file. SAE forms are completed by the clinical interviewer.

5.7.2 Data File

The study file will contain all of the participant's study measures. This file will be identified by study ID only. It will NOT contain PHI or identifiable information. All documents will be labeled with the study ID.

- Run Sheet – The run sheet documents the research assistant responsible for consenting the participant, the interviewer, any relevant notes concerning the participant/interview, and a list of measures to be completed. The research assistant is responsible for completing the run sheet.
- Emergency Contact Template – The emergency contact template documents relevant emergency information for interviewers. Information includes phone numbers for the nearest emergency room, VAMC, as well as the state police. The research assistant will complete this form prior to the clinical interview.
- MINI Suicide Module – The MINI suicide module is administered by the clinician as part of the safety plan. The safety plan is detailed on the back of the MINI as a reference for interviewers.
- SCID – Clinicians complete this worksheet during administration of the SCID.
- Open-Ended questions – If the participant permits his/her interview to be recorded, the clinician can record notes on this document. However, if the participant does not allow for the interview to be recorded the clinician will record the participant's response to the questions here.
- TBI Questionnaire – Clinicians complete this worksheet to document the participant's TBI history.
- Life Events Checklist – Research Assistants fill the LEC out prior to the clinical interview using the participant's responses from the SAQ.
- CPRS/ VISTA Web (electronic medical record) Abstractions – Over the course of the study, research assistants will record 3 data abstractions from the medical record.

5.8. REGISTRY ID NUMBERS

ID numbers are used to ensure the study participant's confidentiality. ID numbers will be taken from a computer generated list of random 6 digit numbers. Study staff will assign a study ID number to all participants upon receipt of an opt-out letter with a positive response. Participants who do not return either of the opt-out letters will be assigned a study ID number at the time of the initial recruitment phone call. The study ID number will only be given to the participant over the phone. Additionally, the study ID will serve as the username for the online SAQ. Research assistants will remind participants that they are unable to send the participant his/her study ID number in written form. Should a participant forget his/her study ID number, the participant will be instructed to call the research assistant who consented him/her.

5.9. RECRUITMENT TARGETS

Given the demands of the Project VALOR timeline, it is important to maintain an efficient recruitment rate during phase II of the study. Project VALOR aims to call all participants on the level 2 roster by month 8 of year 2. The intended recruitment period is 9 months with the aim of recruiting approximately 180 participants per month.

6. Telephone Interview Procedures

6.1. INTERVIEW SCHEDULING

A. Initial Interview Scheduling

For participants who choose to complete the Project VALOR questionnaire online, the phone interview will be scheduled approximately 2 weeks from the date of the phone consent. The participant will be sent a confirmation email (see appendix) with the date and time of the interview. For participants who choose the mailed packet option, a research assistant will contact the participant approximately 2 weeks after the packet was mailed from VA Boston HCS to make sure the packet was received and schedule an interview date. The interview will be scheduled approximately 2 weeks from the date of the check-in call. If the participant has not completed the mailed packet by the scheduled interview date, the research assistant will make a second reminder call to see if the participant is still interested in participating in the study and to reschedule the interview. The interview will be rescheduled 2 weeks from the date of the reminder call. If the participant misses the second interview date, he/she will be dropped from the study. Up to 8 attempts will be made to contact consented individuals before deeming the individual administratively withdrawn from the study.

Once a participant chooses an interview date and time, the research assistant will assign the participant to an available interviewer and make an appointment in the Outlook calendar of the interviewer. The research assistant will note the interview date, time, and name of the assessor in the subject tracking document (see appendix).

If the subject has completed online questionnaire within two days of his/her scheduled interview date, a research assistant will call to confirm the interview appointment a few days in advance of the appointment. If the participant confirms his/her availability for the interview then the research assistant will label the outlook appointment 'confirmed' in the assessor's calendar.

B. Rescheduling the Interview

If the participant has completed his/her questionnaire and needs to reschedule the phone interview, the research assistant will schedule the participant for the next available appointment. Up to 5 attempts will be made to reach participants to reschedule the phone interview for participants who have completed the questionnaire. However, if the participant misses a total of 3 set interview appointments (including the original interview appointment) the participant will be dropped from the study. The research assistant will notify the participant via phone and email (if available) that he/she has been dropped from the study but will still receive partial compensation for completing the questionnaire.

If the participant has not completed his/her questionnaire within 2 days of the interview, the research assistant will call the participant to reschedule the interview within a week of the original interview date. One attempt will be made to reschedule the interview with participants who have not completed the questionnaire at the time of his/her first scheduled interview.

6.2 INTERVIEW PROCEDURES

The clinical interview will be administered by a trained masters or doctoral level clinician over the telephone within 2 to 4 weeks of the completion of the questionnaire. The clinical interview is expected to take approximately 30-60 minutes to complete. All Project VALOR interviewers will receive training on interview administration and protocol prior to the start of the piloting phase. The assessments will be administered in the order listed below. Interviewers should note any deviation from this order in the participant folder. Should a participant become distressed at any time during the interview, the interviewer should stop the interview and use his/her clinical judgment to assess if it is appropriate to continue with the protocol.

The interview will be recorded ONLY if the participant consented to audio recording during the phone consent. The interviewer should check with participant prior to beginning the interview to ensure the participant is still comfortable to the interview being recorded.

6.2.1 Interview Contents and Order of Administration

The project VALOR clinical interview includes the following assessments:

1. <u>Mini-International Neuropsychiatric Interview (M.I.N.I) suicide module</u>

   Clinicians administering the MINI will use the MINI General Instructions to conduct the interview. Sentences in normal font should be read to the participant verbatim. After reading the question verbatim it is acceptable to clarify as needed. Sentences in CAPITALS should not be read to the patient. Sentences in **bold** refer to the timeframe during which the symptoms occurred. The interviewer should emphasize the timeframe as often as needed. The interviewer should ask for clarification in order to gain the best understanding of the symptom or event. Similarly, the interviewer

should make sure that the participant understands he/she can ask questions at any time. For further details about how to use the MINI, refer to the safety plan described in section 4 of the manual of operations.

2. Structured Clinical Interview for DSM-IV (SCID-IV) PTSD module

   The SCID PTSD module is a semi-structured clinical interview used to diagnose PTSD. The interviewer will follow the format on the SCID PTSD module form, beginning by reading the instructions verbatim to the participant. After the participant has listed all of his/her traumatic events, the interviewer should ask the participant to identify the event which the participant considers to be his/her worst traumatic event. The interviewer should complete the assessment using the event the participant indentifies as his/her worst trauma. The interviewer should rephrase and clarify questions if the participant is unclear about the question being asked.

   Interviewers will be given a Life Events Checklist (LEC) for each participant prior to the clinical interview call. The interviewer will review the information on the LEC with the participant prior to starting the SCID to help the participant choose an event to focus on during the interview.

   The interviewer should use his/her judgment in guiding the participant if he/she begins to provide an excessive description of the event. It is acceptable for the interviewer to redirect the participant should the interviewer judge continued discussion of the event to be harmful to the participant. The interviewer should encourage the participant to answer all the questions with an appropriate level of detail. However, should a participant not wish to answer a question he/she is not required to do so. In that event, simply move on to the next question.

3. Open-ended questions (qualitative data)

   The interviewer will ask the following questions:

   A. "How have your military experiences affected your ability to do work after you came home?"
   B. "How have your military experiences affected your personal relationships after you came home?"

   The goal of the open-ended questions is to capture a brief narrative of the participant's experience. Once the question has been read verbatim, the interviewer can use his/her judgment with follow-up questions in order to clarify the participant's response. Overall, the interviewer should aim to keep this portion of the interview to 5 or 10 minutes. Interviewers should tactfully redirect participants who provide more than 10 minutes of narrative by reminding him/her of the time constraints of the interview. The interviewer should encourage the participant to answer both questions, but if the participant does not wish to answer the question he/she is not required to do so.

4. Traumatic Brain Injury Questionnaire (TBI Questionnaire)

   The interviewer will complete the TBI questionnaire on up to 5 TBIs. If the participant has had greater than 5 TBIs, the interviewer should ask the participant to describe the 5 most severe injuries. The interviewer should ask the participant to begin with the most recent TBI. It is important that the information about each TBI is as complete as possible. If the participant has trouble remembering the month and year of the TBI, the interviewer should help the participant to remember by asking questions such as "Do you remember if the event happened in the summer or winter?" or "Did the event occur around a holiday?" Instructions should be read verbatim and repeated as necessary to facilitate understanding.

5. Additional Items

   If the participant was unable to complete the contact and deployment information form during the consent phone call then the interviewer will try to finish this form with the participant during the phone interview. Also, the interviewer will be given a Life Events Checklist (LEC) for each subject. This will serve as a reference for the clinician during the SCID portion of the interview.

6.3 POST INTERVIEW PROCEDURES

6.3.1 Interviewer Responsibilities

After the interview is complete, the interviewer will complete following procedures:

A. The interviewer will save the audio recording from the interview in the 'audio' section in the Dod_PTSD folder. The audio file will be labeled with the subject's study ID number.
B. If the participant did not allow his/her interview to be recorded, the interviewer should make sure all interview notes are legible and complete. This is especially important for the open-ended questions.
C. Regardless of whether the interview was recorded, the interviewer should go over the interview measures to make sure all information is complete prior to returning subject's data file to the research assistant responsible for the participant. The name of the responsible research assistant can be found on the run sheet in the data file.

6.3.2 Research Assistant Responsibilities

Once the interview is complete and the interviewer has returned the participant's recruitment and data files to the research assistant, the research assistant will complete the following procedures:

A. Fill out the remaining fields in your personal section of the subject tracker and highlight the participant in blue.
B. Copy the participant's information from your personal tab and paste it into the 'completed' tab.

C. Open the study bridge and record the date the participant completed the study.
D. Prepare folder for data entry (see section 6 for data entry procedures)

6.4 QUALITY ASSURANCE PROCEDURES

Interviews will be reviewed by the team on a monthly basis to check for consistency and quality. Every month one subject interview will be chosen and reviewed by the interviewers for reliability purposes. Any questions, changes, or inconsistencies will be addressed by the co-investigator and the interviewers. Any changes will be documented and appropriate changes made to the study manual of operations.

7. Safety Plan, Reporting of Adverse Events, and Reporting Responsibilities of the PI

7.1 SAFETY PLAN

Study assessors are doctoral-level or licensed psychologists trained to assess for suicidal and homicidal risk. Additionally, all study personnel with participant contact will receive training on recognizing emotional distress and navigating situations where participants express suicidal and/or homicidal ideation.

In advance of each telephone interview, the assessor will be provided with a list of resources, including VA/DoD healthcare facilities and local police contact information for the area in which the participant lives. The assessor will thus be prepared to use any of these resources in the event that the participant demonstrates safety risk behaviors. If the participant demonstrates risk behaviors prior to the telephone interview during the consent process, research assistants will keep contact with the participant and page the project coordinator or the assessor on call. The project coordinator or assessor on call will then assess the participant's level of risk using the safety plan outlined below.

Assessors will administer and score the Mini-International Neuropsychiatric Interview (M.I.N.I.) suicide module prior to administering the Structured Clinical Interview for DSM-IV (SCID-IV) PTSD module during the telephone interview. Regardless of score on the MINI suicide module, for any participant thought to be at imminent risk, the assessor will contact local VA or DoD facility and inform the mental health provider on call or suicide prevention coordinator, as appropriate. The assessor will administer the further risk assessment measure as necessary to gain additional information regarding risk and protective factors and suicidal ideation risk level. Procedures for the MINI results are:

Low suicide risk (0-8 points on MINI suicide module) and no participant expression of suicidal ideation in other components of the interview:

- Assessor will follow judgment in whether to provide follow-up.
- If participant is mildly symptomatic or distressed, the assessor will:

3) Perform a "check out" with the participant at the conclusion of the interview.
4) Provide the participant with the VA Suicide Hotline number (1-800-273-TALK), number for local VA/DoD.

Moderate suicide risk (9-16 points on MINI suicide module)

The assessor will:

6) Provide the participant with the VA Suicide Hotline number (1-800-273-TALK)
7) Provide the participant with local VA/DOD contact information
8) Offer to provide local treatment referrals within the next 24 hours
9) Offer to contact participant's mental health provider (e.g., therapist, psychiatrist)
10) Take steps to reduce participant risk:

- Ask participant to remove weapons/medications from his/her access

5) Help participant identify important protective factors:

- Religious beliefs
- Dependent children
- Belief in treatment
- Future oriented goals
- Social supports
- The assessor will follow judgment in whether to continue with SCID.

High suicide risk without imminent risk (>= 17 points on MINI suicide module)

The assessor will:

3) Provide VA Suicide Hotline number (1-800-273-TALK)
4) Offer to provide the participant with information on VA/DOD facilities and/or contact the participant's treating clinician, within 24 hours. If the participant identifies barriers to using VA/DOD facilities, the participant will be provided with local/regional resources, including treatment referrals.
5) Follow up with the participant within 24 hours.

6) Mail letter to participant with referral information, including VA Suicide hotline phone number and VA/DOD phone number.

- DO NOT continue current protocol (i.e., do not administer SCID).
- Must follow-up with the participant's treatment provider to confirm that participant is stable before rescheduling the SCID and open-ended interview.

High suicide risk with imminent risk (>= 17 points on the MINI suicide module)
The assessor will:

7) Further assess current SI (plan, means, access, intent)
8) Provide VA Suicide Hotline number (1-800-273-TALK)
9) Contact the VA or DoD suicide prevention coordinator or mental health provider on call, as appropriate, in closest proximity to the participant.
10) If the VA/DoD is unresponsive, contact the local law enforcement and inform them of the participant's emergent psychiatric needs.
11) Follow up with the participant within 24 hours.
12) Follow up with the VA/DoD or local law enforcement within 24 hours to determine the disposition of the case.

- DO NOT continue current protocol (i.e., do not administer SCID).
- Must follow-up with the participant's treatment provider to confirm that participant is stable before rescheduling the SCID and open-ended interview.

An important aspect of the Registry is that it is as inclusive as possible of the entire range of PTSD experiences; thus, it includes high-risk cases when possible, although data on SCID may remain unavailable until high-risk cases are determined to be stable by contact with the treatment provider.

7.2 PROCEDURES FOR REPORTING ADVERSE EVENTS

This non-interventional, observational study poses a low risk to participants. Thus few serious adverse events are expected. Participants may experience emotional distress and communicate this to study staff. Should a participant express suicidal ideation, homicidal ideation, or provide any other indication he/she is experiencing an adverse psychiatric event, the following procedures should be followed.

1) The assessor or staff member will follow the procedures outlined in the safety plan (see section 4.1).
2) The assessor or staff member will document the event using an SAE form (appendix_) and submit it to the project coordinator. Additionally, the assessor will document the termination of data collection in the participant's folder and describe the event.
3) The project coordinator will submit the SAE form to the appropriate regulatory bodies including the USAMRMC and the VA Boston HCS IRB. The project coordinator will also ensure the other study sites are notified of the SAE.
4) Once notified of the SAE by VA Boston HCS, NERI and DC VA will submit the SAE form to their local IRBs as mandated by each site's specific protocols.

7.2.1 Additional Actions

1) If the participant expresses homicidal ideation, the assessor will contact the local police in order for the participant to be transported to the emergency room for a complete psychiatric evaluation. If warranted, the assessor will also fulfill his/her duty to warn/protect a target of homicidal ideation.
2) If the participant is mildly distressed but does not meet criteria for an emergency evaluation, the study assessor will informally debrief the subject at the conclusion of the interview and give the participant the VA suicide hotline number and any other helpful contacts.

7.2.2 Reporting Adverse Events to the Study Sponsor

All unanticipated problems involving risk to subjects or others, serious adverse events related to participation in the study and subject deaths related to participation in the study will be promptly reported by phone (301-619-2165), by email (hsrrb@.amedd.army.mil), or by facsimile (301-619-7803) to the USAMRMC, Office of Research Protections, Human Research Protection Office. A complete written report will follow the initial notification. In addition to the methods above, the complete report will be sent to the U.S. Army Medical Research and Materiel Command, ATTN: MCMR-RP, 504 Scott Street, Fort Detrick, Maryland 21702-5012.

Suspensions, clinical holds (voluntary or involuntary), or terminations of this research by the IRB, the institution, the Sponsor, or regulatory agencies will be promptly reported to the USAMRMC ORP HRPO. Any deviation to the protocol that may have an adverse effect on the safety or rights of the subject or the integrity of the study will be reported to the USAMRMC ORP HRPO as soon as the deviation is identified.

7.3 REPORTING REQUIREMENTS OF THE PI

The protocol will be conducted in accordance with the protocol submitted to and approved by the USAMRMC ORP HRPO and will not be initiated until written notification of approval of the research project is issued by the USAMRMC ORP HRPO.

Accurate and complete study records will be maintained and made available to representatives of the U.S. Army Medical Research and Material Command as a part of their responsibility to protect human subjects in research. Research records will be stored in a confidential manner so as to protect the confidentiality of subject information. Major modifications to the research protocol and any modifications that could potentially increase risk to subjects will be submitted to the USAMRMC ORP HRPO for approval prior to implementation. All other amendments will be submitted with the continuing review report to the USAMRMC ORP HRPO for acceptance.

A copy of the approved continuing review report and the local IRB approval notification will be submitted to the USAMRMC ORP HRPO as soon as these documents become available. A copy of the approved final study report and local IRB approval notification will be submitted to the USAMRMC ORP HRPO as soon as these documents become available.

The knowledge of any pending compliance inspection/visit by the FDA, OHRP, or other government agency concerning this clinical investigation or research, the issuance of Inspection Reports, FDA Form 483, warning letters or actions taken by any Regulatory Agencies including legal or medical actions and any instances of serious or continuing noncompliance with the regulations or requirements that relate to this clinical investigation or research will be reported immediately to USAMRMC ORP HRPO

15. Data Entry and Abstraction Procedures

8.1 DEPARTMENT OF DEFENSE (DOD) AND VHA MEDICAL SAS DATASETS

After the pretesting phase and upon complete enrollment of all participants, investigators at the D.C. VA will abstract military and medical record data. Additional medical record data not available in the D.C. database will be extracted by research technicians at the Boston VA.

To longitudinally follow participants, the medical record abstraction procedures will be repeated up to two more times during the course of the 2-year project.

There are three sources for data abstraction (1) DoD military deployment data (accessed by D.C. VA researchers), (2) medical record data from the VHA Medical SAS Datasets (accessed by D.C. VA), and (3) medical record data from the Veterans Health Information Systems and Technology Architecture (VistA) / Computerized Patient Record System (CPRS) (accessed by researchers at the Boston VA).

8.2 DATA ENTRY FOR COMPUTERIZED PATIENT RECORD SYSTEM (CPRS)/ VISTA WEB INFORMATION

General VISTA WEB instructions:

- Login to CPRS and access the participant's file, either using full name (last,first) or using last initial+last for of SSN.
- Access patient information from the menu on the left hand side of the screen. Record patient information on the CPRS data abstraction template (see appendix).

8.2.1. ACCESSING PCL-C SCORES FOR PARTICIPANTS

1. Go to adhoc report for each site
2. Under "Select Adhoc reports," select "Mha Score" (MHAS) and click the arrow in order to drag those two selections to the "Components Selections" box
3. Once this selection is dragged to the "Components Selections" box, a list of questionnaires will appear in the bottom left box titled, "File Selections." Since the questionnaires are listed in alphabetical order, make sure to click "More" in order to find the PCL-C. Once you select that test, click "run report."
4. If there was a PCL-C administered at that site, there will be a listing with the date and raw score of the PCL-C.

Specific Symptom Scores:

Specific symptom scores are not available with the raw PCL-C score. To access the specific symptom scores the research assistant will check the progress notes for the date corresponding to the PCL-C raw score date.

8.2.2. ACCESSING VITALS

1. Select "Vital Signs"
2. At the top of the page, make sure to click on "all dates" and select "Query"
3. Make sure that there is not an error message at the top of the vital signs chart. If this occurs, not all of the vital signs from each site have appeared.

8.2.3. ACCESSING PARTICIPANT GAF SCORES

In order to find participant GAF scores follow the procedure below:

1. Click on "Outpatient/GAF Encounters," then select "GAF scores"
2. At the top of the page, make sure to click on "all dates" and select "Query"
3. Check each site for the scores and record up to five most recent scores

8.2.4. ACCESSING PARTICIPANT MEDICATIONS

1. Select "Pharmacy" and click on "Medications"
2. Click "View Details" for each active medication in order to receive the dose, frequency, indication, and date filled for each medication.
3. Some participants will buy their medication from a non-va source, which means that the date filled information will not be provided. In this case, include a "99" (unknown) in those cells.
4. The indication for each medication is sometimes not included in the "details" section. *In this scenario, make sure to look at the progress notes with the same date as when the medication was prescribed in order to get a clearer picture of why the participant needs this medication. If it is still not indicated, include a "99" (unknown)*

*For medication doses: **1**= once a day, **2**=2x a day, **3**=3x a day, **4**=4x a day, **5**=5x a day, **6**=6x a day, **7**= As needed, **8**= Other.*

8.3 DATA ENTRY FOR INTERVIEW MEASURES

The basic information concerning data entry is listed below. For more information see the Project VALOR coding manual.

8.3.1 MINI

0= No 1= Yes

Question C4a. on frequency of suicidal ideation: **1**= Occasionally; **2**= Often; **3**= Very Often

Question C4b. on intensity of the suicidal ideation: **1**= Mild; **2**= Moderate; **3**= Severe

Last question on **Suicide Risk Status**: **1**= Low; **2**= Moderate; **3**= High

- Even if a participant answers NO to C4 (Think about suicide?), still make sure to include a yes or no answer for the remaining questions. Clinicians cannot skip these questions.

8.3.2 SCID

Date **Unknown**: Enter **Jan 9999**

Date **Not Applicable:** Enter **Jan 8888**

0 =Inadequate Information

1= Absent or False

2= subthreshold

3= threshold or true

Question F131: **1**=Mild; **2**=Moderate; **3**=Severe

If only the year of certain event is specified, leave it blank until we figure out a way to enter it in the database.

Questions F132 and F133 are no longer applicable variables in the database. Leave those cells blank.

8.3.3 TBI

0=No; 1= Yes

Date **Unknown:** Enter **Jan 9999**

Date **Not Applicable:** Enter **Jan 8888**

Question 1 for each head injury:

0=<12 years**; 1=**12-18 yrs**; 2=**18-30 yrs**; 3=**30-40 yrs**; 4**=>40 yrs

Question 6b for each head injury: **0**=less than 1 minute; **1**=1-15 minutes; **2**=16-30 minutes, **3**=more than 30 minutes, **4**= unknown

Question 9a for each head injury: **0**=No, **1**= Yes, **2**=Unknown

Question 9b for each head injury: **0**=No, **1**= Yes, **2**=Partially

Question 10 for each head injury: **0**= less than one hour; **1**=1-24 hours; **2**= More than 24 hours to 7 days; **3**= More than 7 days; **4**= Unknown

Question 11 for each head injury: **0**=No, **1**= Yes, **2**=Unknown

Question 12 for each head injury: **0**=No, **1**= Yes, **2**=Unknown

In the old version of the TBI, there was not an option to specify what types of problems were associated with the participant's traumatic brain injury **(Variables TBI1a-TBI1d)**, so make sure to discuss the answers to that question with the clinician who conducted the phone interview.

If only the year of certain event is specified, leave it blank until we figure out a way to enter it in the database.

8.3.4 Deployment Information Form:

0=No; 1= Yes

Date **Unknown: Jan 99**

Date **Not Applicable: Jan 88**

When specifying the location for deployments overseas: 1=Iraq**; 2=**Kuwait**; 3;** Afghanistan**; 4=** Kosovo**; 5=**Bosnia**; 6=**Other

1. When entering a participant's MOS information, make sure to enter the MOS that is directly related to their military duties.
2. In addition, when entering the MOS code of a participant, make sure to include the MOS code and brief description of the specialty under the Values section of the MOS string variable, so that techs do not have to constantly search for the meaning of each MOS code.
3. Lastly, when entering whether or not a participant has been deployed since Sept 2001, a tech should not include deployment information that occurred less than 30 days unless traumatic events occurred during that short time period.

8.4. DATA ENTRY PROCEDURES

Data entry for Project VALOR will take place in two phases. The initial phase will involve entering participant from the telephone interview and CPRS. The second phase will involve only abstracted CPRS data.

8.4.1 Initial Data Entry

After the participant has completed his/her questionnaire and the clinical interview the research assistant will do the following:

- Make sure that the participant's file has been downloaded from Psychdata. Psychdata responses are downloaded daily into an SPSS file so the questionnaire responses should already be in the participant's data folder.
- Enter the data from the clinical interview measures
- Complete the initial CPRS abstraction and enter the data.
- Initial the run sheet in the data folder and record the date the data was entered.
- Hand the participant's data folder off to the research assistant responsible for data checking/cleaning.

8.4.2 Secondary Data Entry

After initial data entry and cleaning is complete for all 1600 participants, research assistants will complete the second round of medical record abstraction and data entry using the following procedures.

- Complete the second CPRS abstraction using the procedures outlined in this section.
- Enter the data from the second CPRS abstraction into the SPSS file.
- Double check that the participant's entire data folder has been entered into the SPSS file.
- Initial the run sheet in the data folder. Record the date the secondary data was entered.
- Hand off the participant's data folder to the research assistant responsible for data checking/cleaning.

8.4.3 Data Checking/Cleaning

Once the initial data entry is complete, a research technician will check that the data entered is complete and correct. The participant's data folder will be handed off to a different research assistant who will then check the data. The research assistant responsible for checking the data will initial the run sheet and note the date the data was checked. This will be repeated for the second data entry phase. Any issues or changes will be brought to the attention of the project manager.

8.5 DATA BACKUP

All project VALOR data files will be backed up on a daily basis. The research assistant will back data files up on the N drive and on an external storage device. Hard copies of psychdata files will also be kept in the participant data folder.

9. Data Transfers, Merge and De-Identification Procedures

9.1 DATA TRANSFER: FROM D.C. VA TO BOSTON VA

The abstracted military and medical record data will be sent from the D.C. VA to the Boston VA using the secure file sharing mechanism of the VA. Investigators at the D.C. VA and at the Boston VA will create a file sharing account through the VA network, using the established secure methods. Only key study investigators will have access to this account. Abstracted medical record data will be merged with data from the self-administered questionnaires and interview using subject identifiers. The data merge will take place at the Boston VA.

Because a primary aim of the registry is to track patients longitudinally, medical record data abstraction and transfer from the D.C. VA to the Boston VA will be repeated up to 2 additional times during the study after the initial transfer, which occurs upon completion of recruitment.

9.2 DATA MERGE (BOSTON VA)

The Boston VA will merge the data generated from the D.C. VA and the data collected from the Boston VA into one file for each participant.

9.3. DATA DE-IDENTIFICATION (BOSTON VA)

Each file will be given a participant identification number unrelated to any of that participant's personal identifying information. To prepare the merged data for transfer from the Boston VA to NERI, all participant information will be de-identified in accordance with HIPAA regulations. The only institution with access to linkage data allowing linkage between participants' personal identifying information and participants' study identification numbers will be the VA Boston. This linkage and personal identifying information must be securely stored.

The following identifying information about each participant and each participant's relatives, employers, or household members will be removed from the Registry study dataset in preparation for transfer to NERI for statistical analysis and eventual public use access:

s) Names
t) All geographic subdivisions smaller than a State, except for the initial three digits of a zip code if (i) the geographic unit formed by combining all zip codes with the same three initial digits contains more than 20,000 people, and (ii) the initial three digits of a zip code for all such geographic units containing 20,000 or fewer people is changed to 000
u) All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date and date of death and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older
v) Telephone numbers
w) Fax numbers
x) E-Mail addresses
y) Social security numbers
z) Medical record numbers
aa) Health plan beneficiary numbers
bb) Account numbers
cc) Certificate/license numbers
dd) Vehicle identifiers and serial numbers, including license plate numbers
ee) Device identifiers and serial numbers
ff) Web Universal Resource Locators (URLs)
gg) Internet protocol (IP) address numbers
hh) Biometric identifiers, including voice and finger prints
ii) Full face photographic images and any comparable images
jj) Any other unique identifying number, characteristic or code, except as permitted to re-identify information (i.e. the subject identification number)

9.3.1. Confidentiality and Privacy within the De-identification Program

All de-identification will be performed by research credentialed study personnel, and will be checked by doctoral level study personnel. The only list linking the names of the study participants to their subject numbers will be kept in a secure, password protected computer account accessible only to certain study staff. The servers used to store the personally identifiable information will be kept in a secure, locked environment in a separate location from the portal and website servers at the Boston VA campus. Only team members who need the information to perform a specific job will be granted access to personally identifiable information by the PI.

9.4. DATA TRANSFER: FROM BOSTON VA TO NERI

In order to minimize a breach of confidentiality and privacy during transfer, all research staff involved in the transfer will follow policies as described in VHA Directive 1605.1 (Privacy and Release of Information). As the data will already be de-identified as described in VHA Handbook 1605.1 and Common Rule (38 CFR 16), the encrypted data file will be burned onto a data CD. The CD will be sent to NERI via secure currier service.

10. Subject Payment

10.1. SUBJECT PAYMENT

Subjects who complete the SAQ and the clinical interview will be compensated $50. Participants who complete only the SAQ, but do not complete any part of the clinical interview will be compensated $25.
Participants will be mailed a check within 2 weeks of their interview date. Project VALOR subject payment funds will be held in a checking account at Hanscom Federal Credit Union. Subject payments will be issued from this institution.

10.2. SUBJECT PAYMENT TRACKING

Once a check has been sent to a participant, the subject's name, subject ID, and last 4 of the social security number will be recorded in the password protected Project VALOR subject payment file.

An account reconciliation will be completed every month to account for checks that have not been cashed and general availability of funds. The account reconciliation form (see appendix) will be signed by a project investigator reviewing the form as well as the research assistant completing the form. A copy of the reconciliation form will be provided to Boston VA Research Institute, Inc for their records. Any questions or concerns regarding account reconciliations should be directed the Boston VA Research Institutes, Inc.

11. Statistical Analysis Protocol

11.1. OVERVIEW OF STATISTICAL ANALYSIS

The full database created by the Registry includes abstracted military and medical record data merged with data collected from paper forms and the telephone interview. Descriptive analyses will be conducted to characterize the two enrolled samples in terms of demographics, diagnosis, symptomatology, quality of life, current therapies used, and clinical trajectories. The 1200 PTSD group participants will be considered as the "index group" in most of the analyses, as they are the targets for the majority of the Specific Aims, while the 400 non-PTSD participants will be considered the comparison group. The general analysis plan for each aim is briefly provided below. Most variables will be considered in categorical form to avoid assumptions of linearity in analyses; the operational definitions for selected outcomes of interest are listed in **Table 11.1**. Covariates (and interaction terms) will be retained in the models if they are found to be significant predictors of the outcome (at the 0.05 level of significance) or if they confound the effects of significant predictors, defined as changing the effect estimate by at least 20%. Analyses will be conducted in SAS 9.2 (SAS Institute, Cary, NC) or SUDAAN 9.0.1 (Research Triangle Institute International, Research Triangle Park, NC) as appropriate, considering stratification and matching factors. NERI's computer network and its information systems team support the use of these packages.

Table 11.1. Operational Definitions of Selected Outcomes of Interest

Outcome	Definition	Anticipated Variable Form
PTSD	Diagnosis of PTSD, by electronic medical record (ICD-9 code 309.81) or interview assessment	Dichotomous
Psychiatric comorbidities	Diagnoses of depression, anxiety, substance abuse or other DSM-IV diagnoses	Dichotomous
Treatment Utilization	Number of healthcare visits, pharmaceutical usage	Continuous
Productivity Loss	Self-reported absentee days, decreased accomplishments, decreased diligence	Continuous
Quality of Life	SF-12 scores	Continuous

11.2. ANALYSIS PLANS FOR SPECIFIC AIMS

Specific aims and a brief analysis plan for each follows:

Aim 1: This aim focuses on the describing the natural history of the PTSD group, which includes estimation of comorbidities, disparities in these comorbidities by key subgroups, as well as longitudinal descriptive analyses of the PTSD group. Analyses will be conducted to describe existing and new medical and psychological comorbidities, overall and by sociodemographic, military and post-deployment factors. Confidence intervals for the observed co-morbidities will be constructed. Where there are multiple assessments of one outcome, longitudinal mixed models will be used to test for significant changes over time. If two time points only are available, then a paired t-test or nonparametric equivalent will be used to assess change for continuous outcomes. If the outcome is categorical (presence vs. absence of a condition), a generalized mixed model (e.g., logit, multinomial links) will be utilized. In longitudinal analyses, as it is likely that the correlation of responses will decrease over time, an unstructured or autoregressive correlation will be assumed. Additionally, Cox proportional hazard models can be used to predict the time to event.

Aim 2: These analyses will be a comparison of the PTSD index group to utilizers of the VA medical care who served in OIF/OEF but have not received the PTSD diagnosis. The analyses will use multivariate conditional logistic regression to examine factors associated with the PTSD diagnosis while controlling for matching factors of gender and deployment country. The outcome of interest will be PTSD case status and potential predictors include race/ethnicity, level of social support, socioeconomic status, and military service record variables (e.g., rank, duration of service).

Aim 3: These analyses will describe in detail current treatment approaches and then consider the PTSD treatment(s) as the independent variable(s) and psychosocial and medical outcomes occurring after treatment as dependent variables.

Aim 4: These analyses will establish the prevalence of PTSD in the non-PTSD group. Risk factors for missed diagnoses will be explored by comparing those in this group to those in the index PTSD group, on factors such as age, military service factors, race/ethnicity, medical comorbidities, and health care utilization.

Aim 5: These analyses will obtain estimates of costs of PTSD and its associated treatment, in terms of health care utilization costs, health care staff resource needs, and lost productivity, in the PTSD Registry index group.

Aim 6: There are no statistical analyses for this aim, which is to prepare the database for future applications and research use.

11.3. PROPENSITY SCORES

Because a registry has by definition observational data that arise from a clinically indicated setting, it must be noted that assessment of causality and treatment effects with respect to remission of PTSD are subject to potentially important biases. The veterans who receive treatment for PTSD may have different characteristics than those who do not undergo treatment, and these differences can be related to gender, race/ethnicity, severity of PTSD, accessibility of health care services, and unmeasured factors. Therefore, propensity score analyses may be conducted, in which the likelihood of receiving treatment is considered the outcome, and a multivariate model that identifies correlates of receiving treatment are established. This model is then used to obtain a model-based predicted probability of undergoing treatment, and all subsequent analyses of treatment effectiveness stratifies the analytic dataset according to propensity score quantile, therefore ensuring that at least to some degree, cases within a propensity quantile are most similar to each other, and treatment effect estimates are less biased than those that do not attempt to account for measured and unmeasured differences in the treated vs. untreated groups.

11.4. MISSING DATA

Although every effort will be made to achieve complete interviews and full abstraction of health care visits and treatment, there may be some missing outcome and predictor information in the final database. Initial tasks to address the impact of missing data on statistical inferences include documenting the types of missing data, accounting for different sources of missing data, and assessing the implications of irretrievably missing information for potential biases. Because interview data may not be missing completely at random, statistical analyses must account for possible non-response bias, particularly if missing data are associated with severity of PTSD. Consequently, analyses should adjust in some way for characteristics associated with both non-response and the outcomes of interest. Multiple imputation will be used as appropriate.

11.5. POWER CALCULATIONS

11.5.1. Primary Aims

The primary aim of the registry is to describe the natural history of PTSD, characterized by the long-term psychosocial, medical and quality of life outcomes associated with the disorder, and to assess whether these outcomes differ by subgroups defined by sociodemographic, military and post-deployment factors. In this section, we provide the estimated precision for 90% confidence intervals to describe the underlying annual incidence of co-morbidities, and the power to detect differences in the rate of co-morbidities amongst participants with PTSD by subgroup.

Table 11.5.1a indicates that with 1200 participants with PTSD, there is high precision to estimate co-morbidity rates. If the rate is as high as 40%, the relative precision (half-width) of the confidence interval is less than 6% (.023/.40). If the rate is only 10%, then the relative precision of the confidence interval is 14% (.014/.10).

Table 11.5.1.a. Precision of 90% Confidence Interval for A Range of Co-Morbidity Rates assuming 1200 Participants with PTSD, two-sided α=0.05.

Rate	Precision	90% CI	Estimated Number with Co-Morbidity
.05	.01	(.04, .06)	48 to 72
.10	.014	(.086, .114)	103 to 137
.20	.019	(.181, .219)	217 to 263
.30	.022	(.278, .322)	334 to 386
.40	.023	(.377, .423)	452 to 508

Table 11.5.1b displays power for hypothetical subgroup comparisons that might be conducted to assess whether comorbidity rates differ by subgroup in the PTSD cohort (e.g., males vs. females, high vs. low SES, etc.). The table shows that if the comorbidity rate of the lesser affected subgroup is relatively rare (10%), there is over 84% power to detect an odds ratio of 1.7 (0.10 vs. 0.16 rates). If the co-morbidity rate of the lesser affected subgroup is 20%, there is over 89% power to detect an odds ratio of 1.56 (0.20 vs. 0.28 rates). If the co-morbidity is quite prevalent (40%), there is 87% power to a smaller effect size (odds ratio of 1.44). Of note, if the subgroup sizes are more evenly split amongst the 1200 PTSD cases, power will be greater than shown in Table 11.5.1.b.

Table 11.5.1.b. Power to Detect Subgroup Differences for Co-Morbidity Rates of 0.10, 0.20, 0.40, assuming 1200 Participants with PTSD, Subgroup sizes of 840 vs. 360 (70%/30%), and two-sided α=0.05.

p_0 = 0.10				p_0 = 0.20				p_0 = 0.40		
p_1	Odds Ratio	Power		p_1	Odds Ratio	Power		p_1	Odds Ratio	Power
.13	1.35	.311		.24	1.26	.346		.45	1.23	.391
.14	1.47	.506		.26	1.41	.658		.47	1.33	.663
.15	1.59	.696		.28	1.56	.885		.49	1.44	.869
.16	1.71	.843		.30	1.71	.977		.51	1.56	.966
.17	1.85	.932		.32	1.88	1.00		.53	1.69	.994
.18	1.98	.976		.34	2.06	1.00		.55	1.83	1.00

11.5.2. Secondary Aims

Power calculations are provided in **Table 11.5.2** to address selected secondary aims related to the case-control study comparisons of study outcomes such as social support and quality of life, where it is hypothesized that the cases (1200 PTSD veterans) will have lower social support and quality of life than controls (400 non-PTSD veterans). Therefore, the case: control ratio is 3:1 and this has been incorporated into the power calculations. For simplicity, it is assumed here that the outcome is a dichotomous indicator of low social support/low quality of life defined by a pre-specified cutoff from the overall social support or QOL score derived from interview instruments. Therefore, these power estimates to detect associations are conservative, as continuous analyses of scores will also be conducted (see below). Two scenarios are provided: (a) 20% of controls have low social support or QOL and are compared against rates of low social support of 25% to 31%; and (b) 40% of controls have low social support or QOL and are compared against rates of 47% to 53%, resulting in similar effect sizes to detect in the two scenarios. Table 10.5.2 demonstrates that if the control rate of low social support is 20%, there is approximately 80% power to detect an odds ratio for low social support in cases vs. controls of 1.5, and if the control rate is 40%, there is approximately 80% power to detect odds ratios over 1.4 for low social support in cases vs. controls. If the low social support rate in controls is only 10%, then the current design (1200 cases and 400 controls) will have 85% power (not shown in table) to detect an odds ratio of 1.72, and 70% power to detect an odds ratio of 1.6.

Table 11.5.2. Power to Detect Differences in Rates of Low Social Support or Low Quality of Life for 1200 PTSD cases (p_1) vs. 400 non-PTSD controls (p_0) assuming a two-sided exact test with α=0.05

p_0 = 0.20				**p_0 = 0.40**		
p_1	**Odds Ratio**	**Power**		**p_1**	**Odds Ratio**	**Power**
.25	1.33	.503		.47	1.33	.663
.26	1.41	.658		.48	1.38	.779
.27	1.48	.790		.49	1.44	.869
.28	1.56	.885		.50	1.50	.929
.29	1.63	.945		.51	1.56	.966
.30	1.71	.977		.52	1.62	.985
.31	1.80	.991		.53	1.69	.994

It should be noted that outcomes will also be analyzed continuously, and only 503 cases (vs. 167 controls) are required to detect an effect size (defined as mean difference divided by sample standard deviation) of 0.25 standard deviations with 80% power, which is a minimum clinically significant difference. With 1200 cases and 400 controls, there is >99% power to detect a 0.25 effect size. Therefore, continuous analyses of case-control differences in functioning can support multivariate modeling as well as subgroup analyses defined by gender and race/ethnicity.

APPENDIX D: SELF-ADMINISTERED QUESTIONNAIRE

SECTION A. BACKGROUND INFORMATION

A1. Are you Hispanic, Latino or of Spanish origin? ☐Yes ☐ No

A2. What is your race? (please check one or more)

☐ American Indian or Alaska Native ☐Asian ☐ Black or African American

☐ Native Hawaiian or Other Pacific Islander ☐ White or Caucasian

A3. Which of the following best describes you?

☐ Married
☐ Living with a partner (unmarried)
☐ Divorced/Separated
☐ Widowed
☐ Single, never married
☐ Other (Please specify here):_____

A4. What is the highest level of education you have completed?

☐ Less than High School
☐ High School or equivalent (GED)
☐ Vocational/Technical degree post-High School
☐ Some college
☐ Associate's degree
☐ College graduate (Bachelor's degree)
☐ Masters degree
☐ Doctoral degree

A5. How often do you go to religious meetings or services?

☐ More than once a week ☐ Once a week
☐ Twice a month to once a year ☐ Never or almost never

A6. How many children do you have? Please circle: 0 1 2 3 4 5+

A7. In your household, how many of the following live with you now? (write in a number for each):

Children under 5 years old _____

Children aged 5-10 years old _____

Children aged 11-18 years old _____

Other adults _____

Participant ID: _____ V.2.

A8. Which of the following categories best describes your current work situation?

☐ Working for pay full-time (35 hours or more per week)
☐ Working for pay part-time (less than 35 hours per week)
☐ Unemployed and looking for work
☐ Temporarily laid off, on sick leave, or on another leave
☐ Full-time Homemaker
☐ Full-Time Student
☐ Disabled
☐ Retired
☐ Other SPECIFY: _____

A9. If you are currently working for pay, in the past <u>four weeks</u>, how often did you…..

Miss an entire work day because of problems with your physical or mental health? number of days _____

Miss an entire work day for any other reason (including vacation)? number of days _____

Miss part of a work day for any other reason (including vacation)? number of days _____

Come in early, go home late, or work on your day off? number of days _____

A10. What is (was) your usual occupation? _____

A11. About how much was your total <u>household income</u> before taxes in the last year? Include income from wages, salaries, Social Security or retirement benefits, help from relatives, veteran's benefits, real estate, investments, and other sources.

☐ Less than $20,000

☐ $20,000 to less than $35,000

☐ $35,000 to less than $50,000

☐ $50,000 to less than $75,000

☐ $75,000 to less than $100,000

☐ $100,000 or more

SECTION B. HEALTH QUESTIONNAIRE

B1. In general, would you say your health is:

- ☐ Excellent
- ☐ Very Good
- ☐ Good
- ☐ Fair
- ☐ Poor

B2. The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

	Yes, limited a lot	Yes limited a little	No, not limited at all
a. Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	☐	☐	☐
b. Climbing several flights of stairs	☐	☐	☐

B3. During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. Accomplished less than you would like	☐	☐	☐	☐	☐
b. Were limited in the kind of work or other activities	☐	☐	☐	☐	☐

B4. During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of emotional problems (such as feeling depressed or anxious)?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. Accomplished less than you would like	☐	☐	☐	☐	☐
b. Did work or other activities less carefully than usual	☐	☐	☐	☐	☐

B5. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

Not at all	A little bit	Moderately	Quite a lot	Extremely
☐	☐	☐	☐	☐

B6. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks…

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. Have you felt calm and peaceful?	☐	☐	☐	☐	☐
b. Did you have a lot of energy?	☐	☐	☐	☐	☐
c. Have you felt downhearted and depressed?	☐	☐	☐	☐	☐

B7. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting friends, relatives, etc.)?

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐

B8. During the last four weeks, how much have you been bothered by any of the following problems?

	Not bothered	Bothered a little	Bothered a lot
a. Stomach pain	☐	☐	☐
b. Back pain	☐	☐	☐
c. Pain in your arms, legs, or joints (knees, hips, etc)	☐	☐	☐
d. Menstrual cramps or other problems with your periods	☐	☐	☐
e. Pain or problems during sexual intercourse	☐	☐	☐
f. Headaches	☐	☐	☐
g. Chest pain	☐	☐	☐
h. Dizziness	☐	☐	☐
i. Fainting spells	☐	☐	☐
j. Feeling your heart pound or race	☐	☐	☐
k. Shortness of breath	☐	☐	☐
l. Constipation, loose bowels, or diarrhea	☐	☐	☐
m. Nausea, gas, or indigestion	☐	☐	☐

B9. Over the last 2 weeks, how often have you been bothered by any of the following problems?

	Not at all	Several days	More than half the days	Nearly every day
a. Little interest or pleasure in doing things	☐	☐	☐	☐
b. Feeling down, depressed, or hopeless	☐	☐	☐	☐
c. Trouble falling or staying asleep, or sleeping too much	☐	☐	☐	☐
d. Feeling tired or having little energy	☐	☐	☐	☐
e. Poor appetite or overeating	☐	☐	☐	☐
f. Feeling bad about yourself - or that you are a failure, or have let yourself or your family down	☐	☐	☐	☐
g. Trouble concentrating on things, such as reading the newspaper or watching television	☐	☐	☐	☐
h. Moving or speaking so slowly that other people could have noticed? Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual	☐	☐	☐	☐
i. Thoughts that you would be better off dead or of hurting yourself in some way	☐	☐	☐	☐

B10. Questions about anxiety:

a. In the <u>last 4 weeks,</u> have you had an anxiety attack – suddenly feeling fear or panic?

☐ NO ☐ YES

If you checked "NO," go to question B12 on the next page.

b. Has this ever happened before? ☐ NO ☐ YES

c. Do some of these attacks come suddenly out of the blue – that is, in situations where you don't expect to be nervous or uncomfortable? ☐ NO ☐ YES

d. Do these attacks bother you a lot or are you worried about having another attack? ☐ NO ☐ YES

B11. Think about your last bad anxiety attack.

a. Were you short of breath?	☐NO	☐YES
b. Did your heart race, pound, or skip?	☐NO	☐YES
c. Did you have chest pain or pressure?	☐NO	☐YES
d. Did you sweat?	☐NO	☐YES
e. Did you feel as if you were choking?	☐NO	☐YES
f. Did you have hot flashes or chills?	☐NO	☐YES
g. Did you have nausea or an upset stomach, or the feeling that you were going to have diarrhea?	☐NO	☐YES
h. Did you feel dizzy, unsteady, or faint?	☐NO	☐YES
i. Did you have tingling or numbness in parts of your body?	☐NO	☐YES
j. Did you tremble or shake?	☐NO	☐YES
k. Were you afraid you were dying?	☐NO	☐YES

B12. Over the last 4 weeks, how often have you been bothered by any of the following problems?

	Not at all	Several days	More than half the days
a. Feeling nervous, anxious, on edge, or worrying a lot about different things	☐	☐	☐

If you checked "Not at all," go to question B13.

b. Feeling restless so that it is hard to sit still	☐	☐	☐
c. Getting tired very easily	☐	☐	☐
d. Muscle tension, aches, or soreness	☐	☐	☐
e. Trouble falling asleep or staying asleep	☐	☐	☐
f. Trouble concentrating on things, such as reading a book, watching TV	☐	☐	☐
g. Becoming easily annoyed or irritable	☐	☐	☐

B13. If you checked off <u>any</u> problems on Section B (Health Questions) so far, how <u>difficult</u> have these problems made it for you to do your work, take care of things at home, or get along with other people?

☐ Not difficult at all

☐ Somewhat difficult

☐ Very difficult

☐ Extremely difficult

B14. During the <u>last 4 weeks,</u> how much have you been bothered by any of the following problems?

	Not bothered at all	Bothered a little	Bothered a lot
a. Worrying about your health	☐	☐	☐
b. Your weight or how you look	☐	☐	☐
c. Little or no sexual desire or pleasure during sex	☐	☐	☐
d. Difficulties with husband/wife, partner/lover, or boyfriend/girlfriend	☐	☐	☐

e. The stress of taking care of children, parents, or other family members	☐	☐	☐
f. Stress at work or outside of the home or at school	☐	☐	☐
g. Financial problems or worries	☐	☐	☐
h. Having no one to turn to when you have a problem	☐	☐	☐
i. Something bad that happened recently	☐	☐	☐
j. Thinking or dreaming about something that happened to you in the past – like your house being destroyed, a severe accident, being hit or assaulted, or being forced to commit a sexual act	☐	☐	☐

B15. In the last year, have you been hit, slapped, kicked or otherwise physically hurt by someone, or has anyone forced you to have an unwanted sexual act?

☐NO ☐YES

B16. What is the most stressful thing in your life right now?

_____

_____

B17. Are you taking any medication for anxiety, depression or stress?

☐NO ☐YES

The questions on this page ask about your sleep. Please check one box for each question.

B18. How often in the past month did you:

a) Have trouble falling asleep?

Not at all	1-3 days	4-7 days	8-14 days	15-21 days	22-31 days
☐	☐	☐	☐	☐	☐

b) Wake up several times per night?

Not at all	1-3 days	4-7 days	8-14 days	15-21 days	22-31 days
☐	☐	☐	☐	☐	☐

c) Have trouble staying asleep (including waking far too early)?

Not at all	1-3 days	4-7 days	8-14 days	15-21 days	22-31 days
☐	☐	☐	☐	☐	☐

d) Wake up after your usual amount of sleep feeling tired and worn out?

Not at all	1-3 days	4-7 days	8-14 days	15-21 days	22-31 days
☐	☐	☐	☐	☐	☐

B19. In the past month, on average, how many hours of sleep did you get each night?

0-2 hours	3-4 hours	5-6 hours	6-7 hours	7-8 hours	9-10 hours	Over 10 hours
☐	☐	☐	☐	☐	☐	☐

The questions on this page ask about feelings of anger. Please check the box that best describes how you feel. There are no right or wrong answers.

B20. I often find myself getting angry at people or situations

☐ Not at all ☐ A little ☐ Moderately ☐ A lot ☐ Very much

B21. When I get angry, I get really mad

☐ Not at all ☐ A little ☐ Moderately ☐ A lot ☐ Very much

B22. When I get angry, I stay angry

☐ Not at all ☐ A little ☐ Moderately ☐ A lot ☐ Very much

B23. When I get angry at someone, I want to hit or clobber the person

☐ Not at all ☐ A little ☐ Moderately ☐ A lot ☐ Very much

B24. My anger prevents me from getting along with people as well as I'd like to

☐ Not at all ☐ A little ☐ Moderately ☐ A lot ☐ Very much

SECTION C. HEALTH CARE USE

The following questions ask about any medical treatment or mental health services you may have received from VA or other healthcare providers for emotional problems related to your service in the military. The first few questions cover the period of time when you were in active service, and the others are about the time since your discharge.

C1. Did you request medical treatment or counseling during your time of active duty or after your discharge for any emotional problems, including sleep difficulties, "flashbacks" or other emotional problems?

☐NO (Skip to Question C2)

☐YES (Please answer the next 2 questions below)

↓

C1a. In the past 3 months, how many visits did you have for your emotional problems?

☐ Only 1

☐ 2-5

☐ 6-10

☐ 10-20

☐ More than 20 visits

C1b. In the past 3 months, have you gone for treatment or counseling for your emotional problems from anyone outside the VA or military system?

☐ No. All the care I received was at the VA or in the military system.

☐ Yes. Some of my treatment was from providers who are not part of the VA and military systems.

☐ Yes. All my treatment or counseling was from providers who are not part of the military or VA system.

C2. Did you receive any medications, such as antidepressant medication or sleeping pills, for your emotional problems?

☐NO (Skip to Question C3)

☐YES (Please answer below)

↓

C2a. If yes, did the medications help you to feel better and cope with your emotional problems?

- ☐ I did not take the medications
- ☐ I took the medications, but they did not help
- ☐ I took the medications, and they helped a little
- ☐ I took the medications, and they helped a lot

C3. Did you receive any counseling or therapy for your emotional problems?

☐NO (skip to Question C4)

☐YES (Please answer below)

↓

C3a. If yes, how many sessions of counseling or therapy did you receive?

- ☐ Only 1 session
- ☐ 2-5 sessions
- ☐ 6-10 sessions
- ☐ 10-20 sessions
- ☐ More than 20 sessions

↓

C3b. Did the counseling or therapy help you to feel better and cope with your emotional problems?

- ☐ It did not help me at all
- ☐ It helped me a little
- ☐ It helped me a lot

C4. If you did not get any medical help or counseling for your emotional problems, what was the reason/s? Please check all that apply:

- ☐ I did not think it would help me to cope with my emotional problems.
- ☐ I did not know where to go for the right kind of help
- ☐ I was concerned about my military or VA record
- ☐ Other [please specify] _____

SECTION D. LIFE EXPERIENCES

Listed below are a number of difficult or stressful things that sometimes happen to people. For each event check one or more of the boxes to the right to indicate that: (a) it *happened to you* personally, (b) you *witnessed it* happen to someone else, (c) you *learned about it* happening to someone close to you, (d) you're *not sure* if it fits, or (e) it *doesn't apply* to you. Mark *only one* item for any single stressful event you have experienced. For events that might fit more than one item description, choose the one that fits best. Be sure to consider your *entire life* (growing up as well as adulthood) as you go through the list.

	Event	*Happened to me*	*Witnessed it*	*Learned about it*	*Not Sure*	*Doesn't apply*
D1.	Natural disaster (for example, flood, hurricane, tornado, earthquake)					
D2.	Fire or explosion					
D3.	Transportation accident (for example, car accident, boat accident, train wreck, plane crash)					
D4.	Serious accident at work, home, or during recreational activity					
D5.	Exposure to toxic substance (for example, dangerous chemicals, radiation)					
D6.	Physical assault (for example, being attacked, hit, slapped, kicked, beaten up)					
D7.	Assault with a weapon (for example, being shot, stabbed, threatened with a knife, gun, bomb)					
D8.	Sexual assault (rape, attempted rape, made to perform any type of sexual act through force or threat of harm)					
D9.	Other unwanted or uncomfortable sexual experience					
D10.	Combat or exposure to a war-zone (in the military or as a civilian)					
D11.	Captivity (for example, being kidnapped, abducted, held hostage, prisoner of war)					
D12.	Life-threatening illness or injury					
D13.	Severe human suffering					
D14.	Sudden, violent death (for example, homicide, suicide)					
D15.	Sudden, unexpected death of someone close to you					
D16.	Serious injury, harm, or death you caused to someone else					
D17.	Any other very stressful event or experience					

The statements below are about your combat experiences DURING deployment.
If you've had more than one deployment, please think about the one deployment that affected you the most when answering these questions. Please circle the response that best fits your experiences.

While deployed:	Never	A few times over entire deployment	A few times each month	A few times each week	Daily or almost daily
D18. I went on combat patrols or missions.	1	2	3	4	5
D19. I encountered land or water mines and/or booby traps.	1	2	3	4	5
D20. I received hostile incoming fire from small arms, artillery, rockets, mortars, or bombs.	1	2	3	4	5
D21. I received "friendly" incoming fire from small arms,artillery, rockets, mortars, or bombs.	1	2	3	4	5
D22. I was in a vehicle (for example, a truck, tank, APC, helicopter, plane, or boat) that was under fire.	1	2	3	4	5
D23. I was attacked by terrorists or civilians.	1	2	3	4	5
D24.I was part of a land or naval artillery unit that fired on the enemy.	1	2	3	4	5
D25. I was part of an assault on entrenched or fortified positions.	1	2	3	4	5
D26. I took part in an invasion that involved naval and/or land forces.	1	2	3	4	5
D27. My unit engaged in battle in which it suffered casualties.	1	2	3	4	5
D28. I personally witnessed someone from my unit or an ally unit being seriously wounded or killed.	1	2	3	4	5
D29. I personally witnessed soldiers from enemy troops being seriously wounded or killed.	1	2	3	4	5
D30. I was wounded or injured in combat.	1	2	3	4	5
D31. I fired my weapon at the enemy.	1	2	3	4	5
D32. I killed or think I killed someone in combat.	1	2	3	4	5
D33. I participated in a support convoy	1	2	3	4	5

The statements below are about your experiences AFTER battle. Please circle the response that best fits your experiences.

While deployed:	Never	A few times over entire deployment	A few times each month	A few times each week	Daily or almost daily

D34. I observed homes or villages that had been destroyed.	**1**	**2**	**3**	**4**	**5**
D35. I saw refugees who had lost their homes and belongings as a result of battle.	**1**	**2**	**3**	**4**	**5**
D36. I saw people begging for food.	**1**	**2**	**3**	**4**	**5**
D37. I or my unit took prisoners of war.	**1**	**2**	**3**	**4**	**5**
D38. I interacted with enemy soldiers who were taken as prisoners of war.	**1**	**2**	**3**	**4**	**5**
D39. I was exposed to the sight, sound, or smell of animals that had been wounded or killed from war-related causes.	**1**	**2**	**3**	**4**	**5**
D40. I took care of injured or dying people.	**1**	**2**	**3**	**4**	**5**
D41. I was involved in removing dead bodies after battle.	**1**	**2**	**3**	**4**	**5**
D42. I was exposed to the sight, sound, or smell of dying men and women.	**1**	**2**	**3**	**4**	**5**
D43. I saw enemy soldiers after they had been severely wounded or disfigured in combat.	**1**	**2**	**3**	**4**	**5**
D44. I experienced unwanted sexual activity as a result of force, threat of harm, or manipulation.	**1**	**2**	**3**	**4**	**5**
D45. I saw civilians after they had been severely wounded or disfigured.	**1**	**2**	**3**	**4**	**5**
D46. I saw the bodies of dead civilians.	**1**	**2**	**3**	**4**	**5**
D47. I saw Americans or allies after they had been severely wounded or disfigured in combat.	**1**	**2**	**3**	**4**	**5**
D48. I saw the bodies of dead Americans or allies.	**1**	**2**	**3**	**4**	**5**
D49. I saw the bodies of dead enemy soldiers.	**1**	**2**	**3**	**4**	**5**

You have completed the questions about your deployment. The next set of statements refers to social support AFTER the deployment that affected you the most. Please circle the response that best fits your experiences.

	Strongly disagree	Somewhat disagree	Neither agree nor disagree	Somewhat agree	Strongly agree
D50. The reception I received when I returned from my deployment made me feel appreciated for my efforts.	1	2	3	4	5
D51. The American people made me feel at home when I returned.	1	2	3	4	5
D52. When I returned, people made me feel proud to have served my country in the Armed Forces.	1	2	3	4	5
D53. I am carefully listened to and understood by family members or friends.	1	2	3	4	5
D54. Among my friends or relatives, there is someone who makes me feel better when I am feeling down.	1	2	3	4	5
D55. I have problems that I can't discuss with family or friends.	1	2	3	4	5
D56. Among my friends or relatives, there is someone I go to when I need good advice.	1	2	3	4	5
D57. People at home just don't understand what I have been through while in the Armed Forces.	1	2	3	4	5
D58. There are people to whom I can talk about my deployment experiences.	1	2	3	4	5
D59. The people I work with respect the fact that I am a veteran.	1	2	3	4	5
D60. My supervisor understands when I need time off to take care of personal matters.	1	2	3	4	5
D61. My friends or relatives would lend me money if I needed it.	1	2	3	4	5
D62. My friends or relatives would help me move my belongings if I needed to.	1	2	3	4	5
D63. When I am unable to attend to daily chores, there is someone who will help me with these tasks.	1	2	3	4	5
D64. When I am ill, friends or family members will help out until I am well.	1	2	3	4	5

SECTION E. PERSONAL BACKGROUND INFORMATION

Military service can affect your personal relationships and lifestyle. Please answer the following questions as honestly as you can. Please remember that your answers will be kept confidential and will be used for our research purposes only.

E1. Have you been sexually active in the past 3 months? ☐NO ☐YES

E2. How satisfied are you with your sex life?

Not at all satisfied	Somewhat dissatisfied	Neither satisfied nor dissatisfied	Somewhat satisfied	Completely satisfied
☐	☐	☐	☐	☐

E3. In the last year, have you ever drunk or used drugs more than you meant to?

☐NO ☐YES

E4. Have you felt you wanted or needed to cut down on your drinking or drug use in the last year? ☐NO ☐YES

E5. How often do you have a drink containing alcohol?

☐ Never (Skip to Questions 13-14)

☐ Monthly or less

☐ 2 to 4 times a month

☐ 2 to 3 times a week

☐ 4 or more times a week

E6. How many drinks containing alcohol do you have on a typical day when you are drinking?

☐ 1 or 2

☐ 3 or 4

☐ 5 or 6

☐ 7, 8, or 9

☐ 10 or more

E7. How often do you have six or more drinks on one occasion?

☐ Never

☐ Less than monthly

☐ Monthly

☐ Weekly

☐ Daily or almost daily

E8. How often during the last year have you found that you were not able to stop drinking once you had started?

☐ Never

☐ Less than monthly

☐ Monthly

☐ Weekly

☐ Daily or almost daily

E9. How often during the last year have you failed to do what was normally expected from you because of drinking?

☐ Never

☐ Less than monthly

☐ Monthly

☐ Weekly

☐ Daily or almost daily

E10. How often during the last year have you been unable to remember what happened the night before because you had been drinking?

☐ Never

☐ Less than monthly

☐ Monthly

☐ Weekly

☐ Daily or almost daily

E11. How often during the last year have you needed an alcoholic drink first thing in the morning to get yourself going after a night of heavy drinking?

☐ Never

☐ Less than monthly

☐ Monthly

☐ Weekly

☐ Daily or almost daily

E12. How often during the last year have you had a feeling of guilt or remorse after drinking?

☐ Never

☐ Less than monthly

☐ Monthly

☐ Weekly

☐ Daily or almost daily

E13. Have you or someone else been injured as a result of your drinking?

☐ No

☐ Yes, but not in the last year

☐ Yes, during the last year

E14. Has a relative, friend, doctor, or another health professional expressed concern about your drinking or suggested you cut down?

☐ No

☐ Yes, but not in the last year

☐ Yes, during the last year

INSTRUCTIONS: Answer the questions at the beginning of each section to determine which sections apply to you. Then, within the sections that apply to you, read each statement and rate how often you have acted like that over the past 30 days. Circle only one number for each statement.

Romantic Relationship with Spouse or Partner

Have you been in a romantic relationship with a spouse or partner in the past 30 days? ☐Yes ☐ No

If you have not been in a romantic relationship with a spouse or partner during the past 30 days skip this section and continue with the next section. Otherwise, please answer the following questions.

Over the past 30 days…

	Never			Sometimes			Always
F1. When necessary, I cooperated on tasks with my spouse or partner.	1	2	3	4	5	6	7
F2. I shared household chores or duties with my spouse or partner.	1	2	3	4	5	6	7
F3. I had trouble sharing thoughts or feelings with my spouse or partner.	1	2	3	4	5	6	7
F4. I showed interest in my spouse or partner's activities.	1	2	3	4	5	6	7
F5. I had trouble settling arguments or disagreements with my spouse or partner.	1	2	3	4	5	6	7
F6. I was patient with my spouse or partner.	1	2	3	4	5	6	7
F7. I had trouble giving emotional support to my spouse or partner.	1	2	3	4	5	6	7
F8. I was affectionate with my spouse or partner.	1	2	3	4	5	6	7
F9. My partner or spouse and I did activities that brought us closer together.	1	2	3	4	5	6	7
F10. I was interested in sexual activity with my spouse or partner.	1	2	3	4	5	6	7
F11. I had trouble becoming sexually aroused with my spouse or partner.	1	2	3	4	5	6	7

	Not at all			Somewhat			Very much
12a. Overall, over the past 30 days, I had trouble in my romantic relationship with my spouse or partner.	1	2	3	4	5	6	7
12b. Overall, in the past 30 days, I was distressed or emotionally upset because of the difficulties I had in my romantic relationship.	1	2	3	4	5	6	7

Family

In this section, family refers to all relatives other than your spouse/partner or children (for example, parents, brothers, sisters, grandparents, etc). Do not answer these questions in reference to your spouse/partner or children.

Have you been in contact with family members (parents, brothers, sisters, grandparents, etc.) in the past 30 days? ☐Yes ☐ No

If you have not been in contact with family during the past 30 days skip this section and continue with the next section. Otherwise, please answer the following questions.

Over the past 30 days…

	Never			Sometimes			Always

13. I stayed in touch with family members (e.g. phone calls, e-mails, texts).	1	2	3	4	5	6	7
14. My family and I did activities that brought us closer together.	1	2	3	4	5	6	7
15. I was affectionate with my family members.	1	2	3	4	5	6	7
16. I had trouble being patient with family members.	1	2	3	4	5	6	7
17. I had trouble communicating thoughts or feelings to family members.	1	2	3	4	5	6	7
18. I had trouble giving emotional support to family members.	1	2	3	4	5	6	7
19. I had trouble settling arguments or disagreements with family members.	1	2	3	4	5	6	7

	Not at all			**Somewhat**			**Very much**
20a. Overall, over the past 30 days, I had trouble with my family relationships.	1	2	3	4	5	6	7
20b. Overall, in the past 30 days, I was distressed or emotionally upset because of the difficulties I had in my family relationships.	1	2	3	4	5	6	7

Work (including home-based work)

Have you worked (either for pay or as a volunteer) in the past 30 days?

☐Yes ☐ No

If you have not worked either for pay or as a volunteer during the past 30 days skip this section and continue with the next section. Otherwise, please answer the following questions.

Over the past 30 days…

	Never			**Sometimes**			**Always**
21. I had trouble showing up on time for work.	1	2	3	4	5	6	7
22. I reported for work when I was supposed to.	1	2	3	4	5	6	7
23. I got along well with others at work.	1	2	3	4	5	6	7
24. I stayed interested in my work.	1	2	3	4	5	6	7
25. I had trouble being patient with others at work.	1	2	3	4	5	6	7
26. I performed my job to the best of my ability.	1	2	3	4	5	6	7
27. I completed my work on time.	1	2	3	4	5	6	7
28. I had trouble settling arguments or disagreements with others at work.	1	2	3	4	5	6	7
29. I solved problems or challenges at work without much difficulty.	1	2	3	4	5	6	7
30. I maintained a reasonable balance between work and home.	1	2	3	4	5	6	7
31. I was able to perform my work duties without needing any extra help.	1	2	3	4	5	6	7
32. When necessary, I cooperated on work-related tasks with others.	1	2	3	4	5	6	7
33. I showed my skills and knowledge of the job.	1	2	3	4	5	6	7
34. I showed others at work that they could depend on me.	1	2	3	4	5	6	7
35. I came up with ideas and put them into action at work.	1	2	3	4	5	6	7
36. I took responsibility for my work.	1	2	3	4	5	6	7
37. I prioritized work-related tasks appropriately.	1	2	3	4	5	6	7
38. I worked hard every day.	1	2	3	4	5	6	7
39. I made sure that the work environment was pleasant for others.	1	2	3	4	5	6	7
40. I had trouble expressing my ideas, thoughts or feelings to others at work.	1	2	3	4	5	6	7
41. I had trouble being supportive of others at work.	1	2	3	4	5	6	7

	Not at all			**Somewhat**			**Very much**
42a. Overall, over the past 30 days, I had trouble at work.	1	2	3	4	5	6	7
42b. Overall, in the past 30 days, I was distressed or emotionally upset because	1	2	3	4	5	6	7

of my difficulties at work.

Friendships and Socializing

Have you been in contact with friends in the past 30 days? ☐Yes ☐ No

If you have not been in contact with friends during the past 30 days skip this section and continue with the next section. Otherwise, please answer the following questions.

Over the past 30 days…

	Never			Sometimes			Always
43. I was willing to meet new people.	1	2	3	4	5	6	7
44. I stayed in touch with friends (returning phone calls, emails, visiting).	1	2	3	4	5	6	7
45. My friends and I did activities that brought us closer together.	1	2	3	4	5	6	7
46. I had trouble being patient with my friends.	1	2	3	4	5	6	7
47. I had trouble settling arguments or disagreements with my friends.	1	2	3	4	5	6	7
48. I had trouble sharing my thoughts or feelings with my friends.	1	2	3	4	5	6	7
49. I had trouble giving emotional support to my friends.	1	2	3	4	5	6	7
50. I showed affection for my friends.	1	2	3	4	5	6	7

	Not at all			Somewhat			Very much
51a. Overall, over the past 30 days, I had trouble with my friendships and socializing.	1	2	3	4	5	6	7
51b. Overall, in the past 30 days, I was distressed or emotionally upset because of the difficulties I had with my friendships and socializing.	1	2	3	4	5	6	7

Parenting

In this section, children refers to anyone for whom you had parenting responsibilities.

Do you have children with whom you lived or had regular contact during the past 30 days?

☐Yes ☐ No

If you do not have children with whom you lived or had regular contact during the past 30 days skip this section and continue with the next section. Otherwise, please answer the following questions.

Over the past 30 days…

	Never			Sometimes			Always
52. My children were able to depend on me for whatever they needed.	1	2	3	4	5	6	7
53. I was interested in my children's activities.	1	2	3	4	5	6	7
54. I had trouble communicating with my children.	1	2	3	4	5	6	7
55. I was affectionate with my children.	1	2	3	4	5	6	7
56. I appropriately shared thoughts or feelings with my children.	1	2	3	4	5	6	7
57. My children and I did activities that brought us closer together.	1	2	3	4	5	6	7
58. I talked with, or taught, my children about important life issues.	1	2	3	4	5	6	7
59. I was a good role model for my children.	1	2	3	4	5	6	7

60. I had trouble giving emotional support to my children.	1	2	3	4	5	6	7
61. I had trouble settling conflicts or disagreements with my children.	1	2	3	4	5	6	7

	Not at all			Somewhat			Very much
62a. Overall, over the past 30 days, I had trouble in my relationship with my children.	1	2	3	4	5	6	7
62b. Overall, in the past 30 days, I was distressed or emotionally upset because of the difficulties I had in my relationship with my children.	1	2	3	4	5	6	7

Education (including distance learning)

Have you been involved in a formal educational experience, either in or outside of the school setting, during the past 30 days?

☐Yes ☐ No

If you have not been involved in an educational experience during the past 30 days skip this section and continue with the next section. Otherwise, please answer the following questions.

Over the past 30 days…

	Never			Sometimes			Always
63. I attended classes regularly.	1	2	3	4	5	6	7
64. I stayed interested in my classes and schoolwork.	1	2	3	4	5	6	7
65. I arrived on time for my classes.	1	2	3	4	5	6	7
66. I had trouble being supportive of my classmates' achievements.	1	2	3	4	5	6	7
67. I turned in assignments late.	1	2	3	4	5	6	7
68. I solved problems and challenges in class without much difficulty.	1	2	3	4	5	6	7
69. I took responsibility for my schoolwork.	1	2	3	4	5	6	7
70. I was patient with my classmates and/or instructors.	1	2	3	4	5	6	7
71. I had trouble settling disagreements or arguments with instructors and/or classmates.	1	2	3	4	5	6	7
72. I had trouble remembering what the instructor said.	1	2	3	4	5	6	7
73. I could easily remember what I read.	1	2	3	4	5	6	7
74. I understood course material.	1	2	3	4	5	6	7
75. When necessary, I cooperated with classmates.	1	2	3	4	5	6	7
76. I got along with classmates and/or instructors.	1	2	3	4	5	6	7
77. I completed my schoolwork to the best of my ability.	1	2	3	4	5	6	7

	Not at all			Somewhat			Very much
78a. Overall, over the past 30 days, I had trouble at school.	1	2	3	4	5	6	7
78b. Overall, in the past 30 days, I was distressed or emotionally upset because of my difficulties at school.	1	2	3	4	5	6	7

Day to Day

Over the past 30 days…

	Never			Sometimes			Always
79. I had trouble keeping up with household chores (for example, cleaning, cooking, yard work, etc).	1	2	3	4	5	6	7
80. I maintained good personal hygiene and grooming	1	2	3	4	5	6	7

(for example, showering, brushing teeth, etc).							
81. I had trouble managing my medical care (for example, medications, doctors' appointments, physical therapy, etc).	1	2	3	4	5	6	7
82. I ate healthy and nutritious meals.	1	2	3	4	5	6	7
83. I had trouble keeping up with chores outside the house (shopping, appointments, other errands).	1	2	3	4	5	6	7
84. I had trouble managing my finances.	1	2	3	4	5	6	7
85. I was physically active (for example, walking, exercising, playing sports, gardening, etc).	1	2	3	4	5	6	7
86. I spent time doing activities or hobbies that were fun or relaxing.	1	2	3	4	5	6	7

	Not at all			**Somewhat**			**Very much**
87a. Overall, over the past 30 days, I had trouble taking care of myself.	1	2	3	4	5	6	7
87b. Overall, in the past 30 days, I was distressed or emotionally upset because of the difficulties I had taking care of myself.	1	2	3	4	5	6	7

Instructions: Below is a list of problems and complaints that people sometimes have in response to life experiences. Please read each one carefully, then circle one of the numbers to the right to indicate how much you have been bothered by that problem <u>in the past month</u>.

	Not at all	A little bit	Moderately	Quite a bit	Extremely
1. Repeated, disturbing *memories*, *thoughts*, or *images* of a stressful experience from the past?	1	2	3	4	5
2. Repeated, disturbing *dreams* of a stressful experience from the past?	1	2	3	4	5
3. Suddenly *acting* or *feeling* as if a stressful experience *were happening again* (as if you were reliving it)?	1	2	3	4	5
4. Feeling *very upset* when *something reminded you* of a stressful experience from the past?	1	2	3	4	5
5. Having *physical reactions* (e.g., heart pounding, trouble breathing, sweating) when *something reminded you* of a stressful experience from the past?	1	2	3	4	5
6. Avoiding *thinking about* or *talking about* a stressful experience from the past or avoiding *having feelings* related to it?	1	2	3	4	5
7. Avoiding *activities* or *situations* because *they reminded you* of a stressful experience from the past?	1	2	3	4	5
8. Trouble *remembering important parts* of a stressful experience from the past?	1	2	3	4	5
9. *Loss of interest* in activities that you used to enjoy?	1	2	3	4	5
10. Feeling *distant* or *cut off* from other people?	1	2	3	4	5
11. Feeling *emotionally numb* or being unable to have loving feelings for those close to you?	1	2	3	4	5
12. Feeling as if your *future* will somehow be *cut short*?	1	2	3	4	5
13. Trouble *falling* or *staying asleep*?	1	2	3	4	5
14. Feeling *irritable* or *having angry outbursts*?	1	2	3	4	5
15. Having *difficulty concentrating*?	1	2	3	4	5
16. Being "*super-alert*" or watchful or on guard?	1	2	3	4	5
17. Feeling *jumpy* or easily startled?	1	2	3	4	5

APPENDIX E: TELEPHONE INTERVIEW

INTRODUCTION:

- HELLO MY NAME IS:
  - This is _____ calling from the Boston VA. I believe we have an interview scheduled…
- VOLUNTARY
  - May choose not to answer any question at any time for any reason
- CONFIDENTIAL
  - You answers and interview are only identified by an ID number
- AUDIO RECORDING
  - You agreed to have this interview recorded, is that right?
- ANY OTHER QUESTIONS
  - Before we begin?
- SAFETY
  - I'm going to start by asking you about 10 questions about your safety before we begin

WRAP-UP

- THANKS
  - For your participation – it's been very helpful
- QUESTIONS
  - Do you have any question about anything we've talked about today?
- PAYMENT
  - Should arrive in the coming weeks. If not, please call us back and we'll make sure it gets to you.
- WE MAY BE FOLLOWING UP
  - Don't be surprised if you hear from us again. We hope to be following up on everyone in the future to see how they're doing.

What's this project about anyway?

Epidemiology of PTSD

Aim 1. To describe the natural history of PTSD using the long-term psychosocial, medical and quality of life outcomes associated with the disorder, and to evaluate disparities by sociodemographic, military and post-deployment factors.

Aim 2. To identify risk factors (e.g., demographic, social support, socioeconomic resources) and comorbidities (e.g., other mental health disorders, neurological conditions) of PTSD, by comparing PTSD patients to a “control” group of veterans without PTSD.

PTSD Health Services

Aim 3. To identify treatment approaches through time.

Aim 4. To establish the prevalence of PTSD in a comparison group of service men and women who did not have the PTSD diagnosis in the medical record, and to identify risk factors for a missed PTSD diagnosis.

Aim 5. To assess current referral and health care utilization patterns among patients with PTSD, and also to compare their health care utilization to a group of veterans without PTSD.

Aim 6. To develop a large database of servicemen and women with PTSD and network of treatment sites that are potentially available for further observational and interventional studies, as well as concurrent ancillary studies.

C. SUICIDALITY

In the past month did you:

				Points
C1	Suffer any accident?	NO	YES	0
	IF NO TO C1, SKIP TO C2; IF YES, ASK C1a,:			
C1a	Plan or intend to hurt yourself in that accident either passively or actively?	NO	YES	0
	IF NO TO C1a, SKIP TO C2: IF YES, ASK C1b,:			
C1b	Did you intend to die as a result of this accident?	NO	YES	0
C2	Think that you would be better off dead or wish you were dead?	NO	YES	1
C3	Want to harm yourself or to hurt or to injure yourself?	NO	YES	2
C4	Think about suicide?	NO	YES	6

IF YES, ASK ABOUT THE INTENSITY AND FREQUENCY OF THE SUICIDAL IDEATION:

Frequency		Intensity	
Occasionally	___	Mild	___
Often	___	Moderate	___
Very often	___	Severe	___

→ Can you control these impulses and state that you will not act on them before seeking help/mental health treatment?

Only score 8 points if response is NO.	NO	YES	8
C5 Have a suicide plan?	NO	YES	8
C6 Take any active steps to prepare to injure yourself or to prepare for a suicide attempt in which you expected or intended to die?	NO	YES	9
C7 Deliberately injure yourself without intending to kill yourself?	NO	YES	4
C8 Attempt suicide?	NO	YES	10

Hoped to be rescued / survive ___

Expected / intended to die ___

In your lifetime:

C9 Did you ever make a suicide attempt?	NO	YES	4

IS AT LEAST **1** OF THE ABOVE (EXCEPT C1) CODED **YES**?

NO **YES**

IF YES, ADD THE TOTAL NUMBER OF POINTS FOR THE ANSWERS (C1-C9) CHECKED 'YES' AND SPECIFY THE LEVEL OF SUICIDE RISK AS INDICATED IN THE DIAGNOSTIC BOX:

SUICIDE RISK CURRENT

1-8 points	Low	___
9-16 points	Moderate	___
≥ 17 points	High	___

MAKE ANY ADDITIONAL COMMENTS ABOUT YOUR ASSESSMENT OF THIS PATIENT'S CURRENT AND NEAR FUTURE SUICIDE RISK IN THE SPACE BELOW:

Low suicide risk (0-8 points on MINI suicide module) and no participant expression of suicidal ideation in other components of the interview:

- Assessor will follow judgment in whether to provide follow-up.
- If participant is mildly symptomatic or distressed, the assessor will:

1) Perform a "check out" with the participant at the conclusion of the interview.
2) Provide the participant with the VA Suicide Hotline number (1-800-273-TALK), number for local VA/DoD.

Moderate suicide risk (9-16 points on MINI suicide module)

The assessor will:

1) Provide the participant with the VA Suicide Hotline number (1-800-273-TALK)
2) Provide the participant with local VA/DOD contact information
3) Offer to provide local treatment referrals within the next 24 hours
4) Offer to contact participant's mental health provider (e.g., therapist, psychiatrist)
5) Take steps to reduce participant risk:

- Ask participant to remove weapons/medications from his/her access

4) Help participant identify important protective factors:

- Religious beliefs
- Dependent children
- Belief in treatment
- Future oriented goals
- Social supports
- The assessor will follow judgment in whether to continue with SCID.

High suicide risk without imminent risk (>= 17 points on MINI suicide module)

The assessor will:

1) Provide VA Suicide Hotline number (1-800-273-TALK)
2) Offer to provide the participant with information on VA/DOD facilities and/or contact the participant's treating clinician, within 24 hours. If the participant identifies barriers to using VA/DOD facilities, the participant will be provided with local/regional resources, including treatment referrals.
3) Follow up with the participant within 24 hours.
4) Mail letter to participant with referral information, including VA Suicide hotline phone number and VA/DOD phone number.

- DO NOT continue current protocol (i.e., do not administer SCID).
- Must follow-up with the participant's treatment provider to confirm that participant is stable before rescheduling the SCID and open-ended interview.

High suicide risk with imminent risk (>= 17 points on the MINI suicide module)

The assessor will:

1) Further assess current SI (plan, means, access, intent)
2) Provide VA Suicide Hotline number (1-800-273-TALK)
3) Contact the VA or DoD suicide prevention coordinator or mental health provider on call, as appropriate, in closest proximity to the participant.
4) If the VA/DoD is unresponsive, contact the local law enforcement and inform them of the participant's emergent psychiatric needs.
5) Follow up with the participant within 24 hours.
6) Follow up with the VA/DoD or local law enforcement within 24 hours to determine the disposition of the case.

- DO NOT continue current protocol (i.e., do not administer SCID).
- Must follow-up with the participant's treatment provider to confirm that participant is stable before rescheduling the SCID and open-ended interview.

Project VALOR
Open-Ended Questions in Telephone Interview

1. How have your military experiences affected your ability to do work after you came home?

2. How have your military experiences affected your personal relationships after you came home?

Time Started: [ ]

Time Completed: [ ]

POSTTRAUMATIC STRESS DISORDER SCID CRITERIA
PROJECT VALOR SCID ASSESSMENT FOR PTSD

IF NO SUCH EVENTS, CHECK HERE___AND GO TO *NEXT INTERVIEW*

Date of Birth: ___/___/_____

Traumatic Events List

Brief Description	Civ/Mil	Date Start (M/Y) --	Date End	Ages
_____ F103a	_____	_____/_____ F103b(MS/YS)	-- _____/_____ F103b(ME/YE)	____-____ F103c(S/E)
_____ F103d	_____	_____/_____ F103e(MS/YS)	-- _____/_____ F103e(ME/YE)	____-____ F103f(S/E)
_____ F103g	_____	_____/_____ F103h(MS/YS)	-- _____/_____ F103h(ME/YE)	____-____ F103i(S/E)
_____ F103j	_____	_____/_____ F103k(MS/YS)	-- _____/_____ F103k(ME/YE)	____-____ F103l(S/E)
_____ F103m	_____	_____/_____ F103n(MS/YS)	-- _____/_____ F103n(ME/YE)	____-____ F103o(S/E)
_____ F103p	_____	_____/_____ F103q(MS/YS)	-- _____/_____ F103q(ME/YE)	____-____ F103r(S/E)
_____ F103s	_____	_____/_____ F103t(MS/YS)	-- _____/_____ F103t(ME/YE)	____-____ F103u(S/E)
_____ F103v	_____	_____/_____ F103w(MS/YS)	-- _____/_____ F103w(ME/YE)	____-____ F103x(S/E)
_____ F103y	_____	_____/_____ F103z(MS/YS)	-- _____/_____ F103z(ME/YE)	____-____ F103aa(S/E)
_____ F103bb	_____	_____/_____ F103cc(MS/YS)	-- _____/_____ F103cc(ME/YE)	____-____ F103dd(S/E)
_____ F103ee	_____	_____/_____ F103ff(MS/YS)	-- _____/_____ F103gg(ME/YE)	____-____ F103gg(S/E)

Please place a star (*) next to the index event.

IF ANY EVENTS LISTED: Sometimes these things keep coming back in nightmares, flashbacks, or thoughts that you can't get rid of. Has that ever happened to you?

IF NO: What about being very upset when you were in a situation that reminded you of one of these terrible things?

IF NO TO BOTH OF ABOVE, CHECK HERE ____ AND SKIP TO NEXT INTERVIEW

FOR FOLLOWING QUESTIONS, FOCUS ON TRAUMATIC EVENT(S) MENTIONED IN SCREENING QUESTION ABOVE.	A. The person has been exposed to a traumatic event in which both of the following were present:					
IF MORE THAN ONE TRAUMA IS REPORTED: Which of these do you think affected you the most?_____ _____ _____	(1) the person experienced, witnessed, or was confronted with an event or events that involved actual or threatened death or serious injury, or a threat to the physical integrity of self or others	?	1	2	3	F105
IF UNCLEAR: How did you respond emotionally during (or within one week following) [THE EVENT]?	(2) the person's response involved intense fear, helplessness or horror.	?	1	2	3	F106

GO TO A2 INTERVIEW FORM

A2 - Interview

Start time:_____

Item #1: **How did you respond emotionally during (or within one week following) [THE EVENT]?**
[THIS IS AN OPEN ENDED QUESTION. ALLOW PARTICIPANT TO REPORT AS MUCH OR AS LITTLE AS THEY REMEMBER DURING THE EVENT].

_____

_____

	Emotions	Experienced during or immediately after (within 1 week) the trauma? (Check all that apply)
F106a)	Afraid	
F106b)	Helpless	
F106c)	Horrified	
F106d)	Angry	
F106e)	Sad	
F106f)	Joyful	
F106g)	Disgusted	
F106h)	Surprised	
F106i)	Confused	
F106j)	Relaxed	
F106k)	Excited	
F106l)	Guilty	
F106m)	Ashamed	
F106n)	Humiliated	
F106o)	Embarrassed	
F106p)	Regretful	
F106q)	Frustrated	
F106r)	Anxious	
F106s)	Numb (i.e., lacking in emotion or feeling)	

Item #2: **I'd like to continue discussing how you felt during [THE EVENT]. In situations like these, people often report feeling lots of different emotions. I'm going to go down a list of emotions, and I want you to let me know if you remember feeling each emotion DURING [THE EVENT] .**

[IF PARTICIPANT REPORTS FEELING NUMB, ASK:]

A2a) When did you first start to feel something?

_____

_____

A2b) What were the first emotions you remember feeling?

_____

_____

[AFTER ASSESSING WHAT EMOTIONS WERE EXPERIENCED, ASK:]

A2c) Of the emotions you reported experiencing, which one did you feel the most during the trauma?

_____

Now I'd like to ask a few questions about specific ways that it may have affected you. For example . . .

B. The traumatic event is persistently reexperienced in one (or more) of the following ways:

. . . did you think about (TRAUMA) when you didn't want to or did thoughts about (TRAUMA) come to you suddenly when you didn't want them to?

(1) recurrent and intrusive distressing recollections of the event, including images, thoughts or perceptions

LIFETIME:	?	1	2	3	F107a
CURRENT:	?	1	2	3	F107b

. . . what about having dreams about (TRAUMA)?

(2) recurrent distressing dreams of the event

LIFETIME:	?	1	2	3	F108a
CURRENT:	?	1	2	3	F108b

. . . what about finding yourself acting or feeling as if you were back in the situation?

(3) acting or feeling as if the traumatic event were recurring (includes a sense of reliving the experience, illusions, hallucinations and dissociative flashback episodes, including those that occur on awakening or when intoxicated)

LIFETIME:	?	1	2	3	F109a
CURRENT:	?	1	2	3	F109b

. . . what about getting very upset when something reminded you of (TRAUMA)?

(4) intense psychological distress at exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event

LIFETIME:	?	1	2	3	F110a
CURRENT:	?	1	2	3	F110b

. . . what about having physical symptoms--like breaking out in a sweat, breathing heavily or irregularly, or your heart pounding or racing?

(5) physiological reactivity on exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event

LIFETIME:	?	1	2	3	F111a
CURRENT:	?	1	2	3	F111b

C. Persistent avoidance of stimuli associated with the trauma and numbing of general responsiveness (not present before the trauma), as indicated by three (or more) of the following:

Since (THE TRAUMA) . . .

. . . have you made a special effort to avoid thinking or talking about what happened?	(1) efforts to avoid thoughts, feelings, or conversations associated with the trauma					
		LIFETIME:	?	1	2	3	F113a
		CURRENT:	?	1	2	3	F113b
. . . have you stayed away from things or people that reminded you of (TRAUMA)?	(2) efforts to avoid activities, places, or people that arouse recollections of the trauma					
		LIFETIME:	?	1	2	3	F114a
		CURRENT:	?	1	2	3	F114b
. . . have you been unable to remember some important part of what happened?	(3) inability to recall an important aspect of the trauma					
		LIFETIME:	?	1	2	3	F115a
		CURRENT:	?	1	2	3	F115b
. . . have you been less interested in doing things that used to be important to you, like seeing friends, reading books or watching TV?	(4) markedly diminished interest or participation in significant activities					
		LIFETIME:	?	1	2	3	F116a
		CURRENT:	?	1	2	3	F116b
. . . have you felt distant or cut off from others?	(5) feeling of detachment or estrangement from others					
		LIFETIME:	?	1	2	3	F117a
		CURRENT:	?	1	2	3	F117b
. . . have you felt “numb” or like you no longer had strong feelings about anything or loving feelings for anyone?	(6) restricted range of affect, (e.g., unable to have loving feelings)					
		LIFETIME:	?	1	2	3	F118a
		CURRENT:	?	1	2	3	F118b
. . . did you notice a change in the way you think about or plan for the future?	(7) sense of a foreshortened future (e.g., does not expect to have a career, marriage, children, or a normal life span)					
		LIFETIME:	?	1	2	3	F119a
		CURRENT:	?	1	2	3	F119b

Since (THE TRAUMA) . . .

D. Persistent symptoms of increased arousal (not present before the trauma) as indicated by two (or more) of the following:

. . . have you had trouble sleeping? (What kind of trouble?)	(1) difficulty falling or staying asleep					
		LIFETIME:	?	1	2	3	F121a
		CURRENT:	?	1	2	3	F121b
. . . have you been unusually irritable? What about outbursts of anger?	(2) irritability or outbursts of anger					
		LIFETIME:	?	1	2	3	F122a
		CURRENT:	?	1	2	3	F122b
. . . have you had trouble concentrating?	(3) difficulty concentrating					
		LIFETIME:	?	1	2	3	F123a
		CURRENT:	?	1	2	3	F123b
. . . have you been watchful or on guard even when there was no reason to be?	(4) hypervigilance					
		LIFETIME:	?	1	2	3	F124a
		CURRENT:	?	1	2	3	F124b
. . . have you been jumpy or easily startled, like by sudden noises?	(5) exaggerated startle response					
		LIFETIME:	?	1	2	3	F125a
		CURRENT:	?	1	2	3	F125b

About how long did these problems--(CITE POSITIVE PTSD SYMPTOMS)--last?	E. Duration of the disturbance (symptoms in criteria B, C, and D) is more than one month	?	1	2	3	F127
	LIFETIME:	?	1	2	3	
	CURRENT:					
	F. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning					
	LIFETIME:	?	1	2	3	F128
	CURRENT:	?	1	2	3	

Traumatic Brain Injury (TBI) - lifetime

I am going to ask some questions about injuries to your head or close exposures to explosive blasts that you might have experienced at any time during your life. I am interested only in those injuries that led to certain symptoms.

Have you ever had a head injury or exposure to the force of a blast explosion in which you experienced at least one of the following as a result?

Altered consciousness (by altered consciousness, I mean that you were "dazed" or "knocked out" altogether)	Yes ○	No ○
You lost memory for what was happening during, immediately before, or immediately after the injury or explosion	Yes ○	No ○
Seizures	Yes ○	No ○
Brain surgery	Yes ○	No ○

If "no" to all, DISCONTINUE INTERVIEW

Did you have more than one head injury resulting in one of these problems?

Yes_____ **If yes, how many?** _____
No _____

Have you had any of the following symptoms in the PAST WEEK?
Select **ALL** that apply by filling in the circle

- ○ Memory problems/lapses
- ○ Balance problems or dizziness
- ○ Headaches
- ○ Sensitivity to bright light
- ○ Irritability
- ○ Sleep Problems
- ○ NONE OF THESE

I'm going to ask you now about your injury(ies). (If more than 1), **let's start with the most recent injury.** (If more than 5, ask respondent to consider the 5 most significant injuries, starting with the most recent).

HEAD INJURY #1

1. How old were you at the time?

- ○ < 12 yrs
- ○ 12-17 yrs
- ○ 18-29 yrs
- ○ 30 yrs – 40 yrs
- ○ > 40 yrs

2. Date of Injury: ☐☐ / ☐☐☐☐ (*mm/yyyy*)

3. Was this the most serious head injury you've ever had? ○ Yes ○ No

4. How were you injured?

- ○ Blast or explosion (RPG, landmine, IED, grenade)
- ○ Vehicular accident/crash (include aircraft)
- ○ Fragment or bullet wound above the shoulder
- ○ Fall
- ○ Object Hitting Head or Head Hitting Object
- ○ Knocked out by another person
- ○ Other (specify):

_____

5. Did this injury happen during deployment? ○ Yes ○ No

6. Did you lose consciousness or did you get "knocked out"? ○ Yes ○ No

If YES, **how long were you unconscious?**

Select ONE of the following.

- ○ less than 5 minutes
- ○ 5-15 minutes
- ○ 16-30 minutes
- ○ more than 30 minutes
- ○ unknown

7. Did you have of the following symptoms IMMEDIATELY afterward or after you regained consciousness (if you got "knocked out")?

Select **ALL** that apply by filling in the circle

- ○ Being dazed, confused, or "seeing stars"
- ○ Dizziness
- ○ Blurred Vision
- ○ Loss of coordination
- ○ Ruptured ear drums
- ○ Nausea
- ○ NONE OF THESE

8. Did any of the following problems begin or get worse afterward?

Select **ALL** that apply by filling in the circle

- ○ Memory problems/lapses
- ○ Balance problems or dizziness
- ○ Headaches
- ○ Sensitivity to bright light
- ○ Irritability
- ○ Sleep Problems
- ○ NONE OF THESE

9. a. Immediately after the injury or upon regaining consciousness, were you able to recall the event?

- ○ Yes
- ○ No
- ○ Unknown

b. If no, **Are you able to recall the event now**?

- ○ Yes
- ○ No
- ○ Unknown

10. How long after the injury was it before you started remembering new things again?

- ○ Less than 1 hour
- ○ 1-24 hours
- ○ More than 24 hours to 7 days
- ○ More than 7 days
- ○ Unknown

11. Did the injury result in a skull fracture?

- ○ Yes
- ○ No
- ○ Unknown

12 Did you need brain surgery after the injury?

- ○ Yes
- ○ No
- ○ Unknown

HEAD INJURY #2

"Let's now talk about the next most recent injury."

1. How old were you at the time?

- ○ < 12 yrs
- ○ 12-17 yrs
- ○ 18-29 yrs
- ○ 30 yrs – 40 yrs
- ○ > 40 yrs

2. Date of Injury: ☐☐ / ☐☐☐☐ (*mm/yyyy*)

3. Was this the most serious head injury you've ever had? ○ Yes ○ No

4. How were you injured?

- ○ Blast or explosion (RPG, landmine, IED, grenade)
- ○ Vehicular accident/crash (include aircraft)
- ○ Fragment or bullet wound above the shoulder
- ○ Fall
- ○ Object Hitting Head or Head Hitting Object
- ○ Knocked out by another person
- ○ Other (specify):

_____

5. Did this injury happen during deployment? ○ Yes ○ No

6. Did you lose consciousness or did you get "knocked out"? ○ Yes ○ No

If YES, **how long were you unconscious?**
Select ONE of the following.

- ○ less than 5 minutes
- ○ 5-15 minutes
- ○ 16-30 minutes
- ○ more than 30 minutes
- ○ unknown

7. Did you have of the following symptoms IMMEDIATELY afterward or after you regained consciousness (if you got "knocked out")?
Select **ALL** that apply by filling in the circle

- ○ Being dazed, confused, or "seeing stars"
- ○ Dizziness
- ○ Blurred Vision
- ○ Loss of coordination
- ○ Ruptured ear drums
- ○ Nausea
- ○ NONE OF THESE

8. Did any of the following problems begin or get worse afterward?
Select **ALL** that apply by filling in the circle

- ○ Memory problems/lapses
- ○ Balance problems or dizziness
- ○ Headaches
- ○ Sensitivity to bright light
- ○ Irritability
- ○ Sleep Problems
- ○ NONE OF THESE

9. a. Immediately after the injury or upon regaining consciousness, were you able to recall the event?

- ○ Yes
- ○ No
- ○ Unknown

b. If no, **Are you able to recall the event now**?

- ○ Yes
- ○ No
- ○ Unknown

10. How long after the injury was it before you started remembering new things again?

- ○ Less than 1 hour
- ○ 1-24 hours
- ○ More than 24 hours to 7 days
- ○ More than 7 days
- ○ Unknown

11. Did the injury result in a skull fracture?

- ○ Yes
- ○ No
- ○ Unknown

12 Did you need brain surgery after the injury?

- ○ Yes
- ○ No
- ○ Unknown

HEAD INJURY #3

"Let's now talk about the next most recent injury."

1. How old were you at the time?

- ○ < 12 yrs
- ○ 12-17 yrs
- ○ 18-29 yrs
- ○ 30 yrs – 40 yrs
- ○ > 40 yrs

2. Date of Injury: ☐☐ / ☐☐☐☐ (*mm/yyyy*)

3. Was this the most serious head injury you've ever had? ○ Yes ○ No

4. How were you injured?

- ○ Blast or explosion (RPG, landmine, IED, grenade)
- ○ Vehicular accident/crash (include aircraft)
- ○ Fragment or bullet wound above the shoulder
- ○ Fall
- ○ Object Hitting Head or Head Hitting Object
- ○ Knocked out by another person
- ○ Other (specify):

_____

5. Did this injury happen during deployment? ○ Yes ○ No

6. Did you lose consciousness or did you get "knocked out"? ○ Yes ○ No

If YES, **how long were you unconscious?**
Select ONE of the following.

- ○ less than 5 minutes
- ○ 5-15 minutes
- ○ 16-30 minutes
- ○ more than 30 minutes
- ○ unknown

7. Did you have of the following symptoms IMMEDIATELY afterward or after you regained consciousness (if you got "knocked out")?
Select **ALL** that apply by filling in the circle

- ○ Being dazed, confused, or "seeing stars"
- ○ Dizziness
- ○ Blurred Vision
- ○ Loss of coordination
- ○ Ruptured ear drums
- ○ Nausea
- ○ NONE OF THESE

8. Did any of the following problems begin or get worse afterward?
Select **ALL** that apply by filling in the circle

- ○ Memory problems/lapses
- ○ Balance problems or dizziness
- ○ Headaches
- ○ Sensitivity to bright light
- ○ Irritability
- ○ Sleep Problems
- ○ NONE OF THESE

9. a. Immediately after the injury or upon regaining consciousness, were you able to recall the event?

- ○ Yes
- ○ No
- ○ Unknown

b. If no, **Are you able to recall the event now**?

- ○ Yes
- ○ No
- ○ Unknown

10. How long after the injury was it before you started remembering new things again?

- ○ Less than 1 hour
- ○ 1-24 hours
- ○ More than 24 hours to 7 days
- ○ More than 7 days
- ○ Unknown

11. Did the injury result in a skull fracture?

- ○ Yes
- ○ No
- ○ Unknown

12 Did you need brain surgery after the injury?

- ○ Yes
- ○ No
- ○ Unknown

HEAD INJURY #4

"Let's now talk about the next most recent injury."

1. How old were you at the time?

- ○ < 12 yrs
- ○ 12-17 yrs
- ○ 18-29 yrs
- ○ 30 yrs – 40 yrs
- ○ > 40 yrs

2. Date of Injury: ☐☐ / ☐☐☐☐ (*mm/yyyy*)

3. Was this the most serious head injury you've ever had? ○ Yes ○ No

4. How were you injured?

- ○ Blast or explosion (RPG, landmine, IED, grenade)
- ○ Vehicular accident/crash (include aircraft)
- ○ Fragment or bullet wound above the shoulder
- ○ Fall
- ○ Object Hitting Head or Head Hitting Object
- ○ Knocked out by another person
- ○ Other (specify):

_____

5. Did this injury happen during deployment? ○ Yes ○ No

6. Did you lose consciousness or did you get "knocked out"? ○ Yes ○ No

If YES, **how long were you unconscious?**

Select ONE of the following.

- ○ less than 5 minutes
- ○ 5-15 minutes
- ○ 16-30 minutes
- ○ more than 30 minutes
- ○ unknown

7. Did you have of the following symptoms IMMEDIATELY afterward or after you regained consciousness (if you got "knocked out")?

Select **ALL** that apply by filling in the circle

- ○ Being dazed, confused, or "seeing stars"
- ○ Dizziness
- ○ Blurred Vision
- ○ Loss of coordination
- ○ Ruptured ear drums
- ○ Nausea
- ○ NONE OF THESE

8. Did any of the following problems begin or get worse afterward?

Select **ALL** that apply by filling in the circle

- ○ Memory problems/lapses
- ○ Balance problems or dizziness
- ○ Headaches
- ○ Sensitivity to bright light
- ○ Irritability
- ○ Sleep Problems
- ○ NONE OF THESE

9. a. Immediately after the injury or upon regaining consciousness, were you able to recall the event?

- ○ Yes
- ○ No
- ○ Unknown

b. If no, **Are you able to recall the event now**?

- ○ Yes
- ○ No
- ○ Unknown

10. How long after the injury was it before you started remembering new things again?

- ○ Less than 1 hour
- ○ 1-24 hours
- ○ More than 24 hours to 7 days
- ○ More than 7 days
- ○ Unknown

11. Did the injury result in a skull fracture?

- ○ Yes
- ○ No
- ○ Unknown

12 Did you need brain surgery after the injury?

- ○ Yes
- ○ No
- ○ Unknown

HEAD INJURY #5

"Let's now talk about the next most recent injury."

1. How old were you at the time?

- ○ < 12 yrs
- ○ 12-17 yrs
- ○ 18-29 yrs
- ○ 30 yrs – 40 yrs
- ○ > 40 yrs

2. Date of Injury: ☐☐ / ☐☐☐☐ (*mm/yyyy*)

3. Was this the most serious head injury you've ever had? ○ Yes ○ No

4. How were you injured?

- ○ Blast or explosion (RPG, landmine, IED, grenade)
- ○ Vehicular accident/crash (include aircraft)
- ○ Fragment or bullet wound above the shoulder
- ○ Fall
- ○ Object Hitting Head or Head Hitting Object
- ○ Knocked out by another person
- ○ Other (specify):

_____

5. Did this injury happen during deployment? ○ Yes ○ No

6. Did you lose consciousness or did you get "knocked out"? ○ Yes ○ No

If YES, **how long were you unconscious?**
Select ONE of the following.

- ○ less than 5 minutes
- ○ 5-15 minutes
- ○ 16-30 minutes
- ○ more than 30 minutes
- ○ unknown

7. Did you have of the following symptoms IMMEDIATELY afterward or after you regained consciousness (if you got "knocked out")?
Select **ALL** that apply by filling in the circle

- ○ Being dazed, confused, or "seeing stars"
- ○ Dizziness
- ○ Blurred Vision
- ○ Loss of coordination
- ○ Ruptured ear drums
- ○ Nausea
- ○ NONE OF THESE

8. Did any of the following problems begin or get worse afterward?
Select **ALL** that apply by filling in the circle

- ○ Memory problems/lapses
- ○ Balance problems or dizziness
- ○ Headaches
- ○ Sensitivity to bright light
- ○ Irritability
- ○ Sleep Problems
- ○ NONE OF THESE

9. a. Immediately after the injury or upon regaining consciousness, were you able to recall the event?

- ○ Yes
- ○ No
- ○ Unknown

b. If no, **Are you able to recall the event now**?

- ○ Yes
- ○ No
- ○ Unknown

10. How long after the injury was it before you started remembering new things again?

- ○ Less than 1 hour
- ○ 1-24 hours
- ○ More than 24 hours to 7 days
- ○ More than 7 days
- ○ Unknown

11. Did the injury result in a skull fracture?

- ○ Yes
- ○ No
- ○ Unknown

12 Did you need brain surgery after the injury?

- ○ Yes
- ○ No
- ○ Unknown

APPENDIX F: PUBLICATIONS AND PRESENTATIONS

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Project VALOR: design and methods of a longitudinal registry of post-traumatic stress disorder (PTSD) in combat-exposed Veterans in the Afghanistan and Iraqi military theaters of operations

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Key words
post-traumatic stress disorder (PTSD), study design, disease registry, combat-exposed Veterans, psychosocial outcomes

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Abstract

Few studies have investigated the natural history of post-traumatic stress disorder (PTSD). Project VALOR (Veterans' After-discharge Longitudinal Registry) was designed as a longitudinal patient registry assessing the course of combat-related PTSD among 1600 male and female Veterans who served in Operation Enduring Freedom (OEF) in Afghanistan or Operation Iraqi Freedom (OIF). Aims of the study include investigating patterns and predictors of progression or remission of PTSD and treatment utilization. The study design was based on recommendations from the Agency for Healthcare Quality and Research for longitudinal disease registries and used a pre-specified theoretical model to select the measurement domains for data collection and interpretation of forthcoming results. The registry will include 1200 male and female Veterans with a recent diagnosis of PTSD in the Department of Veteran Affairs (VA) electronic medical record and a comparison group of 400 Veterans without a medical record-based PTSD diagnosis, to also allow for case-control analyses. Data are collected from administrative databases, electronic medical records, a self-administered questionnaire, and a semi-structured diagnostic telephone interview. Project VALOR is a unique and timely registry study that will evaluate the clinical course of PTSD, psychosocial correlates, and health outcomes in a carefully selected cohort of returning OEF/OIF Veterans. *Copyright © 2011 John Wiley & Sons, Ltd.*

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Introduction

Post-traumatic stress disorder (PTSD) is a common and potentially disabling psychiatric disorder that affects a large number of active duty military personnel and Veterans. The prevalence of PTSD in service men and women returning from overseas operations in Afghanistan and Iraq is estimated to be at least 10% immediately post-deployment, with an approximate doubling of the prevalence within five years after deployment (Hoge *et al.*, 2006; Hoge *et al.*, 2004; Tanielian and Jaycox, 2008). Similar or higher rates are reported in Veterans of previous military conflicts (Richardson *et al.*, 2010; Seal *et al.*, 2009). Despite the prevalence and potential impact of PTSD on multiple areas of patient function (Hoge *et al.*, 2007; Kubzansky *et al.*, 2007; Marx *et al.*, 2009a; Schnurr and Jankowski, 1999; Vasterling *et al.*, 2008), surprisingly little is known about the natural history, course of outcomes, and treatment utilization patterns in returning service members (Wolfe *et al.*, 1999). As a result, diagnostic and treatment services for combat-exposed Veterans with PTSD may not be adequately allocated, and long-term health policy and planning in this regard may not be adequately informed.

Epidemiologic studies have identified pre- and post-trauma factors that influence the development of PTSD (Brewin *et al.*, 2000; Ozer *et al.*, 2003). However, the course of PTSD differs across individuals, with some patients recovering quickly and others experiencing symptoms for years or even decades, and the natural history and predictors of remission or progression are not well understood. Knowledge about the efficacy and safety of treatments for PTSD has been obtained from a limited number of randomized controlled trials (RCTs), most of which were performed in non-Veteran populations (Friedman *et al.*, 2007; Monson *et al.*, 2006; Schnurr *et al.*, 2007; Schnurr *et al.*, 2003). While randomized trials are the "gold standard" for assessing efficacy and/or safety of one treatment over another or a suitable control, observational longitudinal studies, such as patient registries, have some unique advantages, such as their ability to evaluate treatment utilization patterns, outcomes, and factors influencing treatment utilization in a real-world setting (Conway and Clancy, 2009). Differences in the course of disease for subgroups of individuals, including men versus women, those with multiple versus few exposures, and those who are actively being treated versus those who are not, can also be assessed in a well-designed patient registry. Moreover, the manner in which treatments for PTSD are applied in everyday practice, including who receives which treatments and for how long, the use of concomitant medical or psychiatric services, and the likely or common psychosocial sequelae, are key areas for assessment, particularly in the context of Veterans with PTSD.

Project VALOR (Veterans' After-discharge Longitudinal Registry) is an observational patient registry study of PTSD among combat-exposed Veterans who served in the recent military operations in Iraq and Afghanistan. The objective of the VALOR registry is to provide data on the natural history and outcomes associated with PTSD in Veterans who have utilized the Department of Veteran Affairs (VA) health care system. An additional goal of this project is to determine predictors of a PTSD diagnosis by comparing diagnosed cases to combat-exposed Veterans without a diagnosis of PTSD.

In this paper, we describe the design and methods of Project VALOR, as well as the strengths, limitations, and challenges of establishing a large patient registry of Veterans with or without a recent medical record-based diagnosis of PTSD.

Methods

Overview

To guide the selection of study measures, we developed a conceptual model (Figure 1) based on current evidence regarding psychosocial predictors of recovery and outcome in PTSD (Brewin *et al.*, 2000; King *et al.*, 1998; Ozer *et al.*, 2003). Although this model does not consider all possible factors that may influence PTSD, it served to guide the selection of conceptual domains and measurement methods in the study, in addition to providing a general conceptual framework for statistical analyses and theoretical interpretation of the final results. Accordingly, the registry is designed to provide relevant data and to allow an evaluation of current theoretical models of symptom development in a large sample of service men and women who utilize the VA medical system. Diagnostic, demographic, and service-related data are being collected from existing medical and military records as well as detailed information on symptoms of PTSD and potential risk factors and outcomes from a diagnostic telephone interview and a self-administered questionnaire. In addition, we plan to collect one-year follow-up data through medical record abstraction; further follow-up, including recontacting study participants, is planned for future years based on continued funding.

This project is the result of a joint effort of researchers at the National Center for PTSD at the VA Boston Healthcare System (clinical center), Washington, DC VA Medical Center, and New England Research Institutes, Inc. (NERI) (data and statistical center). The study has received approval from the Institutional Review Boards (IRBs) of all participating institutions as well as

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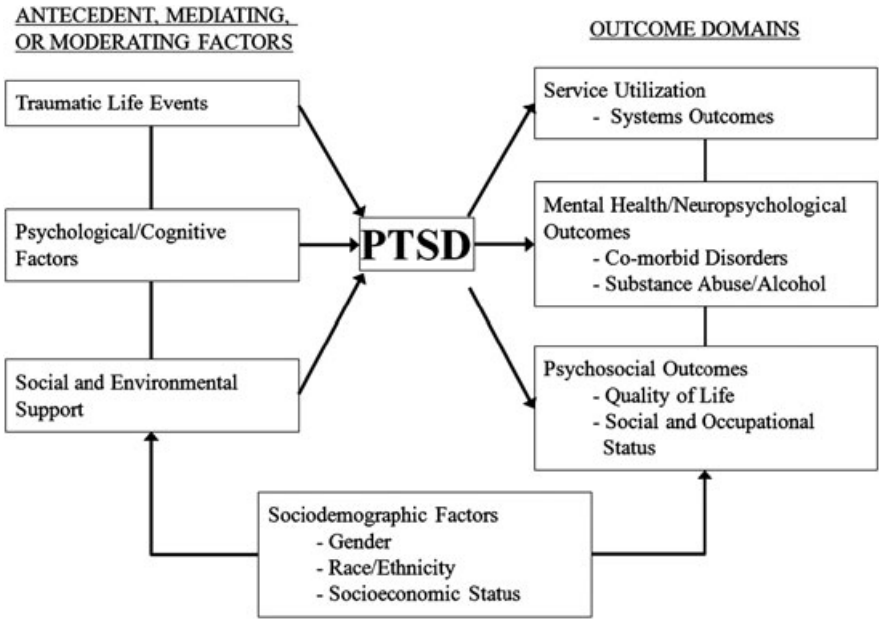

Figure 1 Project VALOR conceptual model.

the US Army Medical Research and Materiel Command Office of Research Protections.

Study population

The source population for study participants is US Army or Marine Veterans who were deployed to combat in support of Operation Enduring Freedom (OEF) or Operation Iraqi Freedom (OIF) and are in the VA health care system inpatient or outpatient databases. To be eligible for this study, participants must have either: (a) separated from active duty after serving in OEF/OIF or (b) completed at least one Reserve/Guard deployment in support of OEF/OIF. In addition, they must have undergone a mental health evaluation at a VA facility, as indicated by a diagnostic interview or psychotherapy procedure code, between July 2008 and December 2009, and must not currently be participating in a clinical (intervention) trial. From this source population, we will enroll in the study 1200 men and women with a recent diagnosis of PTSD in the VA electronic medical record and 400 men and women without a PTSD diagnosis in the medical record. For the purposes of study enrollment, we defined a diagnosis of PTSD as at least two PTSD diagnoses (primary or secondary ICD-9-CM code 309.81) associated with two separate VA visits that occurred on or after the date of the mental health evaluation but before December 2009, and we defined the absence of PTSD as no ICD-9-CM code 309.81 in the VA electronic medical record since the beginning of OEF/OIF (2002 health care records). We exclude individuals with a single PTSD diagnosis during the time period of interest to avoid including those with an unconfirmed referral for PTSD or a diagnostic or coding error. Individuals with major depressive disorder, traumatic brain injury (TBI), or other concomitant psychiatric disorders are included in the registry, so that the registry is inclusive of a broad range of comorbidities associated with PTSD. To evaluate predictors of PTSD risk and recovery separately for men and women, we plan to oversample females to provide adequate power for analyses stratified by gender. Approximately equal numbers of male and female Veterans will be included in each diagnostic group, by recruiting eligible participants until gender-specific enrollment targets are achieved.

Study recruitment

The procedures for recruiting participants are shown in Figure 2. Project VALOR team members from the Washington, DC VA created a roster of potential participants for the PTSD registry and the non-PTSD comparison group using the inclusion criteria described previously. The initial roster included 3000 men and women with a mental health evaluation (defined earlier) completed between July 2008 and July 2009. The target sample for this roster was 2250 individuals with a diagnosis of PTSD between July 2008 and July 2009

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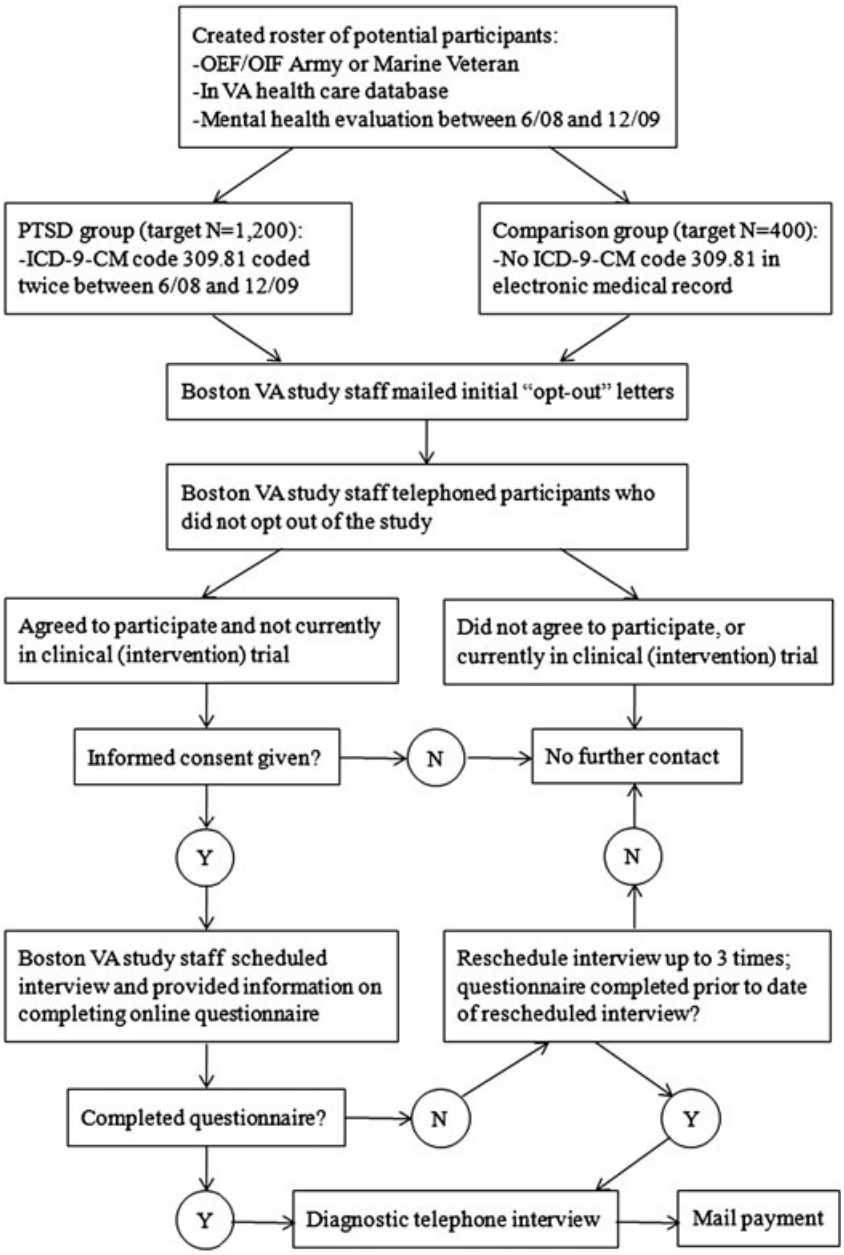

Figure 2 Flowchart of data collection procedures.

and 750 individuals without a PTSD diagnosis in the VA medical record, with equal numbers of men and women within each group. However, due to a limited number of women who met the inclusion criteria for the non-PTSD group, the non-PTSD sample consisted of 527 men and 223 women, while the PTSD sample included equal numbers of men and women. For the second roster of potential participants, we extended the timeframe for selection to December 2009, to increase the number of women without a diagnosis of PTSD who were eligible for the study.

VA Boston study staff mail initial "opt-out" letters to all individuals in the roster, to introduce the study and ask the Veteran whether or not he/she would like further contact about the study. Veterans who request no further contact regarding the study are omitted from the list of potential participants; those who agree to future contact

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are retained as potential participants. Veterans who do not respond to the initial letter within 30 days are sent a second letter, and those who do not respond to the second letter within 14 days are included in the list of potential participants. Demographic data and service-related characteristics of Veterans who decline participation are collected through medical record abstraction, for comparison with registry participants.

Participants who do not opt out of the study are telephoned by VA Boston study staff, who provide additional details about the study, assess the exclusion criteria of no current participation in a clinical (intervention) research trial, and formally invite the Veteran to participate in the study. Those who agree to continue are then provided with an opportunity to give their informed consent for participation in the study. Given the online and telephone nature of the study, a Waiver of Documentation of Informed Consent was granted by the local IRB and consent is obtained verbally, to avoid sending personally identifiable information through the mail. Trained research assistants administer standardized, IRB-approved informed consent and Health Insurance Portability and Accountability Act (HIPAA) release scripts while on the telephone. After informed consent is obtained, the research assistant schedules a date and time for the telephone interview and reminds the participant to complete the self-administered questionnaire prior to the interview. Participants are compensated $50.00 for their participation in the registry.

Data collection and measures

Medical history data were abstracted from the electronic medical records at baseline and will be abstracted again at year one of follow up. The VA health care system database contains information on all inpatient and outpatient visits, including the ICD-9 (International Classification of Diseases) and procedure codes to describe the condition being treated and the nature of the visit, respectively. However, the database is structured chronologically by visit, rather than unique patient identifiers or diagnoses, and it offers no readily accessible way to assess the longitudinal outcomes of patients with PTSD or their utilization of VA health care. Therefore, a fundamental objective of this project is to establish a database of patients with and without PTSD from the existing VA utilization database. However, to do this the data must be extracted, transformed into records indexed by patient, and loaded into a new database, together with data imported from other sources (Gliklich and Dreyer, 2010). Other sources of data for the PTSD registry include the OEF/OIF Veteran roster (particularly for military specific data, such as branch, rank, and deployment dates), a self-administered questionnaire, and a diagnostic interview conducted by telephone (described earlier).

The questionnaire and interview are used to fill key gaps in information obtained from the electronic medical record by assessing factors such as exposure to traumatic events, comorbid symptoms of anxiety or depression, substance abuse, social and occupational status, and overall quality of life. Recognizing the limitations of self-report data, each of these domains are assessed by means of brief, validated scales which measure current symptoms and outcomes (Table 1). The specific measures were selected based on psychometric criteria (reliability, sensitivity, and specificity), public health and policy relevance, and level of burden for the respondent. Details of the validation and utilization of these measures are provided in the references noted in Table 1. For some measures, we selected items from instruments in development or constructed questions based on empirically-demonstrated construct relevance.

Self-administered questionnaire

Participants are required to complete a self-administered questionnaire prior to the interview. The questionnaire, which is a compilation of specific scales (Table 1), is accessed via a secure website hosted by an online survey vendor specializing in psychiatric and social science research (PsychData, LLC, State College, PA, USA). All stored data are encrypted, and no identifying information (including IP address) is collected in the online survey. Participants without access to the internet or who are uncomfortable using the internet are given the option of completing a paper-and-pencil version of the survey through the postal mail. In addition to the measures noted in Table 1, the questionnaire collects background/demographic data and information on current health status and health-related impairment of activities of daily living. This measures broader aspects of daily living than the more psychosocially-focused Psychosocial Functioning Inventory (Marx *et al.*, 2009b).

The process of questionnaire administration is shown in Figure 2. Consented individuals are given approximately two weeks to complete the questionnaire prior to their scheduled telephone interview. If the questionnaire is not completed by the interview date, a research staff member contacts the participant to reschedule the phone interview. Once the participant completes the online questionnaire, the data are transferred to a database at VA Boston and the participant's record is permanently deleted from the PsychData web server, in order to maintain participant

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Table 1 Project VALOR data collection domains, measures and assessment methods

Domain	Assessment measure(s)	Project VALOR administration	References
Suicidal ideation	Mini-International Neuropsychiatric Interview (MINI) suicide module	Telephone interview	(Sheehan *et al.*, 1998)
PTSD	Structured Clinical Interview for DSM-IV (SCID-IV) PTSD module	Telephone interview	(Spitzer *et al.*, 1992; Williams *et al.*, 1992)
Self-assessed effects of military experiences on post-discharge life	Two open-ended questions (qualitative data): "How have your military experiences affected your [ability to do work] *or* [personal relationships] after you came home?"	Telephone interview	—
Traumatic brain injury (TBI)	Defense and Veterans Brain Injury Center TBI questionnaire, modified for brief administration	Telephone interview	(Brown *et al.*, 2005; Levin, 1995; Wilde *et al.*, 2006)
Combat exposure	DRRI Section I (Combat Experiences) and Section J (Post-Battle Experiences)	Self-administered questionnaire	(King *et al.*, 2006)
Quality of life	SF-12v2	Self-administered questionnaire	(Ware *et al.*, 1996)
Sleep	Sleep Problem Scale	Self-administered questionnaire	(Jenkins *et al.*, 1988)
Absenteeism	World Health Organization Health and Work Performance Questionnaire (HPQ)	Self-administered questionnaire	(Kessler *et al.*, 2003)
Life stressors/trauma	Life Events Checklist (LEC)	Self-administered questionnaire	(Gray *et al.*, 2004)
Social support	Deployment Risk and Resilience Inventory (DRRI) Section L (Post-deployment support)	Self-administered questionnaire	(King *et al.*, 2006)
Mental health disorders (including depression, anxiety, panic, somatoform disorder)	Prime-MD Patient Health Questionnaire (PHQ)	Self-administered questionnaire	(Spitzer *et al.*, 1999)
Alcohol/drug use	Alcohol Use Disorder Identification Test (AUDIT) Two-Item Conjoint Screen (TICS)	Self-administered questionnaire	AUDIT (Reid *et al.*, 1999; Saunders *et al.*, 1993) TICS (Brown *et al.*, 2001)
Anger/hostility	Dimensions of Anger Reactions, revised short form (DAR-5)	Self-administered questionnaire	(Forbes *et al.*, 2004; Hawthorne *et al.*, 2006)
Treatment utilization	New questions	Self-administered questionnaire	—
Functional impairment	Psychosocial Functioning Inventory (PFI)	Self-administered questionnaire	(Marx *et al.*, 2009b)

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privacy and data security. In addition, a paper copy of the questionnaire is printed and securely stored at VA Boston, to provide a backup in the event of hardware or software failure.

Diagnostic telephone interview

The diagnostic telephone interviews are administered by doctoral-level clinicians with specialized training in PTSD assessment who are blinded with respect to the participant's PTSD status in the VA medical record. Study interviewers are specifically trained in the administration of the PTSD module of the Structured Clinical Interview for DSM-IV (SCID-IV) (Spitzer *et al.*, 1992; Williams *et al.*, 1992). Assessment measures were selected based on prior use and validation in both clinical and epidemiological studies, and ease of standardization across interviewers (see Table 1). Each interview is digitally recorded, and 5% (i.e. 80 interviews) will be randomly selected and assessed for reliability of the SCID diagnosis by two independent raters.

Prior to administration of the SCID-IV PTSD module, participant suicidality is assessed using the Mini-International Neuropsychiatric Interview (MINI) suicide module. Interviewers follow a standardized protocol for proceeding with the interview based on the participant's score on the MINI suicide module or expression of suicidal ideation in other components of the interview. In the event that a participant is thought to be at imminent risk of suicide, the interviewer discontinues the study protocol, further assesses the participant's suicidal intent, and contacts the participant's local VA or Department of Defense (DoD) health care facility and notifies the mental health provider on call or suicide prevention coordinator, as appropriate.

Participants who complete the questionnaire but do not complete the diagnostic interview as scheduled are telephoned up to four times to reschedule the interview. Those who cannot be reached or who refuse to complete the interview are compensated $25 rather than $50 for their participation in a portion of the study.

Outcomes assessment

An important goal of the interview is to assess the concordance between the PTSD diagnosis found in the electronic medical record and the SCID-based diagnosis from the diagnostic telephone interview. As noted previously, participants' PTSD status at study entry is based on whether or not their VA medical records contain a current or recent (past 18 months) diagnosis of PTSD. Blinded, doctoral-level clinicians administer the SCID-IV PTSD module during the telephone interview to determine each participant's current PTSD status.

Several comorbidities of interest, including TBI, substance use disorders, and depression, are assessed through the online questionnaire or diagnostic interview. In addition, due to the common overlap between PTSD and TBI, the interview includes a retrospective lifetime assessment of history of head injuries that may have led to TBI. The interviewer obtains details regarding the timing, associated events, and injury characteristics of the five most serious head injuries or close exposures to explosive blasts in the participant's life that caused altered consciousness, seizures, and/or required brain surgery. The TBI interview was derived in part from questions used by the Defense and Brain Injury Center, to assure comparability with other recent studies of OEF/OIF Veterans (Schwab *et al.*, 2007). The interview questions also reflect empirically-derived indicators (e.g. duration of post-traumatic amnesia) of brain injury severity (Brown *et al.*, 2005; Wilde *et al.*, 2006) and capture information pertinent to current classification standards (Kay *et al.*, 1993).

Data analysis

The final registry database will include merged data from the self-administered questionnaire and telephone interview, along with select baseline and follow-up data from the Veterans Health Administration (VHA) electronic medical record. We will conduct descriptive analyses to characterize the PTSD and non-PTSD samples in terms of demographics, diagnosis, symptomatology, quality of life, current therapies used, and clinical trajectories. In addition, we will assess the prevalence of PTSD based on both the medical records and the standardized SCID interview assessment, and will examine the concordance between medical record-based and SCID-based diagnoses. We will conduct analyses comparing the 1200 PTSD group participants with the 400 non-PTSD participants. These analyses will include the "false positive" PTSD cases (individuals with a medical record-based diagnosis of PTSD who do not meet the research-based SCID diagnostic criteria for PTSD) and/or the "false negative" cases (individuals in the non-PTSD comparison group who nevertheless meet the SCID diagnostic criteria for PTSD) as appropriate, based on the goal of the analysis. For individuals in the control group who meet SCID criteria for a positive diagnosis but do not have a medical record diagnosis, we will examine potential risk factors and determinants. Conversely, for those individuals who do not meet SCID criteria but have a medical record diagnosis, we will examine likely factors (e.g. treatment or deployment status) that

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might account for the discrepancy. A major strength of the registry design is that it permits examination of potential reasons for and correlates of these discordant diagnostic assessments.

The operational definitions for selected outcomes of interest are listed in Table 2. Covariates (and interaction terms) will be retained in the models if they are found to be significant predictors of the outcome (at the 0.05 level of significance) or if they confound the effects of significant predictors, defined as changing the effect size estimate by at least 20%. Analyses will be conducted in SAS 9.2 (SAS Institute, Cary, NC) and SUDAAN 10.0.1 (Research Triangle Institute International, Research Triangle Park, NC). Because the target population will be oversampled to achieve equal proportions of male and female participants, weighted estimation methods will be used to achieve unbiased overall prevalence estimates of comorbidities and other conditions that reflect the status of the target PTSD population.

Statistical power

The primary aim of the registry is to describe the natural history of PTSD, characterized by the long-term psychosocial, medical, and quality of life outcomes associated with the disorder, and to assess whether these outcomes differ by subgroups defined by socio-demographic, military, and post-deployment factors. The size of each study group and subgroup was determined based on statistical power as well as feasibility, given the duration and resources of the research funding for the project. As noted earlier, we oversampled women to allow for analyses stratified by gender. We plan to continue enrolling participants until we achieve the target number of individuals in each subgroup with a completed questionnaire and diagnostic interview. Our power calculations therefore are based on the goal of 1200 participants with and 400 participants without a PTSD diagnosis. With 1200 participants with a diagnosis of PTSD based on the VA electronic records, there is high precision to estimate comorbidity rates. If the comorbidity rate is as high as 40%, the relative precision (half-width) of a 90% confidence interval is less than 6% (0.023/0.40). If the rate is only 10%, then the relative precision of the confidence interval is 14% (0.014/0.10).

Power is also sufficient for potential subgroup comparisons where moderate to large effect sizes are expected. For example, it is of interest to assess whether comorbidity rates differ by subgroup in the PTSD cohort (e.g. by socio-economic status or service branch). In the case of a subgroup factor that divides the sample according to a 30/70 split (360 versus 840 subjects), if the comorbidity rate of the lesser affected subgroup is relatively rare (10%), there is over 84% power to detect an odds ratio of 1.71 (0.10 versus 0.16 rates). If the comorbidity rate of the lesser affected subgroup is 20%, there is over 89% power to detect an odds ratio of 1.56 (0.20 versus 0.28 rates). If the comorbidity is quite prevalent (40%), there is 87% power to detect a smaller effect size (odds ratio of 1.44). If the subgroup sizes are more evenly split amongst the 1200 PTSD cases, power will be even greater.

Secondary analyses of case-control data from the 1200 Veterans in the PTSD group and 400 Veterans in the comparison group will have sufficient power in numerous scenarios, even for conservative assumptions. For example, if the outcome is low social support as a dichotomous indicator (defined by a pre-specified cutoff), and if the control rate of low social support is 20%, there is approximately 80% power to detect an odds ratio of 1.5 for low social support in cases versus controls. For analyses treating outcomes as continuous variables, only 503 cases (versus 167 controls) are required to detect an effect size (defined as the sample standard deviation divided by the mean difference) of 0.25 standard deviations with 80% power, which is a minimum clinically significant difference. With 1200 cases and 400 controls, there is >99% power to detect a 0.25 effect size. Therefore, continuous analyses of case-control differences in functioning can support multivariate modeling as well as subgroup analyses defined by gender and race/ethnicity.

Results

To test the procedures for study recruitment and data collection, we conducted a pilot study over a three-month period prior to the launch of full study recruitment. Twenty-seven participants (13 men and 14 women) were enrolled during the pilot phase.

Characteristics of the pilot study participants are shown in Table 3. On average, participants were 42 years of age (range: 28 to 58 years), and 74% of participants had a diagnosis of PTSD based on the VA medical records. Concordance between the PTSD diagnosis from the medical records and the SCID was 82%; 18 participants (67%) had a positive diagnosis on both the medical records and the SCID, three (11%) were positive on the SCID but not the medical records, two (7%) were positive based on the medical records but not the SCID, and four (15%) were negative for both.

The pilot phase demonstrated the feasibility of the recruitment and data collection procedures. All participants completed both the self-administered questionnaire and diagnostic telephone interview, and no difficulties related

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Table 2 Operational definitions of selected outcomes of interest

Outcome	Definition	Anticipated variable form
PTSD – clinical diagnosis	Diagnosis of PTSD in electronic medical record (ICD-9 code 309.81)	Dichotomous
PTSD – research-based diagnosis	Meets criteria for PTSD based on SCID assessment	Dichotomous
Psychiatric comorbidities	Diagnoses of depression, anxiety, substance abuse or other DSM-IV diagnoses	Dichotomous
Treatment utilization	Number of health care visits, pharmaceutical usage	Continuous
Productivity loss	Self-reported absentee days, decreased accomplishments, decreased diligence	Continuous
Quality of life	SF-12 scores	Continuous

to comprehension or completion of the questionnaire or interview were reported by the participant or the interviewer. The average length of the diagnostic interview was 32 minutes (range 10 to 59 minutes).

Several changes to the study protocol were implemented as a result of the pilot phase. The number of times an interview can be rescheduled was increased to three, to give participants additional time to complete the self-administered questionnaire. In addition, revisions were made to the TBI scale and the Life Events Checklist was added to the interview to collect detailed information on the participant's trauma history.

The pilot phase was completed in January 2010, and full study recruitment began in May 2010. As of March 4, 2011, 419 study interviews have been completed. With recruitment of additional interviewers for the project, we anticipate completing study enrollment in early 2012.

Discussion

Project VALOR is the first longitudinal patient registry study of PTSD in returning service men and women who have utilized the VA health care system. This study is designed to provide longitudinal data over time to characterize the course of PTSD and associated outcomes in combat-exposed Veterans, as diagnosed by a SCID-based interview and electronic medical record information. The registry will provide a unique opportunity to characterize the diagnostic and treatment services received by a well-defined cohort of Veterans with or without a diagnosis of PTSD, and to describe associated patient characteristics, including demographic, medical and psychosocial information. Our observational registry design will include assessment of the number, type and duration of treatments received, presence or absence of other medical or psychiatric disorders, and the use of conjoint treatments for these disorders. We will use a broad array of functional and psychosocial assessments at baseline, as well as medical record abstraction at baseline and year one of follow-up, to obtain detailed data on potential risk factors for and outcomes of PTSD. Our use of a mixed mode data collection system, including a combination of medical record abstraction, a self-administered questionnaire, and a structured telephone interview, is a unique feature and potential strength of the study design. We will use brief, validated measures to assess PTSD and other outcomes and exposures of interest, with data obtained in a format specifically suited to the topic or domain under investigation. This convergent validity approach is intended to provide internal validity checks on the accuracy and completeness of diagnostic data obtained for each participant. An additional strength of the study design is the large

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Table 3 Baseline characteristics of pilot phase participants in Project VALOR

Covariate	All pilot study participants
N	27
Age (mean and standard deviation [SD])	41.9 (8.6)
Female (%)	52
Race (%)	
Black	15
White	82
Other	3
Hispanic ethnicity (%)	11
Branch of military service (%)	
Army	96
Marines	4
Location of deployment (%)	
Afghanistan only	19
Iraq only	70
Multiple deployments/other	11
PTSD based on SCID (%)	78
Interview duration (mean and SD)	31.9 (12.3)

number of female participants, as this will allow us to examine differences in the predictors of risk and recovery for PTSD by gender.

The registry will create an opportunity, most importantly, to assess the longitudinal trajectory of psychosocial outcomes over time. Funding has been obtained for the first wave (12 months) of follow up, and we plan to seek funding for additional follow-up cycles. The longitudinal component of the registry will provide data not only on progression and remission of PTSD symptoms, but also trajectories of other psychiatric comorbidities (e.g. depression, substance abuse, suicide risk), resource and treatment utilization, and social and occupational outcomes in participants with or without a diagnosis of PTSD. A comparison group of male and female Veterans without a medical record-based diagnosis of PTSD, but with similar service history and combat experience, is included in our design for case-control comparisons. An important aspect of the registry will be assessment of longitudinal data obtained from medical record sources within the VA, compared to the structured, telephone interview and self-administered questionnaire specifically designed for the study. A registry database of potentially eligible participants for future ancillary studies will also be developed.

Although there are several strengths of the study design, limitations include the potential for loss to follow up over time and the possibility that our sample will not be representative of the underlying population of Veterans with PTSD, as our study population will only include those who seek care for PTSD or other mental health conditions at VA health care facilities. Although some loss to follow up is inevitable, we will use proven strategies for maximizing retention in order to retain as many participants as possible at each stage of follow up (Kessler *et al.*, 2008; Scott *et al.*, 2006). Further, by using medical record abstraction we will be able to obtain follow-up data for some participants who are unavailable for recontact but continue to receive care at VA facilities. Due to the sampling strategy, our population will not be broadly representative of the prevalence of PTSD or patterns of treatment utilization in combat-exposed Veterans; however, the influence of known predictors of PTSD risk and recovery, such as social support and exposure to additional life stressors, would not be expected to differ among individuals who seek versus those who do not seek care at VA facilities. In addition, our sample will include some Veterans with a history of PTSD prior to their OEF/OIF deployment. However, the inclusion of these prevalent or historical cases would not be expected to influence our primary aims, as participants will be classified based on their current or recent PTSD status. Other limitations include the possibility of recall bias in assessing trauma history and other exposures, and the inability to definitively determine whether differences in PTSD status based on the medical records versus the study interview are due to true changes in status or diagnostic errors. In addition, we chose not to include a genetic or neurobiological component in our baseline assessment due to the methodological challenges and costs involved; however, we are

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currently evaluating extensions to the registry that will incorporate these and other objectives of interest.

Overall, we anticipate that findings from Project VALOR will inform public health policy and decision-making in the years to come. Specifically, we expect that the study will point to potentially underserved subgroups or populations, such as individuals who have a diagnosis of PTSD or meet criteria for the diagnosis but are not receiving appropriate care for their condition. We expect to learn how specific treatments – medical or psychosocial – are being applied in everyday practice, and how male and female Veterans with PTSD respond to treatment outside the setting of clinical trials. As noted in one recent commentary: "Registries are being used to fill important gaps in evidence and contribute to understanding how trial results can be applied in practice" (Dreyer and Garner, 2009, p. 790). Project VALOR is intended to serve this important function and to provide a complementary viewpoint and means for long-term assessment of outcomes associated with PTSD in an observational setting.

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Declaration of interest statement

The authors have no competing interests.

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Running Head: PTSD IN VETERANS AND MILITARY PERSONNEL

Posttraumatic Stress Disorder in Veterans and Military Personnel:

Epidemiology, Screening, and Case Recognition

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ABSTRACT

Posttraumatic stress disorder (PTSD) is a psychiatric disorder that affects 7-8% of the general U.S. population at some point during their lifetime; however, the prevalence is much higher among certain subgroups, including active duty military personnel and veterans. In this paper, we review the empirical literature on the epidemiology and screening of PTSD in military and veteran populations, including the availability of sensitive and reliable screening tools. Although estimates vary across studies, evidence suggests that the prevalence of PTSD in deployed U.S. military personnel may be as high as 14-16%. Prior studies have identified trauma characteristics and pre- and post-trauma factors that increase risk of PTSD among veterans and military personnel. This information may help to inform prevention and screening efforts, as screening programs could be targeted to high-risk populations. Large scale screening efforts have recently been implemented by the U.S. Departments of Defense and Veterans Affairs. Given the prevalence and potential consequences of PTSD among veterans and active duty military personnel, development and continued evaluation of effective screening methods is an important public health need.

Keywords: epidemiology, military personnel, posttraumatic stress disorder, screening, veterans

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Posttraumatic stress disorder (PTSD) is a psychiatric condition that is experienced by a subset of individuals after exposure to an event that involved life threat and elicited feelings of fear, helplessness, and/or horror in the individual. PTSD is characterized by several interrelated symptom clusters including re-experiencing symptoms (e.g., intrusive thoughts, recurrent dreams, flashbacks, distress and physiologic reactivity upon exposure to trauma cues), avoidance and emotional numbing symptoms (e.g., avoidance of traumatic reminders, anhedonia, detachment from others, restricted emotional experiences, sense of foreshortened future), and hyperarousal symptoms (e.g., sleep difficulties, irritability and anger, concentration problems, hypervigilence, exaggerated startle) (American Psychiatric Association, 2000). Active duty military personnel and veterans are two highly vulnerable, at-risk groups for development of PTSD (Dohrenwend et al., 2006; Hoge, Auchterlonie, & Milliken, 2006; Hoge et al., 2004).

The true prevalence of PTSD among veterans and service members is controversial (Burkett & Whitley, 1998; McHugh & Treisman, 2007; McNally, 2006, 2007; Sundin, Fear, Iversen, Rona, & Wessely, 2010; Young, 1995), in part due to concerns over possible overdiagnosis related to patients seeking secondary gain (Department of Veterans Affairs Office of Inspector General, 2005; McHugh & Treisman, 2007). However, recent, large-scale studies indicate that PTSD may be a highly prevalent disorder among U.S. service men and women returning from current military deployments, with prevalence estimates as high as 14-16% (Hoge et al., 2004; Hoge, Terhakopian, Castro, Messer, & Engel, 2007; Milliken, Auchterlonie, & Hoge, 2007; Tanielian & Jaycox, 2008). Importantly, prior studies may actually underestimate the true number of military personnel and veterans suffering from PTSD and other trauma-related disorders, due to stigma and potential negative consequences associated with disclosing mental health difficulties (e.g., compromising one's military career, delays in returning home)

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(Hoge et al., 2004). Nonetheless, on the basis of the available research findings, PTSD has been referred to as one of the "signature injuries" of active duty service men and women who are deployed to Afghanistan for Operation Enduring Freedom (OEF) or Iraq for Operation Iraqi Freedom (OIF) (*Testimony of Jason Altmire*, 2007).

PTSD is associated with numerous deleterious outcomes for veterans and active duty service personnel, and the costs of PTSD to the individual, their immediate family, and society at large are substantial. In addition to the emotional and cognitive symptoms of PTSD, individuals with PTSD are more likely to experience marital and family problems (Jordan et al., 1992), job instability (Smith, Schnurr, & Rosenheck, 2005), legal difficulties (Kulka et al., 1990), and physical health problems (Boscarino, 2004; O'Toole, Catts, Outram, Pierse, & Cockburn, 2009). Veterans with a history of PTSD have a higher risk of cardiovascular, respiratory, gastrointestinal, infectious, nervous system, and autoimmune disorders (Boscarino, 1997, 2004; Hoge et al., 2007; Kubzansky, Koenen, Spiro, Vokonas, & Sparrow, 2007) and are more likely to experience anxiety, depression, substance abuse, and other psychiatric disorders (Kulka et al., 1990; Long, MacDonald, & Chamberlain, 1996). Some studies also have reported a higher risk of suicidal ideation among veterans with PTSD (Jakupcak et al., 2009; Pietrzak, Goldstein et al., 2009). PTSD often occurs in combination with persistent postconcussive symptoms and chronic pain, complicating the diagnosis and treatment of PTSD (Lew et al., 2009). The economic costs of PTSD and major depression for all currently deployed service members could be over 6.2 billion dollars during only the first two years following return from deployment (Tanielian & Jaycox, 2008). A large proportion of these costs are expected to be due to lost work productivity. Eibner and colleagues (Eibner, Ringel, Kilmer, Pacula, & Diaz, 2008) hypothesized that the economic burden of PTSD could be reduced through the proper

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identification of those with PTSD and use of evidence-based treatments within the first two years after an individual's return from war zone deployment.

In response to the recent estimates of PTSD prevalence among military personnel deployed to OEF/OIF and the associated public health and economic consequences, the U.S. Department of Defense (DoD) and VA have increased the number of available mental health providers and instituted mandatory primary care screenings for PTSD and other associated disorders for military personnel and veterans. In addition, the VA has developed and implemented specialized programs for evidence-based treatment of PTSD, including Cognitive Processing Therapy (CPT) and Prolonged Exposure (PE) therapy (Karlin et al., 2010). However, the provision of adequate services depends upon the use of accurate and reliable screening procedures to identify individuals either at risk for or currently affected by the disorder. Continued evaluation of the current screening efforts is needed to assess their effectiveness in properly identifying individuals with PTSD and reducing the amount of PTSD-related suffering among veterans and active duty military personnel.

In considering the rationale for the development and implementation of PTSD screening programs for armed services personnel and veterans, we first provide an overview of the prevalence and etiology of PTSD in military and veteran populations, followed by a review of current screening initiatives within the DoD and VA and the available screening instruments. We conclude by discussing potential gaps and future research needs in the area of screening for PTSD in veteran and military populations. The primary goal of this manuscript is to provide an overview of PTSD epidemiology and screening for clinicians and researchers, as well as to serve as a resource to guide clinicians in the selection of screening instruments and implementation of screening programs.

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MATERIALS AND METHODS

We searched the U.S. National Library of Medicine's PubMed database and the PsycINFO database for articles related to the prevalence, epidemiology, or screening of PTSD among armed forces personnel and veterans. We identified studies related to the prevalence or epidemiology of PTSD in veterans and military personnel by searching for references with the terms "posttraumatic stress disorder" or "PTSD" and "veterans", "military", or "combat" in the title or abstract, as well as "prevalence" (n=229) or "epidemiology", "risk factor", or "predictor" (n=101) in the title/abstract or subject heading. We reviewed the abstracts for the resulting articles to identify those relevant to our topic, and we also reviewed the references for the most relevant articles to identify additional studies of interest.

To identify articles related to screening for PTSD in veterans and active duty military personnel, we searched for articles with the terms "posttraumatic" or "PTSD" in the major subject heading, "veteran" or "military" in the subjects field, and "screen" in any field, which yielded 177 articles. We reviewed the results to determine whether the study addressed screening for PTSD and the screening measures used. After identifying relevant screening measures, we performed additional searches to locate articles about the measures in question, including original validation studies.

RESULTS

Prevalence of PTSD in veterans and military personnel

Figure 1 displays estimates of the prevalence of lifetime (any history) and current PTSD from studies of active duty military personnel and veterans of the Vietnam War (Boscarino,

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1995; Eisen et al., 2004; Goldberg, True, Eisen, & Henderson, 1990; Kulka et al., 1990; O'Toole et al., 2009; O'Toole et al., 1996; Stretch, 1985), Gulf War (Al-Turkait & Ohaeri, 2008; Department of National Defence, 2002; Gray, Reed, Kaiser, Smith, & Gastanaga, 2002; Holmes, Tariot, & Cox, 1998; Ikin et al., 2004; Jones, Rona, Hooper, & Wesseley, 2006; Kang, Natelson, Mahan, Lee, & Murphy, 2003; Lee, Gabriel, Bolton, Bale, & Jackson, 2002; Perconte, Wilson, Pontius, Dietrick, & Spiro, 1993; Pierce, 1997; Proctor et al., 1998; Stretch et al., 1996; The Iowa Persian Gulf Study Group, 1997; Toomey et al., 2007; Unwin et al., 1999; Wolfe, Erickson, Sharkansky, King, & King, 1999), and OEF/OIF (Duma, Reger, Canning, McNeil, & Gahm, 2010; Fear et al., 2010; Haskell et al., 2010; Hoge & Castro, 2006; Hoge et al., 2004; Hoge et al., 2007; Hotopf et al., 2006; Milliken et al., 2007; Seal, Bertenthal, Miner, Sen, & Marmar, 2007; Seal et al., 2009; Smith et al., 2008; Tanielian & Jaycox, 2008; Vasterling et al., 2006; Vasterling et al., 2010). Although the prevalence estimates vary widely across studies, overall the data in Figure 1 suggest that a large proportion of military personnel and veterans are affected by PTSD. Several factors may contribute to differences in the prevalence estimates across studies, including the study design and methods, the diagnostic criteria used, and characteristics of the study population, such as the intensity of combat exposure or number of deployments (Ramchand et al., 2010). Two recent review articles summarized the data on the prevalence of combat-related PTSD (Richardson, Frueh, & Acierno, 2010; Sundin et al., 2010); we therefore briefly summarize the most recent prevalence data below and refer readers to specific publications for details of older studies.

Prevalence of military-related PTSD in the U.S. The most recent prevalence estimates of deployment-related PTSD come from the ongoing military operations in Iraq and Afghanistan. In a review of the prevalence literature on combat-related PTSD, Richardson et al. reported

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estimates for current PTSD in U.S. OEF/OIF veterans ranging from 4% to 17% (Richardson et al., 2010). In a recent study not included in the reviews noted above, 21.8% of 289,328 OEF/OIF veterans who first received care at a VA facility between 2002 and 2008 were diagnosed with PTSD during the six-year study period, based on ICD-9-CM codes from inpatient and outpatient visits (Seal et al., 2009). However, this study population sought health care at VA facilities and therefore may not be representative of the larger population of OEF/OIF veterans. In addition, PTSD diagnoses were based on electronic medical records and were not confirmed by other methods, likely resulting in false positive as well as false negative diagnoses. In contrast to the study by Seal et al., a study published by the RAND Corporation in 2008 reported that 14% of a representative sample of 1,965 OEF/OIF veterans interviewed by telephone met diagnostic criteria for PTSD (Tanielian & Jaycox, 2008). Extrapolating from these results, the authors estimated that 226,000 individuals who served in OEF/OIF through October 31, 2007 currently have PTSD.

Prevalence of military-related PTSD internationally. Studies of non-U.S. veteran populations generally report similar or lower prevalence estimates than studies of U.S. veterans (Richardson et al., 2010; Sundin et al., 2010). For example, prevalence estimates for UK veterans who served in Iraq and Afghanistan range from 3.4% to 6%, based on studies using self-administered questionnaires (Browne et al., 2007; Fear et al., 2010; Hotopf et al., 2006; Iversen et al., 2008; Mulligan et al., 2010) or a structured telephone interview (Iversen et al., 2009); the lower prevalence of PTSD in these studies, compared with studies of U.S. OEF/OIF veterans, may be due in part to lower levels of combat exposure among UK soldiers (Hoge & Castro, 2006) or methodological differences in the studies.

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Prevalence of military-related PTSD in women and racial/ethnic minorities. Some evidence suggests that the prevalence of PTSD may differ among female and minority service members and veterans, when compared to white, non-Hispanic males. Women generally have lower levels of combat exposure than men, but significantly higher rates of military sexual trauma, which is strongly associated with development of PTSD (Kang, Dalager, Mahan, & Ishii, 2005). In a large study of male and female OEF/OIF veterans seen at VA facilities, the prevalence of PTSD was similar, although statistically more prevalent, in men vs. women (13% vs. 11%) (Seal et al., 2007). In this study the prevalence of PTSD also was similar by race/ethnicity, although black veterans were slightly more likely to be diagnosed with PTSD (14%) than white or Hispanic veterans (13%) (Seal et al., 2007). However, several older studies that examined prevalence differences by race/ethnicity reported marked differences in the prevalence of PTSD by minority status. For example, in the NVVRS the prevalence of PTSD was 20.6% among black veterans and 27.9% among Hispanic veterans, compared to 13.7% among white veterans (Frueh, Brady, & de Arellano, 1998). Additional analyses of the NVVRS data also reported a higher prevalence of PTSD among American Indian veterans, compared to white veterans (Frueh et al., 1998), and high levels of race-related stress and subsequent PTSD among Asian American veterans (Loo, Fairbank, & Chemtob, 2005). Although other individual-level or trauma-related characteristics may have contributed to these differences, as discussed in greater detail below, disparities by gender or race/ethnicity are important to consider in studies of PTSD.

Trends in the prevalence of PTSD. Disparities in estimates of the prevalence of PTSD for different wars could be a function of differences in the study measures or methods (e.g., the diagnostic criteria and the methods of sampling and assessment) or characteristics of the conflict.

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In addition, differences in population characteristics, such as the duration or intensity of combat exposure or the number of deployments also may contribute to the differing prevalence estimates across studies (Ramchand et al., 2010). However, despite these methodological challenges, it is clear that PTSD affects a large number of current and former service men and women at some point during their lifetime. The high prevalence of PTSD in military and veteran populations highlights the importance of screening these populations for PTSD and identifying factors that influence risk and recovery from PTSD.

Risk factors for PTSD in veterans and military personnel

The majority of individuals exposed to trauma do not develop clinical PTSD, suggesting that other factors strongly influence the onset and course of this disorder (Keane, Marx, & Sloan, 2009). Risk factors for PTSD are commonly divided into three categories: individual-level (pre-trauma) factors, characteristics of the trauma, and post-trauma factors (Keane, Marshall, & Taft, 2006). Knowledge of pre-trauma factors and trauma characteristics that influence risk may help to identify populations at higher risk of developing PTSD and who are therefore more likely to benefit from screening, whereas post-trauma factors may help to inform prevention and treatment programs among men and women with trauma exposure.

Table 1 summarizes the epidemiologic factors shown in multiple studies to influence risk of PTSD in veterans and military personnel. Characteristics of the trauma (e.g., trauma severity, perceived life threat, and combat-related injury) and post-trauma factors (e.g., lack of social support and exposure to additional life stressors) have been strongly associated with risk of PTSD in multiple studies. In contrast, weak to moderate associations generally have been reported for pre-trauma factors, such as younger age at trauma and prior psychiatric history.

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Gender, race/ethnicity, and risk of PTSD. In addition to the risk factors included in Table 1, some studies have suggested that gender and race/ethnicity may be important in the development of military-related PTSD (Brewin, Andrews, & Valentine, 2000; Gahm, Lucenko, Retzlaff, & Fukuda, 2007; Koenen, Stellman, Stellman, & Sommer, 2003). In a meta-analysis of 25 studies, Brewin et al. (2000) observed a significantly higher risk of PTSD among women compared with men in civilian but not military populations, although only two military studies of gender and PTSD were included. More recent studies are mixed, with some reporting a higher risk among women and others reporting no association (Street, Vogt, & Dutra, 2009). Similarly, minority race/ethnicity was associated with an increased risk of PTSD in military populations in the meta-analysis by Brewin et al. (2000), but other studies do not support an association (Baker et al., 2009; Frueh et al., 1998). Several factors may contribute to differences in the associations with gender and race observed across studies, including pre-military trauma exposure or confounding by trauma characteristics, social support during deployment, or other stressors (Dohrenwend, Turner, Turse, Lewis-Fernandez, & Yager, 2008; Kimerling, Gima, Smith, Street, & Frayne, 2007; Loo et al., 2005; Street et al., 2009; Vogt, Pless, King, & King, 2005). For example, pre-military/military sexual trauma is an important cause of PTSD that disproportionately affects women (Himmelfarb, Yaeger, & Mintz, 2006; Kimerling et al., 2007); however, studies of military and veteran populations that focus on PTSD due to combat, rather than all military-related trauma, may fail to report cases of PTSD that are primarily due to military sexual trauma.

Complexity of PTSD etiology. Multivariate and meta-analytic studies (Brewin et al., 2000; King, King, Foy, Keane, & Fairbank, 1999; Ozer, Best, Lipsey, & Weiss, 2003; Wolfe et al., 1999) highlight the complexity of predicting who will and will not develop chronic PTSD.

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Risk and resilience factors, including the quality of the family environment during childhood, age at trauma exposure, history of prior adversity, severity of trauma exposure, breadth and strength of the social support network, exposure to additional life stressors, and individual-level characteristics such as hardiness and neurobiology have consistently been found to influence the development of PTSD (King et al., 1999; King, King, Fairbank, Keane, & Adams, 1998; Pietrzak et al., 2010; Pietrzak, Johnson, Goldstein, Malley, & Southwick, 2009). This research suggests that vulnerability to PTSD is not simply a function of trauma exposure, but a function of the interaction between trauma exposure, pre-existing psychological and biological vulnerabilities, and the post-trauma environment. Other research indicates that the factors influencing development and maintenance of PTSD may differ (Schnurr, Lunney, & Sengupta, 2004).

Genetics of PTSD. Finally, although familial studies support a heritable component of PTSD, limited data are available on genetic polymorphisms that may influence risk in military and veteran populations (Afifi, Asmundson, Taylor, & Jang, 2010; Koenen, 2007). In a study of male twin pairs who served during the Vietnam era, True et al. observed that approximately 30% of the variability in PTSD symptoms was due to genetic factors, whereas shared family environment did not appear to influence the development of PTSD (True et al., 1993). Studies of specific genetic variants have focused on the dopaminergic, serotonergic, and other neurobiochemical pathways (Nugent, Amstadter, & Koenen, 2008). Polymorphisms in the dopamine receptor D2 (*DRD2*) gene have been associated with risk of PTSD in some but not all studies of combat-exposed populations (Nugent et al., 2008; Voisey et al., 2009), and one study reported lower dopamine beta-hydroxylase (DBH) activity among veterans with PTSD compared to those without PTSD, suggesting a possible role of the *DBH* gene in the development of PTSD

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(Mustapic et al., 2007). However, studies of genes in other pathways generally have been null in military and veteran populations, although the number of available studies is small (reviewed in Koenen, 2007; Nugent et al., 2008). Large, genome-wide association studies would be helpful in identifying other chromosomal regions that may be important in PTSD. Although future genetic studies may help to elucidate the mechanisms involved in the development of PTSD and may be informative for risk prediction and screening or prevention, currently the evidence is too limited for widespread use of genetic data for screening purposes in military and veteran populations.

Screening programs for PTSD in veterans and military personnel

The high prevalence of PTSD in military and veteran populations and the potential seriousness of the symptoms and associated emotional/physical health consequences highlight the importance of effective screening and early intervention efforts for these groups. The goal of screening in this population is to identify trauma-exposed individuals with undiagnosed or subsyndromal PTSD, or those at risk for developing the disorder, in order to intervene earlier in the course of disease than would occur in the absence of screening. Although screening for PTSD differs from screening for chronic diseases, such as cancer, in that symptoms often are present at the time of screening, the goal of reducing morbidity or mortality from disease is similar, as early intervention may result in a shorter course of disease and fewer negative outcomes related to PTSD (Bryant et al., 2008; Kessler, Sonnega, Bromet, Hughes, & Nelson, 1995; O'Donnell, Bryant, Creamer, & Carty, 2008). Screening may also be of value in identifying subgroups of individuals or specific cohorts at increased risk for developing PTSD, tracking changes in prevalence over time, and assessing the degree of unmet need for services.

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In 2003, the DoD instituted a military-wide screening program – the Post-Deployment Health Assessment (PDHA) – that assesses service members' physical and mental health status following deployment. Specific mental health areas addressed include depression, suicidal ideation, aggression and PTSD (Hoge et al., 2006). Screening occurs within 1-2 weeks of return from deployment and consists of a 3-page self-report questionnaire followed by a brief interview with a healthcare professional, who documents any concerns, determines whether additional evaluation is needed, and provides information on available resources for dealing with post-deployment issues (U.S. Department of Defense Deployment Health Clinical Center). Results of this large-scale screening program suggest that a substantial percentage of service members who served in Iraq and Afghanistan screen positive for probable PTSD; during the first year after implementation of the PHDA, 9.8% of Army soldiers and Marines returning from Iraq and 4.7% returning from Afghanistan screened positive for probable PTSD (Hoge et al., 2006). Although it is possible that these estimates overstate the prevalence of PTSD due to patients seeking secondary gain, it is also possible that these studies underestimate the prevalence of PTSD among active duty military personnel who may not report the presence of PTSD symptoms due to concerns that public knowledge of their symptoms may damage their personal or professional reputations. As part of this ongoing screening program, the DoD mandated in 2005 that service members be assessed again 3-6 months after return from deployment (Milliken et al., 2007). Screening at two time points yielded even higher positive screening rates for probable PTSD and other mental health concerns; at the reassessment, 16.7% of active soldiers and 24.5% of National Guard and Reserve soldiers screened positive for PTSD (Milliken et al., 2007). A second study found that the proportion of individuals screening positive for PTSD and other mental health conditions was higher when screening was delayed until several months post-

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deployment, indicating that screening soon after return from deployment may miss a large number of cases due to delayed onset or false negative screens (Bliese, Wright, Adler, Thomas, & Hoge, 2007).

Despite the apparent success of these screening efforts by the DoD, some researchers have voiced concerns, citing limited evidence of the effectiveness of screening in military populations (Rona, Hyams, & Wessely, 2005). Rona and colleagues argued that the number of positive screens requiring prompt psychological attention is small relative to the total number of individuals screening positive and that several factors may influence over- or underreporting of symptoms in military populations (Rona et al., 2005). However, in a study of 1,578 military personnel returning from a year-long deployment to Iraq, Bliese et al. reported a sensitivity of 0.73 and specificity of 0.88 for the 4-item Primary Care PTSD Screen (PC-PTSD) used in the PDHA compared with a structured interview, indicating that the PDHA has reasonably good validity (Bliese, Wright, Thomas, Adler, & Hoge, 2004, December).

In 2004, the VA implemented the Afghan and Iraq Post-Deployment Screen, a 10-15 minute assessment for PTSD, depression, and high-risk alcohol use (Seal et al., 2008). Veterans seeking care at Veterans Health Administration (VHA) primary care and specialty clinics are routinely screened by their clinician, who is prompted to complete the assessment by an automatic reminder in the VHA's computerized medical record system (Seal et al., 2008; Veterans Health Administration, 2004). PTSD symptoms are assessed using the 4-item PC-PTSD, and clinicians are encouraged to refer veterans with a positive screen to a specialty mental health clinic (Seal et al., 2008). In a study by Seal and colleagues (2008), 45% of OEF/OIF veterans seen at a VHA Medical Center or associated clinic were screened, and 50% of those screened met the criteria for probable PTSD. This is consistent with a study of active duty

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military personnel seen at outpatient mental health clinics in which 44% screened positive for probable PTSD (Gahm & Lucenko, 2008). Although the prevalence of PTSD likely is elevated among active duty military personnel and veterans seen at VHA facilities, as this population includes individuals seeking care for symptoms of PTSD or related conditions, these studies highlight the importance of screening for PTSD in this setting. Beginning in 2010, the VA required that all OEF/OIF veterans being actively treated for PTSD at a VHA facility be evaluated for PTSD symptoms every 90 days using the PTSD Checklist (PCL), to monitor changes in PTSD symptoms and assess whether individuals previously diagnosed with PTSD continue to meet diagnostic criteria (Department of Veterans Affairs, 2009).

Ongoing evaluation of the efforts to screen active duty military personnel and veterans is needed to maximize the effectiveness of these screening programs. For example, studies of the optimal timing of the PDHA and the optimal frequency of the VA screen would help to ensure that cases are detected and treatment is initiated early but that the number of cases missed due to delayed onset is minimized. In addition, validation studies should be conducted where none are available, to evaluate the effectiveness of the screening programs as well as to assess the psychometric properties and diagnostic accuracy of new screening measures in these populations.

Overview of screening instruments for identifying PTSD in military and veteran populations

Various methods have been used to assess the signs and symptoms of PTSD in military and veteran populations; however, the most common approach involves the use of self-report questionnaires. In a review of screening instruments for assessing symptoms of PTSD in the general population, Brewin noted that screening tools designed to assess Diagnostic and

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Statistical Manual of Mental Disorders, 4th Edition (DSM-IV) symptoms were superior to other instruments, and that measures with fewer items, simpler response scales, and simpler methods of scoring usually were superior (Brewin, 2005).

Some screening instruments, including those reviewed by Brewin (2005), more generally assess the presence of PTSD that may or may not be combat related. In contrast, other screening measures are specifically designed to assess combat-related PTSD. Combat-specific PTSD screening instruments may have higher sensitivity and specificity in military and veteran populations than screening tools designed for use in the general population. However, more focused screening tools may fail to identify PTSD cases that are unrelated to combat, such as PTSD due to military sexual trauma (Suris & Lind, 2008); screening measures should therefore be broad enough to effectively screen for both combat-related PTSD and PTSD related to other trauma in military settings.

Screening instruments for PTSD assess some or all of the characteristic symptoms of PTSD and are typically validated against a "gold standard" of clinical diagnosis by a qualified clinician. Additional validation tests include discriminant or known groups validity ("does the test distinguish between individuals with and without the disorder?"), predictive validity ("does the test predict who will develop the disorder?"), and convergent validity ("do the test results correlate with other similar measures?"). Reliability assessment (test-retest, internal consistency) is also necessary. Ideally, PTSD screening tools should have a high degree of sensitivity and at least modest specificity, when compared with expert diagnosis. Although the negative consequences of a false positive screen for PTSD may be acceptable, since a positive screen should always be followed by in-depth diagnostic assessment by a qualified mental health professional, the number of false positives should not be so large as to overwhelm the available

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resources for diagnosing and treating PTSD. In contrast, false negative screens have potentially serious consequences and should be minimized, as individuals with PTSD who are not identified may not receive further assessment and could potentially be symptomatic for several years without receiving diagnosis or treatment.

Review of self-report screening instruments. In Table 2 we provide an overview of the self-report scales and screening instruments that have been used to detect probable PTSD in military and veteran populations (Blanchard, Jones-Alexander, Buckley, & Forneris, 1996; Brewin, 2005; Carlson, 2001; Davidson et al., 1997; Foa, Cashman, Jaycox, & Perry, 1997; Gore, Engel, Freed, Liu, & Armstrong, 2008; Hammarberg, 1992; Horowitz, Wilner, & Alvarez, 1979; Hovens, Bramsen, & van der Ploeg, 2002; Keane, Caddell, & Taylor, 1988; Marx et al., 2008; Meltzer-Brody, Churchill, & Davidson, 1999; Neal et al., 1994; O'Donnell, Creamer et al., 2008; Prins et al., 2003; Weathers, Litz, Herman, Huska, & Keane, 1993; Weathers et al., 1996). In the interest of space we are unable to discuss all of the instruments included in Table 2, but additional information regarding some of the most widely used and/or innovative instruments is presented below.

Early studies, including the NVVRS, used two self-report instruments to screen for PTSD: the 15-item Impact of Events Scale (Horowitz et al., 1979) and the 35-item Mississippi Scale (Keane et al., 1988). The Mississippi Scale was ultimately the biggest contributor to the diagnostic algorithm developed to establish prevalence in the NVVRS. More recently, the PCL has emerged as the standard self-report instrument for screening military and veteran populations (Weathers et al., 1993). The PCL includes 17 items which align with DSM-IV criteria and assess symptoms during the past month, using a scale from 1 ("not at all") to 5 ("extremely"). A positive screen for PTSD is typically determined based on either a cutoff score (e.g., a score of

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50 or higher) or DSM criteria (i.e., the presence of one reexperiencing symptom, three avoidance symptoms, and two arousal symptoms), or a combination of both criteria (Hoge et al., 2007). In a sample of Vietnam veterans, the PCL demonstrated excellent test-retest reliability (0.96) and internal consistency (0.97), and adequate sensitivity (0.82) and specificity (0.83) using a cutoff score of 50 (Weathers et al., 1993). However, more recent studies in veteran populations support the use of a lower cutoff for the PCL (Bliese et al., 2008; Yeager, Magruder, Knapp, Nicholas, & Frueh, 2007); Yeager et al. (2007) reported a sensitivity and specificity of 0.81 using a cutoff of 31, versus a sensitivity of 0.53 and a specificity of 0.95 using a cutoff of 50, while a recent study by Dunn et al. (2011) reported an optimal cutoff of 44 based on a receiver operating characteristic curve, with a sensitivity of 0.81 and a specificity of 0.83. Differences in the sensitivity and specificity for a given cutoff score and the optimal cutoff score across studies may be due to population characteristics such as the severity of PTSD symptoms, the interrater reliability of the screening instrument, or differences in the "gold standard" diagnostic assessment to which the screening instrument is compared (Warner, 2004). Because it is a relatively brief measure, the PCL is easily implemented in survey studies and has been widely used in military (Hoge et al., 2004; Smith et al., 2008) and veteran populations (Hoge et al., 2007; Kline et al., 2010) as a measure of probable PTSD and PTSD symptom severity. In addition, a brief screening instrument has been derived from the PCL (Lang & Stein, 2005).

The Davidson Trauma Scale consists of 17 items, with self-ratings of both frequency and severity for each symptom on a 5-point scale (Davidson et al., 1997). It has been validated for use in military and veteran populations (McDonald, Beckham, Morey, & Calhoun, 2009) and demonstrated adequate test-retest reliability (0.86) and internal consistency (0.97-0.99) in a mixed trauma sample of 353 individuals, including 110 male war veterans (Davidson et al.,

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1997). In a study of U.S. veterans who served after September 11, 2001, a cutoff score of 32 resulted in a sensitivity of 0.97, a specificity of 0.91, and an overall efficiency of 0.94 (McDonald et al., 2009).

A general trend in screening instrument development is the drive to create measures that are as brief as possible but still retain excellent psychometric properties. This, coupled with the fact that PTSD is commonly unrecognized in primary care settings, led to the development of the PC-PTSD, a brief screening tool for PTSD that is easily administered and scored by non-mental health professionals (Prins et al., 2003). The PC-PTSD consists of four items that assess symptoms of reexperiencing, numbing, avoidance, and hyperarousal (Prins et al., 2003). In a validation study conducted among 352 postdeployment soldiers, Bliese et al. (2008) reported a weighted sensitivity and specificity of 0.76 and 0.92, respectively, using a cutoff score of 3.

The Startle, Physiological Arousal, Anger and Numbness instrument is another 4-item self-report measure developed from the severity items of the Davidson Trauma Scale (Meltzer-Brody et al., 1999). Among veterans seen in a VA primary care setting, the sensitivity and specificity were 0.74 and 0.82, respectively, using a cutoff score of 5 and comparing the results to the Clinician-Administered PTSD Scale (Yeager et al., 2007).

Gore and colleagues (2008) recently developed a single-item PTSD measure with a 3-point response scale ranging from “not bothered” to “bothered a lot”. However, the psychometric properties of the single-item measure were inferior to the 4-item PC-PTSD; the sensitivity and specificity in a military primary care setting were 0.76 and 0.79, respectively, for those who were “bothered a little” by a past traumatic experience. In contrast, the PC-PTSD had a sensitivity of 0.91 and a specificity of 0.84 in this population, based on a cutoff score of 2 (Gore et al., 2008).

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Screening for PTSD due to pre-military or military sexual trauma. In addition to combat, PTSD symptoms among veterans and military personnel may originate from pre-military or military sexual trauma. VA surveillance data suggest that 22% of females and 1% of males experience sexual trauma while in the military (Suris & Lind, 2008); however, estimates vary across studies and the true prevalence may be even higher due to underreporting (Suris & Lind, 2008; Valente & Wight, 2007). Given the scope of the problem, specific screening measures have been developed to assess PTSD symptoms related to military sexual trauma. For example, the VHA implemented universal screening for military sexual trauma using a 2-item instrument, which has been successful in identifying individuals for referral to mental health services (Kimerling et al., 2007; Kimerling, Street, Gima, & Smith, 2008). Both questions have high sensitivity (0.89-0.92) and specificity (0.89-0.90), compared to a clinical interview, and a positive screen has been associated with a significantly increased odds of PTSD (adjusted odds ratio = 8.83 for women and 3.00 for men) (Kimerling et al., 2007).

Screening for PTSD in women and racial/ethnic minorities. As noted above, military sexual trauma is an important consideration when screening women for PTSD. Screening instruments should be designed to accurately diagnose PTSD regardless of the gender or race/ethnicity of the individual being screened, and the reliability and validity of instruments should be assessed in diverse populations (Frueh et al., 1998). Since several studies have reported racial/ethnic differences and a high prevalence of PTSD among minority veterans (Frueh et al., 1998; Loo et al., 2005; Seal et al., 2007), validation studies of current and future screening instruments should include adequate numbers of minority participants to ensure the representativeness of relevant domains and items in minority respondents.

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Predictive assessments for risk of developing PTSD. Although symptom-based PTSD screening instruments may help to reduce morbidity related to PTSD by allowing for earlier intervention, they are limited by their inability to prevent the onset of PTSD in individuals exposed to trauma. Recent research suggests that measures designed to quantify information about risk and resilience factors for PTSD can be used to identify asymptomatic, trauma-exposed individuals who are more likely to develop PTSD. O'Donnell and colleagues developed a screening tool that identifies hospitalized adults at high risk of PTSD or major depression (O'Donnell, Creamer et al., 2008). In this study, 527 civilians hospitalized with non-lethal injuries answered questions related to 13 risk factors for PTSD. Patients were assessed 12 months later for the presence of PTSD or major depression. Responses from half of the participants were used in factor analyses to derive the 10-item Posttraumatic Adjustment Scale, which was then validated in the remaining participants. After 12 months, 8% of participants had developed PTSD, and the scale had moderate sensitivity (0.82) and specificity (0.84) when predicting PTSD diagnoses (O'Donnell, Creamer et al., 2008).

In another recent study, Marx et al. (2008) used data from 1,081 Vietnam era veterans to develop and test a similar screening instrument for combat-related PTSD. Participants completed self-report measures and structured interviews for PTSD and supplied information on risk and resilience variables. Participants were divided into three subsamples, two of which were used to identify variables that differentiated between individuals with and without PTSD. Twelve risk and resilience items were included in the resulting PTSD Statistical Prediction Instrument, which was validated using the remaining subsample. This instrument displayed adequate sensitivity (0.86) and moderate specificity (0.77) in the validation sample, using a cutoff score of 6, and strong internal consistency (0.84) (Marx et al., 2008). These results

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suggest that primary prevention of PTSD may be possible in military and veteran populations, which would be expected to result in improved outcomes and decreased healthcare utilization by PTSD patients.

Psychophysiological screening. In addition to traditional questionnaire-based assessments, some research suggests that psychophysiological testing, such as the acoustic startle response and heart rate variability, may have potential applications for PTSD screening. Several studies have reported that veterans with PTSD have decreased heart rate variability (Tan, Dao, Farmer, Sutherland, & Gevirtz, 2011; Tan et al., 2009) and a heightened acoustic startle response (Butler et al., 1990; Morgan, Grillon, Southwick, Davis, & Charney, 1996; Orr, Lasko, Shalev, & Pitman, 1995), raising the possibility that these measures could be used to identify individuals with undiagnosed or preclinical PTSD. However, the use of biological assays and psychophysiological methods for assessment and screening is still in the early developmental stages and additional research on the utility of these measures for screening purposes is needed.

Risks and limitations of screening instruments. Despite the intense effort and interest in developing methods to screen for symptoms of PTSD in military and veteran populations, all of the current methods have inherent limitations. For example, all self-report scales may be vulnerable to response bias from various sources (Elhai, Frueh, Davis, Jacobs, & Hamner, 2003). Concerns about the potential implications of positive (or negative) screening results may lead to over- or underreporting of symptoms, depending on the individual and circumstances of testing. In addition, reliance on a single measure or assessment methodology may lead to inaccurate diagnosis in many cases and a large number of false positives and negatives.

As a result of these limitations, it has become standard practice to employ multiple methods and measures to better inform diagnostic decisions (Weathers, Keane, & Foa, 2009).

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Such multi-method assessment of PTSD takes advantage of each individual measure's relative strengths, overcoming the potential psychometric limitations of any single instrument and maximizing correct diagnostic decisions. On the other hand, the use of multiple assessment methods reduces cost efficiency and increases the respondent and clinician burden in proportion to the number of instruments used. In determining cutpoints or criteria for further evaluation, it is generally preferable to err on the side of increased sensitivity, rather than specificity, in the use of such screeners. All other things being equal, a modest number of false positives may be acceptable on the initial shorter screening measure, followed by perhaps longer, but increasingly accurate and specific measures. For instance, Felker and colleagues (Felker, Hawkins, Dobie, Gutierrez, & McFall, 2008) used the 4-item PC-PTSD followed by the longer PCL. Other researchers found that using a composite measure, created from various self-report symptom-based measures, led to increased diagnostic accuracy, compared to the use of several individual measures (Wright et al., 2007).

Additional resources for clinicians. In addition to the references noted above and those included in Table 2, several resources related to PTSD screening are available through the VA. The VA/DoD Clinical Practice Guideline for the Management of Post-Traumatic Stress (Department of Veterans Affairs, 2004) includes information on PTSD screening and treatment, as well as monitoring and follow-up of patients with potential PTSD. The VA National Center for PTSD website (Department of Veterans Affairs, 2011) includes extensive resources on PTSD for both clinicians and researchers, including an overview of PTSD screening instruments.

DISCUSSION

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Although numerous symptom checklists and self-administered questionnaires have been developed, there is no compelling evidence that one screening instrument outperforms the others in veteran and military populations. Several instruments have adequate psychometric properties and have been used successfully to screen for PTSD in active duty military personnel and veterans. In general, short measures seem to do as well as longer questionnaires and therefore should be used whenever possible to decrease the time and effort required to screen for PTSD. When appropriate, short screening instruments may be followed by longer measures with greater specificity to decrease the number of false positive screens. Continued evaluation of new and existing screening measures, and in particular validation against more rigorous diagnostic methods, is needed to ensure that the screening measures in use are detecting cases of probable PTSD while minimizing the number of missed diagnoses.

Screening programs such as those implemented by the DoD and VA have been successful in identifying individuals with presumptive or probable PTSD. Individuals who screen positive are then referred for further clinical assessment and diagnostic evaluation by a mental health professional, who might also provide treatment of the disorder as needed. By detecting and treating patients as soon as possible after the onset of symptoms, screening may contribute to a shorter duration of disease and more favorable outcomes (Kessler et al., 1995). In addition, screening instruments have been used in large-scale surveys to evaluate the prevalence of key symptoms of PTSD before and after deployment, and to identify subgroups of individuals at increased risk for PTSD and related conditions, such as substance abuse and depression. However, despite the potential benefits of screening, there are also several limitations. Current screening programs detect symptoms of PTSD in individuals who already show signs of the disorder; therefore, these programs may lead to earlier diagnosis and treatment, but may not

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prevent the onset of PTSD symptoms. Although some research has evaluated the effectiveness of predeployment screening, the question remains as to whether screening asymptomatic individuals can result in accurate identification of a sufficient number of military personnel at risk for future PTSD, and whether those who screen positive are more likely to obtain and benefit from services. Rona and colleagues found little benefit of predeployment screening for predicting subsequent onset of PTSD, in part due to the low prevalence of PTSD in the sample (Rona et al., 2006). Additional limitations of screening include the fact that individuals with symptoms of PTSD may be less likely to participate in screening programs (Rona, Jones, French, Hooper, & Wessely, 2004) or seek treatment (Sayer et al., 2009). These findings raise serious concerns, as the individuals with greatest need of diagnosis and treatment may be least likely to receive it.

Further, individuals exposed to military-related trauma may have multiple adverse effects, and PTSD may not be the most immediate concern following trauma exposure. For example, in a recent study of British troops deployed to Iraq or Afghanistan the prevalence of probable PTSD was only 4%, compared with 13% for alcohol abuse and 20% for symptoms of other psychiatric disorders (Fear et al., 2010). However, several studies have reported an increase in PTSD prevalence with increasing time since return from deployment (Bliese et al., 2007; Kang, Li, Mahan, Eisen, & Engel, 2009; Milliken et al., 2007), suggesting that continued surveillance and screening for PTSD are needed.

In summary, PTSD is a potentially disabling mental disorder that is common among active duty military personnel and veterans. Prevalence studies and large scale screening programs have helped to define the scope of the problem in military and veteran populations, while epidemiologic studies have improved our understanding of the etiology of the disorder and

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the characteristics of those at highest risk. Although research and interest in this field has grown in recent years, there is still much to be learned about the risk, detection, natural history, and treatment of PTSD. In particular, prospective studies of military cohorts that begin prior to deployment and follow individuals for trauma exposure and its sequelae will help to improve our understanding of the epidemiology and detection of PTSD, while longitudinal registries of PTSD patients will help to elucidate the most effective treatment regimens and other factors influencing recovery. Given the debilitating nature of the symptoms of PTSD and the seriousness of the associated medical conditions, additional research on PTSD should be an area of high priority.

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Figure 1. Current/lifetime prevalence of posttraumatic stress disorder in military and veteran populations

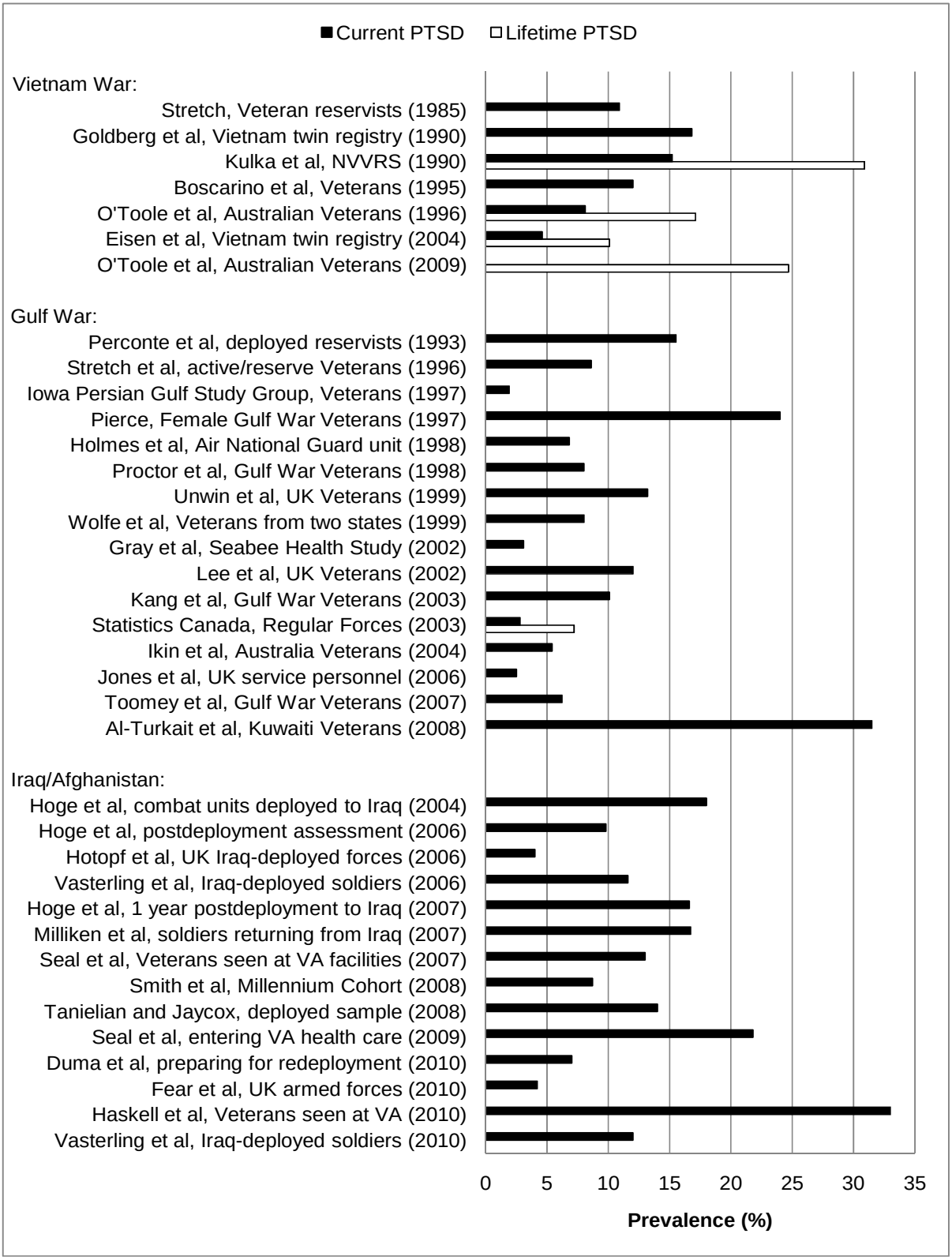

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Table 1. Epidemiologic factors associated with increased risk of posttraumatic stress disorder in veterans and military personnel

Risk factor	Strength of Association*	References
Pre-trauma factors		
Younger age at trauma	+	(Brewin et al., 2000; Nasky, Hines, & Simmer, 2009)
Lower education	++	(Brewin et al., 2000; Iversen et al., 2008; Schnurr et al., 2004; Zohar et al., 2009)
Lower intelligence	++	(Brewin et al., 2000; Gale et al., 2008; Zohar et al., 2009)
Lower military rank	++	(Iversen et al., 2008; Nasky et al., 2009; Zohar et al., 2009)
Lower socioeconomic status	++	(Brewin et al., 2000; Schnurr et al., 2004)
Prior trauma	++	(Brewin et al., 2000; Ozer et al., 2003)
Prior psychiatric history/symptoms	++	(Brewin et al., 2000; Rona et al., 2009)
Family psychiatric history	++	(Brewin et al., 2000; Ozer et al., 2003)
Behavioral problems in childhood	++	(Helzer, Robins, & McEvoy, 1987; King, King, Foy, & Gudanowski, 1996; Koenen et al., 2005)
Childhood abuse or adversity	++	(Brewin et al., 2000; Cabrera, Hoge, Bliese, Castro, & Messer, 2007; Gahm et al., 2007; Iversen et al., 2008)
Trauma characteristics		
Trauma/combat exposure severity	+++	(Brewin et al., 2000; Cabrera et al., 2007; Gahm et al., 2007; Koenen et al., 2003; O'Toole et al., 1996; Rona et al., 2009; Schnurr et al., 2004)
Perceived life threat	+++	(King et al., 1998; Schnurr et al., 2004)
Combat-related injury	+++	(Koren, Norman, Cohen, Berman, & Klein, 2005; MacGregor et al., 2009)
Exposure to death, killing, or abusive violence	++	(Gahm et al., 2007; Iversen et al., 2008; Maguen et al., 2010; Marx et al., 2010; McCarroll, Ursano, Fullerton, Liu, & Lundy, 2001)
Peritraumatic distress or dissociation	+++	(Ozer et al., 2003; Schnurr et al., 2004)
Post-trauma factors		
Lack of social support	+++	(Brewin et al., 2000; Ozer et al., 2003)
Negative homecoming experience	+++	(Johnson et al., 1997; Koenen et al., 2003)
Exposure to additional life	+++	(Brewin et al., 2000)

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stressors

*Weak effect (+), intermediate effect (++), or strong effect (+++)

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Table 2. Posttraumatic stress disorder screening instruments

Name	# of items	Psychometrics			Item structure and description	Cutoff score
		Sensitivity	Specificity	Efficiency		
PTSD Checklist (PCL) (Blanchard et al., 1996; Weathers et al., 1993)	17	0.78-0.94	0.83-0.86	0.83-0.90	Rate how much specific problems have bothered patient in the past month ranging from 1 (not at all) to 5 (extremely)	Varies
Primary Care Posttraumatic Stress Disorder Screen (PC-PTSD) (Prins et al., 2003)	4	0.78	0.87	0.85	Indicate presence/absence of nightmares, avoidance, hypervigilance, and numbness in the past month due to a traumatic event	3
Davidson Trauma Scale (DTS) (Davidson et al., 1997)	17	0.69	0.95	0.83	Rate frequency/severity of each symptom in the past week from 0=not at all to 4=every day/extremely distressing. Reexperiencing symptoms are tied to a specific event.	40
Startle, Physiological arousal, Anger, and Numbness (SPAN) (Meltzer-Brody et al., 1999)	4	0.84	0.91	0.88	Rate frequency/severity of symptoms from 0-4	5
Screen for Posttraumatic Stress Disorder (SPTSS) (Carlson, 2001)	17	0.94	0.60		Rate frequency of symptoms over the past two weeks from 0 (never) to 10 (every day)	4
Impact of Event Scale (IES) (Horowitz et al., 1979; Neal et al., 1994)	15	0.89	0.88	0.88	Rate frequency of symptoms in past week (not at all, rarely, sometimes, and often) in response to a specific life event	35

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Mississippi PTSD Scale (Keane et al., 1988)	35	0.93	0.89	0.90	Items rated on a 5-point scale (responses vary by item), time period “since the event”	107
Single Item PTSD Screen (SIPS) (Gore et al., 2008)	1	0.76	0.79		“Not bothered at all,” “bothered a little,” or “bothered a lot” by a past traumatic experience	“Bothered a little”
War-Zone Related PTSD Scale (WZ-PTSD) (Brewin, 2005; Weathers et al., 1996)	25	0.87-0.90	0.65-0.72	0.81-0.82	Rate current PTSD symptoms (occurring in the past 7 days) on a 5-point scale	1.3
PTSD Statistical Prediction Instrument (PSPI) (Marx et al., 2008)	12	0.86-0.99	0.36-0.8	0.78-0.87	Twelve items that significantly predict PTSD diagnostic status	Optimally efficient at 6, optimally sensitive at 3
Posttraumatic Adjustment Scale (PAS-P) (O'Donnell, Creamer et al., 2008)	10	0.82	0.84		5-item severity-based Likert scale ranging from “Not at all” to “Totally”	16
Self-Rating Inventory for PTSD (SRIP) (Hovens et al., 2002)	22	0.86	0.71	0.78	4-point Likert scale from “not at all” to “very much” rating symptom intensity	52
Penn Inventory for PTSD (Hammarberg, 1992)	26	0.90-0.98	0.94-1.00	0.94-0.97	4 scaled sentences measuring presence/absence of PTSD symptoms, along with degree, frequency, or intensity of symptoms.	35
Posttraumatic	49	0.89	0.75		Symptom frequency in the past month rated	

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Diagnostic Scale (PTDS) (Foa et al., 1997)	on a 4-point scale from 0=”not at all” to 3=”five or more times a week”

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Psychological Trauma: Theory, Research, Practice, and Policy

The Prevalence and Latent Structure of Proposed DSM-5 Posttraumatic Stress Disorder Symptoms in U.S. National and Veteran Samples

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The Prevalence and Latent Structure of Proposed DSM-5 Posttraumatic Stress Disorder Symptoms in U.S. National and Veteran Samples

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The *Diagnostic and Statistical Manual, Fourth Edition* (*DSM–IV*) is currently undergoing revisions in advance of the next edition, *DSM-5*. The *DSM-5* posttraumatic stress disorder workgroup has proposed numerous changes to the PTSD diagnosis. These include the addition of new symptoms, revision of existing ones, and a new four-cluster organization (Friedman, Resick, Bryant, & Brewin, 2011). We conducted two Internet-based surveys to provide preliminary information about how proposed changes might impact PTSD prevalence and clarify the latent structure of the new symptom set. We used a newly developed instrument to assess event exposure and lifetime and current *DSM-5* PTSD symptoms among a nationally representative sample of American adults (N = 2,953) and a clinical convenience sample of U.S. military veterans (N = 345). Results from both samples indicated that the originally proposed *DSM-5* symptom criteria (i.e., requiring 1 B, 1 C, 3 D, and 3 E symptoms) yielded considerably lower PTSD prevalence estimates compared with *DSM–IV* estimates. These estimates were more comparable when the DSM-V D and E criteria were relaxed to 2 symptoms each (i.e., the revised proposal). Confirmatory factor analyses (CFA) indicated that the factor structure implied by the four-symptom criteria provided adequate fit to the data in both samples, and a *DSM-5* version of a dysphoria model (Simms, Watson, & Doebbeling, 2002) yielded modest improvement in fit. Item-response theory and CFA analyses indicated that the psychogenic amnesia and new reckless/self-destructive behavior symptom deviated from the others in their respective symptom clusters. Implications for final formulations of *DSM-5* PTSD criteria are discussed.

Keywords: DSM-5, Posttraumatic Stress Disorder, Diagnosis

The *Diagnostic and Statistical Manual for Mental Disorders, Fourth Edition* (*DSM–IV*; American Psychiatric Association, 2000) is currently undergoing revisions in advance of the next edition, *DSM-5*. The *DSM-5* posttraumatic stress disorder (PTSD) workgroup has proposed numerous changes to the PTSD diagnosis, including moving the diagnosis out of the anxiety disorders section and into a new class of "trauma- and stressor-related disorders," the elimination of criterion A2 (i.e., the peri-traumatic fear, helplessness, or horror requirement), the addition of new symptoms and revision of existing ones, and a new four-cluster organization to the symptoms (Friedman, Resick, Bryant, & Brewin, 2011). The aims of this study were to examine how these changes might impact PTSD prevalence rates and to clarify the latent structure of the proposed symptom set using confirmatory factor analysis (CFA) and item-response theory (IRT).

The reorganization and redefinition of PTSD symptoms includes several changes that could impact diagnostic prevalence and/or the latent structure of the symptoms. Most notably, the *DSM-5* PTSD workgroup has proposed to add three new symptoms, for a new total of 20 symptoms, and organize all symptoms under four symptom clusters (i.e., the B, C, D, and E symptom clusters) as opposed to the three clusters listed in *DSM–IV*. Criterion B was left essentially unchanged in the *DSM-5* proposal

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though renamed from "reexperiencing" to "intrusion" symptoms to underscore the new emphasis on intrusive versus ruminative processes, as evident for symptom B1 ("intrusive distressing memories of the traumatic event") (Friedman et al., 2011). The new Criterion C, termed "persistent avoidance of stimuli associated with the traumatic event(s)," is comprised of the two effortful avoidance symptoms from *DSM–IV* (C1 and C2) that were previously located within the broader *DSM–IV* Criterion C. This revision was based on results of prior *DSM–IV* CFA studies that emphasized the distinction between effortful avoidance and the other symptoms that fell under the rubric of "numbing of general responsiveness" (Elhai, Ford, Ruggerio, & Frueh, 2009; Forbes et al., 2011; Friedman et al., 2011). Criterion D, titled "Negative alterations in cognitions and mood that are associated with the traumatic event," lists seven symptoms. Two are new and were intended to reflect the persistent negative appraisals and pervasive negative moods associated with the syndrome (Criteria D3 and D4). A third symptom, previously known as "sense of a foreshortened future" (D7 in *DSM–IV*), was expanded in scope and substantially revised to read "persistent and exaggerated negative expectations about one's self, others, or the world." The *DSM–IV* symptom "restricted range of affect" also received a subtle revision to emphasize specific deficits in the capacity to experience positive emotion. The hyperarousal cluster, formerly Criterion D, will become Criterion E in *DSM-5* and is titled "alterations in arousal and reactivity that are associated with the traumatic event(s)." This cluster includes two major changes, the addition of a new symptom "Reckless or self-destructive behavior" (E2), and an irritability/anger symptom that places a new emphasis on aggressive behavior, that is, "irritable or aggressive behavior" (E1), in contrast to "irritable or angry feelings," which are subsumed within the negative mood symptom (D4). The item order of the hyperarousal criteria are also changed from DSM-*IV* to *DSM-5*. Finally, at the time this research was initiated, the *DSM-5* proposal included a new diagnostic algorithm requiring the presence of a minimum of one Criterion B, one Criterion C, three Criterion D, and three Criterion E symptoms. Since then, the requisite number of Criterion D and Criterion E symptoms have each been reduced from 3 to 2 symptoms.

In this study, we evaluated the impact of these changes on diagnostic prevalence and the latent structure of PTSD symptoms using data collected through Internet surveys of two samples using a new *DSM-5* instrument. To our knowledge, only one previously published study has addressed these questions and was based on a nonclinical college student sample (Elhai et al., 2012). We used CFA to examine the fit of the new factor structure implied by the four symptom criteria and compared this model to logical alternatives suggested by prior research and initial study findings. CFA is uniquely suited for this purpose because it permits examination of the relations between manifest indicators (i.e., in this case symptom data) and the latent constructs believed to underlie their covariation, as well as the correlations among the factors themselves. Thus, CFA can provide information about the relative strengths of association between each symptom and the factors hypothesized to underlie them (e.g., the construct represented by the overarching criterion). We then used IRT analyses to examine the relationship between the probability of endorsement of each item and symptom severity within a given symptom cluster. In this context, IRT can be thought of as complementing CFA by providing information about how items within a cluster perform relative to each other with respect to a severity metric; that is, the analysis indicates whether symptoms within a given cluster measure similar or different levels of symptom intensity.

Study 1

Method

Participants. Participants were adults recruited from a probability-based online panel of U.S. adults (age 18 and older) who had indicated that they would consider participating in online surveys if asked to do so. Such panels are constructed to be generally representative of the U.S. adult population with respect to age, gender, and socioeconomic status. Potential participants are sent e-mail invitations about online surveys and then go to a website containing a brief description of the self-administered survey and decide whether they wish to participate. For this study, participants were recruited from a probability-based online panel of U.S. adults maintained by Survey Sampling International (SSI). Participants who completed the survey received points worth approximately $3 and were entered into a raffle with a prize equivalent to $25,000 held every 3 months for which participants completing all types of SSI surveys were eligible. Approximately 20% of U.S. households lack home Internet coverage, but some individuals from such households have Internet access through school, work, or smartphones. Therefore, although this sampling method does not produce a true national probability sample, it does provide a nonconvenience sample that is highly representative of U.S. adults.

A total of 3,756 adults accessed the URL containing the National Stressful Events Survey (NSES) description and survey, and 3,457 (92%) agreed to participate. Of those who agreed to participate, 2,953 completed the survey (85.4% of adults who agreed to participate and 78.6% of those who accessed the URL). Survey data were weighted by age and gender to adjust for discrepancies between the 2010 Census and survey data on these variables, with a corresponding weighted sample of 2,955. Prevalence data presented from the full sample were weighted. Individual item-level analyses (including structural analyses) were based on unweighted data. Comparison of weighted and unweighted symptom prevalence and severity rating data indicated minimal, and in most cases, no differences in prevalence.

Of the survey completers, 345 endorsed exposure to a *DSM-5* Criterion A event and met criteria for a probable lifetime diagnosis of PTSD, as defined by endorsement of at least 1 Criterion B, 1 Criterion C, 3 Criterion D, and 3 Criterion E lifetime symptoms in addition to endorsement of significant distress or impaired functioning in conducting activities in their personal life, relationships, or work or school. Demographic characteristics for this lifetime PTSD subset (whose data was used in the structural analyses described below) were as follows: 78.8% were women, 84.9% self-identified as White, 6.1% as Black, 1.7% as Native American, and 1.7% as Asian/Pacific Islander; 3.8% endorsed Hispanic ethnicity. A substantial proportion, 11.6%, had served in the U.S. Armed Forces, National Guard, or Military Reserves. Approximately one-quarter (25.5%) were between the ages of 18 and 34, 40.6% were between the ages of 35 and 54, and 33.3% were age 55 or older. Nearly all of these participants (97.1%) had at least a

high school degree, and 30.4% had obtained at least a 4-year college degree.

Measures

NSES. The NSES (Kilpatrick, Resnick, Baber, Guille, & Gros, 2011) was developed for this study to assess exposure to different types of traumatic events and the presence and severity of each of the 20 proposed *DSM-5* PTSD symptoms. The language for each symptom item was developed in collaboration with members of the *DSM-5* PTSD workgroup through a process aimed at reflecting the committee's conceptualization of each symptom and the precise wording of the drafted *DSM-5* language. The survey began with a life events section comprised of 28 questions that assessed exposure to a range of events that would meet the proposed *DSM-5* definition for a Criterion A event. Participants who endorsed exposure to at least one event then completed a symptom assessment featuring a conditional branching structure that administered follow-up items on the basis of prior responses. Specifically, for each symptom item, an initial stem question assessed whether the respondent had "ever" experienced the symptom (yes/no). If this question was not endorsed affirmatively, no further questions related to that symptom were administered. If the initial item was endorsed, then participants were asked to indicate when the symptom was last experienced using a four category temporal response option that ranged from "within the past month" to "more than 1 year ago." Participants who endorsed a given symptom within the past month were then asked to rate how much they had been *bothered* by it in the past month using the 1–5 severity scale of the PTSD Checklist (PCL; Weathers, Litz, Herman, Huska, & Keane, 1993), with anchors that ranged from "*not at all*" to "*extremely*." Coefficient alpha for the symptom severity items was .94 among those with *DSM-5* defined PTSD (i.e., those participants included in the structural analyses). Items assessing *DSM-5* PTSD Criteria D3 through E6 (which are not implicitly linked to a prior event) included a follow-up item that asked participants to indicate (yes or no) whether the symptom "began or got worse after the event." Endorsement of this item was required for these symptoms to contribute to calculation of probable diagnostic status but not required for individual item-level frequency of endorsement analyses or structural analyses. In addition, if the amnesia item (D1) was endorsed, participants were administered a follow-up item inquiring whether the symptom was because of loss of consciousness or intoxication. If either of these options were endorsed, the symptom was coded as not present for all analyses. Finally, in keeping with *DSM–IV* and *DSM-5* conceptualizations, a positive diagnosis required significant distress or impairment from the symptoms as indexed by responses to at least one of four additional items assessing this criterion.

Procedure

Participants were recruited by email invitation from a panel of U.S. adults (age 18 and older) in the United States who were registered with SSI. Potential participants were e-mailed the link to the web-based survey by the SSI study manager. Participants who accessed the link were then presented with a brief description of the survey as well as an online consent document in which they had the option to indicate consent or decline participation. The survey was described as a national survey of exposure to extremely stressful events/experiences and how they affect people. It was emphasized that, to get a good understanding of how common different stressful events are and how they affect people's lives, it was important that people participate whether or not they had experienced stressors or had problems. Participants who indicated that they were 18 years old or older and consented to the study were administered survey questions regarding exposure to events and, if events were reported, questions regarding PTSD symptoms.

Data Analyses

Three types of analyses were conducted. First, descriptive statistics were computed pertaining to event exposure and probable PTSD diagnosis. For these analyses (in Study 1 only) weighted data were used because this procedure provides the best population estimates of PTSD diagnostic prevalence for adults 18 and older in the United States. The number of weighted cases for these analyses was 2,955. Second, descriptive statistics for data at the individual symptom level were computed and CFA and IRT analyses were performed using the Mplus statistical software, version 5.2 (Muthén & Muthén, 1998–2009). CFA and IRT analyses were based on data from the subsample of participants who met criteria for probable lifetime PTSD (n = 345) to ensure that structural findings would be based on a clinically relevant sample. For CFA, we used the robust maximum likelihood (MLR) estimator to account for the non-normal distribution of some items. Ninety-five percent of participants provided complete data across all symptom rating items evaluated in the CFAs. Cases with missing data were included and modeled directly under maximum likelihood estimation. Analyses were based on 5-point severity rating data for symptoms experienced "within the past month." Data for participants who did not endorse a given symptom in the past month (and not administered the severity scale for that symptom) were recoded using the minimum scale value corresponding to "not at all bothered by the symptom."

We compared the fit of 4 alternative models for the structure of *DSM-5* symptoms. The first was the four-factor model defined by the proposed *DSM-5* diagnosis. The second was a *DSM-5* version of a "dysphoria" model (Simms, Watson, & Doebbeling, 2002), which has provided good fit to *DSM–IV* symptom data in many prior CFA studies (for a recent meta-analysis, see Yufik, & Simms, 2010). The defining feature of this model was a broad "dysphoria" factor comprised of all of the *DSM-5* Criterion D and E symptoms except for hypervigilance and exaggerated startle, which defined a separate "hyperarousal" factor. The third model was based on the findings from preliminary analyses, which revealed a high degree of intercorrelation between the reexperiencing and avoidance symptoms. This led us to wonder about the relative fit of a model that merged these two symptom clusters onto a single factor. The fourth model represented the *DSM–IV* three-factor configuration by combining the DSM-5 criteria C and D symptoms together onto a single Criterion C. Finally, we also examined the fit of a simple one-factor model.

Fit statistics were selected from the absolute (χ^2; standardized root-mean-square residual [SRMR]), parsimony (root mean square error of approximation [RMSEA]), and comparative-fit (Tucker-Lewis index [TLI], and comparative fit index [CFI]) classes of fit indices, and we applied cut-off guidelines recommended by Hu

and Bentler (1999) and Kline (2005) to determine the acceptability of each model. Specifically, RMSEA values ≤.06 and SRMR values ≤.08 were considered an indication of good model fit. CFI and TLI values ≥.90 and ≥.95 were considered as indicators of adequate and good model fit, respectively. In addition, we evaluated the Akaike (1987) and Bayesian (Schwartz, 1978) information criteria (Akaike information criterion [AIC] and Bayesian information criterion [BIC], respectively) to assist in model comparison across non-nested models. AIC and BIC are population based fit indices that favor model parsimony and fit. With these statistics, the preferred model is associated with lower relative values although there are no universally agreed upon guidelines regarding the interpretation of the difference in AIC/BIC values across any two models. In general, greater discrepancy across models suggests the superiority of the model with the lower value whereas models in which these values are more similar may be harder to discriminate (Preacher & Merkle, 2012); this highlights the need to collectively evaluate all fit statistics (Brown, 2006).

IRT analysis was used to evaluate the performance of each item in relation to others within a given symptom cluster. A primary assumption of this type of analysis is that the construct being measured is unidimensional. Because prior factor analytic research on the structure of PTSD symptoms has demonstrated a multidimensional structure, with symptoms within a cluster covarying unidimensionally, we only compared items belonging within the same cluster. IRT analysis generates information curves and item-characteristic curves (ICCs). Information curves depict the strength of the association between a given item and the latent trait underlying its covariation with other symptoms in the analysis and identifies where on the range of the trait information is maximized. ICCs illustrate the relationship between the amount of the trait being measured and the probability of endorsing a given item aggregated, in this case, across the 5 levels of the Likert-like severity scale. Our presentation of IRT results focused on ICCs because these figures convey results for multiple symptoms in the same figure. Information curves for each individual symptom are available from the corresponding author upon request.

Results

Trauma Exposure

The majority of participants within the full sample (88%) reported exposure to one or more of 10 nominal *DSM-5* Criterion A events, including disaster, accident, fire, exposure to hazardous chemicals, combat or experience in a war zone, physical or sexual assault, witnessing physical or sexual assault, unexpectedly witnessing dead bodies or body parts, life threat or serious injury to or violent death of a close friend or family member, or exposure to repeated accounts of traumatic events or images primarily because of occupational exposure. The six most prevalent forms of trauma exposure were: physical or sexual assault (52%), accident or fire (50%), death of a close family member or friend because of violence (49%), natural disaster (48%), threat or injury to a close family member or friend (32%), and witnessing physical or sexual assault (31%). The modal number of Criterion A events was 3, with a mean of 3.18 and *SD* of 2.27.

Frequency of Symptom Endorsement and Estimated Prevalence of PTSD

The frequency of symptom endorsement across the 20 proposed *DSM-5* symptoms within the lifetime PTSD subsample is listed in Table 1. Several noteworthy findings are evident. First, the frequency of symptom endorsement diminished in a step-like fashion across the lifetime ("ever"), past month, and "severity >3 in the past month" columns. Second, the frequency of endorsement of 18 of 20 symptoms in both past month columns was between 26 and 55%. Two symptoms had markedly lower rates of endorsement than all of the others: D1 (amnesia) and E2 (reckless/self-destructive).

Table 2 lists lifetime and past 12-month PTSD prevalence estimates using 3 different diagnostic criteria in the full sample. The prevalence of probable lifetime PTSD using the originally proposed *DSM-5* criteria of 1 Criterion B, 1 Criterion C, 3 Criterion D, and 3 Criterion E symptoms, was 10.4%. A greater percentage of women compared with men met the original criteria for lifetime *DSM-5* PTSD (14.8% of women vs. 5.5% of men), χ^2 (1, 2936) = 67.99, $p < .0005$. The percentage of participants meeting each criterion individually was as follows: one B symptom (59%), one C symptom (47%), 3 D symptoms (26%), 3 E symptoms (17%), indicating that Criterion D and E were the most strict of the four symptom criteria. We then examined the effect of reducing the requisite number of Criteria D and E symptoms to two each (i.e., reflecting the revised proposal); this yielded an estimated lifetime prevalence of 16.6%. A greater number of women (23.1%) compared with men (9.7%) met lifetime criteria for the revised definition, χ^2 (1, 2936) = 94.38, $p < .0005$. The lifetime prevalence of *DSM-5* PTSD using the original criteria among the *subset* of trauma-exposed participants (i.e., 88% of the full sample) was 6.3% for men and 16.7% for women, and the lifetime prevalence using the revised *DSM-5* criteria (i.e., requiring only 2D and 2E

Table 1
Study 1 (National Sample) Frequency of Symptom Endorsement (%) for Participants With Probable Lifetime Posttraumatic Stress Disorder (PTSD)

DSM-5 item	Ever	Past month	Severity ≥3
B1: Intrusions	94	53	41
B2: Nightmares	66	30	26
B3: Flashbacks	68	31	28
B4: Emotional reactivity	93	52	46
B5: Physical reactivity	69	38	32
C1: Avoid thoughts	93	52	45
C2: Avoid places/activity	81	43	38
D1: Amnesia	38	11	8
D2: Negative beliefs	79	35	31
D3: Guilt	83	34	29
D4: Negative emotions	93	40	37
D5: Loss of interest	87	39	35
D6: Distant and cut-off	91	46	42
D7: Low positive emotions	76	35	32
E1: Aggression	70	30	27
E2: Reckless/self-destructive	41	8	7
E3: Hypervigilance	77	34	29
E4: Startle	78	40	32
E5: Concentration	80	43	40
E6: Sleep	93	55	51

Note. DSM = Diagnostic and Statistical Manual of Mental Disorders.

Table 2
Study 1 (National Sample) Posttraumatic Stress Disorder (PTSD) Prevalence Across Various Criteria

Criterion	Past 12 months	Lifetime
DSM-5 (1B, 1C, 3D, 3E)	5.4	10.4
DSM-5 (1B, 1C, 2D, 2E)	9.1	16.6
DSM-IV (1B, 3C, 2D)	9.8	16.4

Note. DSM = Diagnostic and Statistical Manual of Mental Disorders. The *DSM-IV* prevalence estimate was computed using the 17 National Stressful Events Survey (NSES) items that corresponded most closely with the *DSM-IV* symptoms. The diagnostic algorithm included exposure to a *DSM-5* criterion A event.

symptoms) was 11.0% for men and 26% for women. Finally, using the 17 NSES items that corresponded to *DSM–IV* symptoms with the *DSM–IV* algorithm (including the *DSM–IV* Criterion A definition), we computed a lifetime *DSM–IV* PTSD prevalence estimate of 16.4%. Of those with lifetime *DSM–IV* PTSD, 63.1% met the original criteria for a lifetime *DSM-5* PTSD diagnosis, and 89.8% met the revised definition for lifetime *DSM-5* PTSD.

The estimate of the prevalence of past 12-month *DSM-5* PTSD using the original criteria was 5.4%.[1] Using this definition, a greater percentage of women compared with men met full criteria for past 12-month *DSM-5* PTSD (7.6% of women vs. 2.9% of men; χ^2 (1, 2936) = 31.00, $p < .0005$. The percentage of participants meeting each criterion individually within the past 12 months was as follows: one B symptom (43%), one C symptom (31%), 3 D symptoms (15%), 3 E symptoms (9%). When we examined the effect of reducing the requisite number of past 12-month Criterion D and E symptoms to two (i.e., the revised criteria), we found that this increased past 12-month PTSD prevalence to 9.1%. As with the lifetime data, there was a greater number of women (12.4%) compared with men (5.4%) who met the revised criteria for past 12-month PTSD, χ^2 (1, 2936) = 43.95, $p < .0005$. We estimated a past 12-month *DSM–IV* PTSD prevalence of 9.8%. Of those with past 12-month *DSM–IV* PTSD, 55.2% also met the original criteria for past 12-month *DSM-5* PTSD, and 86.1% met the revised *DSM-5* criteria for past 12-month PTSD (i.e., with both criteria D and E relaxed to 2 symptoms each).

CFA

Model fit statistics for the four CFA models that we evaluated are listed in Table 3. Results showed that the proposed *DSM-5* model provided acceptable, albeit not excellent, fit to the data. Figure 1 shows the factor loadings and factor correlations for this model. All symptoms loaded strongly (i.e., .58 or greater) on their respective factors with two exceptions: criterion D1 (dissociative or psychogenic amnesia) showed a .41 loading on the negative alterations factor and criterion E2 (reckless or self-destructive behavior) showed only a .41 loading on the hyperarousal factor. In comparison, all other items loaded on negative alterations within the range of .62 to .86 and all of the other hyperarousal items loaded in the range of .58 to .72. BIC and AIC values for the alternative "dysphoria" model suggested a substantial improvement in fit relative to the proposed *DSM-5* model. The third model, combining Criteria B and C as suggested by the high correlations between these factors in the first two models yielded no significant improvement in fit relative to the proposed *DSM-5* model. The *DSM–IV* model yielded poor fit relative to the other models tested. Finally, because of the strong factor intercorrelations in the *DSM-5* and dysphoria models, we also evaluated the fit of a one-factor model. As shown in Table 3, this model provided poor fit to the data.

IRT Analysis

IRT analyses for the Criteria B, D, E symptoms terminated normally and yielded no error messages. However, the analysis of the two symptom avoidance cluster yielded multiple error messages that we believe to be related to the use of only two highly correlated items in the analysis. This rendered results for the Criteria C symptom cluster uninterpretable. ICCs for the B, D, E criteria are depicted in Figure 2. In each panel, the *x*-axis is a standardized symptom cluster score with a mean of zero and a *SD* of 1. The *y*-axis is the probability of item endorsement. The curves are a logistic function with each figure permitting comparison of the performance of items within a cluster relative to each other. A basic principle of these graphs is that the steeper and taller the curve, the better the discrimination level between individuals high and low in symptom severity. Conversely, the flatter and lower the curve, the worse the discrimination between individuals differing in symptom severity. In each figure, at the low end of the *x*-axis, increases in symptom severity resulted in only small increases in the probability of endorsing the item. The same was true at the high end of this axis. In the middle though, relatively small increases in symptom severity were associated with large increases in the likelihood of item endorsement.

Comparison of the ICC figures revealed several noteworthy findings. Items within the Criterion B (intrusions) cluster showed largely overlapping curves indicating comparable levels of discrimination and item difficulty across items. The exception to this was symptom B2 (nightmares; the curve the farthest to the right within Criterion B), which showed a slightly elevated level of difficulty, relative to the other intrusion symptoms that more closely paralleled each other. A more distinct pattern of results emerged for the Criterion D and E items. Specifically, item D1 (psychogenic amnesia) deviated considerably from the other items in the D cluster. The shift to the upper end of the *x*-axis indicated that it was the most difficult item (i.e., endorsed by individuals with more severe symptoms) and discriminated relatively poorly (as indicated by the flatter slope) between individuals high and low in severity of symptoms within that cluster. Similarly, within the Criterion E symptoms, item E2 (recklessness or self-destructive behavior) showed the highest level of difficulty, but less discrimination, relative to the other hyperarousal items. Item E1 (irritable or aggressive behavior) evidenced similar, albeit less extreme characteristics. In contrast, item E6 (sleep disturbance; the curve farthest to the left on this figure) was the least difficult item.

[1] For this sample, we present past 12-month and lifetime PTSD estimates to permit direct comparison with estimates of PTSD prevalence from the National Comorbidity Surveys (Kessler, Sonnega, Bromet, Hughes, & Nelson, 1995; Kessler, Chiu, Demler, Merikangas, & Walters, 2005).

Table 3
Study 1 (National Sample) Confirmatory Factor Analysis (CFA) Fit Statistics for Each Model

Model	χ^2 (*df*)	RMSEA	SRMR	CFI	TLI	AIC	BIC
Proposed *DSM-5* (4 factors)	310.75 (164)	.05	.05	.94	.93	21,130	21,383
Reexperiencing, avoidance, dysphoria, hyperarousal (4 factors)	299.25 (164)	.05	.05	.94	.93	21,114	21,368
Trauma (B + C), negative alterations, hyperarousal (3 factors)	317.13 (167)	.05	.05	.94	.93	21,133	21,375
DSM-IV (3 factors)	379.24 (167)	.06	.05	.91	.90	21,233	21,475
1 factor	522.34 (170)	.08	.06	.85	.83	21,461	21,692

Note. RMSEA = root mean square error of approximation; SRMR = standardized root mean square residual; AIC = Akaike information criterion; CFI = comparative fit index; TLI = Tucker-Lewis Index; BIC = Bayesian information criterion; DSM = Diagnostic and Statistical Manual of Mental Disorders.

Study 2

The aim of Study 2 was to collect preliminary *DSM-5* PTSD data from a clinical sample of trauma-exposed veterans with an elevated prevalence of PTSD using the same instrument. Aside from necessary changes to the recruitment method (described below), procedures were identical to Study 1 with the following exceptions. First, Criterion C "Persistent avoidance of stimuli associated with the traumatic event(s)" was divided into three rather than two items. The rationale for this exploratory modification was that symptom C2, which reads "Avoids external reminders [people, places, conversations, activities, objects, situations] that arouse recollections of the traumatic event[s]," combines avoidance of discrete external stimuli (people, places, objects) with avoidance of behavioral engagement with the environment (i.e., via conversations and activities). Separating these two seemingly distinct forms of avoidance yielded three items reflecting avoidance of (a) internal reminders, (b) external reminders, and (c) activities.

A second methodological difference between the two studies was that the Veteran's Affairs (VA) version of the NSES organized the traumatic life events checklist portion of the survey into three life span intervals: (a) events experienced prior to joining the military, (b) events experienced during military service, and (c) events experienced after discharge from the military. The categories of events assessed within the pre- and postmilitary intervals were the same as those used in Study 1. The military service interval included four categories of events: (a) combat or its aftermath, (b) military sexual trauma, (c) other military-related trauma, (d) and nonmilitary service related event.

Finally, the VA study included the *DSM–IV* PTSD Checklist-Civilian Version (PCL-C; Weathers et al., 1993) administered in a counterbalanced order with the NSES. The PCL is the most widely used self-report measure of PTSD in both research and clinical contexts (Ruggiero, Rheingold, Resnick, Kilpatrick, & Galea, 2006). It consists of 17 items that correspond directly to the *DSM–IV* PTSD symptoms, with each one rated on a 5-point severity (i.e., "bothered") scale. The Civilian as opposed to Military version of the PCL was used to allow for the assessment of PTSD symptoms in response to either military or nonmilitary related traumas (and to correspond more closely to the methodology used in Study 1).

Method

Participants. Veteran participants were recruited via two methods. The first was a recruitment letter mailed to 700 veterans of all service eras (since World War II) who had previously consented to be contacted for research studies at the National

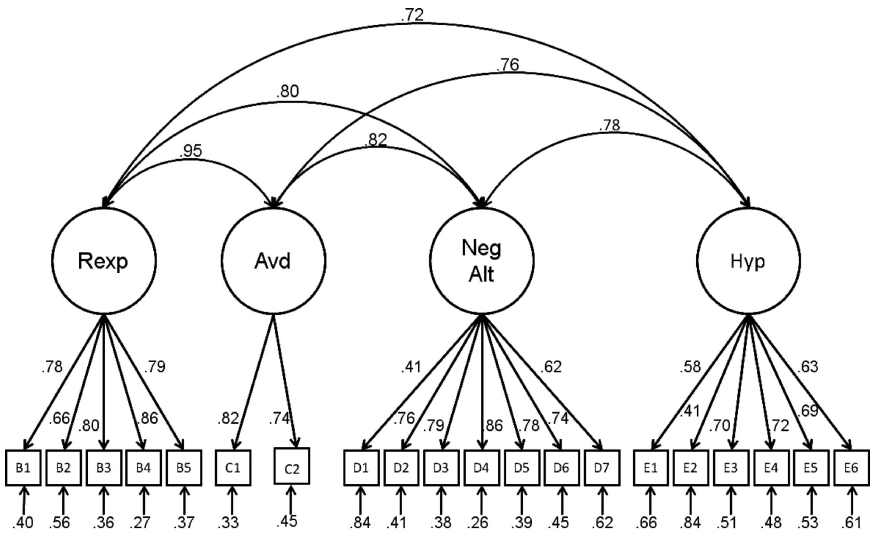

Figure 1. Study 1 (Community Sample) confirmatory factor analysis of the symptom structure implied by the four *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (*DSM-5*) symptom criteria. The figure lists factor correlations and the completely standardized factor loadings and residual variances for each item.

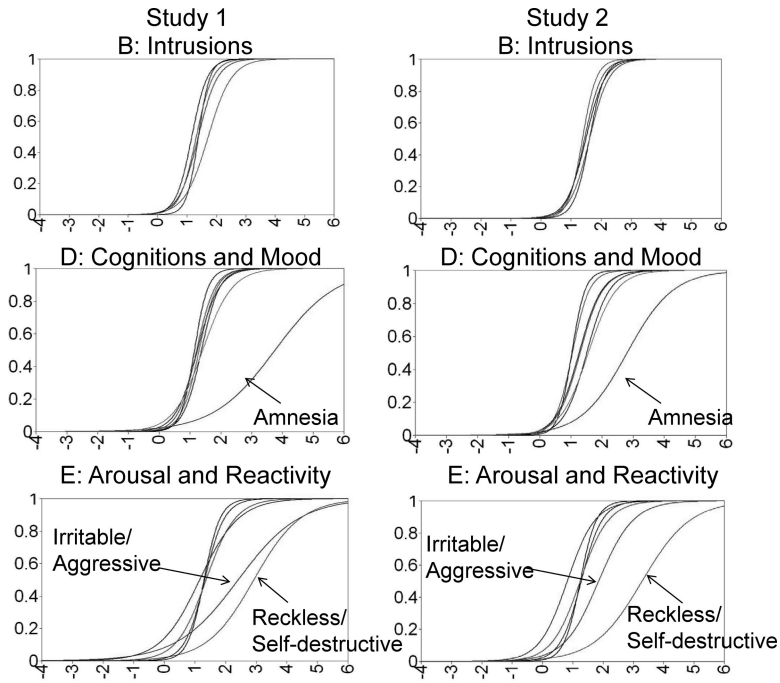

Figure 2. Item characteristic curves for items reflecting the B, D, and E criteria. Study 1 is in the left panel; Study 2 is in the right panel. In each figure, the *x*-axis is a standardized symptom cluster score with a mean of zero and a *SD* of 1. The *y*-axis is the probability of item endorsement. [1] For this sample, we present past 12 month and lifetime PTSD estimates to permit direct comparison with estimates of PTSD prevalence from the National Comorbidity Survey (Kessler, Chiu, Demler, Merikangas, & Walters, 2005). [2] In the VA sample we focused on estimates of current PTSD (i.e., past-month as opposed to past 12-month) so we could directly compare NSES estimates to the PCL estimate which was based on reports of symptoms in the past month. [3] It is noteworthy also that the correlation between total current severity scores on the NSES and the PCL-C was $r = .82$ ($p < .001$). [4] Coefficient alpha for the symptom severity items was .95. [5] This may not be surprising since lowering these thresholds make the *DSM-5* criteria more comparable to those of *DSM-IV* (i.e., since 1 C and 2 D symptoms in *DSM-5* = 3 C symptoms in *DSM IV*; and 2E symptoms in *DSM-5* = 2 D symptoms in *DSM-IV*).

Center for PTSD in Boston. One hundred seven letters were returned for bad addresses. One hundred twenty-three of the 593 (21%) remaining completed the survey. The second recruitment method involved emailing an invitation to complete the survey to 278 veterans of Operations Enduring Freedom and Iraqi Freedom (OEF/OIF) who were enrolled in an ongoing longitudinal PTSD registry study, the Veterans' Afterdischarge Longitudinal Registry (Rosen et al., 2011). Of these, 222 veterans (80%) endorsed trauma exposure and completed the survey, yielding a total across the two recruitment mechanisms of 345 study participants. Twenty-two participants (8 from the first cohort, 14 from the second) did not complete the symptom assessment and were omitted from data analysis, yielding a final sample of 323 survey completers. Of these, 61% were male and self-reported race and ethnicity was as follows: 80% White, 16% Black, 4% American Indian or Alaskan Native, and 1% Asian. In addition, 5% endorsed Hispanic, Latino, or Spanish ethnicity. The mean age of the sample was 44 (range = 23–85). The majority of the sample (75%) had served in the Operation Iraqi Freedom or Operation Enduring Freedom era; 15% served in the Vietnam War era, 4% served during the Operation Desert Storm era, 1% served in the Korean War or World War II eras. Most (76%) served in the Army; 14% served in the Marine Corps, 7% served in the Navy, and 4% served in the Air Force. With respect to education, 76% had earned at least a high school diploma or equivalent and 24% had completed a bachelor's or more advanced degree.

Results

Trauma Exposure

All participants endorsed having experienced at least one Criterion A event. The five most commonly endorsed types of premilitary trauma exposure were sudden, unexpected death of a close relative or friend due to disease (endorsed by 34% of the sample), physical or sexual assault (28%), having a close family member or friend experience an extraordinary stressful event (27%), death of a close relative or friend due to violence (21%), and witnessing dead bodies or parts of bodies (17%). Combat exposure was the most common type of trauma endorsed during participants' military service (reported by 83% of the sample), followed by exposure to other stressful military experiences (48%), nonmilitary trauma occurring during the time of military service (18%), and military sexual trauma (16%). The five most common traumatic events occurring after participants' military service were the sudden, unexpected death of a close relative or friend due to disease

(32%), a close family member or friend experiencing an extraordinarily stressful event (25%), the death of a close friend or relative because of violence (21%), exposure to details of traumatic events for occupational or other reasons (20%), and witnessing dead bodies or parts of bodies (17%).

Frequency of Symptom Endorsement and Estimated Prevalence of Probable PTSD

The frequency of symptom endorsement for the VA sample is listed in Table 4. A *t* test revealed that there were no differences in mean total scores on the PCL or the NSES as a function of which measure was presented first (i.e., no significant order effects). Results for the NSES paralleled those observed in the community sample, that is, the frequency of symptom endorsement diminished in a step-like fashion across the lifetime ("ever"), past month, and "severity ≥ 3" columns. Also, as observed in the community sample, items D1 (Amnesia) and E2 (reckless/self-destructive) were endorsed much less frequently than the other items. Table 4 also shows that the frequency of endorsement of past month symptoms with a severity rating greater than or equal to three was lower for NSES items than for the corresponding PCL item despite using similar item language and identical cut-offs using the same 5-point rating scale.

As shown in Table 5, 30.3% of the VA sample met criteria for a probable current diagnosis of PTSD, using the originally proposed *DSM-5* criteria of 1 Criterion B, 1 Criterion C, 3 Criterion D, and 3 Criterion E symptoms, with each symptom endorsed at level of at least moderate severity (a score of 3 or greater on the 1–5 symptom severity scale) in the past month.[2] There were no differences in the prevalence of the original definition of current PTSD by gender (31.4% of women vs. 29.9% of men) χ^2 (1, 318) = .08, p = .78. In addition, 67.5% percent met criteria for a probable lifetime diagnosis of *DSM-5* PTSD, using the original definition. A greater percentage of women compared with men met the original criteria for lifetime *DSM-5* PTSD (76.5% of women vs. 64.6% of men), χ^2 (1, 314) = 4.87, p = .027. The percentage of participants meeting each current criterion individually was as follows: one B symptom (67.5%), one C symptom (59.1%), 3 D symptoms (44.9%), 3 E symptoms (40.9%), indicating that Criteria D and E were the most strict of the four symptom criteria. As in Study 1, we also examined the effect of reducing the requisite number of symptoms in these clusters to two (i.e., the revised proposal) and found this to increase the percentage of cases meeting diagnostic criteria to 38.7% and 75.2% for current and lifetime PTSD, respectively. There were no gender differences in the prevalence of current PTSD using the revised criteria: 40% of women versus 38.6% of men met the current revised criteria for PTSD, χ^2 (1, 317) = .06, p = .80. Significant gender differences did emerge when evaluating the lifetime revised PTSD criteria: 86.4% of women compared to 72.2% for men met this criteria, χ^2 (1, 312) = 8.59, p = .003. In comparison, the PCL-C yielded an estimate of current probable PTSD of 61.0% using an established *DSM–IV* PCL-C diagnostic rule (i.e., defined as endorsement of at least one Criterion B, three Criterion C, and two Criterion D symptoms each at a level of 3 [moderate] or greater; Weathers et al., 1993). When this rule was combined with the additional requirement of a PCL-C total score of 50 or greater, estimated prevalence dropped to 51.7%.[3]

Of those who met criteria for a current diagnosis of *DSM–IV* PTSD, as defined by the NSES, 73.6% also met the original criteria for *DSM-5* current PTSD and 86% met the revised *DSM-5* current PTSD criteria. Finally, of those who met *DSM–IV* defined lifetime PTSD, 90.4% met the original *DSM-5* definition for lifetime PTSD and 97.9% met the revised criteria for a *DSM-5* lifetime PTSD diagnosis.

Table 4
Study 2 (Veterans Affairs [VA] Sample) Frequency of Symptom Endorsement (%)

DSM-5 item	Ever	Past month	Severity ≥3	PCL ≥3
B1: Intrusions	88	71	59	65
B2: Nightmares	78	51	45	54
B3: Flashbacks	74	38	33	49
B4: Emotional reactivity	85	55	51	66
B5: Physical reactivity	81	49	43	59
C1: Avoid thoughts	84	57	50	63
C2: Avoid places	82	51	44	59
C3: Avoid activities	78	49	42	
D1: Amnesia	45	18	14	40
D2: Negative beliefs	68	47	44	46
D3: Guilt	53	41	35	
D4: Negative emotions	74	43	42	
D5: Loss of interest	81	43	40	60
D6: Distant and cutoff	85	48	44	64
D7: Low positive emotions	64	37	35	60
E1: Anger	57	28	26	63
E2: Reckless/self-destructive	43	14	11	
E3: Hypervigilance	83	45	40	65
E4: Startle	86	47	39	60
E5: Concentration	79	51	47	65
E6: Sleep	81	58	53	69

Note. DSM = Diagnostic and Statistical Manual of Mental Disorders; PCL = PTSD Checklist. *DSM-IV* PCL items are aligned with the *DSM-5* item that is most similar in content (i.e., not by criterion number since the proposed order of symptoms has changed in *DSM-5*).

CFA of Proposed *DSM-5* Factor Structure

Model fit statistics for the four CFA models in this sample of trauma exposed veterans are listed in Table 6.[4] Results showed that the *DSM-5* model provided adequate fit to the data. Figure 3 shows the factor loadings and factor correlations for this model. All symptoms loaded on their respective factors at the $p < .001$ level, although the magnitudes of loadings of two symptoms on their respective factors were substantially lower than the others. Specifically, criterion D1 (dissociative or psychogenic amnesia) loaded on the Negative Alterations factor at .48 and criterion E2 (reckless or self-destructive behavior) loaded on the hyperarousal factor at .41. In comparison, all other items loaded on negative alterations within the range of .67 to .85 and all of the other hyperarousal items loaded on that factor in the range of .62 to .75.

[2] In the VA sample we focused on estimates of current PTSD (i.e., past-month as opposed to past 12-month) so we could directly compare NSES estimates to the PCL estimate which was based on reports of symptoms in the past month.

[3] It is noteworthy also that the correlation between total current severity scores on the NSES and the PCL-C was r = .82 ($p < .001$).

[4] Coefficient alpha for the symptom severity items was .95.

Table 5
Study 2 (Veterans Affairs [VA] Sample) Posttraumatic Stress Disorder (PTSD) Prevalence Across Various Criteria

Criterion	Current	Lifetime
DSM-5 (1B, 1C, 3D, 3E)	30.3	67.5
DSM-5 (1B, 1C, 2D, 2E)	38.7	75.2
DSM-IV (1B, 3C, 2D)	39.9	74.0
PCL-C	61.0/51.7	

Note. DSM = Diagnostic and Statistical Manual of Mental Disorders; PCL-C = PTSD Checklist (Civilian version) *DSM-IV* prevalence estimate was computed using the 17 National Stressful Events Survey items that most closely correspond with *DSM-IV* items. The PCL estimate lists two figures: The first was based on the *DSM-IV* algorithm with each item endorsed at a level of 3 or greater, the second is the *DSM-IV* algorithm combined with total score of 50 or more.

As in the community sample, BIC and AIC values for the dysphoria model suggested slightly better fit than the *DSM-5* model, though the magnitude of the difference was only 5 points. The third model, combining Criteria B and C yielded poorer fit compared to the first two models across most indices and, as in Study 1, the *DSM–IV* model showed the worst fit of the four models. As in Study 1, we also evaluated the fit of a 1 factor model in the veteran sample and found that it provided poor fit to the data (Table 6).

IRT of Proposed *DSM-5* Scales

As in Study 1, symptoms within the reexperiencing cluster showed largely overlapping curves indicating comparable levels of discrimination and difficulty. Again, a more distinct pattern of results emerged for the Criterion D and E items. Specifically, item D1 (psychogenic amnesia) deviated considerably from the other items in that cluster indicating that it tended to be endorsed by individuals with more severe symptoms and discriminated relatively poorly between those with high versus low symptom severity. Within the Criterion E symptoms, item E2 (recklessness or self-destructive behavior) again showed the highest level of difficulty, but less discrimination, relative to the other hyperarousal items. Item E1 (irritable/aggressive behavior) evidenced similar, albeit somewhat less extreme, characteristics as E2.

Discussion

These two studies were designed to provide preliminary information about how proposed changes to the PTSD diagnosis might impact prevalence rates and clarify the latent structure of the new symptom set using CFA- and IRT-based approaches. To do this, we developed an Internet survey to assess event exposure and *DSM-5* PTSD symptoms (Kilpatrick et al., 2010) that was then completed online by a large nationally representative community sample and a second clinical sample of trauma-exposed veterans with a high prevalence of PTSD. Results from the community sample suggested a weighted lifetime prevalence of probable PTSD using the originally proposed *DSM-5* criteria (i.e., 3 D and 3 E symptoms) of 10.4% and past 12-month estimate of 5.4%; the prevalence using the revised *DSM-5* criteria (i.e., 2 D and 2 E symptoms) was 16.6% for lifetime and 9.1% for past 12 months. These findings are somewhat higher than prior estimates of PTSD prevalence in nationally representative U.S. community samples such as the National Comorbidity Survey (7.8% for lifetime prevalence; Kessler, Sonnega, Bromet, Hughes, & Nelson, 1995) and National Comorbidity Survey Replication (3.5% for past 12-month prevalence; Kessler, Chiu, Demler, Merikangas, & Walters, 2005). We further compared our results with those of Kessler et al. (1995) by comparing the prevalence of PTSD among the trauma-exposed samples of the two studies: Kessler et al. (1995) reported that among those exposed to any type of traumatic event, the lifetime prevalence of PTSD was 8.1% in men and 20.4% in women. In comparison, the lifetime prevalence of *DSM-5* PTSD using the 3D/3E criteria among trauma-exposed participants in Study 1 was 6.3% for men and 16.7% for women. Lifetime prevalence using the revised *DSM-5* definition of PTSD (i.e., 2D and 2E symptoms) was 11.0% for men and 26% for women.

In the VA clinical sample, 30.3% of veterans met the original criteria for a probable current diagnosis of PTSD using the proposed *DSM-5* criteria with each symptom endorsed at a level of at least moderate severity in the past month. In addition, 67.5% of the sample met the original criteria for a probable lifetime diagnosis of *DSM-5* PTSD. Reducing the requisite number of symptoms in the Criteria D and E clusters to two (i.e., the revised proposal) increased the percentage of cases meeting *DSM-5* diagnostic criteria to 38.7% and 75.2% for current and lifetime PTSD, respectively. In comparison, the *DSM–IV* PCL-C yielded an estimate of probable current PTSD of 61.0% using the *DSM–IV* diagnostic rule (i.e., one Criterion B, three Criterion C, and two Criterion D symptoms all endorsed at a level of at least moderate severity in the past month).

The large discrepancy between diagnostic prevalence estimates derived from the PCL-C versus NSES in the veteran sample was remarkable given that both assessments were based on past month

Table 6
Study 2 (Veterans Affairs [VA] Sample) Confirmatory Factor Analysis (CFA) Fit Statistics for Each Model

Model	χ^2 (*df*)	RMSEA	SRMR	CFI	TLI	AIC	BIC
Proposed *DSM-5* (4 factors)	386.18 (183)	.06	.04	.93	.92	19,469	19,730
Reexperiencing, avoidance, dysphoria, hyperarousal (4 factors)	381.50 (183)	.06	.04	.93	.92	19,464	19,725
Trauma (B + C), negative alterations, hyperarousal (3 factors)	435.31 (186)	.06	.05	.92	.91	19,529	19,778
DSM-IV (3 factors)	474.16 (186)	.07	.05	.90	.89	19,584	19,833
1-factor	641.23 (189)	.09	.06	.85	.83	19,807	20,045

Note. RMSEA = root mean square error of approximation; SRMR = standardized root mean square residual; CFI = comparative fit index; TLI = Tucker-Lewis Index; AIC = Akaike information criterion; BIC = Bayesian information criterion; DSM = Diagnostic and Statistical Manual of Mental Disorders.

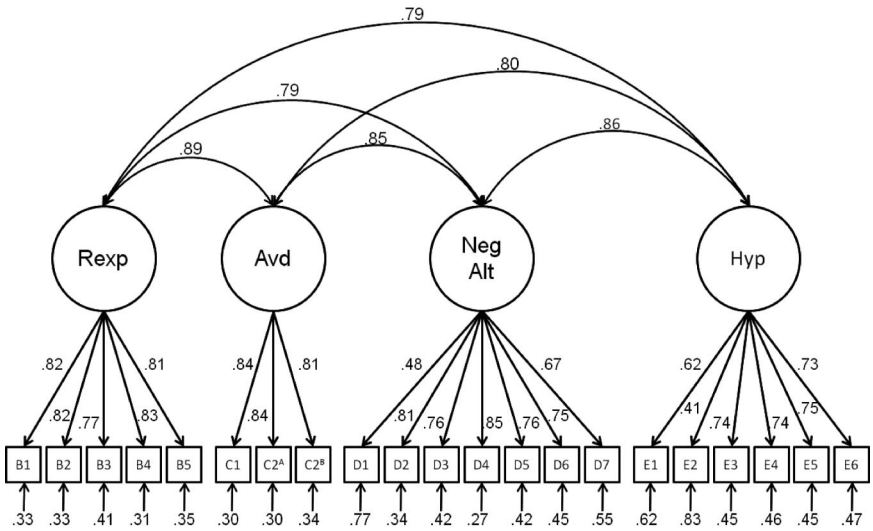

Figure 3. Study 2 (Veteran's Affairs [VA] sample) confirmatory factor analysis of the symptom structure implied by the four *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (*DSM-5*) symptom criteria. In this study criterion C2 was subdivided into two items. Factor correlations are listed, as well as the completely standardized factor loadings and residual variances for each item.

symptom endorsement using the same severity metric. The correlation between the two measures for current symptom severity was high, suggesting that they were measuring the same construct. So what might account for the discrepancy? Previous research suggests that the PCL-C *DSM–IV* scoring rule that we used to compare with the NSES may yield inflated prevalence estimates compared with estimates derived from clinical interview. Keen, Kutter, Niles, and Krinsley (2008), for example, found that although 32.5% of a veteran sample met criteria for a probable diagnosis on the PCL-C using this algorithm, only 22% met criteria as defined by the Clinician Administered PTSD Scale (CAPS; Weathers, Ruscio, & Keane, 1999). It is also conceivable that the discrepancy reflects the difference between the checklist-type assessment of the PCL-C and the interactive conditional-branching assessment of the NSES (which is more similar to structured clinical interviews). The NSES, CAPS, and other measures of this type begin the assessment of each symptom with an inquiry about whether the respondent has ever experienced the symptom (i.e., which can then be used in the assignment of a lifetime diagnosis). If the respondent denies ever having experienced the symptom, no further questions about that symptom are asked and then the next item is presented. In the NSES, if the lifetime symptom was endorsed, then participants were asked to indicate when the symptom was last experienced using a four category temporal scale that ranged from "within the past month" to "more than 1 year ago." Only those who endorsed a given symptom within the past month were then given an opportunity to rate how much they had been bothered by it in the past month using the PCL-like severity scale. It appears from the pattern of results that the more detailed temporal assessment of the NSES yielded significantly reduced endorsements of current symptomatology compared to the checklist approach of the PCL-C. Unfortunately, without a clinical interview-based diagnosis it is not possible to determine which estimate is more accurate though this question can (and should) be addressed in future research.

Given the major differences in response format between the NSES and PCL-C, we also computed *DSM–IV* prevalence estimates using the 17 NSES items that correspond to *DSM–IV* symptoms. In both study samples, *DSM-5* prevalence estimates more closely approximated the *DSM–IV* estimate when the minimum number of Criterion D and Criterion E symptoms was lowered from 3 to 2.[5] Based, in part, on these findings, the *DSM-5* PTSD workgroup is now planning to reduce both the D and E diagnostic thresholds to 2, rather than 3 symptoms as proposed originally.

Structural Findings

CFAs indicated that the structural model implied by the proposed *DSM-5* B, C, D, and E criteria provided adequate, albeit not excellent, fit to the data. This was true in both the community sample of individuals who met criteria for PTSD using the originally proposed (i.e., 3D and 3E symptoms) definition and for the veteran sample comprised of individuals with trauma exposure and a high prevalence of PTSD, suggesting that the results generalize to both the threshold and subthreshold trauma-exposed populations. We also evaluated four alternative models: a *DSM-5* version of the "dysphoria" model (Simms et al., 2002), a model suggested by preliminary analyses which had the five intrusion and two avoidance symptoms loading on the same factor, one representing the *DSM–IV* structure with criteria C and D combined, and a one-factor model. Results from both studies suggested that the dysphoria model provided the best fit of the five models tested. However, as in prior studies of this type (Yufik & Simms, 2010), the magnitude of improvement relative to the proposed *DSM-5* model was modest. Given the preliminary nature of this research,

[5] This may not be surprising since lowering these thresholds make the *DSM-5* criteria more comparable to those of *DSM-IV* (i.e., since 1 C and 2 D symptoms in *DSM-5* = 3 C symptoms in *DSM IV*; and 2E symptoms in *DSM-5* = 2 D symptoms in *DSM-IV*).

we limited our CFA model testing to only the most obvious and logical comparisons. Future studies will undoubtedly examine alternative models, and while it is likely that other solutions may prove better fit to the data, it is also clear that a diagnostic model cannot be validated using CFA fit statistics alone and that obtaining a psychometrically pure diagnostic construct was not the primary objective of the *DSM-5* PTSD workgroup.

Examination of the pattern of factor loadings in the proposed *DSM-5* model indicated that the two new items, "Persistent and exaggerated negative expectations about one's self, others, or the world" and "Persistent distorted blame of self or others about the cause or consequences of the traumatic event(s)," showed strong loadings on the latent variable reflecting the new Criterion D titled "Negative alterations in cognitions and mood." The high degree of intercorrelation between items on this factor is compatible with the notion that they share a common cause, that is, are manifestations of the same underlying construct. The results of IRT analyses echoed these observations and indicated that these two new items yielded item-characteristic curves that closely paralleled all but one of the other symptoms in this cluster.

In contrast, results of both studies suggested that the amnesia ("Inability to remember an important aspect of the traumatic event(s)" and new reckless/self-destructive behavior item yielded relatively weak loadings on their respective factors in CFA and deviated considerably from the others on their respective factors in IRT analyses. The finding of a relatively weak factor loading for the amnesia item replicates, in a new constellation of symptoms, a finding that has been observed in many prior factor analytic studies of PTSD symptoms (e.g., King, Leskin, King, & Weathers,1998; Palmieri, Weathers, Difede, & King, 2007; Simms et al., 2002). The IRT results shed new light on this result indicating that psychogenic amnesia tended to be endorsed by more highly symptomatic individuals relative to the other items within Criterion D. The ICC curve for the reckless/self-destructive behavior item deviated in a similar fashion from the other items within Criterion E in both samples. These observations would not be necessarily problematic if the slope of the ICC curves for these two items more closely approximated the others within the cluster. However, in both samples, these items showed considerably flatter curves, suggesting poorer discrimination between individuals high and low in symptom severity.

The finding that the amnesia item tended to be endorsed by individuals with higher levels of symptom severity is consistent with prior research on the relationship between dissociation and PTSD. Psychogenic amnesia has long been conceptualized as a manifestation of dissociation (Carlson, Dalenberg, & McDade-Montez, 2012) and recent findings suggest that this symptom is most likely to be endorsed by individuals with a proposed subtype of PTSD defined by marked elevations in depersonalization, derealization, and flashbacks (Lanius, Brand, Vermetten, Frewen, & Spiegel, in press; Wolf et al., 2012). If psychogenic amnesia is indeed a marker of a qualitatively distinct subgroup of individuals with PTSD characterized by marked dissociation, then perhaps there would be benefit to dropping this item from the core symptoms of the disorder and redefining it as a marker of a dissociative subtype. Alternatively, one could argue that this symptom has been viewed as a rare but important part of the PTSD construct since its establishment in 1980, thereby justifying its retention.

Similarly, the "reckless/self-destructive behavior" symptom showed relatively low factor loadings on the latent variable reflecting Criterion E "alterations in arousal and reactivity." Its item characteristic curve also suggested that it tended to be endorsed by individuals with more severe symptoms and provided relatively poor discrimination between those high versus low in symptom severity. According to members of the PTSD workgroup, this item was intended to address "an important posttraumatic symptom often seen in adolescents" (Friedman et al., 2011, p. 761). Results of these two studies of adults suggest that this item did not cohere well with the core symptoms of hyperarousal. One alternative would be to eliminate this symptom from the core diagnostic criteria and list it instead as an associated feature seen most often among adolescents. However, the problematic behaviors described by this symptom have been identified by many clinicians and researchers as a clinically important feature among many individuals with PTSD, so another view is that it should remain as a core symptom. The latter perspective has the advantage of stimulating more research that may help resolve this issue. In sum, results of these two studies suggest that the PTSD workgroup (and future researchers) may wish to reconsider whether psychogenic amnesia and problems in the domain of reckless/self-destructive behavior would be better conceptualized as core symptoms of PTSD, "associated features" of the disorder, markers of a subtype, or manifestations of PTSD associated primarily with a particular stage of development.

Finally, IRT analyses of both studies showed that many NSES items, particularly within the Criterion B symptoms, showed largely overlapping ICCs. When items overlap like this, it indicates that they are showing equivalent associations with the latent trait (i.e., the relationship between the amount of the trait being measured and the probability of endorsing a given item is equivalent across items). The implications of this are mixed. On the one hand, in this context, similarities in the ICC curves within a symptom cluster may indicate that the items are mapping onto the same latent construct (or symptom cluster). On the other hand, from a test construction perspective, this may be undesirable because it indicates that the items are providing largely redundant information. In future research on the development of PTSD assessment instruments, it may be useful for investigators to develop items that provide greater coverage of the full range of the latent trait.

These conclusions should be weighed in light of study limitations. First, findings were based on Internet surveys using a newly developed instrument that has yet to undergo thorough psychometric refinement and validation in relation to a clinical interview. Second, given the scope of the analyses presented in this preliminary report, we left a number of issues to be addressed in future analyses including more detailed examinations of the relationships between events of various types and subsequent symptoms. Third, the focus of the assessment in both studies was on event exposure and PTSD symptoms and we did not assess many relevant variables such as comorbidity. That said, our findings provide important preliminary findings regarding the effect of changes to the PTSD diagnosis proposed for *DSM-5* and identify several issues for further consideration by the workgroup.

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ABSTRACT

Creation of a PTSD Registry for Veterans: Project VALOR

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Objectives: The objective of this project is to develop the first longitudinal registry of combat-exposed men and women with PTSD. The Veteran's After-discharge Longitudinal Registry (VALOR) will provide essential data on the natural history and outcomes associated with PTSD in military service men and women who have utilized the Department of Veterans Affairs (VA) health care system. An additional goal of this project is to determine risk factors for PTSD among combat-exposed service men and women (through comparison to a combat-exposed non-PTSD group of veterans). Thus, the registry will allow an evaluation of current theoretical models of symptom development in a large sample of service men and women who utilize the VA medical system. Furthermore, the registry will allow the assessment of referral and health care utilization as well as treatment approaches used within VA. The final objective of this study is to develop a large database of servicemen and women with PTSD for further observational, interventional and ancillary studies.

Research Design and Methodology: A sample of potential PTSD patients will be selected randomly from VA's electronic OIF/OEF veteran patient records. Following their initial consent, 1200 participants with a diagnosis of PTSD in their medical file will be mailed a package containing a description of the study, informed consent form and a self-report questionnaire packet to be returned to the researchers. Once these materials are received, participants will be contacted be telephone to conduct a brief clinical interview. A comparison sample of 400 veterans, deployed to combat but without a recorded diagnosis of PTSD, will also be selected from the same database and will undergo the same assessment procedures. In addition to clinical interview and self-report data, data will be extracted from all veteran's computerized VA medical files pertaining to diagnoses, treatment and other health care data. Data will be collected using these various methods to assess the following domains: PTSD diagnosis, additional mental health difficulties and diagnoses, alcohol/drug use, traumatic brain injury, anger/hostility, sleep difficulties, combat exposure, additional trauma exposure social support, quality of life, absenteeism, functional impairment and treatment utilization. Data from these multiple sources will be merged into one centralized database for analysis and storage.

Results: Data collection for this study is currently underway. Preliminary results of pilot testing will be presented.

Impact: The PTSD registry will provide information to assist researchers, military leaders, and treatment providers to better understand the etiology and course of PTSD, how it can be identified at early stages, and the responsiveness of recent returnees to various treatment options. This knowledge will be of benefit to current service members as well as victims of trauma in the broader community.

ABSTRACT (ABCT)

Creation of a PTSD Registry for Veterans: Project VALOR

Terence M. Keane[1,2], Ray Rosen[3], Nancy N. Maserejian[3], Darren W. Holowka[1,2], Paola Rodriguez[1], Brian P. Marx[1,2], Han K. Kang[4], Jennifer J. Vasterling[1,2], Kathryn B. Wunderle[1], Nicole A. Rodier[1], Denise M. Sloan[1,2], Matthew J. Friedman[1], Lynn A. Sleeper[3]

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Preliminary evidence suggests that veterans of the current conflicts in Afghanistan (Operation Enduring Freedom; OEF) and Iraq (Operation Iraqi Freedom; OIF) are at significant risk for posttraumatic stress disorder (PTSD) and other mental health difficulties as well as significant barriers to care (Hoge et al., 2004). Furthermore, PTSD and deployment to these warzones has been associated with increased incidence of physical problems and overall healthcare utilization (Hoge, Terhakopian, Castro, Messer, & Engel, 2007). To examine these issues in more detail, we are developing the first longitudinal registry of combat-exposed men and women with PTSD. The Veteran's After-discharge Longitudinal (VALOR) Registry will gather data on the natural history and outcomes associated with PTSD in veterans who have utilized the Department of Veterans Affairs (VA) health care system. The present study was designed to address the epidemiology of PTSD and the effectiveness of PTSD health services within VA. In terms of epidemiology, the goals are to (1) describe the natural history of PTSD and to evaluate disparities by sociodemographic, military and post-deployment factors and (2) to identify risk factors and comorbidities of PTSD by comparing patients to a group of veterans without PTSD. In terms of health services, the goals of this study are to (1) identify treatment approaches over time, (2) identify risk factors for a missed PTSD diagnosis, (3) assess current referral and health care utilization patterns and (4) develop a large database of servicemen and women with PTSD and network of treatment sites that are potentially available for further studies.

A national sample of potential PTSD patients will be randomly selected from VA's electronic OIF/OEF veteran patient records. Following their initial consent, 1200 participants with a diagnosis of PTSD in their medical file will complete a self-report questionnaire packet to be returned to the researchers. Participants will then be contacted by telephone to conduct a 60-minute clinical interview. A comparison sample of 400 veterans, deployed to combat but without a recorded diagnosis of PTSD, will also be selected from the same database and will undergo the same assessment procedures. In addition to clinical interview and self-report data, data will be extracted from participants' computerized VA medical files pertaining to diagnoses, treatment and other health care data. During the interview, PTSD diagnosis will be verified using the PTSD module of the Structured Clinical Interview for DSM-IV and open-ended questions will be used to elicit descriptions of perceived effects of their military service and a traumatic brain injury interview will also be administered. Measures in the self-report packet will assess additional mental health difficulties and diagnoses, alcohol/drug use, anger/hostility, sleep, combat exposure, additional trauma exposure, social support, quality of life, absenteeism, functional impairment and treatment utilization. Data from these multiple sources will be merged into one centralized database for analysis and storage. Data collection for this study is currently underway. Preliminary results will be presented and implications will be discussed.

The Natural History of Combat-Related Posttraumatic Stress Disorder: Project VALOR

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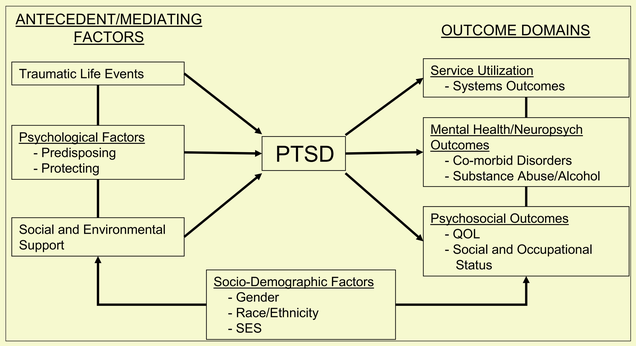
OVERVIEW

- Posttraumatic stress disorder (PTSD) is a disabling psychiatric disorder affecting 10% or more of service men and women
- Data are lacking regarding the natural history, comorbid psychiatric disorders, psychosocial outcomes, and treatment utilization for PTSD in VA and non-VA settings
- Current models of antecedents and consequences of PTSD have not been systematically evaluated in longitudinal studies
- Project VALOR (Veterans' After-Discharge Longitudinal Registry) is the first large-scale, PTSD registry to address these and other needs

Fig 1: Conceptual Model



SPECIFIC AIMS

- **Aim 1**: To assess the long-term progression of PTSD using the psychosocial, medical and quality of life outcomes associated with the disorder, and to evaluate disparities by sociodemographic, military and post-deployment factors
- **Aim 2:** To identify risk factors and comorbidities of PTSD by comparing OEF/OIF Veterans with PTSD to a control group of OEF/OIF Veterans without PTSD

  Aim 3: To identify treatment approaches for PTSD over time in a naturalistic VA setting
- **Aim 4:** To assess prevalence, risk factors, and outcomes associated with undiagnosed PTSD in a comparison group of post-combat OEF/OIF Veterans
- **Aim 5:** To compare healthcare utilization patterns among OEF/OIF Veterans with and without PTSD
- **Aim 6:** To develop a comprehensive database of former OEF/OIF service men and women with PTSD for future observational, interventional, or concurrent ancillary studies

STUDY DESIGN

- Potential participants identified using VA health care system database
- Cohort 1: Registry of 1,200 Veterans with a diagnosis of PTSD within the past 12 months
- Cohort 2: Comparison group of 400 Veterans without a PTSD diagnosis within the past 12 months
- Approximately equal numbers of male and female Veterans will be included in both diagnostic groups
- All subjects will provide informed consent to participate

INCLUSION CRITERIA

- OEF/OIF Army or Marine Veteran (deployed to combat)
- In the VA health care system database
- Not currently participating in a clinical (intervention) research trial
- Mental health evaluation conducted in the past 12 months and coded in the electronic medical record
- Additional criteria for participants in the PTSD Registry:
  - PTSD diagnosis (ICD9-309.81) coded in the electronic medical record within the past 12 months (primary or secondary diagnosis)
  - PTSD diagnosis code appears at least once subsequent to the date of the mental health evaluation coding
- Additional criteria for participants in the non-PTSD comparison group
  - No PTSD diagnosis (ICD9-309.81) coded in the electronic medical record within the past 12 months

DATA COLLECTION

Conducted in 2 phases over 3 years:

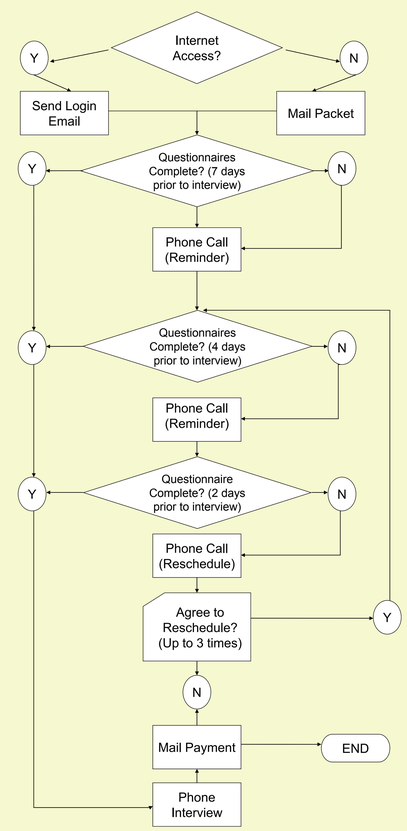
Phase I (months 1-12): Preliminary PTSD database will be created by data transfer, query reports/resolutions will be addressed, analyses of existing data extracted from the VA medical record system will be conducted, and target cohorts for follow-up assessment will be identified

Phase II (months 12-36): Subject recruitment and structured telephone interviews will be conducted, data will be coded, de-identified, and merged with the overall study database, and analyses will be conducted on the combined data set. The data collection procedure is illustrated in Figure 2.

- Interviews are scheduled based on availability of participants and interviewers
- Reasons for ineligibility and refusal are recorded

DATA COLLECTION (CONTINUED)

Fig. 2: Data Collection Procedure



Study Domains and Assessment Measures

Domain	Measure
PTSD	SCID-IV PTSD module
Mental Health Disorders and Stresses	Prime-MD PHQ
Self-Assessed Effects of Military Experiences on Post-discharge Life	Two open-ended questions (qualitative data)
Alcohol/Substance Abuse	AUDIT;TICS
Traumatic Brain Injury	Study-Specific Questions
Social and Occupational Support	DRRI Post-Deployment Interview
Quality of Life	SF-12v2
Sleep Quality	Jenkins Sleep Questionnaire
Treatment and Service Utilization	Study-Specific Questions
PTSD related functional impairment	Inventory of Functional Impairment (IFI)
Combat Exposure	DRRI Section I (Combat Exposures) and Section J (Post-Battle Experiences)
Suicide Ideation	M.I.N.I. Module
Absenteeism	HPQ
Life Stressors/Trauma	Life Events Checklist (LEC)
Anger Hostility	DAR-5

ANALYSIS PLAN

- Descriptive analyses to characterize two enrolled samples in terms of demographics, diagnosis, symptomatology, quality of life, current therapies used, and clinical trajectories
- Examine changes in medical and psychological comorbidities and other outcomes over time
- Use multivariable-adjusted logistic regression to examine factors associated with PTSD diagnosis
- Examine prevalence of PTSD in the non-PTSD group and risk factors for missed diagnosis
- Use propensity score analyses to obtain model-based predicted probability of undergoing treatment, and stratify all analyses of treatment effectiveness by propensity score quantile

IMPLICATIONS

- Findings from Project VALOR will inform public health policy and planning
- Application of current treatments in everyday practice
- Assessment of gender differences in health utilization and associated correlates
- Fill in gaps in RCT's and other observational studies – the "real world" situation

Medical Chart PTSD Diagnostic Accuracy among OEF/OIF Veterans: Preliminary Results

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Background: Posttraumatic Stress Disorder (PTSD) is considered to be among the signature wounds of the conflicts in Iraq and Afghanistan, with new cases continuing to present to the Veteran's Administration (VA) for assessment and treatment on a regular basis. Accurate diagnosis is important for a variety of reasons: It has serious implications for (1) compensation and pension decisions (2) reimbursement and billing and (3) ongoing healthcare. To date, however, no research has examined the accuracy of routine diagnoses in VA medical charts and factors associated with diagnostic accuracy.

Methods: Participants were 268 Army and Marine Veterans (49% female) deployed in support of Operations Enduring Freedom (OEF) or Iraqi Freedom (OIF). Participants were randomly selected from the VA patient database (with females oversampled) by the Environmental Epidemiology Service of the Veteran's Health Administration in Washington, DC.

Table 1. Demographics

Age	M= 37.3 (SD=10.1)
Gender	
Male	51%
Female	49%
Branch	
Army	90%
Marines	10%
Race/Ethnicity	
White	78%
Black	17%
Latino	13%
Multiracial	5%
Native	3%
Asian	2%
Marital Status	
Married	47%
Single	21%
Divorced	19%
Cohabitating	9%

Measures

Chart Diagnosis of PTSD was defined as at least two instances of a diagnosis of PTSD (309.81) by a mental health professional associated with a scheduled visit in the Veteran's electronic medical files within the past year.

SCID Diagnosis. Current (past-month) diagnosis was used as the standard and was obtained using the SCID Module for PTSD[1], administered by doctoral level clinicians in a telephone interview. Numbers of symptoms as well as past month DSM-IV PTSD diagnosis were calculated.

Stressful Life Events were counted using the Life Events Checklist[2]. Respondents indicate which of 17 stressful events has "happened to" them, was "witnessed" or "leaned about".

Combat exposure was assessed using two scales from the Deployment Risk and Resilience Inventory[3] (DRRI): the Combat Experiences Subscale, which assesses stereotypical warfare experiences, such as being shot at, firing a weapon, and witnessing injury and death, which is measured on a five point scale. The Aftermath of Battle subscale assesses exposure to additional stressors that occur following combat, including handling human remains, and witnessing human suffering with items rated "yes" or "no".

Post-deployment Social Support was also assessed using the DRRI scale and refers to the extent to which family, friends and other members of the community. Items are rated on a 5-point scale from "Strongly disagree" to "Strongly agree".

Sleep difficulty was assessed using the Sleep Problems Scale[4] (SPS), a five-item questionnaire that asks respondents to rate the numbers of days that have experienced a variety of sleep problems in the past month. These responses are grouped into 6 categories ranging from “Not at all” to “22-31 days”

Anger was measured using the Dimensions of Anger Reactions[5] (DAR5), a 5-item scale that assesses trait anger. Items are scored on a five-point Likert-type scale from 0 “Not at all” to 4 “Very much”.

Substance abuse was measured using the Alcohol Use Disorders Identification Test[6] (AUDIT) and the Two Item Conjoint Screen[7] (TICS).

Suicide risk was assessed using the suicide module of the Mini International Neuropsychiatric Interview[8] yielding a total risk score.

Functional Impairment was assessed using the Inventory of Psychosocial Functioning[9] (IPF) is an 87-item self-report measure designed to assess multiple dimensions of functional impairment experienced by active duty service members and veterans. Respondents rate how often they have acted that way over the past 30 days. Items are rated on a 7-point scale ranging from 1 (“never”) to 7 (“always”). The IFI yields a total score and scores for seven subscales: Romantic Relationships with a Spouse or Partner, Family, Work, Friendships and Socializing, Parenting, Education, and Day-to-Day functioning.

Results:

Results indicated 73% agreement between diagnoses, with 17% false positives and 10% false negatives (See Table 2). Current PTSD diagnosis (SCID) was associated with more PTSD symptoms, greater exposure to life and war zone stressors

greater functional impairment, less social support, and more anger and sleep problems. (See Table 3)

Factors associated with occurrences of false positives included fewer overall PTSD symptoms (including fewer sleep problems and less anger), greater social support, less combat exposure, less alcohol and drug abuse and increased suicide risk.

Factors associated with false negatives included higher AUDIT scores, and younger age at the time of assessment.

Table 2. Crosstabulation of PTSD diagnoses

		SCID	
		No PTSD	PTSD
Chart	No PTSD	50	27
	PTSD	46	145

Table 3. Correlations among study measures

	SCID Diagnosis	False Positive	False Negative
Age	.14	-.08	-.14*
Sex	.01	-.13*	.09
PTSD Current Symptoms	.81**	-.34**	.13*
PTSD Lifetime Symptoms	.64**	-.09	.09
Life Events	.29**	-.03	-.03
Combat Exposure	.24**	-.08	-.03
Post-battle Exposure	.33**	-.15*	-.05
Social Support	-.33**	.18**	-.01
Anger	.42**	-.14*	.01
Sleep Problems	.46**	-.18**	-.02
AUDIT	.13*	-.13*	.17**
TICS	.13*	-.14*	.08
Functional Impairment	.21**	-.10	.02
Suicide Risk	-.17**	.20**	.03

* p <.05 **p <.01

Conclusions:

- Preliminary results indicate more than 25% of VA chart diagnoses are in error.
- Reporting fewer PTSD symptoms was a risk for false positives, which may indicate
  - more difficult diagnostic distinctions or
  - that recovery has occurred and the diagnosis remains in the chart
- Social Support was also associated with false positives, which could indicate that having the support of family and friends makes it more likely that a Veteran will perceive their problems to be severe enough to pursue a claim more vigorously, or possibly that these are cases of recovery.
- Suicide Risk was also associated with false positives, likely due by influencing clinician perceptions of severity and functional impairment.
- False negatives were associated with being younger at the time of interview and could indicate that younger Veterans were less likely to report symptoms at the t
- Alcohol abuse was also associated with false negatives, possibly through being identified as the more serious problem.
- Strengths of this study include the use of a random sample and interview method of assessment of PTSD. Weaknesses include a relatively small sample size.
- While these results are preliminary, they point toward questionable validity of a substantial number of diagnoses in VA medical charts.
- Future research ought to (1) examine these associations in a larger sample longitudinally, and (2) evaluate additional factors (such as clinician or context variables) that may contribute to diagnostic error.

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A Longitudinal Registry of Post-Traumatic Stress Disorder in OEF/OIF Veterans: The Early Recruitment Experience

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Background

- Post-traumatic stress disorder (PTSD) is a disabling psychiatric disorder affecting 10% or more of service men and women returning from overseas operations
- Little is known about the natural history and treatment utilization patterns for PTSD in returning service members
- Project VALOR (Veterans' After-Discharge Longitudinal Registry) was designed as a longitudinal patient registry assessing the course of PTSD in 1,600 male and female Veterans who served in Operation Enduring Freedom (OEF) in Afghanistan or Operation Iraqi Freedom (OIF)
- Aims of the study include investigating predictors of progression or remission of PTSD and treatment utilization

Methods

- Study population:
  - U.S. Army or Marine Veteran deployed to combat in support of OEF or OIF
  - In the VA health care system database
  - Mental health evaluation conducted between June 2008 and December 2009
  - PTSD group (target N=1,200): ICD-9-CM code 309.81 coded twice between June 2008 and December 2009
  - Comparison group (target N=400): No ICD-9-CM code 309.81 coded in electronic medical record
  - Approximately equal numbers of men and women included in each diagnostic group
- Study recruitment
  - Created roster of Veterans meeting inclusion criteria
  - Mailed 'opt-out' letters to introduce the study
  - Telephoned individuals who did not opt out of the study to invite them to participate and obtain informed consent
- Data collection:
  - Medical history abstracted from electronic medical record at baseline and year one of follow-up
  - Military-specific data obtained from the OEF/OIF roster
  - Self-administered questionnaire
  - Telephone diagnostic interview

Table 1. Data collection domains and assessment measures

Domain	Measure
PTSD	SCID-IV PTSD Module
Suicidal Ideation	M.I.N.I. Suicide Module
Mental Health Disorders	Prime-MD Patient Health Questionnaire
Effects of military experiences on post-discharge life	Two open-ended questions (qualitative data)
Traumatic Brain Injury	Study-specific questions
Alcohol/Drug Use	AUDIT, TICS
Social Support	DRRI Post-Deployment Interview
Quality of Life	SF-12v2
Sleep Quality	Jenkins Sleep Problem Scale
Treatment Utilization	Study-specific questions
Functional Impairment	Psychosocial Functioning Inventory (PFI)
Combat Exposure	DRRI sections on Combat Exposures and Post-Battle Experiences
Absenteeism	WHO Health and Work Performance Questionnaire (HPQ)
Life Stressors/Trauma	Life Events Checklist (LEC)
Anger/Hostility	Dimensions of Anger Reactions (DAR-5)

Methods

- Outcome assessment:
  - PTSD status at study entry based on VA medical record
  - Blinded, doctoral-level clinicians assessed each participant's current PTSD status during the diagnostic interview using the Structured Clinical Interview for DSM (SCID-IV) PTSD module
  - Also assessed the presence of comorbidities of interest, including traumatic brain injury, substance use disorders, and depression, in the self-administered questionnaire or diagnostic interview
- Data analysis:
  - Final registry database will include merged data from the self-administered questionnaire and interview, along with select baseline and follow-up data from the electronic medical record
  - Conducted descriptive analyses to characterize participants in terms of demographics, diagnoses, and symptomatology
  - Examined concordance between medical record-based and SCID-based PTSD diagnoses

Results

- To test the study procedures, we conducted a pilot study over a 3-month period prior to the launch of full study recruitment
- 27 participants (13 men and 14 women) were enrolled during the pilot phase

Table 2. Baseline characteristics of pilot phase participants in Project VALOR

Covariate	Pilot Study Participants
N	27
Age (mean and standard deviation [SD])	41.9 (8.6)
Female (%)	52
Race (%)	
Black	15
White	82
Other	3
Hispanic ethnicity (%)	11
Branch of military service (%)	
Army	96
Marines	4
Location of deployment (%)	
Afghanistan only	19
Iraq only	70
Multiple deployments/other	11
PTSD diagnosis based on SCID (%)	78
Interview duration (mean and SD)	31.9 (12.3)

- On average, participants were 42 years of age (range: 28 to 58 years)
- 74% of participants had a diagnosis of PTSD based on the VA medical records
- Concordance between the PTSD diagnosis from the medical records and the SCID was 82%
- All pilot phase participants completed both the self-administered questionnaire and diagnostic telephone interview, and no difficulties related to comprehension or completion of either component were reported by the participant or the interviewer
- The average length of the diagnostic interview was 32 minutes (range: 10 to 59 minutes)

Results

Table 3. Concordance between medical record-based and SCID-based PTSD diagnoses in pilot phase participants

		Medical record-based diagnosis	
		PTSD	No PTSD
SCID-based diagnosis	PTSD	N=18 (67%)	N=3 (11%)
	No PTSD	N=2 (7%)	N=4 (15%)

- Full study recruitment began in May 2010 and is ongoing
- As of May 2011, 601 study interviews have been completed

Strengths

- Study design will provide longitudinal data over time and will allow us to characterize the course of PTSD and associated outcomes in combat-exposed Veterans
- Use of a mixed mode data collection system, including medical record abstraction, a self-administered questionnaire, and a diagnostic interview, will allow for internal validity checks on the accuracy and completeness of diagnostic data
- Large number of female participants

Limitations

- Unable to determine whether differences in PTSD status based on the medical records vs. the diagnostic interview are due to diagnostic errors or true changes in status (remission or new onset of PTSD)
- Sample may not be representative of the underlying population of Veterans with PTSD, as our study population only includes those who seek care for PTSD or other mental health conditions at VA health care facilities
- Possibility of recall bias in assessing trauma history and other exposures

Conclusions

- Our results suggest that confirmation of medical record-based diagnoses is needed in studies of PTSD
- In future analyses, we plan to examine predictors of discordance between the medical record-based and SCID-based diagnoses

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Posttraumatic Stress Disorder, Mild Traumatic Brain Injury, & Psychosocial Functioning among Iraq and Afghanistan Veterans

Darren W. Holowka, Brian P. Marx, Margaret Gates, Lin Guey, Raymond Rosen, Jennifer J. Vasterling
Terence M. Keane

Posttraumatic Stress Disorder and Traumatic Brain Injury have been identified as the signature wounds of the conflicts in Iraq and Afghanistan. Hoge et al. (2008) reported associations between mild TBI (mTBI) and health concerns among active duty military personnel. Research has also linked both PTSD and TBI to certain kinds of functional impairment (Marx et al, 2008; Rassovsky et al, 2005). What remains unclear is whether these relationships are observed in different populations, and the extent to which these factors interfere in psychosocial functioning domains.

Participants were 268 US Army and Marine OEF/OIF Veterans; 49% were female, and 34% identified as members of a racial or ethnic minority. Participants completed online questionnaires and a brief telephone interview. Questionnaires included the Health and Work Performance Questionnaire, the Patient Health Questionnaire and the Psychosocial Functioning Inventory. Participants were interviewed regarding the occurrence of TBI and the presence of PTSD symptoms.

Of the total sample, 172 met criteria for current PTSD (66 with mTBI) and 72 did not (24 with mTBI). Results indicated significant associations between PTSD symptoms and all areas of functioning. Significant correlations were also observed between mTBI and absenteeism, depression, PTSD symptoms and decreased physical health. Mild TBI was also associated with impairments in family, work and friendships, but not romantic relationships, parenting, education or self-care. The association between mTBI and absenteeism remained significant, while controlling for PTSD symptoms and Depression.

Peritraumatic response, PTSD and functional impairment among OEF/OIF veterans.

Bovin, M. J., Wisco, B. E., Holowka, D. W., Marx, B. P., Gates, M. A., Guey, L. T., Rosen, R. C., & Keane, T. M.

Although the DSM-IV-TR specifies that an event must elicit fear, helplessness or horror for it to be considered a traumatic stressor (i.e., PTSD Criterion A2; APA, 2000), prior research has suggested that additional peritraumatic responses may occur during a trauma and may be related to the onset of cardinal PTSD symptomatology (Bovin & Marx, 2010). Importantly, only a handful of studies have examined the nature of peritraumatic responses among Veterans (e.g., Adler, Wright, Bliese, Eckford, & Hoge, 2008; Schnurr, Spiro, Vielhauer, Findler, & Hamblen, 2002). These studies are limited because they examined a truncated number of potential peritraumatic responses among predominantly male Veterans. The current study addresses these limitations by providing data concerning a broadened range of peritraumatic responses in both male and female Veterans. A sample of 678 OEF/OIF veterans (54% female) ranging in age from 21-67 years old was recruited from VA medical centers across the country. As part of a larger study, participants completed a novel interview regarding their peritraumatic emotional reactions, in addition to the SCID module for PTSD and various self-report questionnaires. Initial results indicated that, after controlling for the Criterion A2 emotions, a number of peritraumatic responses (including peritraumatic sadness, guilt, and emotional numbing) were associated with PTSD. In addition, a number of the peritraumatic responses assessed were associated with depressive symptoms and functional impairment. The implications of these findings in the context of the assessment and treatment of trauma symptoms will be discussed.

Post-Deployment Social Support as a Mediator Between Military Sexual Trauma and PTSD among OIF/OEF Veterans

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Background: Studies suggest that both military sexual trauma (MST; Suris & Lind, 2008) and post-deployment social support (i.e., Pieterzak et al., 2009) significantly impact the risk of PTSD among veterans, yet no studies to date have examined the influence of post-deployment social support on MST-related PTSD. Research has found that post-deployment social support mediates the relationship between other traumatic events, such as combat exposure, and PTSD (Taft et al., 1999). Therefore, we hypothesized that post-deployment social support would similarly mediate the relationship between MST and PTSD symptoms. **Methods:** Participants were 675 OIF/OEF veterans recruited as part of a national registry study (Project VALOR). Veterans completed a telephone interview administered by doctoral level clinicians, which included the SCID module for PTSD. Participants also completed an online questionnaire, which included questions from the Deployment Risk and Resilience Inventory (DRRI; King et al., 2006) regarding unwanted sexual activity in the military and post-deployment social support. **Results:** MST was significantly correlated with post-deployment social support ($p < .001$) and with PTSD ($p < .05$). In order to test for the effects of mediation, we utilized a bootstrapping method to estimate the indirect effects. Results indicate that zero was not in the 95% confidence interval for the indirect effect, signifying that post-deployment social support significantly mediated the association between MST and PTSD symptoms. **Conclusion:** These findings suggest that post-deployment social support significantly impacts the risk of developing PTSD following MST. Implications for increasing post-deployment social support will be discussed.

Educational Objectives

1. Evaluate the negative impact of MST on PTSD symptomatology among veterans of OEF/OIF.
2. Recognize the role of post-deployment social support in mediating the relationship between MST and PTSD symptoms.
3. Discuss the implications of increasing post deployment social su**p**port among OIF/OEF veterans, particularly among those who experienced MST.

Posttraumatic Stress and Depressive Symptoms in a Sample of Returning OIF/OEF Veterans

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Background: Elevated rates of psychiatric disorders have been identified in soldiers returning from Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF). Posttraumatic stress disorder (PTSD) and major depressive symptoms frequently co-occur in veteran samples and are associated with worse psychosocial functioning. Utilizing a sample of veterans from the OIF/OEF conflicts, the aims of the present analysis are to identify associations between comorbid PTSD and major depressive symptoms, identify factors predictive of this comborbidity, and assess its impact on psychosocial functioning.

Methods: Data from a sample of 432 OIF/OEF veterans (53% female, 33% racial or ethnic minority) recruited for Project VALOR were used for this analysis. Participants were assessed for PTSD by clinician-administered diagnostic interviews (CAPS). Measures of combat experiences and post-deployment support (DRRI), depressive symptoms (PHQ-9), and psychosocial functioning (IFI) were obtained by self-report.

Results: 233 participants met criteria for PTSD and major depressive syndrome (MDS) (197 PTSD without MDS). Multiple logistic regression showed low post-deployment social support was most predictive of comorbid PTSD and MDS compared to PTSD alone when controlling for PTSD severity, other comorbid disorders, and demographic variables. Multiple linear regression showed comorbid PTSD and MDS was predictive of impaired psychosocial functioning when controlling for PTSD severity and other comorbid disorders.

Conclusion: The results of this analysis show significant rates comorbidity between PTSD and major depressive symptoms. Results also confirm findings from previous studies that this comorbidity is related to low post deployment support and it has a significant impact on psychosocial functioning.

Posttraumatic Stress Disorder, Mild Traumatic Brain Injury, & Psychosocial Functioning among Iraq and Afghanistan Veterans

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BACKGROUND

•Posttraumatic Stress Disorder and Traumatic Brain Injury have been identified as the signature wounds of the conflicts in Iraq and Afghanistan.

• Hoge et al. (2008) reported associations between mild TBI (mTBI) and health concerns among active duty military personnel.

•Research has also linked both PTSD and TBI to certain kinds of functional impairment (Marx et al, 2008; Rassovsky et al, 2005).

•What remains unclear is whether these relationships are observed in different populations, and the extent to which these factors interfere with psychosocial functioning.

METHODS

Participants: 1,065 US Army and Marine OEF/OIF Veterans; 51.3% were female, and 33.5% identified as members of a racial or ethnic minority.

Measures: ***Health and Work Performance Questionnaire*** (Kessler et al., 2003; HPQ). The HPQ is a comprehensive questionnaire used to address job performance, sickness absence and work related accidents or injuries. For the purposes of this study, questions pertaining to absenteeism were used to estimate the number of missed work days in the past 28 days.

Patient Health Questionnaire. **(**PHQ; Spitzer, Kroenke, Williams et al., 1999) The PHQ is a self-report version of the PRIME-MD that assesses the presence of various mood and anxiety disorders and syndromes. For the purposes of the present study a dichotomous variable was computed that determined the presence or absence of a Major Depressive Disorder.

Inventory of Psychosocial Functioning (IPF; Marx et al., 2009). The Inventory of Psychosocial Functioning (IPF) is an 80-item self-report measure designed to assess multiple dimensions of functional impairment over the past 30 days. Items are rated on a 7-point scale ranging from 1 ("never") to 7 ("always"). The IPF yields an overall mean score and scores for seven subscales: Romantic Relationships with a Spouse or Partner, Family, Work, Friendships and Socializing, Parenting, Education, and Self-care functioning.

Veterans RAND 12-item Health Survey. (VR-12; Selim et al., 2009). The VR-12 is brief 12-item questionnaire that assesses health-related quality of life. It provides various standardized subscales including Physical and Mental Component Summaries, as well as scales for Role Limitation (Physical & Emotional), Pain, General Health, Vitality, Social Functioning.

METHODS

Alcohol Use Disorders Identification Test (AUDIT; Saunders, Aasland, Babor, De La Fuente & Grant, 1993). The AUDIT is a ten item screening questionnaire that assesses harmful or hazardous alcohol consumption habits. It is composed of 10 items rated on likert-type scales.

TBI Interview. A structured interview was used to assess the presence of TBI in this sample. Participants were first asked to indicate whether they had ever had a head injury or exposure to a blast that led to (1) altered consciousness, (2) memory loss, (3) seizures, or (4) brain surgery. More detailed information is gathered about the 5 worst injuries, including symptoms that arose or were exacerbated after the injury. For the purposes of this study, mTBI was defined as any head injury that occurred while deployed and caused daze, confusion, loss of consciousness or retrograde amnesia.

Structured Clinical Interview for DSM-IV, PTSD Module. (First, Spitzer, Gibbon & Williams, 1997). The SCID is a semi-structured interview that was administered to determine the presence of DSM-IV symptoms and disorders. For the purposes of this study, only the PTSD module was administered by doctoral level interviewers.

Age	36.2(SD=9.3)	
Gender	Female	51.3%
	Male	48.7%
Branch	Army	91.0%
	Marines	9.0%
PTSD Diagnosis	PTSD	64.2%
	No PTSD	35.8%
Ethnicity	Hispanic	12.0%
Race	Asian	2.3%
	Native	3.1%
	Black	16.1%
	White	79.2%
Marital Status	Single	18.6%
	Married/Cohabitating	57.4%
	Divorced/Separated	20.9%

RESULTS

• Of the total sample, 684 met criteria for current PTSD.

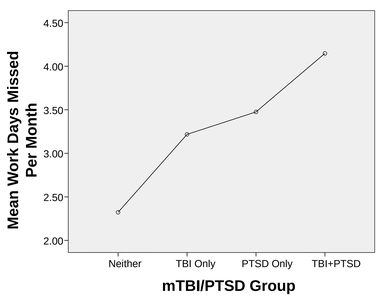
• Mean number of missed days of work in the past 28 days was 3.2 (SD=4.1), although this information was present only for 500 participants. (566 did not answer these questions).

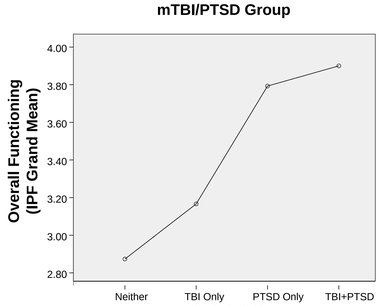
• Results indicated significant associations between PTSD symptoms and all areas of functioning (range r=.36 to r=.56) . Small but significant correlations were also observed between mTBI and Absenteeism (r=.11), PTSD symptoms (r=.18) decreased physical health (r=-.14) and functional impairment (r=.15). T-tests revealed significant mean differences between those with and without mTBI on all subscales of the VR-12 (all ps <.01). Multiple regression revealed that the association between mTBI and functioning remained significant while controlling for gender, minority status and age, but not when controlling for comorbid psychiatric diagnoses.

• Four groups were constructed based on the presence of PTSD and/or mTBI, and ANOVA revealed significant differences among groups on both Absenteeism (F=4.84, p<.01) and Functional Impairment (F=90.94, p<.001).

• Tukey's HSD post-hoc tests revealed that for Absenteeism, the only significant pairwise comparisons were (1) between the group that had Neither TBI nor PTSD and those with both, with a mean difference of almost two (1.8) additional missed work days per month, and (2) between the group that had Neither TBI nor PTSD and those with PTSD only, with a mean difference of one (1.2) additional missed work day per month. For Functional Impairment, however, all pairwise comparisons were significant except for those between the PTSD Only group and the TBI+PTSD Group.

	No PTSD	PTSD
No mTBI	298 (28%)	426 (40%)
mTBI	83 (8%)	258 (24%)





RESULTS

Model 1: Regression results for prediction of functional impairment from gender, minority status, and age. (Adj R^2=.02)

	B	*SE B*	β
Gender	.15	.06	.08*
Minority	.16	.07	.08*
Participant age at T1	.01	.00	.12***

*p<.05. ***p<.001

Model 2: Regression results for prediction of functional impairment from gender, minority status, age, and mTBI. (Adj R^2=.05)

	B	*SE B*	β
Gender	.09	.06	.04
Minority	.18	.07	.09 **
Participant age at T1	.013	.003	.13***
mTBI	.32	.07	.15***

**p<.01. ***p<.001

Model 3: Regression results for prediction of functional impairment from gender, minority status, age, mTBI, depression, anxiety , AUDIT score, and PTSD diagnosis. (Adj R^2=.40)

	B	*SE B*	β
Gender	.05	.05	.02
Minority	.07	.05	.03
Participant age at T1	.01	.003	.06*
mTBI	.08	.05	.04
Major Depressive Syndrome	.73	.06	.37***
Other Anxiety Syndrome	.26	.06	.13***
Total Audit Score	.02	.004	.11***
Current PTSD	.48	.06	.24***

*p<.05. ***p<.001

DISCUSSION

• Overall results indicate significant associations between PTSD, mTBI and functional impairment, with PTSD symptoms explaining more of the variance.

• Interestingly, the presence of PTSD and comorbid mTBI was associated with overall worse functional impairment compared to those with TBI only.

• Mild TBI was also associated with deficits in functioning even while controlling for the effects of demographics and psychopathology through other factors (especially Major Depression).

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Posttraumatic Stress Disorder, Mild Traumatic Brain Injury, & Psychosocial Functioning among Iraq and Afghanistan Veterans

Brian P. Marx [1,2], Darren W. Holowka [1,2]Margaret Gates[3], Lin Guey[3], Raymond Rosen[3], Jennifer J. Vasterling [1,2] & Terence M. Keane [1,2]

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Research has linked both posttraumatic stress disorder (PTSD) and traumatic brain injury (TBI) to certain kinds of functional impairment. What remains unclear is the extent to which each of these factors interferes with psychosocial functioning. Participants were 729 US Army and Marine OEF/OIF Veterans; 46.3% were female and 34% identified as members of a racial or ethnic minority. Participants completed online questionnaires and a brief telephone diagnostic interview for PTSD and mTBI. Results showed that, of the total sample, 39% met criteria for current PTSD only, 28% met criteria for mTBI only and 23% met criteria for both PTSD and mTBI. Results indicated significant associations between PTSD symptoms and functional impairments across several domains (r=.35 to r=.57). Small but significant correlations were also observed between mTBI and work absenteeism (r=.11), PTSD symptoms (r=.15) decreased physical health (r=-.12) and overall functional impairment (r=.08). Multiple regression analyses revealed that the association between mTBI and overall functional impairment remained significant while controlling for gender, minority status and age, as well as for depression, PTSD symptoms, other anxiety syndromes and alcohol abuse. Although mTBI was still a significant predictor, other variables (e.g., depression, PTSD, alcohol use) were more strongly associated with functional impairment in the final model. Using PTSD and mTBI diagnostic status, we examined group differences on functional outcomes. Analyses revealed significant differences among groups on both work absenteeism and overall functional impairment. Post-hoc tests revealed that, for work absenteeism, the only significant pairwise comparison was between the group that had neither TBI nor PTSD and those with both diagnoses. For functional impairment, however, all pairwise comparisons were significant except (1) between participants with neither diagnosis and those with mTBI only, and (2) between those with PTSD only and those with both mTBI and PTSD. These results will be discussed.

Psychosocial Outcomes in OEF/OIF Veterans with PTSD

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Background

- Post-traumatic stress disorder (PTSD) is a disabling psychiatric disorder affecting 10% or more of service men and women returning from overseas operations.
- Little is known about psychosocial outcomes of PTSD symptoms in Veterans with or without a confirmed mental health diagnosis.
- Project VALOR (Veterans' After-Discharge Longitudinal Registry) was designed as a longitudinal, observational registry for studying these effects in combat-exposed Veterans with and without a PTSD diagnosis.
- The Specific Aims were to examine psychosocial outcomes in Veterans with and without PTSD, including the prevalence and severity of sleep disorders, alcohol abuse, anger reactions, depressive or anxiety disorders, and suicidality.
- Additionally, we aimed to compare psychosocial outcomes of PTSD in male and female Veterans with confirmed, non-confirmed or no diagnosis of PTSD.

Design and Methods

Design:

- Project VALOR (Veterans' After-Discharge Longitudinal Registry) was designed as a longitudinal patient registry assessing the course of PTSD in 1,600 male and female Veterans who served in Operation Enduring Freedom (OEF) in Afghanistan or Operation Iraqi Freedom (OIF).
- Data on prior PTSD diagnoses were abstracted from the VA electronic medical records (EMR) at baseline. Participants completed an online self-administered questionnaire at study entry, and current/lifetime PTSD status was assessed during a diagnostic telephone interview using the Structured Clinical Interview for DSM (SCID) Module for PTSD.

Methods:

- Outcomes of interest were assessed using validated instruments including the Jenkins Sleep Questionnaire, Alcohol Use Disorder Identification Test (AUDIT), Dimensions of Anger Reactions revised short form, Prime-MD Patient Health Questionnaire, Mini-International Neuropsychiatric Interview (MINI) suicide module (9 or above indicating moderate/high suicide risk) and Inventory of Psychosocial Functioning (IPF).
- Study population:
  - U.S. Army or Marine Veteran deployed to combat in support of OEF or OIF
  - Mental health evaluation conducted between June 2008 and December 2009
  - PTSD group (target N=1,200): ICD-9-CM code 309.81 coded twice between June 2008 and December 2009
  - Comparison group (target N=400): No ICD-9-CM code 309.81 coded in electronic medical record
  - Approximately equal numbers of men and women included in each diagnostic group
- Study recruitment
  - Created roster of Veterans meeting inclusion criteria
  - Mailed 'opt-out' letters to introduce the study
  - Telephoned individuals who did not opt out of the study to invite them to participate and obtain informed consent
- Data collection:
  - Medical history abstracted from electronic medical record at baseline and year one of follow-up
  - Military-specific data obtained from the OEF/OIF roster
  - Self-administered questionnaire
  - Telephone diagnostic interview

Methods (Contd.)

Outcome assessment:

- PTSD status at study entry based on VA medical record.
- Blinded, doctoral-level clinicians assessed current PTSD status during the diagnostic interview using the Structured Clinical Interview for DSM (SCID-IV) PTSD module.
- Suicide risk was assessed by the MINI suicide module following standard scoring for none or low risk (0-8 points); moderate risk (9-16 points); or high risk (17+ points). For purposes of these analyses, none and low risk groups were combined as "low risk" and moderate and high risk groups were combined as "high risk".
- We also assessed the presence of key comorbid conditions, including traumatic brain injury (mTBI), sleep disorders, substance use, anger control problems, and depression via self-administered questionnaire and diagnostic interview.

Data analysis:

- We classified participants based on their PTSD status from the EMR and SCID. We used chi-square and Kruskal-Wallis tests (as appropriate) to assess differences in the prevalence or severity of each outcome of interest by PTSD status.

Results

- Of 1064 combat-exposed veterans with available data, 577 had PTSD on the EMR and the SCID, 183 had PTSD on EMR only, 197 did not have a PTSD diagnosis according to either the EMR or the SCID and 106 had PTSD on the SCID only (this last group is not included in subsequent analyses). Similar proportions of men and women had discordant and concordant diagnoses (See Table 1).

Table 1. PTSD diagnostic status in 958 combat-exposed veterans.

	Concordant for PTSD (n=577)	PTSD on EMR only (n=184)	Concordant for no PTSD (n=197)	Total
Male	293	81	95	469
Female	284	103	102	489

- Participants were on average 37 years of age and 51% were female. Most were army Veterans and in a long-term relationship with a partner (See Table 2).
- Few differences between male and female Veterans were observed.

Table 2. Baseline characteristics of 958 combat-exposed veteran participants in study sample.

Covariate	Overall (n=958) Mean (SD) or %	Men (n=469) Mean (SD) or %	Women (n=489) Mean (SD) or %
Age	37.0 (9.9)	37.5 (10.1)	36.6 (9.7)
Female (%)	51.0	N/A	N/A
Race/ethnicity			
Black (%)	10.3	7.7	12.9
Hispanic (%)	8.4	7.7	9.0
White (%)	58.5	61.8	55.2
Other/unknown (%)	22.9	22.8	22.9
Military branch			
Army (%)	91.3	85.9	96.5
Marines (%)	8.7	14.1	3.5
Married or living with partner (%)	57.0	66.1	48.3

Results (Contd.)

- Veterans with confirmed PTSD (PTSD on both the EMR and SCID) were significantly more likely to have reported anxiety or depression compared to Veterans with PTSD based on the EMR only or no PTSD at both assessments (all P < 0.001).
- Almost 16% of the Veterans with a confirmed diagnosis had a significant suicide risk compared to 11% of those with PTSD diagnosis in medical record only and 2.5% in Veterans without PTSD diagnoses by interview or medical record (See Table 3).

Table 3. Emotional/mental disorders and psychosocial adjustment characteristics of 1,064 participants in Project VALOR by concordance between PTSD status in electronic medical record (EMR) problem list and SCID-based diagnostic interview for current PTSD.

Covariate	Concordant for PTSD (n=577)	PTSD in EMR only (n=184)	Concordant for no PTSD (n=197)	p-value
Emotional/mental disorders				
Major depressive syndrome (%)	57.7	22.8	13.2	<0.001
Panic syndrome (%)	52.3	27.2	10.2	<0.001
Other anxiety syndrome (%)	48.2	16.3	9.6	<0.001
Moderate/high suicide risk (%)	15.9	10.9	2.5	<0.001
Did you ever make a suicide attempt (%)	26.9	17.5	10.2	<0.001
Mean and SD				
AUDIT alcohol use total score (range 0-40)	7.0 (7.1)	5.2 (5.6)	4.7 (5.1)	<0.001
Dimensions of Anger Reactions (DAR-5) score (range 0-20)	11.6 (5.2)	7.6 (5.0)	5.8 (4.8)	<0.001
Jenkins sleep disturbance index (range 0-5)	3.8 (1.1)	2.8 (1.4)	2.2 (1.5)	<0.001
Psychosocial adjustment characteristics				
Treatment seeking for emotional problems (%)	95.7	91.3	57.9	<0.001
Mean and SD				
Family distress (range 1-7)	3.9 (2.1)	2.8 (2.0)	2.5 (1.9)	<0.001
DRRI postwar social support total score (range 15-75)	45.9 (11.0)	52.8 (10.1)	54.3 (12.8)	<0.001
IPF grand mean score (range 1-7)	3.9 (0.9)	3.1 (0.9)	2.8 (0.8)	<0.001

Discussion and Recommendations

- Veterans with clinically confirmed PTSD are at significantly higher risk of psychosocial comorbidities and related sequelae, including suicidality, when compared to Veterans with suspected/transient PTSD or no history of recent PTSD.
- Similar increased risk of emotional/mental disorders and psychosocial issues were found for both genders.

Implications/Future Directions

- Our results suggest that confirmation of medical record-based diagnoses is needed in studies of PTSD.
- These results highlight the importance of clinically confirming PTSD diagnoses and providing treatment and support for Veterans with confirmed PTSD.
- In future analyses, we plan to examine predictors of discordance between the medical record-based and SCID-based diagnoses.

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Problem Drinking Moderates the Effect of Social Support on PTSD and Suicide Risk

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Prior research suggests that social support may be a protective factor for suicidality and PTSD among Veterans. Conversely, there is strong evidence that high alcohol use is associated with greater risk of suicidality and PTSD. However, no studies to date have looked at how the presence of high alcohol use might mitigate the protective impact of social support on suicide and PTSD. The present study examined whether social support would be less protective for suicide risk and PTSD among Veterans reporting problem drinking relative to Veterans without problem drinking. Participants were 774 men and women OEF/OIF Veterans who participated in a national registry study (Project VALOR). Participants were assessed for PTSD and suicidality over the phone by a doctoral-level clinician and completed measures of postdeployment social support and alcohol use. Regression analyses indicated that problem drinking significantly moderated the relationship between social support and PTSD symptoms *(β =.09, t =2.86, p <.01)* and between social support and suicide risk *(β =.075, t =2.21, p <.05)*. The pattern of results suggests that problematic drinking diminishes the protective effects of social support on elevated suicide risk and PTSD symptoms.

Learning Objectives

1. To increase awareness of factors contributing to suicidality and PTSD among OEF/OIF Veterans
2. To examine the interactions between risk and resilience factors in predicting suicidality and PTSD.
3. To recommend ways to tailor PTSD and suicide interventions for Veterans that account for variable levels of alcohol use and social support.

Anger Mediates the Relationship between Combat Exposure and Functioning

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Prior research suggests that Veterans who experienced military-related traumatic events (i.e., combat exposure) tended to report higher rates of anger (Jakupcak et al., 2007; Elbogen et al., 2010), and more problems functioning (Dohrenwend et al., 2006; Hoge et al., 2006). However, few studies have looked specifically at the relationship between anger, combat exposure, and functional impairment among Veterans with a history of trauma. The current study explored the role of anger as a potential mediator in the relationship between combat exposure and functional impairment. Participants were 813 US Army and Marine OEF/OIF Veterans who completed online questionnaires and a brief telephone interview. Questionnaires included the combat exposure module of the Deployment Risk and Resilience Inventory (DRRI), and the Dimensions of Anger Reactions, revised short form (DAR-5). The Inventory of Psychosocial Functioning (IPF) was used to assess functional impairment. Significant correlations were observed between anger and all domains of functioning (range r=.42 to r=.54), between combat exposure and anger (r = .31), and between combat exposure and functioning (range r=.11 to r=.19). Bootstrapping analyses demonstrated that anger mediated the relationship between combat exposure and functioning. These findings suggest that anger problems might be another mechanism through which combat exposure causes functional impairment.

Learning Objectives

1. To elucidate the relationship between combat exposure and functional impairment following military experiences.
2. To assess the potential role anger as a mediator between combat exposure and functional impairment.
3. To highlight the significance of clinical interventions that account for anger among combat-exposed Veterans with problems functioning

PTSD Symptoms and Parental Functioning among Male and Female OEF/OIF Veterans

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Despite the growing number of studies indicating interpersonal impairments among combat veterans with PTSD, little is known about the impact of PTSD on parenting among Veterans. Studies of earlier cohorts indicate that PTSD symptoms differentially affect parenting among male and female Veterans but they were limited in that 1) men and women were not assessed in the same study, 2) studies used small samples, 3) participants were assessed many years after their military experiences and 4) analyses did not uniformly control for confounding variables. This study addressed these limitations of earlier studies with a sample of Veterans of the wars in Iraq and Afghanistan. Participants were 442 OEF/OIF Veteran parents (50% women) recruited as part of a national registry study. Regression analyses indicate that the avoidance/numbing symptoms of PTSD were most significantly associated with parental functioning ($p < .001$) for both men and women, even after controlling for the presence of other psychopathology. Results also showed that different PTSD avoidance and numbing symptoms were more strongly related to parenting difficulties for men and women, suggesting different mechanisms by which PTSD disrupts parental functioning for men and women Veterans.

1. To summarize previous research on PTSD-related interpersonal impairments among Veterans and to identify gaps in the literature.

2. To consider the implications of results and to discuss potential reasons for differential findings between men and women Veterans.

3. To apply findings to clinical interventions designed to address impairments in parenting among men and women Veterans with PTSD.

Deployment and Post-Deployment Experiences in Iraq-deployed Soldiers: Comparison of Soldiers Deployed during the Iraq Invasion, Insurgency, and Surge

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Background: The Iraq War was an extensive and expansive campaign marked by phases reflecting different degrees of combat intensity, varied combatant tactics, and evolving counter strategies employed by the US military. While many studies have examined deployment experiences of OIF Veterans (Ramchand 2010, Baker 2009, Fontana 2008), there is a dearth of research comparing the deployment and post-deployment experiences of Veterans deployed during different phases of the Iraq War. Generally, combat and post-battle experiences as well as post-deployment social support have shown strong associations with PTSD (Vasterling 2010) and functional impairment (Maguen 2009). The aim of the present analysis is to compare deployment and post-deployment experiences as well as PTSD and functional impairment endorsed by soldiers and marines deployed during three distinct phases of the Iraq war: the initial invasion and occupation of Iraq (2002-2004), the insurgency (2004-2007), and the surge (2007-2011) **Methods:** Data from a sample of 548 OIF/OEF veterans (321 female) were used for this analysis. Participants completed an online survey, which included the combat experiences, post-battle experiences, and post-deployment social support scales of the Deployment Risk and Resilience Inventory (DRRI)and the Inventory of Psychosocial Functioning (IPF). Participants also completed a telephone interview, which included a clinician-administered SCID module for PTSD. **Results:** Soldiers deployed during the initial invasion and occupation and during the insurgency reported significantly higher combat experiences ($p<0.001$) and post-battle experiences ($p<0.01$) than soldiers deployed during or after the surge as well as higher levels of impairment in work ($p<0.05$), education ($p<0.05$), and day-to-day functioning ($p<0.01$). Post-deployment social support did not differ between groups; however among participants with a current diagnosis of PTSD, social support was significantly lower for those deployed during the last phase than those deployed during the first two ($p<.01$). Current diagnoses of PTSD did not differ between groups ($\chi^2=4.78$, $p=0.09$); however PTSD severity was significantly higher for those deployed during the first two phases ($p<0.01$). **Conclusions:** Results highlighted the heterogeneous nature of the Iraq conflict and the varied impact it has had on Veterans. Consistent with military and civilian reports, the invasion and insurgency phases were characterized by more frequent and intense combat, a factor which could contribute to greater PTSD symptom severity and functional impairment for Veterans of those deployments. While the overall experience of post-deployment social support did not differ between groups, results show differential support for those with PTSD deployed in the last phase of the war.