Award Number: W81XWH-12-1-0576

TITLE: A Randomized, Controlled Trial of Meditation Compared to Exposure Therapy and Education Control on PTSD in Veterans

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REPORT DATE: October 2015

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
October 2015	Annual	30Sep2014 - 29Sep2015

4. TITLE AND SUBTITLE

A Randomized, Controlled Trial of Meditation Compared to Exposure Therapy and Education Control on PTSD in Veterans

5a. CONTRACT NUMBER
W81XWH-12-1-0576

5b.Grant Number

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S) : Initiating Principal Investigator: Sanford Nidich, Ed.D., Maharishi University of Management
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5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

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Veterans Medical Research Foundation, San Diego, CA 92161

8. PERFORMING ORGANIZATION REPORT

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

This single-blinded, RCT will: 1) evaluate effects of Transcendental Meditation (TM) vs. Prolonged Exposure (PE) and PTSD health education control (EC), using the Clinician Administered PTSD Scale (CAPS) (primary outcome); 2) evaluate effects of TM vs. controls on PTSD symptoms (PCL-M), depressive symptoms and other psychological distress measures, quality of life, and physiological/biochemical stress markers; and 3) evaluate treatment compliance. The study will enroll 210 subjects (70 per group). The VA San Diego is the field site with testing conducted at 0 and 3 months The research will provide data on the feasibility and efficacy of TM as an alternative therapy for PTSD. Our collaborative group (Maharishi University of Management Research Institute, VA San Diego Healthcare System, University of California at San Diego) has made excellent progress. We are currently on target for randomization, with 157 subjects randomized (target of 162) and have good treatment compliance, with over 70% treatment sessions attended. Post-testing compliance is greater than 80%.

15. SUBJECT TERMS
PTSD, Meditation, Prolonged Exposure, Veterans

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
					USAMRMC
a. REPORT	b. ABSTRACT	c. THIS PAGE			19b. TELEPHONE NUMBER *(include area code)*
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INTRODUCTION

Posttraumatic stress disorder (PTSD) is a common and debilitating condition that affects up to 20% of all Veterans. PTSD is often a chronic problem for Veterans, affecting reintegration into society, family and marital relationships, sleep, employment stability, substance abuse rates, and risk for depression and suicide. Although standard treatments exist to treat PTSD, research shows that up to 50% of patients continue to have elevated symptoms. This suggests a need for developing and evaluating additional, alternative treatment options.

We are currently engaged in a collaborative research project that includes Maharishi University of Management Research Institute, VA San Diego Healthcare System, and the University of California at San Diego. This single-blinded, randomized controlled trial (RCT) will: 1) evaluate effects of Transcendental Meditation (TM) vs. Prolonged Exposure (PE) and a PTSD health education control (EC), using the Clinician Administered PTSD Scale (CAPS), as the primary outcome; 2) evaluate effects of TM vs. controls on PTSD symptoms (PCL-M), depressive symptoms and other psychological distress measures, quality of life, and physiological/ biochemical stress markers; and 3) evaluate treatment compliance. The study will enroll 210 subjects (70 per group) over four years. The intervention period for each arm is three months, with testing conducted at 0 and 3 months.

The research will provide important data on the feasibility and efficacy of the Transcendental Meditation program as an effective alternative therapy for PTSD. The results will serve to inform policy decisions on the study and application of this standardized and validated stress reduction program in Veteran populations.

BODY

The following tasks describe the actual Year 3 (Oct 1, 2014 thru Sept 30, 2015) achievements/milestones compared to the tasks originally outlined in the Statement of Work (SOW) (July, 2012, final-revised)

Task 1: Regulatory Review and Approval Processes (Completed)
Final DoD ORP approval was given for our staff to begin recruitment on May 31, 2013. This approval came after we made several human subjects-related adjustments based upon DoD ORP requests. The most significant of these requests involved receiving approval from the VASDHS IRB to do consenting over the phone prior to conducting initial phone screens. All subjects complete written informed consent, approved by the local IRB and DoD ORP, prior to baseline testing.

Task 2: Hiring and Training of Staff (Completed)
We completed the hiring and training of our three full-time staff coordinators during Year 1. After final approval from the DoD ORP, we were also able to officially hire the Prolonged Exposure study therapist – allowing us to have all of our study therapists in place.

Task 3: Development of Case Report Forms and Operation and Treatment Manuals (Completed)
We completed Case Report Forms and Operation and Treatment Manuals prior to beginning the study June 2013.

Task 4: Recruitment of Study Subjects (Consistent with Target Number)
After final DOD approval on May 31, 2013, we began recruitment of subjects. Since June 2013, we randomized (enrolled) 157 subjects, with a target goal of 162 (5.8 per month). To date, there have been approximately 406 phone screens with 361 potentially eligible, 216 consented (written consents) and completing baseline testing one, 157 completing baseline visit 2 and randomized. The number of subjects randomized over each quarter has been fairly consistent (see Supporting Data below).

Recruitment methods have included the use of posters, flyers, presentations to Veterans groups and community centers, placing information in VA and Veterans newsletters and presenting the study to VA healthcare providers for referrals. Weekly teleconference meetings are held on an ongoing basis with all staff and investigators, led by the initiating and partnering PIs.

Task 5: Testing of Subjects – baseline and 3-month post-testing (on target)
Baseline testing began June 2013. Through September 2015, 157 subjects, meeting eligibility criteria and completing baseline testing, were randomized (18% female; mean age= 48). Three-month posttesting compliance is 82% (136 eligible for 3-month posttesting as of September 30, 2015 with 112 actually posttested).

Task 6: Delivery of Treatments (on target)
Through the end of September, 2015, 157 subjects have been randomized which meets our target goal. Of these, over 90% of the randomized subjects have gotten into treatment or were scheduled for their first treatment session. Treatment sessions are held at the VASDHS for all treatment arms and last approximately 60-75 minutes. Sessions are provided by trained instructors in each of the treatment arms: Transcendental Meditation, Prolonged Exposure, and PTSD Health Education, and are supervised by the research team for quality control.

No study-related adverse events have been reported to date.

Task 7: Treatment Compliance (on target)
Overall approximately 72% of the treatment sessions have been attended. Treatment sessions are held at the VASDHS for all treatment arms and last approximately 60-75 minutes. Sessions are provided by trained instructors in each of the treatment arms: Transcendental Meditation, Prolonged Exposure, and PTSD Health Education, and are supervised by the research team for quality control. For home practice, over 70% of subjects have indicated compliance with their home practice program (at least once per day). These figures satisfy the 70% milestones for treatment compliance.

Task 8: Data Entry and Management (on target)
The Access database for data entry at VASDHS was developed and completed by study statistician, Maxwell Rainforth, and pilot tested by the VA data manager in Spring 2013. Data entered and stored is under strict quality control procedures. 100% of the data received thus far has been entered. This meets our milestone established of collected data being entered.

Task 9: Data Analysis (on target)
Baseline data for the March, 2015 DSMB report is shown in the Appendices section. The data is presented by treatment arm in a blinded manner. Posttest data is not being analyzed or presented in any form per the instructions of our Data Safety and Monitoring Board. Data analysis procedures are on target.

Task 10: Overall Project Management (on target)
The initiating PI, Dr. Nidich at MUMRI, and partnering PI, Dr Rutledge at VASDHS, and their teams along with Dr. Mills at UC San Diego have been engaged in weekly or bi-monthly teleconference calls since the first month of the award, October 2012. In addition, Dr. Nidich and Dr. Rutledge frequently communicate each week on study management issues by phone and email. Other group members and staff have also frequently communicated by email and phone on a regular basis on study implementation issues, supervised by Drs. Nidich and Rutledge. Group conference calls with PIs, investigators, and staff will be ongoing throughout the trial.

Dr. Nidich from MUMRI made a site visit in March, 2015 to VASDHS and had several important meetings with Dr. Rutledge, Dr. Mills, study staff, and treatment providers.

Drs. Nidich, Rutledge, Mills, Rainforth attended all meetings of the Data Safety and Monitoring Board (DSMB), chaired by the study's medical monitor, Dr. Charles Elder, M.D. Other members of the DSMB include Dr. Kerri Boutelle, psychologist, Dr. Arpi Minassian, psychologist, and Dr. Loki Natarajan, biostatistician.

Task 11: Quarterly and Annual Reports
This document represents the study's third Annual report. All previous quarterly and annual reports to the DoD were written, submitted and received in a timely manner.

KEY ACCOMPLISHMENTS

- Study recruitment began in June 2013 immediately following DOD ORP human subjects approval.
- All study staff and treatment therapists were hired and trained as of the end of May 2013.
- We assembled a four-member Data Safety and Monitoring Board (DSMB) on July 18, 2013. The DSMB membership is chaired by Dr. Charles Elder, M.D., the study's medical monitor, and includes two clinical psychologists, who are active researchers and faculty at the UC San Diego Dept of Psychiatry and a biostatistician with the Dept. of Family and Preventive Medicine at UC San

Diego. The DSMB met twice during the first year of the study and annually thereafter. The DSMB last met March, 2015 to review the progress of the study.

- As of Sept 30, 2015, 157 subjects have been recruited (162 target). Posttest compliance is >80% and intervention meeting attendance and home practice compliance is >70%.
- Dr. Nidich will be presenting study results to the DoD In-Person Meeting at Ft. Detrick, MD in September 2016.

REPORTABLE OUTCOMES

Due to the study being blinded, there are no reportable outcomes. There were no study publications or conference presentations during this past year. It is expected that there will be several publications and conferences presentations, based on the final study data in Fall, 2015 and in 2016.

CONCLUSION

This report summarized the study progress through Year 3. We are meeting all of our Statement of Work targets for the study. Study recruitment began on June 2013 immediately following DoD ORP human subjects approval. All study staff and treatment therapists have been hired and trained, operation manuals completed, and baseline testing and treatment sessions started. As of the end of September 2015, 157 subjects have been randomized, which meets our target goals for the study. The March, 2015 Data Safety and Monitoring Board (DSMB) report is included in this annual report. There have been no “substantive” amendments the study protocol. There were no study-related adverse events to date.

SUPPORTING DATA

Table 1 Overall Enrollment

Quarterly Period		# Randomized	Cumulative No.	Cum. Target
From	To			
6/1/13	9/30/13	24	24	23
10/1/13	12/31/13	17	41	41
1/1/14	3/31/14	19	60	58
4/1/13	6/30/14	18	78	75
7/1/14	9/30/14	17	95	93
10/1/14	12/31/14	16	111	110
1/1/15	3/31/15	16	127	127
4/1/15	6/30/15	14	141	144
7/1/15	9/30/15	16	157	162

APPENDICES

1) DSMB Report to Data & Safety Monitoring Board meeting, Thursday, March 19, 2015 9:00 am (PST)

Principal Investigators: Sanford Nidich, Ed.D., Thomas Rutledge, Ph.D.

Field Site: VA Hospital, San Diego.
Coordinating Center: M.U.M. Research Institute, Maharishi Vedic City, IA

Starting and ending dates: 9/30/2012—9/29/2016

Research Design and Methods: (proposed sample size N=210) randomized controlled clinical trial over a 3 month intervention period, with 3 arms—Transcendental Meditation (TM) versus Prolonged Exposure (PE) versus Health Education. Comparison of TM versus PE will be based on non-inferiority design. Subject inclusion criteria: Military veteran over age of 18 with current PTSD diagnosis due to service-related trauma and CAPS score ≥45. Exclusion criteria: Service related trauma within last 3 months, history of schizophrenia, bipolar disorder, dementia, moderate or severe cognitive impairment, current intent to physically harm self or others.

Primary Outcome: Clinician Administered PTSD Scale for DSM-IV (CAPS)

Secondary Outcomes: PTSD Checklist—Military Version (PCL-M), Patient Health Questionnaire (PHQ-9), Profile of Mood States (POMS 2 adult version), Quality of Life & Enjoyment Satisfaction Scale. Social Support Scale

General narrative description of study progress: On 5/31/2013 notification was received that the study protocol had been reviewed and approved by the US Army Medical Research and Materiel Command (USAMRMC), Office of Research Protections (ORP), Human Research Protection Office (HRPO) and found to comply with applicable DOD, US Army, and USAMRMC human subjects protection requirements. Recruitment began on 6/10/2013. Randomization is stratified by gender and number of years since last active duty (≥15 or <15); the latter stratification variable was added on 3/18/2014. As of 2/28/2015, 306 subjects have been screened, 172 have been consented, and 122 have been randomized to treatment.

Table 1.1 Overall Enrollment

Quarterly Period		No. of Subjects Randomized
From	To	
6/1/2013	9/30/2013	24
10/1/2013	12/31/2013	17
1/1/2014	3/31/2014	19
4/1/2013	6/30/2014	18
7/1/2014	9/30/2014	17
10/1/2013	12/31/2013	16
1/1/2014	2/28/2014	11
Total:		122

Table 1.2

Recruitment Progress*

Screened for Eligibility	306
Eligible	204
Eligible and willing to participate	204
Consented	172
Randomized	122

* Data as of February 28, 2015

Table 1.3

Completeness of Data Collection and Entry*

	Number of Subject Visits			Reasons for Data Not Received	
Time Point	Expected	Received	Data Not Received	Dropped Out	Delayed Completion Of Testing
Baseline	122	122	0	0	0
12 Weeks	104	86	18	18	0

* Data as of February 28, 2015; currently at 82.7% post-testing retention rate

Table 1.4

Post-testing Rates by Treatment Group

Treatment Group	Number Posttested*	Number Due for Post-testing†	Post-testing Rate
X	32	36	88.9%
Y	27	34	79.4%
Z	27	34	79.4%
All Groups	86	104	82.7%

* Number of subjects tested on the primary outcome as of February 28, 2015.
† Subjects are due for post-testing 90 days after randomization.

Table 2.1

Sample Characteristics at Baseline: Demographics and Medical History by Intervention Group

Variable	Group			P value
	X	Y	Z	
# Participants randomized	39	39	36	
Gender, % male	84.6%	84.6%	83.3%	0.985
Age, yrs				
Mean (std. dev.)	49.4 (16.4)	48.7 (12.9)	47.9 (16.2)	0.911
Median	52.0	50.0	46.5	
(Min, Max)	(23.0,82.0)	(24.0,70.0)	(25.0,85.0)	
Married / domestic partnership, %	51.3%	56.4%	41.7%	0.435
Education				0.704
Some high school	0.0%	2.6%	0.0%	
High school graduate	15.4%	17.9%	19.4%	
Post secondary	84.6%	79.5%	80.6%	
Race				0.473
African American / African descent	30.8%	28.2%	22.2%	
Asian American / Asian descent	10.3%	2.6%	2.8%	
Caucasian	48.7%	64.1%	66.7%	
Native American	2.6%	0.0%	5.6%	
Other	7.7%	5.1%	2.8%	
Ethnicity, % Hispanic	25.6%	10.3%	38.9%	0.016

Based on data received and entered up through January 31, 2015.
Chi-Square tests were used for comparisons on categorical variables. ANOVA was used for continuous variables.

Table 2.1 (continued)

Sample Characteristics at Baseline: Demographics and Medical History by Intervention Group

Variable	Group			P value
	X	Y	Z	
Income				0.495
< $10,000	20.5%	17.9%	11.1%	
$10,000 - $24,999	25.6%	33.3%	47.2%	
$25,000 - $49,999	28.2%	20.5%	22.2%	
$50,000 - $99,999	23.1%	17.9%	16.7%	
> $100,000	2.6%	10.3%	2.8%	
Accommodation				0.128
Own home	35.9%	17.9%	22.2%	
Rent	35.9%	56.4%	58.3%	
Living with friends / family	17.9%	5.1%	2.8%	
Hotel, lodging house, or rooming	0.0%	5.1%	8.3%	
Community shelter	7.7%	12.8%	5.6%	
Homeless (no address)	2.6%	2.6%	2.8%	
Service branch				0.739
Army	33.3%	38.5%	37.1%	
Marines	38.5%	23.1%	37.1%	
Air Force	7.7%	7.7%	2.9%	
Navy	20.5%	28.2%	22.9%	
Other	0.0%	2.6%	0.0%	
Combat duty, %	43.6%	56.4%	61.1%	0.285
Years of active duty				
Mean (std. dev.)	9.3 (8.6)	8.2 (6.9)	7.7 (6.7)	0.628
Median	6.0	5.0	5.0	
(Min, Max)	(1.0,33.0)	(0.5,26.0)	(1.0,28.0)	

Based on data received and entered up through January 31, 2015.
Chi-Square tests were used for comparisons on categorical variables. ANOVA was used for continuous variables.

Table 2.1 (continued)

Sample Characteristics at Baseline: Demographics and Medical History by Intervention Group

Variable	Group			P value
	X	Y	Z	
Number of years since discharged				
Mean (std. dev.)	20.6 (16.7)	21.4 (15.6)	21.1 (17.6)	0.976
Median	17.5	20.0	15.0	
(Min, Max)	(1.0,59.0)	(0.0,46.0)	(0.0,67.0)	
Last served				0.600
Within last 5 years	28.9%	17.9%	16.7%	
5-10 years ago	15.8%	17.9%	25.0%	
More than 10 years ago	55.3%	64.1%	58.3%	
Service-related condition, %				
Mean (std. dev.)	27.9 (35.3)	29.7 (35.6)	41.7 (34.8)	0.222
Median	0.0	0.0	35.0	
(Min, Max)	(0.0,100.0)	(0.0,100.0)	(0.0,100.0)	
Schizophrenia, %	7.7%	0.0%	8.3%	0.191
Bipolar disorder, %	7.7%	10.3%	13.9%	0.681
Substance use disorder, %	30.8%	43.6%	41.7%	0.458
Major depressive disorder, %	64.1%	59.0%	61.1%	0.897
Anxiety disorder, %	28.2%	44.7%	38.9%	0.314
Suicidal ideation, %	12.8%	12.8%	13.9%	0.988
Cognitive impairment, %	15.4%	17.9%	11.1%	0.705
Traumatic brain injury, %	17.9%	20.5%	19.4%	0.959
Combat Exposure Scale (7 items, 0-41)				
Mean (std. dev.)	15.9 (12.6)	17.8 (12.8)	17.1 (12.5)	0.800
Median	16.0	18.0	18.5	
(Min, Max)	(0.0,41.0)	(0.0,41.0)	(0.0,41.0)	

Based on data received and entered up through January 31, 2015.
Chi-Square tests were used for comparisons on categorical variables. ANOVA was used for continuous variables.

Table 2.1 (continued)

Sample Characteristics at Baseline: Demographics and Medical History by Intervention Group

Variable	Group			P value
	X	Y	Z	
Life Events Checklist (0-17, 17 items)				
Mean (std. dev.)	8.0 (3.6)	8.5 (3.9)	8.5 (2.9)	0.761
Median	8.0	9.0	8.0	
(Min, Max)	(0.0,15.0)	(0.0,14.0)	(2.0,15.0)	
Systolic blood pressure (mm Hg)				
Mean (std. dev.)	128.8 (13.9)	128.8 (13.9)	134.9 (16.8)	0.134
Median	126.5	126.0	130.5	
(Min, Max)	(103.5,167.0)	(97.5,173.5)	(89.5,176.5)	
Diastolic blood pressure (mm Hg)				
Mean (std. dev.)	78.8 (9.6)	81.8 (10.2)	82.3 (9.5)	0.255
Median	80.0	81.0	82.5	
(Min, Max)	(50.0,98.5)	(53.5,103.0)	(58.0,99.5)	
Weight (kg)				
Mean (std. dev.)	91.1 (18.3)	94.9 (16.2)	93.3 (17.0)	0.618
Median	89.8	97.6	92.4	
(Min, Max)	(52.3,130.5)	(67.0,127.9)	(57.8,132.3)	
Body mass index				
Mean (std. dev.)	30.7 (5.4)	30.8 (5.8)	30.6 (5.4)	0.982
Median	32.0	29.7	31.2	
(Min, Max)	(18.0, 43.7)	(23.2, 50.1)	(19.8, 44.6)	

Based on data received and entered up through January 31, 2015.
Chi-Square tests were used for comparisons on categorical variables. ANOVA was used for continuous variables.

Table 2.2

Comparison of Intervention Groups on Primary and Secondary Outcomes at Baseline

Variable †	Group			P value
	X	Y	Z	
CAPS total score (17: 0-136)	79.7 (19.2)	81.1 (18.3)	80.6 (19.3)	0.950
PCL-M score (17: 17-85)	60.5 (11.3)	61.3 (13.5)	60.9 (12.0)	0.964
PHQ-9 score (9: 0-27)	16.1 (5.6)	17.7 (6.0)	17.5 (4.8)	0.377
Profile of Mood States				
Tension/Anxiety (10: 0-40)	23.7 (7.4)	24.3 (8.6)	24.6 (7.5)	0.886
Depression/Dejection (13: 0-52)	22.6 (11.4)	23.7 (12.7)	24.0 (10.2)	0.869
Anger/Hostility (11: 0-44))	19.8 (8.9)	20.2 (10.1)	20.5 (10.7)	0.957
Vigor/Activity(9: 0-36)	13.3 (5.1)	14.2 (6.9)	13.1 (6.0)	0.724
Fatigue/Inertia (6: 0-24)	14.8 (5.7)	14.0 (5.3)	15.4 (5.1)	0.531
Confusion/Bewilderment (10: 0-40)	19.3 (5.5)	19.0 (5.7)	19.2 (5.9)	0.971
POMS Total Score (59: 0-236)				
Alcohol intake (drinks/week)	1.2 (2.3)	2.2 (6.7)	3.5 (6.7)	0.230
Cigarettes (no./day)	1.2 (4.2)	2.1 (4.5)	3.3 (6.8)	0.236
Satisfaction with Social Support (6: 0-6)	26.1 (8.4)	27.1 (9.5)	25.3 (9.0)	0.699
Quality of Life & Enjoyment Satisfaction Scale (14: 0-100)	43.4 (13.5)	41.0 (20.3)	42.4 (13.1)	0.799

† The measurement scale for psychometric variable is indicated in parentheses: (# items: min. score-max. score)

Based on data received and entered up through January 31, 2015.

All data are reported as means (SD). P-values for comparisons of groups are based on ANOVA.

Table 2.3

Comparison of Intervention Groups on PTSD Medication Status at Baseline

Type of Medication	Group			P value
	X	Y	Z	
Anti-depressants, %	28.2%	53.8%	33.3%	0.049
Anti-convulsants, %	7.7%	10.3%	11.1%	0.871
Anxiolytics, %	61.5%	66.7%	61.1%	0.854
Mood stabilizers, %	17.9%	35.9%	19.4%	0.127
Anti-psychotics, %	10.3%	30.8%	8.3%	0.014
Sleep medications, %	56.4%	59.0%	44.4%	0.409
Any of the above, %	66.7%	82.1%	72.2%	0.295

Based on data received and entered up through January 31, 2015.
P-values for comparisons of groups are based on chi-square tests.

Table 2.4
Comparison of Intervention Groups on Biochemical Measures at Baseline

Variable	X	Y	Z	P value
Pro-inflammatory 2 Panel				
IL-1 beta (pg/mL)				
Mean (std. dev.)	0.3 (0.1)	0.2 (0.2)	0.2 (0.1)	0.956
Median	0.2	0.2	0.2	
(Min, Max)	(0.0,0.6)	(0.0,1.0)	(0.0,0.7)	
n	20	33	22	
IL-6 (pg/mL)				
Mean (std. dev.)	2.0 (0.7)	1.7 (0.9)	2.0 (0.8)	0.276
Median	2.0	1.5	1.8	
(Min, Max)	(1.0,4.1)	(0.6,4.8)	(1.0,4.2)	
n	20	33	22	
IL-8 (pg/mL)				
Mean (std. dev.)	9.8 (7.2)	11.1 (6.0)	14.3 (9.9)	0.141
Median	7.2	9.6	11.4	
(Min, Max)	(4.6,35.2)	(4.8,30.2)	(3.8,47.3)	
n	20	33	22	
TNF-alpha (pg/mL)				
Mean (std. dev.)	2.1 (0.9)	2.1 (0.7)	2.2 (1.1)	0.877
Median	1.9	2.1	1.8	

Variable	X	Y	Z	P value
(Min, Max)	(1.2,4.4)	(1.3,4.2)	(1.1,5.9)	
n	20	33	22	

Based on data received and entered up through January 31, 2015.
P-values for comparisons of groups are based on ANOVA.

Table 2.4 (continued)

Variable	X	Y	Z	P value
Urinary Catecholamines				
ADR, daytime (ng/mL)				
Mean (std. dev.)	7.0 (4.1)	3.9 (2.8)	10.0 (7.2)	0.002
Median	5.8	3.0	7.4	
(Min, Max)	(3.7,17.6)	(0.2,12.9)	(2.6,22.9)	
n	11	25	11	
ADR, nighttime (ng/mL)				
Mean (std. dev.)	5.3 (2.7)	2.6 (4.6)	7.3 (10.0)	0.093
Median	3.9	0.9	3.2	
(Min, Max)	(2.1,9.7)	(0.1,21.4)	(1.2,34.2)	
n	11	25	11	
NAD, daytime (ng/mL)				
Mean (std. dev.)	45.1 (30.0)	26.5 (21.5)	66.7 (39.5)	0.001
Median	34.0	28.9	55.7	
(Min, Max)	(18.4,118.4)	(1.9,74.8)	(14.1,146.5)	
n	11	25	11	
NAD, nighttime (ng/mL)				
Mean (std. dev.)	42.9 (21.9)	28.8 (28.6)	52.3 (43.4)	0.108
Median	46.7	25.5	36.0	
(Min, Max)	(11.8,72.9)	(0.5,124.3)	(4.2,150.4)	
n	11	25	11	
Urinary Cortisol				
Cortisol, daytime (ng/mL)				
Mean (std. dev.)	155.7 (227.0)	56.7 (47.7)	75.5 (54.1)	0.056
Median	88.3	28.1	86.7	
(Min, Max)	(20.4,914.8)	(1.6,155.7)	(8.2,200.4)	
n	15	25	15	

Based on data received and entered up through January 31, 2015; P-values for comparisons of groups are based on ANOVA.

Table 2.4 (continued)

Variable	X	Y	Z	P value
Cortisol, nighttime (ng/mL)				
Mean (std. dev.)	199.1 (357.8)	39.3 (38.1)	52.3 (34.4)	0.043
Median	59.4	29.1	49.2	
(Min, Max)	(6.4,1240.3)	(4.8,149.7)	(15.6,126.8)	
n	16	24	12	
VASC-II Assay				
CRP (mg/L)				
Mean (std. dev.)	7.9 (10.0)	6.1 (9.7)	12.5 (28.3)	0.407
Median	5.3	2.4	3.8	
(Min, Max)	(0.4,43.0)	(0.4,48.8)	(0.4,131.5)	
n	20	33	22	
SAA (ng/mL)				
Mean (std. dev.)	7680.9 (10646.0)	14402.8 (43786.5)	7735.6 (19164.1)	0.660
Median	3003.6	2237.1	2175.1	
(Min, Max)	(1020.4,45646.2)	(411.8,208800.5)	(519.8,90303.6)	
n	20	33	22	
sICAM-1 (ng/mL)				
Mean (std. dev.)	571.8 (326.3)	514.9 (223.5)	585.7 (336.2)	0.627
Median	497.6	473.6	503.0	
(Min, Max)	(215.0,1496.3)	(219.9,1376.1)	(265.2,1396.4)	
n	20	33	22	
sVCAM-1 (ng/mL)				
Mean (std. dev.)	642.9 (232.2)	591.1 (269.8)	643.8 (355.7)	0.740
Median	573.5	538.0	513.4	
(Min, Max)	(341.1,1205.8)	(272.3,1881.5)	(305.2,1807.3)	
n	20	33	22	

Based on data received and entered up through January 31, 2015.
P-values for comparisons of groups are based on ANOVA.

Table 3.1

Compliance: Attendance at Intervention Meetings*

Group	# Randomized	# Actual Meetings*	# Possible Meetings†	% Attendance
X	38	298	437	68.2%
Y	37	324	415	78.1%
Z	36	270	413	65.4%

*Based upon attendance records through January 31, 2015 for all subjects randomized through December 31, 2014.
† Number of intervention meetings scheduled between start of treatment and January 31, 2015. There are 12 intervention meetings for each treatment group.

Table 4.1.

Summary of Adverse events and Actions

Type of Event	# of Events	Study related?
Suicide/homicide attempt	1	No
Psychiatric hospitalization	3	No
New mental health diagnosis	1	No
Death	0	N/A
Non-fatal Medical event or hospitalization	7	No
ER visit	12	No
Other	3	No
Actions Indicated		
Event Rated to Study	0	N/A
Reported to IRB	0	N/A
Participant referred to treatment	0	N/A
Participant terminated from study	1	No
Other action	0	N/A

Data as of February 28, 2015

2) DSMB March 19, 2015 Minutes

Data & Safety Monitoring Board meeting
Thursday, March 19, 2015 9:00 am (PST)

Overview of study

- Overall study progress
    - Dr. Nidich attended DoD meeting in September to present study progress

- Overall monthly randomization target is on track. However, recruitment is becoming more difficult due to the following: 1) Other newly funded PTSD studies @ San Diego VA 2) Strict VA flyer posting criteria
- PI's are considering opening inclusion criteria to allow veterans with non-military related trauma to be enrolled in the study.
- Study additions: Telomerase and gene expression sub studies
  - Phase I: PBnC's shipped to Dr. Rissman to run Telomerase analysis.
  - Phase II: Currently collecting samples for Dr. Fagan for DNA and RNA analysis.
  - IRB approvals already obtained in prior fiscal year and reported to DoD in fiscal year two quarterly and annual reports
  - Funds obtained from private TM donors

Review of data and comments

- Table 1.3 & 1.4 Post-testing data completeness (baseline and posttest)
  - 82.7 % post-test attendance
  - Post-testing must be completed within 30 days of anticipated post-testing date

- Table 2.3 Comparison of Intervention Groups on PTSD Medication Status at Baseline
  - Group Y has high use of psychotropic medications though no participants in this sub group have schizophrenia. May be due to VA prescribing antipsychotic medication to PTSD patients as mood stabilizers.
  - Medications may be classified in more than one category. Further review required.
  - The team will closely monitor if differences in medication types could affect the primary outcome results.
  - How is medication use going to be reported in final paper?
  - Do we know how medications could affect primary outcome? I.e. could certain medications impact a patient engaging in the interventions? (Response to treatment)
  - Medication variable could be controlled for to analyze between group changes.

- Table 2.4 Comparison of Intervention Groups on Biochemical Measures at Baseline
  - Overall data reveals cortisol levels of this population much higher than non-psychiatric populations.
  - A few extreme outliers. Those samples will be analyzed again. Maybe excluded from final analysis
  - Urinary catecholamines levels for this population are not decreasing at night. Why? May be due to PTSD symptoms (i.e. hyperarousal). Catecholamines levels decrease at night for non-psychiatric populations.
  - Blood and urine measures relate to secondary aims of study
  - All inflammatory markers in sample high (sICAM-1 mean = ~500) in comparison to non-psychiatric sample (sICAM-1 mean = ~300). Some elevations of inflammatory markers can be due to current infections or other factors.
  - Post intervention data not reported

- Table 4.1 Adverse Events
  - No study related serious adverse events.
  - ER visits include an array of reasons. I.e. VA protocol requires patients to go to ER if blood sugar or blood pressures are below or above a certain threshold.

- Recommendations/suggestions from DSMB

- Continue monitoring medications of group X,Y and Z
- Dr. Nidich suggested expanding inclusion criteria to allow veterans with non-military related trauma to be enrolled.
  - DSMB has previously approved potential change at PIs' discretion
  - Tom and Sandy decided to wait 2 months and closely monitor recruitment and randomization. If recruitment slows significantly, this change may be implemented.

The DSMB congratulated the study team on excellent report and excellent progress to date.

Next DSMB meeting: One year from today.

Respectfully submitted,

Charles Elder MD MPH FACP
DSMB Chair
4/1/15