Cognitive Behavioral Therapy for Posttraumatic Stress Disorder in Women

A Randomized Controlled Trial

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Context The prevalence of posttraumatic stress disorder (PTSD) is elevated among women who have served in the military, but no prior study has evaluated treatment for PTSD in this population. Prior research suggests that cognitive behavioral therapy is a particularly effective treatment for PTSD.

Objective To compare prolonged exposure, a type of cognitive behavioral therapy, with present-centered therapy, a supportive intervention, for the treatment of PTSD.

Design, Setting, and Participants A randomized controlled trial of female veterans (n=277) and active-duty personnel (n=7) with PTSD recruited from 9 VA medical centers, 2 VA readjustment counseling centers, and 1 military hospital from August 2002 through October 2005.

Intervention Participants were randomly assigned to receive prolonged exposure (n=141) or present-centered therapy (n=143), delivered according to standard protocols in 10 weekly 90-minute sessions.

Main Outcome Measures Posttraumatic stress disorder symptom severity was the primary outcome. Comorbid symptoms, functioning, and quality of life were secondary outcomes. Blinded assessors collected data before and after treatment and at 3- and 6-month follow-up.

Results Women who received prolonged exposure experienced greater reduction of PTSD symptoms relative to women who received present-centered therapy (effect size, 0.27; $P=.03$). The prolonged exposure group was more likely than the present-centered therapy group to no longer meet PTSD diagnostic criteria (41.0% vs 27.8%; odds ratio, 1.80; 95% confidence interval, 1.10-2.96; $P=.01$) and achieve total remission (15.2% vs 6.9%; odds ratio, 2.43; 95% confidence interval, 1.10-5.37; $P=.01$). Effects were consistent over time in longitudinal analyses, although in cross-sectional analyses most differences occurred immediately after treatment.

Conclusions Prolonged exposure is an effective treatment for PTSD in female veterans and active-duty military personnel. It is feasible to implement prolonged exposure across a range of clinical settings.

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EVENTS SUCH AS THE TERRORIST attacks on September 11, 2001, the war in Iraq, and Hurricane Katrina have focused attention on posttraumatic stress disorder (PTSD), an anxiety disorder that can result from exposure to traumatic events like combat, rape, assault, and disaster. Posttraumatic stress disorder is characterized by symptoms of reexperiencing the traumatic event, avoiding reminders of the event or feeling emotionally numb, and hyperarousal.[1] The disorder is associated with psychiatric and physical comorbidity, reduced quality of life,[2-4] and substantial economic costs to society.[5] Lifetime prevalence in US adults is higher in women (9.7%) than in men (3.6%)[6] and is especially high among women who have served in the military.[3,7] Thus, research aimed at testing treatments for PTSD in this population is important.

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This study is the first randomized clinical trial, to our knowledge, to assess PTSD treatment for active-duty and veteran women. We focused on women because prior studies of PTSD treatment in veterans[8-11] had focused on men. (There are no studies of PTSD treatment among active-duty men.)

Practice guidelines for PTSD[12,13] recommend cognitive behavioral therapy (CBT) and selective serotonin reuptake inhibitors as primary treatments. Although most clinicians do not regularly use CBT,[14] we studied CBT because meta-analytic findings indicated that it has the largest effects.[15,16] With few exceptions,[11,17] evidence has come from well-controlled single-site trials conducted in research settings using expert therapists and no-treatment control groups.[10,18-23] Although these studies typically have allowed use of psychotropic medications and a range of psychiatric comorbidities,[10,18-23] patients are sometimes removed from analysis after randomization for nonadherence to a treatment protocol.[17,19,20,23] The generalizability of such findings to clinical practice settings needs to be examined.[16]

Our study included features of practical clinical trials[24] to enhance relevance to clinicians and policy makers: a clinically relevant comparison group rather than a no-treatment control; diverse clinical settings rather than academic research centers; relatively broad inclusion criteria that created a sample with characteristics similar to patients in clinical settings; use of non-expert therapists rather than experts working in academic research centers; allowance of cotherapies likely to be used by patients in clinical settings; and measurement across a range of outcomes to permit evaluation of treatment effects beyond target symptoms.

We studied prolonged exposure,[25] an especially effective type of CBT in previous single-site trials.[19,20,22,23] In prolonged exposure, a patient is asked to vividly recount a traumatic event repeatedly until the patient's emotional response decreases and to gradually confront safe but fear-evoking trauma reminders.[25] Prolonged exposure was compared with present-centered therapy, a supportive intervention, to control for the nonspecific benefits of therapy. A supportive, present-centered approach is clinically realistic because it is typically used by Department of Veterans Affairs (VA) clinicians[14] to address the problems of female veterans with PTSD.[26] We hypothesized that prolonged exposure would be more effective than present-centered therapy in reducing symptoms of PTSD and comorbid problems.

METHODS

An institutional review board at each site approved the protocol. Participants gave written informed consent prior to enrollment. Details of the methods have been published elsewhere.[27]

Participants

Female veterans were recruited from 9 VA medical centers (n=255), 2 VA readjustment counseling centers (n=22), and 1 military hospital; due to recruitment difficulties, only 7 active-duty personnel were enrolled at the participating military hospital. The 284 women were randomized to prolonged exposure (n=141) or present-centered therapy (n=143). Inclusion criteria were current PTSD according to *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* criteria[1]; symptom severity of 45 or higher on the Clinician-Administered PTSD Scale (CAPS)[28]; 3 or more months since experiencing trauma; a clear memory of the trauma that caused PTSD; agreement to not receive other psychotherapy for PTSD during study treatment; and, if being treated with psychoactive medication, a stable regimen (no change in drugs or dose) for at least 2 months before the trial. Psychotherapy for other problems, brief visits with an existing therapist, and self-help groups were allowed. Exclusion criteria were substance dependence not in remission for at least 3 months; current psychotic symptoms, mania, or bipolar disorder; prominent current suicidal or homicidal ideation; cognitive impairment indicated by chart diagnosis or observable cognitive difficulties; current involvement in a violent relationship (defined as more than casual contact; eg, dating or living with an abusive partner); or self-mutilation within the past 6 months.

Measures

A master's- or doctoral-level assessor, blinded to treatment assignment, performed assessments before and after treatment and at 3- and 6-month follow-up appointments. The primary outcome measure was PTSD symptom severity on the CAPS[28] structured interview. For diagnosis, we used the "1/2 rule," which stipulates that symptoms occur at least monthly with moderate intensity, and required that the overall CAPS score was 45 or higher. To aid clinical interpretation, we also assessed 3 secondary outcomes: loss of diagnosis (no longer meeting symptom criteria and CAPS severity score <45); response (decrease from baseline ≥ 10 points on CAPS score[11,28]); and total remission (CAPS score <20[28]).

The PTSD Checklist (PCL)[29] provided an additional measure of PTSD severity. Comorbid symptoms and functioning were measured using several questionnaires.[30-34] The Structured Clinical Interview for the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (SCID)[35] was used to establish exclusion diagnoses. The Life Events Checklist[28] was used to assess direct exposure to 17 types of traumatic events. Patients identified as their index trauma the event causing the most current distress. Military sexual trauma was defined, using a question from the Military Stress Inventory for Women,[26] as at least 1 sexual experience during military service that was unwanted and involved force or threat of force. Participants reported treatment satisfaction on a scale ranging from 1 (very satisfied) to 7 (very dissatisfied). Additional treatment was measured with questions about whether a participant received individual, group, or family therapy[36]; psychotropic medication[36]; and new medication or increases in current medication. Demographic information included questions

about race to facilitate sample description. Two questions with investigator-defined response options were used to determine participants' self-reported racial/ethnic categorization.

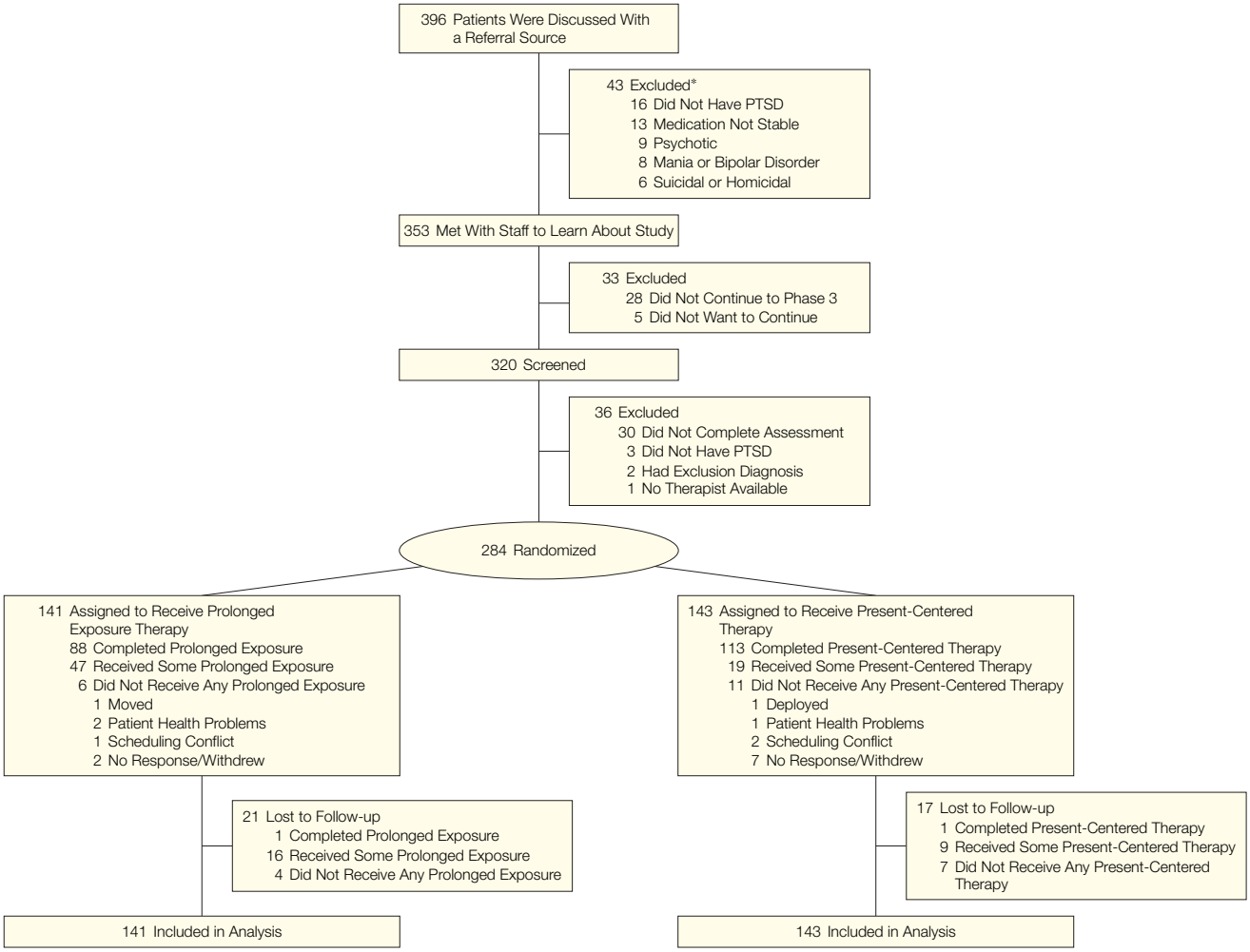
Twenty-five percent of SCIDs and 12.5% of CAPS interviews, which were audiotaped, were randomly selected for monitoring by a doctoral-level psychologist. The intraclass correlation for CAPS severity was 0.92. κ Statistics for SCID diagnoses ranged from 0.65 to 0.83.

Blinding was maintained by ensuring that assessors did not have access to study files or know the identity of patients' therapists and attended only part of the study team meetings. The site coordinator, therapist, and assessor also reminded patients to keep treatment condition confidential. If a patient began to mention information during an interview that could lead to unblinding, the assessor reminded the patient of the importance of blinding. With these procedures, unblinding occurred for 33 patients in the prolonged exposure group and 17 in the present-centered therapy group. For 11 patients (12 interviews), interviews performed subsequent to the unblinding were also rated by the assessment monitor. Discrepancies between the monitor and the assessor were small on average and did not differ between groups.

Procedure

Recruitment and follow-up occurred from August 2002 to October 2005. Recruitment involved a 3-stage process (FIGURE 1): (1) referring clinicians provided information about inclusion and exclusion criteria; (2) study staff met with potential participants to explain the study; and (3) assessors obtained consent and administered the CAPS and SCID. Participants meeting eligibility criteria then completed the assessment battery. Study staff called a com-

Figure 1. Flow of Participants Through the Trial



PTSD indicates posttraumatic stress disorder.
*May have multiple reasons.

puterized voice information system at the study coordinating center to obtain the treatment assignment for participants. The voice information system first verified entry criteria to ensure accuracy and reduce errors. Verified eligible participants were randomized within each site to prolonged exposure or present-centered therapy using permuted blocks with random block sizes of 4 or 6. All study data were stored at the study coordinating center.

Treatment

Prolonged exposure and present-centered therapy were delivered in 10 weekly 90-minute sessions according to a manual that specified the content and structure of each session. Prolonged exposure included education about common reactions to trauma; breathing retraining; prolonged (repeated) recounting (imaginal exposure) of trauma memories during sessions; homework (listening to a recording of the recounting made during the therapy session and repeated in vivo exposure to safe situations the patient avoids because of trauma-related fear); and discussion of thoughts and feelings related to exposure exercises.[25,27] Sessions 1 and 2 were introductory and included provision of the treatment rationale and education about PTSD. Imaginal exposure occurred in sessions 3 through 10.

Exposure is used to enhance emotional processing of traumatic events by helping patients face trauma memories and situations associated with them. Patients learn to distinguish memories and associated situations from the event itself. They also learn they can safely experience reminders and tolerate any resulting distress and that distress decreases over time.

The focus in prolonged exposure can be a single event or multiple events. In the latter case, the therapist establishes which memory will be the focus of imaginal exposure—typically, the most distressing memory. Successfully processing the most distressing memory usually generalizes to other memories. If another event still triggers significant distress, imaginal exposure is then used with that memory.

Sometimes confronting feared situations or memories triggers urges to escape or avoid. When this occurs, the therapist acknowledges the patient's feelings, reminding the patient that avoidance reduces anxiety in the short term but maintains fear and prevents learning that the feared situations or memories are not dangerous. The therapist also breaks exposure into a more gradual progression.

Instead of focusing on trauma, present-centered therapy focuses on current life problems as manifestations of PTSD. The aim of using present-centered therapy in this study was to provide a credible therapeutic alternative to control for nonspecific therapeutic factors[27] so that observed effects of prolonged exposure could be attributed to its specific effects beyond the benefits of good therapy. Treatment followed the same format as prolonged exposure, although the content differed. Sessions 1 and 2 were introductory and included provision of the treatment rationale and education about PTSD. Sessions 3 through 9 focused on discussing and reviewing general daily difficulties. Session 10 focused on reviewing accomplishments made during therapy and making plans for the future. No instructions for exposure or cognitive restructuring were given. Instead, therapists helped patients identify daily stresses and discussed them in a supportive, nondirective mode.

Treatment was discontinued if a participant developed problems requiring immediate attention, eg, she became actively suicidal or homicidal or failed to attend 3 consecutive therapy sessions without an acceptable reason. A reason's acceptability was determined by consensus, typically among the therapist, the supervisor, and the master therapist for the participant's condition. We attempted to have patients complete treatment within 16 weeks, although 20 weeks was allowed if the therapist's supervisor and the master therapist for the participant's condition agreed. (Master therapists were E.B.F. for prolonged exposure and M.T.S. for present-centered therapy. Master therapists developed the training plan and coordinated all training and supervision for their respective condition.)

Supervision and Fidelity Monitoring

There were 52 female therapists who were master's- or doctoral-level clinicians experienced in treating women with PTSD. Prior CBT experience was not required. Therapists treated 1 to 2 training cases before treating study participants. By design, there were 2 therapists per condition per site. Initial therapists were randomized to treatment condition.[25] Replacements were made as needed. Two therapy training centers, 1 for prolonged exposure and 1 for present-centered therapy, coordinated training and supervision. All therapy sessions were videotaped and reviewed by supervisors, who provided weekly or biweekly individual telephone supervision and conducted monthly group conference calls.

A senior clinician independent of treatment delivery rated 11.7% of the videotapes (n=269) using measures adapted from several trials of psychotherapy for PTSD.[17,18,21] A 5-point scale (1 [poor] to 5 [excellent]) was used to rate therapists' competence and adherence to essential manual elements that were (1) unique to that approach and (2) not unique to that approach. Proscribed elements, eg, encouraging a patient in present-centered therapy to expose herself to feared situations, were rated present/absent and were converted to a percentage for each tape because the number and content of elements varied across sessions and treatments. Data from the multiple tapes for each therapist were aggregated across patients into an average for that therapist on each measure.

Prolonged exposure and present-centered therapy therapists did not differ in global ratings of competence or adherence, which averaged between very good and excellent: competence (prolonged exposure=4.53; present-

centered therapy = 4.32; $P = .21$), unique and essential elements (4.48 vs 4.24, respectively; $P = .21$), and essential but not unique elements (4.65 vs 4.46, respectively; $P = .14$). The percentage of proscribed elements was low and did not differ (0.5 vs 1.5, respectively; $P = .33$).

Statistical Analysis

The study biostatistician (B.K.C.) performed all analyses. Baseline characteristics were compared using χ^2 or t tests. Primary analyses were performed on the intention-to-treat sample, using data from all randomized participants. Multiple imputation[37] (using SAS PROC MI and MI ANALYZE, SAS statistical software, version 9.1.3, SAS Institute Inc, Cary, NC) with the Markov chain Monte Carlo method[38] was used to impute missing values. Secondary analyses were performed using data from participants who completed treatment.

Outcomes were analyzed using the generalized linear mixed model (SAS PROC MIXED with iteratively reweighted likelihoods GLIMMIX macro[39]). The analysis for each outcome consisted of a longitudinal model that included therapist as a random cluster effect and baseline severity, treatment group, and site as fixed effects, with the treatment × time interaction to test the consistency of the treatment effect over time. For brevity, we report only the main effect of treatment and the treatment × time interaction. We tested 2 additional models for the CAPS, our primary outcome, to determine whether service-connected PTSD disability and military sexual trauma modified the treatment effect. Within- and between-groups effect sizes were computed as d, the standardized mean difference.[40] Cohen[40] defines effect sizes as small ($d = 0.20$), medium ($d = 0.50$), and large ($d = 0.80$). With each therapist seeing 6 patients on average and an intraclass correlation of 0.05, a sample of 284 has 85% power to detect an effect size of $d = 0.36$ for the CAPS in a longitudinal model (2-tailed $\alpha = .05$).

Longitudinal analyses were supplemented by cross-sectional comparisons. When planning the trial, we expected the maximum effect would be observed at 3 months based on studies showing that patients who received prolonged exposure continued to improve after treatment.[20,21]

RESULTS

Women randomized to prolonged exposure and present-centered therapy did not differ at baseline. TABLE 1 shows that participants were exposed to an average of almost 10 different types of trauma in their lifetime. The type most commonly identified as the worst, or index, event was sexual trauma (n = 194 [68.3%]), followed by physical assault (n = 39 [15.8%]) and war-zone exposure (n = 16 [5.6%]). On average, the index trauma had occurred many years prior to the study: 23.0 years in prolonged exposure (range, 0-58 years) and 22.8 years in present-centered therapy (range, 0-50 years) ($P = .99$). The groups did not differ in age at which the index trauma occurred: for prolonged exposure, 21.2 years (range, 3-53 years) vs for present-centered therapy, 21.7 years (range, 4-54 years) ($P = .81$).

Treatment dropout was higher in prolonged exposure (n = 53 [38%]) than in present-centered therapy (n = 30 [21%]) ($P = .002$). The average number of sessions attended was 8.0 in prolonged exposure and 9.3 in present-centered therapy ($P < .001$). Satisfaction was high and did not differ between prolonged exposure (mean, 1.96) and present-centered therapy (mean, 1.58) ($P = .11$). There were 5 serious adverse events in prolonged exposure (4 psychiatric hospitalizations and 1 suicide attempt) and 14 in present-centered therapy (2 deaths [nonsuicidal], 9 psychiatric hospitalizations, and 3 suicide attempts). No events were regarded as study-related; the suicide attempt in prolonged exposure was coded as possibly related.

Intention-to-Treat Analyses

FIGURE 2A presents observed CAPS means. TABLE 2 presents least squares means and pre-post effect sizes. CAPS scores improved from pretreatment to posttreatment in both groups. According to mixed-model analysis, CAPS scores were lower in prolonged exposure than in present-centered therapy overall ($d = 0.27$; $P = .03$). The treatment × time interaction was not significant, indicating that the treatment effect did not differ across time ($P = .37$). However, despite the absence of the interaction, scores were lower in prolonged exposure than in present-centered therapy at posttreatment ($d = 0.29$; $P = .01$) and 3-month follow-up ($d = 0.24$; $P = .047$) but not at 6-month follow-up ($d = 0.15$; $P = .21$). Neither PTSD service-connected disability nor military sexual trauma modified the overall treatment effect ($F < 1$ for both).

Most participants showed a clinically meaningful response on the CAPS (TABLE 3). According to mixed-model analysis, women in the prolonged exposure group were more likely than women in the present-centered therapy group to lose their diagnosis (41.0% vs 27.8%; odds ratio, 1.80; 95% confidence interval, 1.10-2.96; $P = .01$) and achieve total remission (15.2% vs 6.9%; odds ratio, 2.43; 95% confidence interval, 1.10-5.37; $P = .01$). The treatment × time interactions were not significant ($P = .14$-$.49$). At posttreatment, loss of diagnosis and total remission were more likely with prolonged exposure than with present-centered therapy. At 3 and 6 months, there were no differences.

Self-reported PTSD, depression, and overall mental health improved from pretreatment to posttreatment in both groups (Table 2). Anxiety decreased and quality of life improved with prolonged exposure. Findings for self-reported PTSD were similar to CAPS findings. Scores on the PCL were lower in the prolonged exposure group than in the present-centered therapy group overall ($d = 0.40$; $P < .001$), at posttreatment ($P < .001$), at 3-month follow-up ($P = .008$), and at 6-month follow-up

($P=.049$). The treatment × time interaction was not significant ($P=.18$). There were no overall effects of treatment on other outcomes. There was a treatment × time interaction for anxiety ($P<.05$). In cross-sectional comparisons, prolonged exposure led to greater improvement than present-centered therapy at posttreatment in depression ($P=.04$), anxiety ($P=.01$), and overall mental health ($P=.01$). At 3 months, prolonged exposure led to greater improvement in depression ($P=.04$).

We reran the analyses for the CAPS outcome and all secondary outcomes after omitting the 7 active-duty participants. Findings remained the same, except that the difference between prolonged exposure and present-centered therapy on the CAPS at 3 months was no longer statistically significant.

Prolonged exposure and present-centered therapy participants did not differ in the percentage who received additional psychotherapy during treatment (18.4% vs 15.4%), at 3 months (59.6% vs 52.5%), or at 6 months (58.2% vs 57.3%) or in the percentage of participants receiving psychotropic medication (61.0%-76.6%). Drug classes included antidepressants, antipsychotics, sedatives (including hypnotics and anxiolytics), mood stabilizers, antiadrenergics, stimulants, and other miscellaneous drugs (such as methadone). Comparisons within classes at each time showed only 1 difference: at 6 months, the present-centered therapy group (14.0%) was more likely than the prolonged exposure group (6.4%) to be taking an antipsychotic ($P=.03$). More present-centered therapy than prolonged exposure participants (28.7% vs 14.9%) received an increased or new medication during study treatment ($P<.01$) but not during 3-month (21.0% vs 20.6%) or 6-month (21.0% vs 22.0%) follow-up. Data for specific drug classes indicated that during treatment, the present-centered therapy group was more likely than the prolonged exposure group to have increased or started new antidepres-

Table 1. Baseline Participant Characteristics*

Characteristics	Prolonged Exposure (n = 141)	Present-Centered Therapy (n = 143)
Age, mean (95% CI), y	44.6 (43.1 to 46.2)	44.9 (43.4 to 46.5)
Post–high school education	129 (91.5)	124 (86.7)
Unemployed	53 (37.6)	56 (39.2)
Married/cohabitating	45 (31.9)	45 (31.5)
Race/ethnicity		
White, non-Hispanic	79 (56.0)	76 (53.1)
Black, non-Hispanic	47 (33.3)	46 (32.2)
Hispanic	8 (5.7)	9 (6.3)
Other	7 (5.0)	12 (8.4)
Lifetime trauma exposure, mean (95% CI) No. of event types (of 17)†	9.9 (9.4 to 10.4)	9.4 (8.9 to 9.9)
Any sexual trauma	131 (92.9)	131 (93.0)
Military sexual trauma	98 (69.5)	109 (76.2)
Physical assault	129 (91.4)	120 (83.8)
Combat exposure	35 (24.8)	36 (25.2)
Disaster exposure	106 (75.2)	99 (69.2)
Serious accident	117 (83.0)	115 (80.4)
Life-threatening illness or injury	65 (46.1)	58 (40.6)
Other traumatic event (eg, sudden, unexpected death of someone close)	125 (88.7)	127 (88.9)
Active-duty status	3 (2.1)	4 (2.8)
PTSD disability		
Approved	28 (19.9)	34 (23.8)
Pending	28 (19.9)	38 (26.6)
Denied	14 (9.9)	7 (4.9)
Never applied	68 (48.2)	59 (41.3)
Approved PTSD disability, mean (95% CI), %	56.8 (46.8 to 66.7)	48.1 (38.6 to 57.5)
Receiving psychotherapy	95 (67.4)	82 (57.3)
Taking psychotropic medication	108 (76.6)	105 (73.4)
Any current comorbid psychiatric disorder	106 (75.2)	115 (80.4)
Mood disorder	87 (61.7)	94 (65.7)
Anxiety disorder	69 (48.9)	67 (46.9)
Substance abuse	3 (2.1)	3 (2.1)
Any lifetime comorbid psychiatric disorder	136 (96.5)	141 (98.6)
Mood disorder	131 (92.9)	137 (95.8)
Anxiety disorder	79 (56.0)	82 (57.3)
Substance abuse/dependence	81 (57.4)	74 (51.7)
Psychological assessment tools, mean (95% CI) score		
Clinician-Administered PTSD Scale	77.6 (74.8 to 80.4)	77.9 (75.1 to 80.6)
PTSD Checklist	58.2 (56.0 to 60.3)	57.1 (55.0 to 59.2)
Beck Depression Inventory	25.3 (23.8 to 26.9)	23.9 (22.4 to 25.5)
Spielberger State Anxiety Inventory	52.1 (49.9 to 54.4)	52.4 (50.2 to 54.7)
Quality-of-Life Inventory	0.06 (–0.24 to 0.35)	0.09 (–0.26 to 0.44)
Short Form-36 mental component	30.1 (28.4 to 31.7)	30.6 (28.7 to 32.6)
Short Form-36 physical component	38.3 (36.4 to 40.2)	39.7 (37.5 to 41.8)
Addiction Severity Index, alcohol	0.05 (0.03 to 0.07)	0.03 (0.02 to 0.04)
Addiction Severity Index, drug	0.006 (0.002 to 0.010)	0.004 (0.001 to 0.007)

Abbreviations: CI, confidence interval; PTSD, posttraumatic stress disorder.
*Data are expressed as No. (%) unless otherwise indicated. *t* Tests were used for continuous variables and χ^2 tests for categorical variables. There were no significant differences between groups.
†The 17 categories of the Life Events Checklist[28] were aggregated as shown to simplify presentation. Military sexual trauma was determined from a separate questionnaire.[26]

sants ($P=.005$) and antipsychotics ($P=.02$). Exploratory analyses to determine whether medication change during treatment modified the treatment effect for CAPS severity scores indicated that the interaction between medication change and treatment was not significant ($P=.63$).

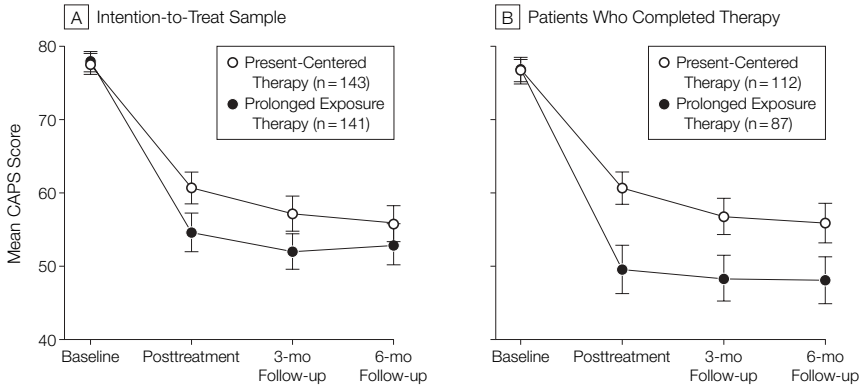
Completer Analyses

Among women providing outcome data, 87 in prolonged exposure and 112 in present-centered therapy completed treatment. Groups did not differ on any baseline measure. Results were similar to results of intention-to-treat analyses; only CAPS findings are presented herein.

CAPS scores improved from pretreatment to posttreatment with prolonged exposure ($d=1.15$; $P<.001$) and with present-centered therapy ($d=0.67$; $P<.001$). In mixed-model analysis, CAPS scores were lower with prolonged exposure than with present-centered therapy overall ($d=0.46$; $P=.005$) (Figure 2B). The treatment × time interaction was not significant ($P=.37$). In cross-sectional comparisons, scores were lower with prolonged exposure than with present-centered therapy at posttreatment ($d=0.54$; $P=.001$) and at 3 months ($d=0.34$; $P=.03$) but not at 6 months ($d=0.29$; $P=.10$).

Most participants showed a clinically meaningful CAPS response (Table 3). According to mixed-model analysis, women in the prolonged exposure group were more likely than women in the present-centered therapy group to lose their diagnosis (odds ratio, 2.43; 95% confidence interval, 1.33-4.44) and to achieve total remission (odds ratio, 3.66; 95% confidence interval, 1.40-9.57). The treatment × time interactions were not significant ($P=.21$-$.47$). At posttreat-

Figure 2. PTSD Severity on the Clinician-Administered PTSD Scale (CAPS) as a Function of Treatment Group



PTSD indicates posttraumatic stress disorder. Data are observed means with standard error bars. Values were imputed for missing data at immediate posttreatment and 3- and 6-month follow-up in the intention-to-treat sample.

Table 2. Outcomes as a Function of Treatment Group (N = 284)*

Outcome Assessment Tools	Pre-Post Effect Size† PE	Pre-Post Effect Size† PCT	Between-Group Effect Size‡	Immediate Posttreatment‡ PE	Immediate Posttreatment‡ PCT	3-Month Follow-up‡ PE	3-Month Follow-up‡ PCT	6-Month Follow-up‡ PE	6-Month Follow-up‡ PCT
Clinician-Administered PTSD Scale	.80§	.62§	0.27‖	52.9 (47.7 to 58.0)	60.1 (55.3 to 64.8)‖	49.7 (44.7 to 54.7)	56.0 (50.5 to 61.5)‖	50.4 (45.0 to 55.8)	54.5 (49.3 to 59.7)
PTSD Checklist	.80§	.43§	0.40§	41.6 (38.4 to 44.9)	48.9 (45.8 to 52.0)§	43.5 (40.2 to 46.7)	48.8 (45.3 to 52.4)¶	44.6 (41.2 to 48.1)	48.5 (45.2 to 51.8)‖
Beck Depression Inventory	.59§	.36§	0.23	17.4 (15.3 to 19.5)	19.9 (18.0 to 21.9)‖	18.5 (16.3 to 20.7)	21.1 (19.1 to 23.1)‖	19.2 (17.1 to 21.3)	20.4 (18.2 to 22.7)
Spielberger State Anxiety Inventory	.34§	.09	0.17	45.7 (42.6 to 48.7)	50.3 (47.4 to 53.3)‖	48.8 (45.9 to 51.8)	50.5 (47.7 to 53.3)	50.4 (47.3 to 53.6)	50.8 (48.0 to 53.6)
Quality-of-Life Inventory	.18‖	.05	–0.09	0.56 (0.19 to 0.93)	0.24 (–0.12 to 0.60)	0.35 (–0.05 to 0.75)	0.22 (–0.14 to 0.60)	0.23 (–0.12 to 0.58)	0.14 (–0.26 to 0.53)
Short Form-36 mental component	.47§	.19‖	–0.21	37.5 (35.0 to 40.0)	33.4 (30.9 to 35.8)¶	35.6 (33.2 to 38.1)	33.8 (31.1 to 36.4)	35.3 (33.0 to 37.7)	33.4 (30.9 to 35.9)
Short Form-36 physical component	.05	.01	–0.02	38.1 (36.1 to 40.2)	39.5 (37.5 to 41.4)	39.1 (37.1 to 41.1)	38.8 (36.7 to 40.9)	38.8 (36.7 to 40.8)	38.3 (36.2 to 40.5)
Addiction Severity Index, alcohol	.16	.05	0.04	0.03 (0.01 to 0.05)	0.03 (0.01 to 0.05)	0.03 (0.01 to 0.06)	0.04 (0.02 to 0.06)	0.04 (0.01 to 0.06)	0.04 (0.02 to 0.06)
Addiction Severity Index, drug	.10	.10	0.02	0.003 (–0.002 to .007)	0.001 (–0.003 to 0.005)	0.001 (–0.001 to 0.004)	0.002 (0 to 0.005)	0.0005 (–0.001 to 0.002)	0.002 (0 to 0.003)

Abbreviations: PCT, present-centered therapy; PE, prolonged exposure; PTSD, posttraumatic stress disorder.
*Pre-post effect sizes were calculated from analyses to generate least square means. Between-group effects indicate the overall difference between PE and PCT in longitudinal analysis. Analyses were performed using PROC MIXED (95% confidence intervals are provided in parentheses).
†Within-group comparisons.
‡Between-group comparisons.
§$P<.001$.
‖$P<.05$.
¶$P<.01$.

ment, response, loss of diagnosis, and total remission were more likely with prolonged exposure than with present-centered therapy. At 3 months, total remission was more likely in the prolonged exposure group.

COMMENT

Prolonged exposure was more effective than present-centered therapy for treating PTSD in female veterans and active-duty personnel. Treatment groups did not consistently differ in comorbid symptoms, quality of life, substance abuse, or functional impairment. Effects of prolonged exposure among treatment completers were larger but similar to effects in the intention-to-treat sample. Both treatments were safe and well tolerated.

Groups were comparable in receipt of additional treatments, except for an increased likelihood of medication changes in present-centered therapy during treatment. This difference may reflect an attempt to compensate for the smaller improvements in present-centered therapy. However, medication change during treatment did not affect treatment outcome.

We initially expected the maximum effect would be observed at 3-month follow-up given data from an older prolonged exposure protocol showing that patients continued to improve after treatment.[20,21] Subsequent studies using the version of the prolonged exposure protocol used in our study found that the maximum benefits of prolonged exposure are observed immediately after treatment and persist over time.[17,19,23] Our longitudinal findings indicating that the effects of prolonged exposure did not differ over time are consistent with these studies. However, cross-sectional comparisons showed no differences at 6 months except for a secondary measure of self-reported PTSD. Differences between the longitudinal and cross-sectional findings are likely due to greater statistical power for the longitudinal tests and slight (nonsignificant) decreases in symptom severity in the present-centered therapy group and/or increases in the prolonged exposure group. Regardless of the reason, the effects of prolonged exposure were less persistent than expected.

Although this is the first study of PTSD in female veterans and active-duty personnel, some comparison with prior studies is possible because most women in our study were treated for sexual trauma, which often has been the focus of treatment in women with PTSD.[17,19-21,23] The high prevalence of sexual trauma among our participants is noteworthy, as is the fact that sexual trauma—occurring more than 20 years prior—was chosen by the majority of participants as the most distressing trauma from among the many types they had experienced. Of further note is the high prevalence of military sexual trauma—more than 70%. A prior study of female VA health care users found that 23% reported military sexual trauma.[41] In this light, it is not surprising that women seeking treatment for PTSD would have such high prevalence.

The effect size between prolonged exposure and present-centered therapy (d=0.27) was similar to that found in

Table 3. PTSD Response and Remission Criteria by Treatment Group*

Analysis	Between-Group Effect, OR (95% CI)	Immediate Posttreatment, No. (%)		3-Month Follow-up, No. (%)		6-Month Follow-up, No. (%)	
		PE	PCT	PE	PCT	PE	PCT
Intention to treat (n = 284)		(n = 141)	(n = 143)	(n = 141)	(n = 143)	(n = 141)	(n = 143)
Response	1.35 (0.80-2.30)	99 (70.2)	84 (58.7)	110 (78.0)	102 (71.3)	97 (68.8)	98 (68.5)
NNT		9		15		381	
Loss of diagnosis	1.80 (1.10-2.96)†	55 (39.0)	29 (20.3)‡	55 (39.0)	40 (28.0)	56 (39.7)	47 (32.9)
NNT		6		10		15	
Total remission	2.43 (1.10-5.37)†	24 (17.0)	10 (7.0)§	21 (14.9)	9 (6.3)	24 (17.0)	16 (11.2)
NNT		10		12		18	
Treatment completers (n = 199)		(n = 83)	(n = 111)	(n = 84)	(n = 106)	(n = 84)	(n = 105)
Response	1.29 (0.69-2.41)	62 (74.7)	66 (59.5)‖	70 (83.3)	76 (71.7)	61 (72.6)	72 (68.6)
NNT		7		9		25	
Loss of diagnosis	2.43 (1.33-4.44)¶	39 (47.0)	22 (19.8)¶	36 (42.9)	30 (28.3)	39 (46.4)	36 (34.3)
NNT		4		7		8	
Total remission	3.66 (1.40-9.57)¶	18 (21.7)	7 (6.3)‡	15 (17.9)	6 (5.7)§	17 (20.2)	12 (11.4)
NNT		6		8		11	

Abbreviations: CI, confidence interval; NNT, number needed to treat; OR, odds ratio; PCT, present-centered therapy; PE, prolonged exposure; PTSD, posttraumatic stress disorder.
*All outcomes are defined based on the Clinician Administered PTSD Scale[28]: response indicates decrease from baseline of 10 points or more[11,28]; loss of diagnosis, no longer meeting symptom criteria and severity score less than 45; total remission, severity score less than 20.[28] The between-group effect is the overall difference between PE and PCT in longitudinal analysis. Analyses were performed using PROC MIXED with the GLIMMIX macro[39] (95% confidence intervals are provided in parentheses).
†P = .01.
‡P = .002.
§P = .02.
‖P = .04.
¶P<.001.

most other studies that have compared exposure-based and nonspecific treatments[11,20,21] (see Bryant et al[42] for an exception). In contrast, the pre-post effect size within the prolonged exposure group (d=0.80) was smaller than in prior studies of prolonged exposure and other CBT treatment in nonveterans but was comparable with findings from male veterans. As reported in a recent meta-analysis,[16] pre-post effect sizes for prolonged exposure in prior studies of women were d=1.21,[20] d=2.04,[19] and d=2.95.[23] Studies of mixed-sex samples and/or exposure-based treatments also typically yielded larger pre-post effect sizes as well.[16] However, our pre-post effect size is comparable with findings for male veteran samples (d=0.81),[16] which was significantly lower than effect sizes for mixed trauma (d=1.24) and assault (d=1.82) samples.[16]

It is inappropriate to conclude from our study or prior studies that veterans are less treatment-responsive than nonveterans. Samples in veteran and nonveteran treatment studies differ in ways that could affect treatment responsiveness. In particular, our sample is distinctive in its chronicity. In some studies of CBT, the average time since trauma was 8 to 13 months.[18,41] Even in studies with longer intervals, the average time was less than 10 years.[17,23] In contrast, the average time since trauma in our sample was 23 years. Such extremely chronic cases may need more treatment than the relatively small number of sessions typically provided in a clinical trial. The greater chronicity in our sample also may explain why effects on outcomes other than PTSD were more limited than in prior studies.[17-23]

Yet it is unlikely that chronicity alone explains our more limited findings. Furthermore, between-group effect sizes were comparable with those observed in studies of nonveteran women. Also, a recent study found excellent response to CBT in a male VA sample.[10] It also is unlikely that relatively smaller within-group improvement and limited effects on outcomes other than PTSD in our study resulted from poor therapy quality. Therapy protocol adherence and therapist competence were excellent in both conditions. Patients were highly satisfied with care.

The study design may have contributed to the differences between our findings and those from prior studies, which have tended to be more strictly controlled.[16,27] Our study included features of practical clinical trials[24]: a clinically relevant comparison group, diverse settings, relatively broad inclusion criteria, use of nonexpert therapists, allowance of cotherapy, and measurement across a range of outcomes. The design may have reduced the relative *efficacy* of prolonged exposure compared with nonspecific treatment for PTSD, but we believe that including such features is a strength. By combining them with strategies to enhance internal validity (eg, randomization, careful training and supervision), we hoped to generate useful findings to inform the VA and Department of Defense about the about the *effectiveness* of prolonged exposure if it were more widely adopted in clinical practice across these systems. The sample size is also a strength because it afforded adequate power to detect relatively small differences.

Like other randomized clinical trials of CBT for PTSD,[8-11,17-23] we enrolled patients who were receiving a stable regimen of psychotropic medication. Unlike prior studies, we compared outcomes in medication users and nonusers. Our design did not specifically allow us to test whether prolonged exposure augments the effect of medication because the comparison group also received psychotherapy, but evidence from a recent study[43] indicates that prolonged exposure (vs continued sertraline) augments outcomes in PTSD patients who have only partially responded to sertraline.

Although roughly two thirds of participants in both groups had a clinically meaningful response, those who received prolonged exposure were 1.8 times more likely to no longer meet diagnostic criteria and 2.4 times more likely to have full remission. However, the number needed to treat for these outcomes indicates that the effect was modest. Furthermore, the magnitude of pre-post change in prolonged exposure for outcomes other than PTSD was only medium at best. Although these were secondary outcomes, they are important. As suggested above, more treatment or additional types of treatment may be needed to achieve greater total benefit in patients with chronic PTSD who have significant comorbidity.

Because of the careful training and supervision of present-centered therapy therapists and the high degree of adherence and competence they displayed, this study provides a stringent test of the advantage of prolonged exposure over present-centered treatment, the approach used most often by VA clinicians.[14] According to program evaluation data from VA women's specialized PTSD treatment programs, PTSD symptoms decreased 3.7% to 5.0% over a 4-month period during which patients received just less than 10 sessions of individual psychotherapy.[44] (Similar data for the Department of Defense are not available). In our prolonged exposure group, self-reported change from pretreatment to posttreatment (roughly comparable in amount of time and number of sessions with the program evaluation study) was 31.8% on the CAPS and 28.5% on the PCL. Admittedly, this is an informal comparison, so it only suggests that prolonged exposure would be more effective than the usual care delivered in the VA.

We enrolled few active-duty women. Anecdotal evidence indicated that some potential active-duty patients worried about the stigmatizing effects of PTSD treatment, a concern that has been expressed by soldiers serving in Iraq and Afghanistan.[45] The small number of active-duty participants prevented us from examining whether they differ from veteran women in treatment response. It is possible that younger, active-duty women would be more responsive, as is true for civilian women.[17,19,23]

Our study has additional limitations to consider when interpreting the

results. Dropout from treatment was higher in prolonged exposure than in present-centered therapy. Thus, to maximize the potential benefit of prolonged exposure in clinical practice, strategies to enhance retention may be needed. The fact that results were stronger in women who completed treatment lends support to this need. Another potential limitation is that we included women only. Our findings may be generalized to men, with some caution, because prolonged exposure and other CBT are effective for treating men.[8-10,18,22,42]

Practice guidelines for PTSD[12,13] recommend prolonged exposure and other CBT, but the treatments are not widely used.[14] Along with recent findings,[10,17] our study demonstrates the feasibility of implementing CBT across a range of clinical settings. With the high prevalence of PTSD among military personnel returning from service in Iraq and Afghanistan,[45] the challenge for large health care systems like those of the VA and the Department of Defense is to find efficient ways to train personnel to promote dissemination of these effective treatments.

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