Received: 22 June 2018 | Revised: 26 November 2018 | Accepted: 1 December 2018

DOI: 10.1002/da.22871

RESEARCH ARTICLE

WILEY ADAA ANXIETY AND DEPRESSION ASSOCIATION OF AMERICA

Residual symptoms following prolonged exposure and present-centered therapy for PTSD in female veterans and soldiers

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Funding information
U.S. Department of Defense; U.S. Department of Veterans Affairs, Grant/Award Number: CSP #494

Background: Despite the effectiveness of evidence-based treatments for posttraumatic stress disorder (PTSD), some symptoms, such as sleep disturbance, can be difficult to treat regardless of treatment type.

Methods: We examined residual PTSD symptoms in 235 female veterans and soldiers who were randomized to receive 10 weekly sessions of either Prolonged Exposure (PE) or Present-Centered Therapy (PCT). PTSD symptoms were assessed using the Clinician-Administered PTSD Scale. Analyses examined the effects of PE and the effects of clinically significant improvement (loss of diagnosis, operationalized as meaningful symptom reduction and no longer meeting diagnostic criteria).

Results: Both treatments resulted in reductions in PTSD symptoms. PE had lower conditional probabilities than PCT of retaining intrusive memories, avoidance of people/places, detachment/estrangement, and restricted range of affect. Loss of diagnosis had lower conditional probabilities of almost all symptoms, although hyperarousal symptoms—especially irritability/anger (60.7%) and sleep difficulties (50.9%)—were the most likely to remain.

Conclusions: Results are consistent with previous findings on sleep difficulties being difficult to treat, but also show that hyperarousal symptoms overall may not be resolved even after substantial improvement. Additional strategies may be needed to treat the full range of PTSD symptoms in some patients.

KEYWORDS
cognitive-behavioral therapy, PTSD, veterans, women

1 | INTRODUCTION

There are a number of effective treatments for posttraumatic stress disorder (PTSD). For example, the practice guideline recently published by the Department of Veterans Affairs and Department of Defense (2017) recommends trauma-focused psychotherapies such as Prolonged Exposure (PE), Cognitive Processing Therapy (CPT), and Eye-Movement Desensitization and Reprocessing, and selected medications (sertraline, paroxetine, fluoxetine, and venlafaxine). The guideline also suggests (a weaker recommendation) several manualized nontrauma-focused psychotherapies (present-centered therapy [PCT], interpersonal therapy, and stress inoculation training) and additional medications (nefazodone, imipramine, and phenelzine).

But despite these effective treatments, some symptoms persist in some patients. Most research has focused on the persistence of sleep problems following psychotherapy (e.g., Belleville, Guay, & Marchand, 2011; Gutner, Casement, Gilbert, & Resick, 2013; Pruiksma et al., 2016; Woodward et al., 2017; Zayfert & DeViva, 2004). Although treatment improves sleep problems and nightmares, these symptoms remain to some degree. One of the earliest studies (Zayfert & DeViva, 2004) found that 48% of patients who no longer met PTSD diagnostic criteria and had substantial reductions in PTSD symptoms after cognitive-behavioral therapy (CBT) reported difficulty falling or staying asleep. The average item severity at posttreatment for sleep problems (M = 3.6 on a 0–8 scale) was significantly higher than severity for all other symptoms except anger (M = 2.5) and startle (M = 1.5). In a more recent study, 44% of patients who had undergone cognitive

therapy (that was shown to be highly effective) had difficulty falling or staying asleep after treatment (Woodward et al., 2017).

Other studies have identified additional residual symptoms. In Zayfert and DeViva's (2004) study of treatment responders, 52% of the sample retained anger. A recent study examined the prevalence of all 17 DSM-IV symptoms of PTSD before and after treatment in completers of either PE or CPT (Larsen, Fleming, & Resick, 2018). Prevalences at posttreatment were highest for distress related to reminders, inability to recall the trauma, hypervigilance, startle, and sleep difficulty (31%–40%). Among the subsample of treatment responders, prevalences were in this range for inability to recall and sleep difficulty. The conditional probability of retaining a symptom at long-term (5–10 year) follow-up exceeded 30% in PE for inability to recall, sleep difficulty, and hypervigilance and in CPT for distress related to reminders, inability to recall, startle, and reactivity.

It is possible that sleep and other symptoms may persist simply because current PTSD treatments are not effective enough, or because PTSD is especially difficult to treat. However, evidence does not support these explanations. Effect sizes of treatments for PTSD (e.g., Lee et al., 2016; Watts et al., 2013) are comparable with effect sizes of treatments for other mental disorders (e.g., Bandelow et al., 2015; Carpenter et al., 2018; Cuijpers et al., 2013). Furthermore, the occurrence of residual symptoms is not unique to PTSD. For example, in a sample of depressed patients who met criteria for remission following treatment with duloxetine, almost 60% retained core depression symptoms, just over 50% retained insomnia symptoms, and almost 70% retained anxiety symptoms (Romera et al., 2014). The literature on residual symptoms in mood disorders highlights several types of symptoms, but, as in the PTSD literature, consistently emphasizes the persistence of sleep problems (e.g., Conradi, Ormel, & de Jonge, 2011; Culpepper, Muskin, & Stahl, 2015; Geoffroy et al., 2015; Romera et al., 2014; Zajecka, 2013).

Research on the topic of residual symptoms in PTSD is still emerging. The literature suggests that residual symptoms are common, as in depression, but few studies (Larsen et al., 2018; Zayfert & DeViva, 2004) have examined all PTSD symptoms. Most studies have focused only on sleep. Because of this focus, there is incomplete knowledge about which symptoms persist following specific treatments and treatment in general. There is also variability in how residual symptoms are defined, with most studies reporting the percentage of people who had a symptom after treatment, regardless of whether the symptom was present before treatment. Therefore, we conducted secondary analyses of a trial of PE, a trauma-focused CBT, in female veterans and soldiers (Schnurr et al., 2007). Prior studies of residual symptoms in PTSD had focused on female civilians (e.g., Gutner et al., 2013; Larsen et al., 2018), mixed samples of civilians (e.g., Belleville et al., 2011; Woodward et al., 2017; Zayfert & DeViva, 2004), and largely male samples of veterans or military personnel (e.g., Pruiksma et al., 2016).

The initial trial had found that PE was more effective than Present-Centered Therapy (PCT) for reducing PTSD severity and leading to clinically significant outcomes (loss of diagnosis and remission). Subsequent analysis of individual symptoms and symptom clusters found that averages of almost all clinician-rated symptoms improved following both treatments (Schnurr & Lunney, 2015). For clinician-rated PTSD, PE had greater benefit than PCT on the avoidance and numbing clusters, most individual symptoms in these clusters, and distress related to reminders. Such information is useful for understanding the specific effects of PE, but because the analyses focused on averages, is not informative about symptom retention—which should be determined at the level of an individual, and account for symptom presence before treatment.

We first examined the effects of treatment on residual symptoms by comparing PE and PCT and then examined the effects of clinically significant improvement, defined as loss of diagnosis. We chose this measure because prior analyses had shown it to be robustly associated with clinically significant improvements in functioning and quality of life (Schnurr & Lunney, 2012, 2016; Schnurr et al., 2009). Given the limited evidence, it was difficult to make predictions for most symptoms, but we expected that sleep difficulties and anger would be especially likely to remain even following PE and loss of diagnosis. The primary outcome in both sets of analysis was the conditional probability of retaining a symptom at posttreatment.

2 | MATERIALS AND METHODS

Details about the original study have been published previously (Schnurr et al., 2005, 2007). An institutional review board at each site approved the research protocol. Participants provided written informed consent after they had been given a complete description of the study. Data were collected between August 2002 and October 2005.

2.1 | Participants

Participants were 232 female veterans and three Army soldiers drawn from a randomized clinical trial of PTSD treatment (Schnurr et al., 2007). Participants were recruited from nine VA hospitals, two VA community Vet Centers, and one Army hospital. Inclusion criteria were current PTSD according to the "1/2" rule and minimum severity ≥ 45 on the Clinician-Administered PTSD Scale (CAPS; Weathers, Keane, & Davidson, 2001); 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, for those on psychoactive medication, a stable regimen for the prior 2 months. Exclusion criteria were current psychotic symptoms, mania, or bipolar disorder; current substance dependence; prominent current suicidal or homicidal ideation; cognitive impairment; current involvement in a violent relationship; and self-mutilation within the past 6 months.

The 235 women were selected from the 284 enrolled in the trial because they participated in outcome measurement at posttreatment. The 235 did not differ from the 49 excluded women on PTSD symptom severity or any of the quality-of-life measures at pretreatment, nor on race, marital status, work status, or VA PTSD disability status.

2.2 | Measures

We assessed PTSD using the CAPS (Weathers et al., 2001), a structured interview in which the frequency and intensity of the 17

TABLE 1 Pretreatment demographic and clinical characteristics by treatment type and loss of diagnosis

	Total		PE		PCT		Lost PTSD diagnosis		Retained PTSD diagnosis	
	N = 235		(*n* = 111)		(*n* = 124)		(*n* = 68)		(*n* = 167)	
Variable	*M*/%	*SD*/*n*	*M*/%	*SD*/*n*	*M*/%	*SD*/*n*	*M*/%	*SD*/*n*	*M*/%	*SD*/*n*
Age (*M*)	45.0	9.4	44.6	9.4	45.4	9.4	44.6	9.5	45.2	9.4
Post-high-school education[a]	87.2	205	89.2	99	85.5	106	94.1	64	84.4	141
Non-white race	45.5	107	43.2	48	47.6	59	45.6	31	45.5	76
Married/living as married	29.8	70	30.6	34	29.0	36	33.8	23	28.1	47
Working full- or part-time	39.6	93	36.0	40	42.7	53	38.2	26	40.1	67
VA PTSD service-connected disability	21.6	50	19.8	22	23.1	28	22.7	15	21.1	35
Current comorbid psychiatric disorder	77.5	182	75.7	84	79.0	98	69.1	47	80.8	135
Lifetime comorbid psychiatric disorder	97.9	230	97.3	108	98.4	122	95.6	65	98.8	165
CAPS PTSD symptom severity (*M*)[b]	77.5	16.6	78.0	17.1	77.1	16.1	69.4	14.8	80.8	16.1

Note. *N* = 235. PE: Prolonged Exposure; PCT: Present-Centered Therapy; PTSD: posttraumatic stress disorder; CAPS: Clinician-Administered PTSD Scale. There were no significant differences between the two treatment types on any of the variables listed in the table.

[a]Participants who lost their PTSD diagnosis were more likely to have post-high-school education than those who retained their PTSD diagnosis ($P < 0.05$).

[b]Participants who lost their PTSD diagnosis had lower pretreatment PTSD symptom severity than those who retained their PTSD diagnosis ($P < 0.001$).

DSM-IV PTSD symptoms are rated on a 5-point scale. Severity scores range from 0 to 136. Baseline assessments were performed using the CAPS 1-month version, and posttreatment assessments were performed using the 1-week version. We used the "1/2" rule to define symptom presence, counting a symptom as present if it occurred at least monthly with at least moderate intensity (Weathers, Ruscio, & Keane, 1999). Loss of diagnosis was defined as a decrease of at least 10 points plus no longer meeting criteria for PTSD diagnosis and having a severity score of <45 (Schnurr & Lunney, 2016). Other Axis 1 diagnoses were measured using the Structured Clinical Interview for DSM-IV (SCID; First, Spitzer, Gibbon, & Williams, 1995). Interrater reliability was high for the CAPS (intraclass correlation = 0.92) and moderate to high for SCID diagnoses (κ values ranged from 0.62 to 0.83; Schnurr et al., 2007).

2.3 | Procedure

Referring clinicians provided information about potential participants to study staff, who then met with the referrals to explain the study and obtain informed consent. A master's- or doctoral-level clinician who was blind to participants' treatment assignment performed all assessments. Posttreatment assessments were performed at least 1 week following the end of treatment. Eligible women were randomized to receive 10 weekly sessions of PE (Foa, Hembree, & Rothbaum, 2007) or PCT (Schnurr et al., 2005). Therapists were 52 female master's or doctoral-level clinicians who were randomized to deliver one of the two treatments. All received specialized training in their assigned treatment, consisting of a training workshop followed by 1–2 practice cases. Sessions were videotaped and reviewed by an expert supervisor, who provided individual weekly or biweekly telephone supervision. Therapist adherence (4.2–4.7) and competence (4.3–4.5), rated on a 5-point scale ranging from 1 = poor to 5 = excellent) by an independent fidelity monitor, were excellent and equivalent across treatments (Schnurr et al., 2007).

2.4 | Statistical analysis

We operationalized symptom retention as the conditional probability of retaining a symptom at posttreatment among individuals who had that symptom before treatment, using logistic regression to examine the effects of PE (vs. PCT), and the effects of loss of diagnosis (vs. retaining diagnosis). Additional analyses including loss of diagnosis, treatment type, and the treatment type by loss-of-diagnosis interaction were conducted but are not presented here, as the substantive findings remained the same.

3 | RESULTS

Table 1 contains descriptive information about the sample by treatment type and loss of diagnosis. On average, participants were in their mid-40s and ranged in age from 22 to 78 years. Most had more than a high school education, and almost one third were married or living as married. Just under half were non-white. Sexual trauma was the type of trauma most commonly identified as the index event to address in treatment (68.5%, *n* = 161), followed by physical assault (14.9%, *n* = 35) and war-zone exposure (6.0%, *n* = 14). The index trauma occurred when participants were 21.18 years of age (*SD* = 10.19, range = 3 to 54 years). Women randomized to PE and PCT did not differ at baseline in demographic, exposure, or clinical characteristics (Schnurr et al., 2007).

Figure 1 displays information about symptom presence before and after treatment for PE and PCT. The three most prevalent symptoms before treatment were detachment/estrangement (C5), distress

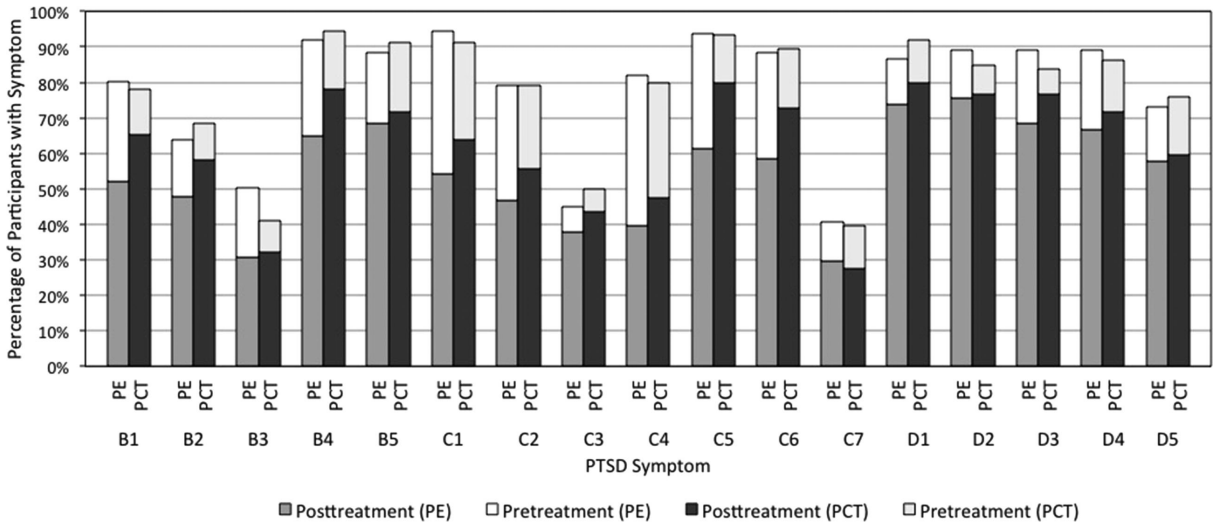

FIGURE 1 Symptom presence for each posttraumatic stress disorder symptom before and after treatment by treatment type. PE: Prolonged Exposure; PCT: Present-Centered Therapy

at reminders (B4), and avoidance of thoughts and feelings (C1). Before treatment, fewer than half of participants experienced psychogenic amnesia (C3), dissociative reminders (B3), or foreshortened future (C7). After treatment, difficulty falling asleep (D1), anger/irritability (D2), and difficulty concentrating (D3) were the most prevalent symptoms, experienced by about three fourths of participants. Psychogenic amnesia (C3), dissociative reminders (B3), and foreshortened future (C7) remained the least common symptoms after treatment.

Table 2 presents the conditional probability of retaining each symptom following treatment. Probabilities were lower in PE than PCT for four symptoms: intrusive recollections (B1), avoidance of places, people, or activities (C2), detachment/estrangement (C5), and restricted range of affect (C6). In PE, conditional probabilities of symptom retention were highest for all hyperarousal symptoms, ranging from 70.7% to 80.2%, and physiological reactivity (B5; 71.4%). In PCT, conditional probabilities were highest for the first four hyperarousal symptoms (difficulty falling asleep, anger/irritability, difficulty concentrating, and hypervigilance), ranging from 77.6% to 81.6%, the two avoidance symptoms (C1, 81.0% and C2, 78.4%), and distress about reminders (B4, 77.8%).

After treatment, 28.9% of participants ($n = 68$) no longer met diagnostic criteria, 38.8% ($n = 43$) who received PE and 20.2% ($n = 25$) who received PCT. Their decrease in CAPS scores ranged from 10 to 83 points ($M = -44.5$, $SD = 16.4$) and they retained an average of 4.3 ($SD = 2.2$) symptoms. In contrast, change in CAPS scores ranged from a decrease of 59 points to an increase of 34 points ($M = -9.4$, $SD = 16.6$) among participants who still met diagnostic criteria, and they retained an average of 12.3 ($SD = 2.8$) symptoms. Figure 2 shows descriptive information about symptom presence before and after treatment as a function of loss of diagnosis.

Table 3 presents information about the conditional probability of retaining each symptom as a function of loss of diagnosis. For all symptoms, participants who no longer met diagnostic criteria had much lower conditional probabilities of symptom retention. However, probabilities were high for all hyperarousal symptoms among these participants, with difficulty falling asleep (D1) and anger/irritability (D2) having the highest probabilities, 50.9% and 60.7%, respectively. Symptom retention was also relatively higher for distress about reminders (B4; 41.0%) and physiological reactivity (B5; 37.3%).

TABLE 2 Percentage of participants retaining each posttraumatic stress disorder symptom after treatment by treatment type

	PE		PCT		
Symptom	%	*n*	%	*n*	OR (95% CI)
B1. Intrusive memories*	58.4	52	74.2	72	0.49 (0.26–0.91)
B2. Recurrent/distressing dreams	62.0	44	72.9	62	0.61 (0.31–1.19)
B3. Dissociative reactions	48.2	27	52.9	27	0.83 (0.39–1.77)
B4. Distress about reminders	67.6	69	77.8	91	0.60 (0.33–1.09)
B5. Physiological reactivity	71.4	70	73.5	83	0.90 (0.49–1.66)
C1. Avoidance of thoughts/feelings	56.2	59	66.4	75	0.65 (0.38–1.13)
C2. Avoidance of people/places*	47.7	42	64.3	63	0.51 (0.28–0.91)
C3. Psychogenic amnesia	52.0	26	67.7	42	0.52 (0.24–1.11)
C4. Diminished interest in activities	42.9	39	53.5	53	0.65 (0.37–1.16)
C5. Detachment/ estrangement**	63.5	66	81.0	94	0.41 (0.22–0.75)
C6. Restricted range of affect**	60.2	59	78.4	87	0.42 (0.23–0.77)
C7. Foreshortened future	53.3	24	51.0	25	1.10 (0.49–2.47)
D1. Difficulty falling asleep	80.2	77	81.6	93	0.92 (0.46–1.83)
D2. Irritability/anger	79.8	79	79.0	83	1.05 (0.53–2.07)
D3. Difficulty concentrating	70.7	70	78.8	82	0.65 (0.34–1.23)
D4. Hypervigilance	71.7	71	77.6	83	0.73 (0.39–1.38)
D5. Exaggerated startle	72.8	59	66.0	62	1.38 (0.72–2.65)

Note. Symptoms were measured using the Clinician-Administered PTSD Scale. PE: Prolonged Exposure; PCT: Present-Centered Therapy; *$P < 0.05$; **$P < 0.01$.

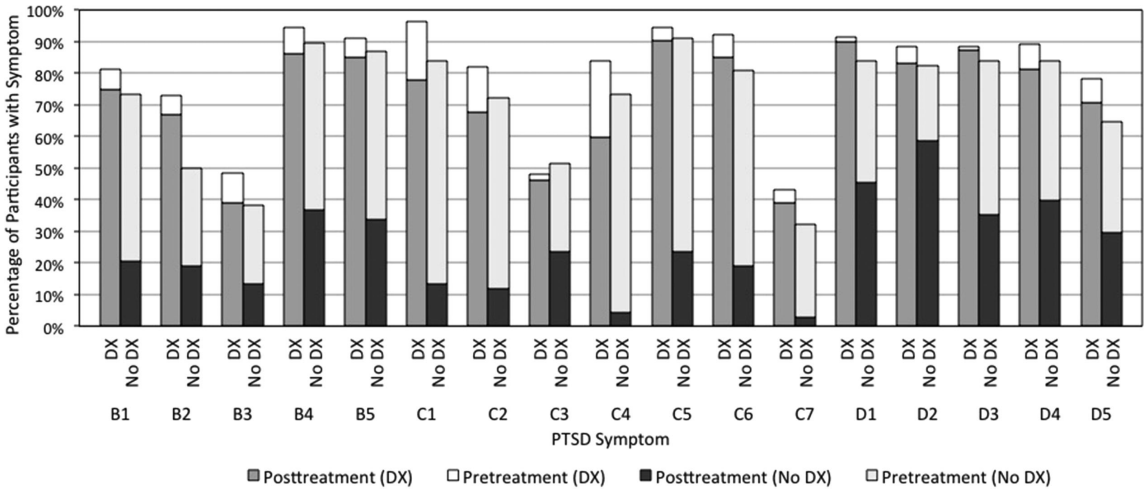

FIGURE 2 Symptom presence for each posttraumatic stress disorder symptom before and after treatment by loss of diagnosis. DX: retained diagnosis of posttraumatic stress disorder following treatment; no DX: lost diagnosis of posttraumatic stress disorder following treatment

4 | DISCUSSION

We examined residual symptoms among female veterans and soldiers following treatment for PTSD and found that the probability of symptom retention was high for most symptoms unless improvement resulted in loss of diagnosis. PE improved symptom severity relative to PCT, but the conditional probability of retaining symptoms in PE was high, especially for physiological reactivity and all hyperarousal symptoms. Women who no longer met diagnostic criteria following treatment had substantially lower conditional probabilities of all symptoms relative to those women who still had PTSD. Yet even among women who no longer met diagnostic criteria, hyperarousal symptoms—especially irritability/anger and sleep difficulties—were the most likely to remain.

In the analyses comparing treatment types, PE was associated with lower conditional probabilities than PCT of retaining several symptoms—intrusive memories, avoidance of people/places, detachment/estrangement, and restricted range of affect. These findings are generally consistent with analyses that examined average symptom improvement (Schnurr & Lunney, 2015), although those analyses had identified the avoidance and numbing clusters and most symptoms in those clusters as improving more in PE. Using symptom retention, rather than improvement, as a criterion for examining treatment outcome resulted in a smaller number of symptoms for which PE had a unique effect.

Improvement in avoidance symptoms in PE is not surprising given that avoidance is a specific target of exposure-based therapies. In PE, exposure is used to activate dysfunctional perceptions and beliefs associated with the traumatic event in order to modify emotional processing of the traumatic event (e.g., Foa & Kozak, 1986; Foa et al., 2007). Reductions in intrusive recollections may be a result of reduced fear associated with aspects of the traumatic event. Theoretical conceptualizations (e.g., Foa, Zinbarg, & Rothbaum, 1992; Litz, 1992; Litz & Gray, 2002) and factor analytic evidence (e.g., Elhai & Palmieri, 2011; King, Leskin, King, & Weathers, 1998) suggest numbing and avoidance may result from different mechanisms, but because avoidance and numbing symptoms were grouped in a single cluster prior to DSM-5, few studies have compared the effects of different treatments on numbing separately from avoidance. If numbing results from depleted emotional resources as a consequence of traumatic reminders, treatments such as PE that reduce intrusive memories may in turn result in improvements in emotional numbing (Litz & Gray, 2002). Further study is needed to understand the effectiveness of different treatments in improving numbing symptoms, especially given the unique association between numbing and greater distress and poorer functioning and quality of life for veterans (e.g., Hassija, Jakupcak, & Gray, 2012; Schnurr et al., 2009; Sippel, Watkins, Pietrzak, Hoff, & Harpaz-Rotem, 2018).

The conditional probability of symptom retention in both PE and PCT was highest for difficulty falling asleep (81%), replicating the findings of investigations that have examined additional treatments (e.g., Belleville et al., 2011; Gutner et al., 2013; Larsen et al., 2018; Pruiksma et al., 2016; Woodward et al., 2017; Zayfert & DeViva, 2004). The treatment-resistant nature of sleep symptoms may indicate that although PTSD may initiate these symptoms, that they may later develop into a primary sleep disorder that requires additional sleep-focused treatment to resolve (e.g., Spoormaker & Montgomery, 2008; Zayfert & DeViva, 2004). Our results are also consistent findings of residual sleep problems in studies of treatment for depression and bipolar disorder (e.g., Conradi et al., 2011; Culpepper et al., 2015; Geoffroy et al., 2015; Romera et al., 2014; Zajecka, 2013). Because it appears that residual sleep problems are not a phenomenon that occurs only in PTSD, but in the treatment of mental disorders more broadly, targeted interventions such as CBT for insomnia (e.g., Wu, Appleman, Salazar, & Ong, 2015) may be indicated across disorders in some patients.

In contrast to the circumscribed findings of the analyses of treatment type, analyses examining loss of diagnosis revealed broader and more substantial improvement. Although symptom reduction is necessary to define loss of diagnosis, all conditional probabilities were meaningfully reduced. However, hyperarousal symptoms, especially sleep difficulty and anger, had highest conditional probabilities of retention.

TABLE 3 Percentage of participants retaining each posttraumatic stress disorder symptom after treatment by loss of diagnosis

	Lost PTSD diagnosis ($n = 68$)		Retained PTSD diagnosis ($n = 167$)		
Symptom	%	*n*	%	*n*	OR (95% CI)
B1. Intrusive memories***	26.0	13	81.6	111	0.08 (0.04–0.20)
B2. Recurrent/ distressing dreams***	23.5	8	80.3	98	0.08 (0.03–0.19)
B3. Dissociative reactions*	30.8	8	56.8	46	0.34 (0.13–0.87)
B4. Distress about reminders***	41.0	25	85.4	135	0.12 (0.06–0.23)
B5. Physiological reactivity***	37.3	22	86.2	131	0.10 (0.05–0.19)
C1. Avoidance of thoughts/feelings***	15.8	9	77.6	125	0.05 (0.02–0.12)
C2. Avoidance of people/places***	16.3	8	70.8	97	0.08 (0.04–0.19)
C3. Psychogenic amnesia***	34.3	12	72.7	56	0.20 (0.08–0.46)
C4. Diminished interest in activities***	4.0	2	64.3	90	0.02 (0.01–0.10)
C5. Detachment/ estrangement***	24.2	15	91.8	145	0.03 (0.01–0.06)
C6. Restricted range of affect***	20.0	11	87.7	135	0.04 (0.02–0.08)
C7. Foreshortened future***	4.6	1	66.7	48	0.02 (0.01–0.19)
D1. Difficulty falling asleep***	50.9	29	92.2	141	0.09 (0.04–0.19)
D2. Irritability/ anger***	60.7	34	86.5	128	0.24 (0.12–0.49)
D3. Difficulty concentrating***	38.7	22	89.0	130	0.08 (0.04–0.16)
D4. Hypervigilance***	45.6	26	85.9	128	0.14 (0.07–0.28)
D5. Exaggerated startle***	34.1	15	80.9	106	0.12 (0.06–0.26)

Note. Symptoms were measured using the Clinician-Administered PTSD Scale. $^{*}P < 0.05$. $^{***}P < 0.001$.

The finding on sleep is consistent with Larsen et al.'s (2018) findings that the prevalence of sleep problems remained high (over 30%) among treatment responders and the conditional probability of sleep problems was over 40% at long-term follow-up in PE. Larsen et al.'s (2018) long-term follow-up data also showed elevations of other hyperarousal symptoms—hypervigilance and startle—in PE. In addition, our finding on elevated residual anger is consistent with Zayfert and DeViva's (2004) finding of residual anger in patients who no longer met diagnostic criteria for PTSD and had meaningful reductions in symptom severity. It is possible that the persistence of anger/irritability may be due to in part its relationship with sleep disturbances. Network analyses of PTSD symptoms show close connections between sleep and anger/irritability (e.g., Bryant et al., 2017; McNally et al., 2015; McNally, Heeren, & Robinaugh, 2017). Research is needed to determine the generalizability of our findings on sleep, anger, and other hyperarousal symptoms to other treatments and other disorders. Because scales exist to measure aspects of some of these symptoms more fully—for example, the Insomnia Severity Index (Morin, 1993) for sleep and the Dimensions of Anger Reactions for anger (Novaco, 1975)—it would be useful to include these measures in treatment studies when possible.

Instruments like the CAPS provide a standardized way to determine if a symptom is *present*, but it appears that there is no clear consensus on how to define a symptom as being *residual*. We suggest that the measure be computed at the level of the person, and not based on post-treatment group averages exceeding a specific threshold (e.g., Gutner et al., 2013). We also suggest that simply reporting what percentage of participants have a given symptom after treatment (e.g., Pruiksma et al., 2016) is not optimal because a participant may not have a given symptom before treatment. We recommend a measure that is person-specific and accounts for symptom presence before treatment, such as a conditional probability. We further recommend conditional probabilities calculated at posttreatment rather than follow-up as the best indicator of that symptom's continued presence; conditional probabilities calculated at longer follow-ups (e.g., Larsen et al., 2018) are useful, but do not address the question of whether the symptom remained after treatment. Longer-term measures may need to account for symptom presence at posttreatment as well, for example, to determine if a symptom that remitted following treatment had returned.

When interpreting our findings, it is important to remember that our sample consisted of female veterans and active duty personnel who had severe and chronic PTSD with multiple comorbidities. Almost all had experienced sexual trauma, which was the index trauma for two thirds (Schnurr et al., 2007). The sample was large and ethnically diverse, but results may not generalize to men, non-veterans, and individuals who have experienced other types of traumatic events or are less clinically complex. The data were collected between 2002 and 2005 (Schnurr et al., 2007). It is also important to remember that we examined only two treatments, and that other treatments may lead to the identification of different residual symptoms. In addition, the PE manual used was based on an earlier version of the manual currently in use, and participants were diagnosed using DSM-IV criteria. Regarding the latter point, the VA/DoD PTSD guideline (2017) argues that the evidence based on DSM-IV should generalize to treating PTSD diagnosed according to DSM-5. However, the effects of PE or any treatment on the three new symptoms added to the diagnostic criteria are unknown. With regard to measurement, because this was a secondary analysis, symptoms were assessed using single items rather than more detailed measures. We also did not assess comorbid psychiatric diagnoses at posttreatment and therefore were unable to explore to what extent comorbidity might account for the residual symptoms observed.

5 | CONCLUSION

Our findings suggest that the cluster of hyperarousal symptoms is difficult to treat among PTSD patients, even among those who have a substantial clinical response. Although findings on sleep and anger are consistent with prior research, more investigation of residual

symptoms in PTSD is needed in order to optimally understand which symptoms are residual across treatments—specifically, studies of different treatments that use comparable definitions of symptom presence and examine the effects of both specific treatments (various medications and psychotherapies) and treatment success (loss of diagnosis, remission). Studies that examine which treatments are most effective for which symptoms are needed. Research should also examine whether residual comorbid disorders account for residual symptoms—e.g., depression might explain the residual sleep symptoms observed in this and other studies—and whether patient characteristics predict these symptoms. The ultimate goal is to learn what our treatments do—and do not do—so that we can enhance treatment effectiveness for individuals recovering from traumatic experiences.

ACKNOWLEDGMENTS

This study was conducted with grant CSP #494 from the VA Cooperative Studies Program and support from the Department of Defense for CSP #494. However, the views expressed in this article are those of the authors and do not necessarily represent the views of the Department of Veterans Affairs, the Department of Defense, or any U.S. government agency. Trial registration information for CSP #494: clinicaltrials.gov Identifier NCT00032617. Data reported were presented at the Annual Meeting of the International Society for Traumatic Stress Studies, November 2017.

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REFERENCES

Bandelow, B., Reitt, M., Röver, C., Michaelis, S., Görlich, Y., & Wedekind, D. (2015). Efficacy of treatments for anxiety disorders: A meta-analysis. *International Clinical Psychopharmacology*, *30*, 183–192. https://doi.org/10.1097/YIC.0000000000000078

Belleville, G., Guay, S., & Marchand, A. (2011). Persistence of sleep disturbances following cognitive-behavior therapy for posttraumatic stress disorder. *Journal of Psychosomatic Research*, *70*, 318–327. https://doi.org/10.1016/j.jpsychores.2010.09.022

Bryant, R. A., Creamer, M., O'Donnell, M., Forbes, D., McFarlane, A. C., Silove, D., & Hadzi-Pavlovic, D. (2017). Acute and chronic posttraumatic stress symptoms in the emergence of posttraumatic stress disorder: A network analysis. *JAMA Psychiatry*, *74*, 135–142. https://doi.org/10.1001/jamapsychiatry.2016.3470

Carpenter, J. K., Andrews, L. A., Witcraft, S. M., Powers, M. B., Smits, J. A. J., & Hofmann, S. G. (2018). Cognitive behavioral therapy for anxiety and related disorders: A meta analysis of randomized placebo controlled trials. *Depression and Anxiety*, *35*, 502–514. https://doi.org/10.1002/da.22728

Conradi, H. J., Ormel, J., & de Jonge, P. (2011). Presence of individual (residual) symptoms during depressive episodes and periods of remission: A 3-year prospective study. *Psychological Medicine*, *41*, 1165–1174. https://doi.org/10.1017/S0033291710001911

Cuijpers, P., Sijbrandij, M., Koole, S. L., Andersson, G., Beekman, A. T., & Reynolds, C. F., III (2013). The efficacy of psychotherapy and pharmacotherapy in treating depressive and anxiety disorders: A meta-analysis of direct comparisons. *World Psychiatry*, *12*, 137–148. https://doi.org/10.1002/wps.20038

Culpepper, L., Muskin, P. R., & Stahl, S. M. (2015). Major depressive disorder: Understanding the significant of residual symptoms and balancing efficacy with tolerability. *The American Journal of Medicine*, *128*, S1–S15.https://doi.org/10.1016/j.amjmed.2015.07.001

Department of Veterans Affairs and Department of Defense. (2017). *VA/DoD clinical practice guideline for the management of posttraumatic stress disorder and acute stress disorder*. Washington, DC: Author.

Elhai, J. D., & Palmieri, P. A. (2011). The factor structure of posttraumatic stress disorder: A literature update, critique of methodology, and agenda for future research. *Journal of Anxiety Disorders*, *25*, 849–854. https://doi.org/10.1016/j.janxdis.2011.04.007

First, M. B., Spitzer, R. L., Gibbon, M., & Williams, J. B. W. (1995). *Structured clinical interview for DSM–IV (patient ed; SCID-I/P; Version 2.0)*. New York, NY: Biometrics Research.

Foa, E. B., Hembree, E. A., & Rothbaum, B. O. (2007). *Prolonged exposure therapy for PTSD: Emotional processing of traumatic experiences, therapist guide*. New York, NY: Oxford University Press.

Foa, E. B., & Kozak, M. J. (1986). Emotional processing of fear: Exposure to corrective information. *Psychological Bulletin*, *99*, 20–35. Retrieved from http://doi.org/10.1037/0033-2909.99.1.20

Foa, E. B., & Zinbarg, R. E., & Rothbaum, B. O. (1992). Uncontrollability and unpredictability in post-traumatic stress disorder: An animal model. *Psychological Bulletin*, *112*, 218–238. https://doi.org/10.1037//0033-2909.112.2.218.

Geoffroy, P. A., Scott, J., Boudebesse, C., Lajnef, M., Henry, C., Leboyer, M., … Eitan, B. (2015). Sleep in patients with remitted bipolar disorders: A meta-analysis of actigraphy studies. *Acta Psychiatrica Scandinavica*, *131*, 89–99. https://doi.org/10.1111/acps.12367

Gutner, C. A., Casement, M. D., Gilbert, K. S., & Resick, P. A. (2013). Changes in sleep symptoms across cognitive processing therapy and prolonged exposure: A longitudinal perspective. *Behaviour Research and Therapy*, *51*, 817–822. https://doi.org/10.1016/j.brat.2013.09.008

Hassija, C. M., Jakupcak, M., & Gray, M. J. (2012). Numbing and dysphoria symptoms of posttraumatic stress disorder among Iraq and Afghanistan war veterans. *Behavior Modification*, *36*, 834–856. https://doi.org/10.1177/0145445512453735

King, D. W., Leskin, G. A., King, L. A., & Weathers, F. W. (1998). Confirmatory factor analysis of the clinician-administered PTSD scale: Evidence for the dimensionality of posttraumatic stress disorder. *Psychological Assessment*, *10*, 90–96. https://doi.org/10.1037/1040-3590.10.2.90

Larsen, S. E., Fleming, C. E., & Resick, P. A. (2018). Residual symptoms following empirically supported treatment for PTSD. *Psychological Trauma: Theory, Research, Practice, and Policy*, Advance online publication. https://doi.org/10.1037/tra0000384

Lee, D. J., Schnitzlein, C. W., Wolf, J. P., Vythilingam, M., Rasmusson, A. M., & Hoge, C. W. (2016). Psychotherapy versus pharmacotherapy for posttraumatic stress disorder: Systematic review and meta-analyses to determine first-line treatments. *Depression and Anxiety*, *33*, 792–806. https://doi.org/10.1002/da.22511

Litz, B. T. (1992). Emotional numbing in combat-related post-traumatic stress disorder: A critical review and reformulation. *Clinical Psychology Review*, *12*, 417–432. https://doi.org/10.1016/0272-7358(92)90125-R

Litz, B. T., & Gray, M. J. (2002). Emotional numbing in posttraumatic stress disorder: Current and future research directions. *Australian and New Zealand Journal of Psychiatry*, *36*, 198–204. https://doi.org/10.1046/j.1440-1614.2002.01002.x

McNally, R. J., Heeren, A., & Robinaugh, D. J. (2017). A Bayesian network analysis of posttraumatic stress disorder symptoms in adults reporting childhood sexual abuse. *European Journal of Psychotraumatology*, *8*, S1341276. https://doi.org/10.1080/20008198.2017.1341276

McNally, R. J., Robinaugh, D. J., Wu, G. W. Y., Wang, L., Deserno, M., & Borsboom, D. (2015). Mental disorders as causal systems: A network approach to posttraumatic stress disorder. *Clinical Psychological Science*, *3*, 836–849. https://doi.org/10.1177/2167702614553230

Morin, C. M. (1993). *Insomnia, psychological assessment, and management*. New York, NY: Guilford Press.

Novaco, R. W. (1975). *Dimensions of anger reactions*. Irvine, CA: University of California.

Pruiksma, K. E., Taylor, D. J., Wachen, J. S., Mintz, J., Young-McCaughan, S., Peterson, A., … Resick, P. A. (2016). Residual sleep disturbances following PTSD treatment in active duty military personnel. *Psychological Trauma*, *8*, 697–701. https://doi.org/10.1037/tra0000150

Romera, I., Pérez, V., Quail, D., Berggren, L., Lenox-Smith, A., & Gilaberte, I. (2014). Individual residual symptoms and functional impairment in patients with depression. *Psychiatry Research*, *220*, 258–262. https://doi.org/10.1016/j.psychres.2014.07.042

Schnurr, P. P., Friedman, M. J., Engel, C. C., Foa, E. B., Shea, M. T., Chow, B. K., … Bernardy, N. (2007). Cognitive behavioral therapy for posttraumatic stress disorder in women: A randomized controlled trial. *JAMA: Journal of the American Medical Association*, *297*, 820–830. https://doi.org/10.1001/jama.297.8.820

Schnurr, P. P., Friedman, M. J., Engel, C. C., Foa, E. B., Shea, M. T., Resick, P. M., … Chow, B. K. (2005). Issues in the design of multisite clinical trials of psychotherapy: VA cooperative study no. 494 as an example. *Contemporary Clinical Trials*, *26*, 626–636. https://doi.org/10.1016/j.cct.2005.09.001

Schnurr, P. P., & Lunney, C. A. (2012). Work-related outcomes among female veterans and service members after treatment of posttraumatic stress disorder. *Psychiatric Services*, *63*, 855–861. https://doi.org/10.1176/appi.ps.201100415

Schnurr, P. P., & Lunney, C. A. (2015). Differential effects of prolonged exposure on posttraumatic stress disorder symptoms in female veterans. *Journal of Consulting and Clinical Psychology*, *83*, 1154–1160. https://doi.org/10.1037/ccp0000031

Schnurr, P. P., & Lunney, C. A. (2016). Symptom benchmarks of improved quality of life in PTSD. *Depression and Anxiety*, *33*, 247–255. https://doi.org/10.1002/da.22477

Schnurr, P. P., Lunney, C. A., Bovin, M. J., & Marx, B. P. (2009). Posttraumatic stress disorder and quality of life: Extension of findings to veterans of the wars in Afghanistan and Iraq. *Clinical Psychology Review*, *29*, 727–735. https://doi.org/10.1016/j.cpr.2009.08.006

Schnurr, P. P., Lunney, C. A., Forshay, E., Thurston, V. L., Chow, B. K., Resick, P. A., & Foa, E. B. (2009). Sexual function outcomes in women treated for posttraumatic stress disorder. *Journal of Women's Health*, *18*, 1549–1557. https://doi.org/10.1089/jwh.2008.1165

Sippel, L. M., Watkins, L. E., Pietrzak, R. H., Hoff, R., & Harpaz-Rotem, I. (2018). The unique roles of emotional numbing and arousal symptoms in relation to social connectedness among military veterans in residential treatment for PTSD. *Psychiatry*, *81*, 271–282. https://doi.org/10.1080/00332747.2017.1395313

Spoormaker, V. I., & Montgomery, P. (2008). Disturbed sleep in posttraumatic stress disorder: Secondary symptom or core feature? *Sleep Medicine Reviews*, *12*, 169–184. https://doi.org/10.1016/j.smrv.2007.08.008

Watts, B. V., Schnurr, P. P., Mayo, L., Weeks, W., Young-Xu, Y., & Friedman, M. J. (2013). Meta-analysis of the efficacy of treatments for posttraumatic stress disorder. *Journal of Clinical Psychiatry*, *74*, 541–550. https://doi.org/10.4088/JCP.12r08225

Weathers, F. W., Keane, T. M., & Davidson, J. R. T. (2001). Clinician-administered PTSD scale: A review of the first ten years of research. *Depression and Anxiety*, *13*, 132–156. https://doi.org/10.1002/da.1029

Weathers, F. W., Ruscio, A., & Keane, T. M. (1999). Psychometric properties of nine scoring rules for the clinician-administered posttraumatic stress disorder scale. *Psychological Assessment*, *11*, 124–133. https://doi.org/10.1037/1040-3590.11.2.124

Woodward, E., Hackman, A., Wild, J., Grey, N., Clark, D. M., & Ehlers, A. (2017). Effects of psychotherapies for posttraumatic stress disorder on sleep disturbances: Results from a randomized clinical trial. *Behaviour Research and Therapy*, *97*, 75–85. https://doi.org/10.1016/j.brat.2017.07.001

Wu, J. Q., Appleman, E. R., Salazar, R. D., & Ong, J. C. (2015). Cognitive behavioral therapy for insomnia comorbid with psychiatric and medical conditions: A meta-analysis. *JAMA Internal Medicine*, *175*, 1461–1472. https://doi.org/10.1001/jamainternmed.2015.3006

Zajecka, J. M. (2013). Residual symptoms and relapse: Mood, cognitive symptoms, and sleep disturbances. *Journal of Clinical Psychiatry*, *74*(Suppl. 2), 9–13. https://doi.org/10.4088/JCP.12084su1c.02

Zayfert, C., & DeViva, J. C. (2004). Residual insomnia following cognitive behavioral therapy for PTSD. *Journal of Traumatic Stress*, *17*, 69–73. https://doi.org/10.1023/B:JOTS.0000014679.31799.e7

How to cite this article: Schnurr PP, Lunney CA. Residual symptoms following prolonged exposure and present-centered therapy for PTSD in female veterans and soldiers. *Depress Anxiety*. 2019;36:162–169. https://doi.org/10.1002/da.22871