



The efficacy of recommended treatments for veterans with PTSD: A metaregression analysis



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HIGHLIGHTS

- Veterans with PTSD benefit less from psychotherapy than other populations.
- We performed meta-analyses to identify psychotherapy efficacy predictors.
- Group-only therapy formats should not be used to treat PTSD.
- Exposure therapy and CPT are preferred above SMT and EMDR.
- Patients with low and high PTSD symptom severity levels risk lower treatment gains.

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ABSTRACT

Soldiers and veterans diagnosed with PTSD benefit less from psychotherapy than non-military populations. The current meta-analysis identified treatment predictors for traumatised soldiers and veterans, using data from studies examining guideline recommended interventions, namely: EMDR, exposure, cognitive, cognitive restructuring, cognitive processing, trauma-focused cognitive behavioural, and stress management therapies. A systematic search identified 57 eligible studies reporting on 69 treated samples. Exposure therapy and cognitive processing therapy were more effective than EMDR and stress management therapy. Group-only therapy formats performed worse compared with individual-only formats, or a combination of both formats. After controlling for study design variables, EMDR no longer negatively predicted treatment outcome. The number of trauma-focused sessions, unlike the total number of psychotherapy sessions, positively predicted treatment outcome. We found a relationship between PTSD pretreatment severity levels and treatment outcome, indicating lower treatment gains at low and high PTSD severity levels compared with moderate severity levels. Demographic variables did not influence treatment outcome. Consequently, soldiers and veterans are best served using exposure interventions to target PTSD. Our results did not support a group-only therapy format. Recommended interventions appear less effective at relatively low and high patient PTSD severity levels. Future high-quality studies are needed to determine the efficacy of EMDR.

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1. Introduction

Deployed soldiers and veterans have risked exposure to life-threatening stressors, such as combat, injury, and witnessing suffering and death. Whilst most veterans were healthy, resilient individuals able to cope with such stressors, between 3 and 17% developed post-traumatic stress disorder (PTSD) in the first years after deployment (Engelhard et al., 2007; Richardson, Frueh, & Acierno, 2010). PTSD is a mental disorder that evokes severe distress, chronic suffering and impairment. Its core symptoms comprise re-experiencing traumatic content, persistent avoidance of traumatic content, negative alterations in cognitions, and arousal and reactivity (American Psychiatric Association, 1994, 2013). More than half a million American veterans sought PTSD care at a cost of three billion dollars (Institute of Medicine [IOM], 2014).

Clinical-practice guidelines recommend psychological treatment interventions to target PTSD (Australian Centre for Posttraumatic Mental Health (ACPMH), 2007; IOM, 2008; International Society for Traumatic Stress Studies (ISTSS), 2009; National Institute for Clinical Excellence (NICE), 2005; The management of post-traumatic stress Working Group, 2004, 2010). The following first-choice interventions are recommended by most or all clinical practice guidelines: eye movement desensitization and reprocessing (EMDR), exposure therapy (ET), cognitive therapy (CT), cognitive restructuring therapy (CR), cognitive processing therapy (CPT), and trauma-focused cognitive behavioural therapy (TF-CBT). Stress management therapy (SMT) has also been mentioned because the VA-DoD guidelines (The management of post-traumatic stress Working Group, 2010) recommend stress inoculation therapy (SIT), which is a SMT intervention. Recent empirical evidence confirmed that veterans respond reasonably well to these recommended interventions (Kitchiner, Roberts, Wilcox, & Bisson, 2012). However, veterans benefitted less from psychotherapy than non-military PTSD populations (Watts et al., 2013) and meta-analyses reported smaller treatment effect sizes for traumatised veterans ($d = .68-.81$) versus non-veterans ($d = 1.04-1.83$) (Bradley, Greene, Russ, Dutra, & Westen, 2005; Goodson et al., 2011). The majority of veterans with PTSD (78%) still receive PTSD treatment after four years of treatment (Congress of the United States (CBO), 2012). Psychotherapies apparently deliver only limited PTSD symptom-reduction in the veteran population. Psychotherapy studies face further critique that their findings are mostly based on the average responses of large treatment groups that ignore within-person variability (i.e., individual factors that influence outcome). As a response, researchers have begun to emphasize the importance of individual treatment responses and mechanisms of therapeutic change as 'the surest way to enhance efficacy' (Barlow, Bullis, Comer, & Ametaj, 2013).

There are various explanations why veterans benefit less from treatment than other PTSD populations. Several authors highlighted the intensive, repetitive and interpersonal nature of combat-related traumatic events as a complicating factor (Pietrzak, Whealin, Stotzer, Goldstein, & Southwick, 2011). Traumatic combat experiences are often less straightforward than single traumatic events (e.g., a car accident) and are known to decrease PTSD treatment effectiveness (Price, Gros, Strachan, Ruggiero, & Acierno, 2013). On a patient level, treatment complications are reported among more symptomatic veterans. These veterans experienced more severe symptoms and more

comorbid disorders, and include severe PTSD levels (Belsher, Tiet, Garvert, & Rosen, 2012; Boden, Bernstein, et al., 2012; Boden, Kimerling, et al., 2012; Johnson & Lubin, 1997; Owens, Chard, & Cox, 2008), severe anger issues (Forbes, Creamer, Hawthorne, Allen, & McHugh, 2003; Forbes et al., 2008; Lloyd et al., 2014; Owens et al., 2008), comorbid alcohol abuse (Forbes et al., 2003, 2008), and comorbid depression (Forbes et al., 2003). The results however are not unequivocal, a minority of studies reported no negative and even positive treatment effects for more symptomatic veterans (Fontana, Rosenheck, & Desai, 2012; Forbes et al., 2002; Richardson et al., 2014; Steindl, Young, Creamer, & Crompton, 2003). From a developmental perspective, veterans diagnosed with a borderline personality disorder (Forbes et al., 2002), a 'disorders of extreme stress not otherwise specified' (DESNOS) diagnosis (Ford & Kidd, 1998), and dysfunctional attachment style (Forbes, Parslow, Fletcher, McHugh, & Creamer, 2010), fared worse in treatment. The results are again not unequivocal, Walter, Kiefer, and Chard (2012) did not find any effects for personality disorders on PTSD treatment, and early childhood experiences did not predict treatment outcome (Johnson & Lubin, 1997). From a social perspective, veterans performed worse in treatment if they were socially isolated (Forbes et al., 2002), had poor functioning families, and experienced marital distress (Evans, Cowlshaw, Forbes, Parslow, & Lewis, 2010; Evans, Cowlshaw, & Hopwood, 2009). Last, organisational and treatment factors also influence outcome. For example, PTSD treatment success was predicted by positive treatment expectations and longer treatment duration (Belsher et al., 2012), as well as a willingness for patients to therapeutically change (Rooney et al., 2007).

The evidence for treatment predictors may seem abundant from these articles, but is in reality scant. Most of these factors were studied only once or twice which does not offer a firm base for predictive statements. The vast majority of studies examined univariate relationships between a single predictor and treatment outcome, thus not taking the interrelatedness between predictor variables into account. Only a few studies investigated the effects of multiple predictors simultaneously (e.g., Forbes et al., 2008). Many questions related to mechanisms of change also remain unanswered. It is unclear whether important veteran patient characteristics such as age and gender, should be treated in the same manner as civilians (IOM, 2008). There is also debate about the most optimal content and format for delivering treatment; is group-therapy formats as effective as individual-therapy formats (The management of post-traumatic stress Working Group, 2010), and is a trauma-focus imperative for PTSD treatment (Benish, Imel, & Wampold, 2008; Ehlers et al., 2010; Wampold et al., 2010). Consequently, there is a need to assess the influence of veteran patient and treatment characteristics on treatment outcome. Using meta-analysis, the information from numerous studies can be combined to strengthen predictive evidence, test treatment guideline recommendations and help resolve conflicting predictor study outcomes. Up till now, meta-analyses about predictive factors are however lacking.

Prognostic research offers novel opportunities to assess the impact of specific factors on treatment outcome. The term prognosis refers to the probability of an individual developing a particular state of health (e.g., treatment outcome) over a specific time, based on his or her clinical and non-clinical profile (Moons, Royston, Vergouwwe, Grobbee, & Altman, 2009). Prognostic research thus allows us to make inferences or predictions about expected treatment outcomes for individual

patients. It advances understanding of therapeutic change mechanisms, enables psychotherapy improvements, and the creation of clinical decision making tools (Altman, 2001; Moons, Altman, Vergouwe, & Royston, 2009). Such tools enable clinicians to select suitable interventions tailored to the specific needs of each individual. The present prognostic study aims to identify PTSD psychotherapy treatment efficacy predictors for traumatised veterans. It is the first meta-analysis to use data from guideline recommended PTSD psychotherapy intervention studies in search of predictors.

2. Method

2.1. Search strategy

We undertook a systematic literature search to retrieve all first-choice psychotherapy studies that target PTSD among veterans and active military personnel. The search was performed in the following databases and their accompanied search registries: PubMed (NCBI), Pilots (ProQuest), PsycINFO (Ovid), Embase (Elsevier), Medline (OvidSP), CINAHL (Ebsco Host), and Web of Science (ISI Web of Knowledge). The search domains and their respective synonyms were combined into search syntaxes using Boolean operators. For example, the PubMed search syntax was: (PTSD OR "Posttraumatic stress disorder" OR "Post traumatic stress disorder" OR "Post-traumatic stress disorder" OR "Combat disorder" OR Psychotrauma OR Traumatized OR Traumatized) AND (Treatment OR Treatments OR Therap* OR Psychotherap* OR Intervention OR Interventions) AND (Veteran OR Veterans OR Troops OR War OR Ex-military OR Army OR Soldier OR Soldiers OR Peacemaker OR Peacemakers) AND (Effectiveness OR Effect OR Effectively OR Efficacy OR Efficiency OR Efficacious OR Efficient OR Success OR "Symptom reduction" OR "Symptom decrease" OR "Treatment outcome" OR "Treatment response"). The first author screened the reference list of each included study for additional suitable studies.

2.2. Study selection

Two researchers independently reviewed the retrieved studies consecutively on title, abstract and full text, using identical selection criteria. The retrieved studies were considered eligible for inclusion if they: (a) were peer-reviewed, (b) consisted of help-seeking veterans or active duty soldiers, (c) had a PTSD diagnosis, (d) examined a first-choice PTSD psychotherapy trial, and (e) reported pre- and post-treatment PTSD symptom severity data. No time, linguistic and geographical restrictions were employed. Twenty studies reported the proportion of veterans on psychotropic drugs. Over three quarters (76%) of the patients received medication at the start of psychotherapy. These results show that medication is a common practice among veterans and soldiers with PTSD. It was not considered an exclusion criteria because it reflects standard clinical practice.

The interventions were allowed to be imbedded in more extensive treatment programmes that included other interventions. This enables inferences concerning the influence of inpatient and day treatment settings that almost exclusively involve programmes in which trauma-focused interventions consist of a single aspect of the total treatment programme. However, we excluded treatment programmes that did not define the content and number of first-choice treatment sessions, as well as case studies, secondary data-analyses, reviews and meta-analyses. Studies designed to investigate the effects of a specific medication to augment psychotherapy were also excluded.

The search identified 57 eligible studies that tested 69 interventions among 6878 patients (see Appendix A). Authors were contacted for: (a) missing data, (b) pre- and post-treatment PTSD symptom severity outcome correlations, and (c) clarification regarding suspected secondary data analysis. A follow-up e-mail was sent if no response was forthcoming.

2.3. Data extraction

The first author extracted and coded all the reports. A second coder checked the accuracy of the first coder. Both coders were in agreement 95.8% of the time. The disagreement observations (4.2%) were further scrutinised and, after reaching consensus, led to (1%) coding changes.

Various predictors were included in the meta-analyses. Patient characteristics: age (mean age in years), gender (% male), ethnicity (% Caucasian, Afro-American, and Hispanic), marital (% divorced), employment (% unemployed), and military status (veteran versus active duty), and pretreatment PTSD symptom severity level (% of severity calculated by dividing the mean sample score by the maximum score on the instrument). Treatment characteristics: treatment setting (outpatient or inpatient), modality (individual, group, or combination format), delivery (face-to-face, internet-based, or using virtual reality simulations), number of sessions, and number of trauma-focused sessions. The number of trauma-focused sessions was only examined in outpatient settings because most inpatient studies were unclear about the number of trauma-focused sessions compared to the total number of sessions. Study characteristics: PTSD measurement instrument, treatment allocation strategy (randomised versus not-randomised), and whether intent-to-treat or completer analyses were used.

We gathered pre- and post-treatment correlations to calculate the effect size for each intervention. The majority of the correlations (57%) between the pre- and post-treatment PTSD measures were attained directly from the article, or calculated from dependent t-test analyses provided in the article, or via author communications. The remaining correlations (43%) were imputed using predictive mean matching (10 imputations). Predictive mean matching is a recommended multiple imputation technique to increase the reliability of the results (Vink, Frank, Pannekoek, & Van Buuren, 2014). To inform the prediction of the missing data in the imputation models, we included variables that were considered missing at random (MAR). These consisted of a range of demographic, treatment, and design variables, as well as the dependent variable (treatment effect size). Multiple instruments ascertained the PTSD severity; the Clinician-Administered PTSD Scale (CAPS) was considered the 'gold standard'.

2.4. Methodological quality

The first author assessed the methodological quality of each study using the 'Methodology checklist for prognostic studies'—an assessment tool developed by NICE (2009). Several topics were inspected regarding their potential for bias, namely: (a) study sample representability, (b) loss of follow-up data, (c) adequate measurement of prognostic factors, (d) adequate measurement of outcome of interest, and (e) potential confounders. The appropriateness of the topic of statistical analysis was not inspected, since the current meta-analysis did not include pre-analysed data. Instead of reporting a 'yes', 'no', or 'unclear' risk of bias, the current study reported 'low', 'moderate', or 'high' risk of bias. The risk of bias was assessed based on an appraisal of the quality of each topic as formulated in the employed methodology checklist. For example, to address the quality of the study sample representability, points to consider were: is the population of interest adequately described with respect to key characteristics, sampling frame and recruitment, inclusion and exclusion criteria, etc. (see NICE, 2009 Appendix J for the complete checklist). After evaluating the quality of each topic the overall quality of each article was assessed. Articles with a low risk of bias on each topic and a moderate risk of bias on no more than one topic were considered to be at low risk of bias. Articles with a moderate risk of bias on two or more topics and with no more than one high risk of bias topic were considered to be at moderate risk of bias. Articles with two or more high risk of bias topics were considered to be at high risk of bias. Twenty percent of the studies were independently assessed for risk of bias by a second rater. The interrater reliability was good (.85 kappa).

2.5. Statistical analysis

The treatment effect sizes were calculated using Hedges' g for each intervention. We calculated the pooled effect size using macro's developed by Wilson (2005) for SPSS statistical software. The same macro was used to perform subgroup analysis (analogue to the one-way ANOVA) and meta-regression analyses for categorical and continuous predictors. Categorical variables that were significantly associated with effect sizes in univariate analyses were dummy coded to enable inclusion in multivariate regression analyses. Pretreatment PTSD severity was also investigated using quadratic regression because of conflicting predictive findings from previous studies (Forbes et al., 2003; Perconte & Griger, 1991). Quadratic regression variables were standardised (mean-centred) to avoid multicollinearity. A random-effects model was chosen because of the expected heterogeneity between the studies. We estimated the model using the iterative maximum likelihood estimation.

The authors assessed the heterogeneity using the Q statistic and a significance test of the Q statistic (p -value), the ratio of true heterogeneity to total observed variation (I^2), and investigated the possibility of publication bias using an Egger test to detect funnel plot asymmetry (Borenstein, Hedges, Higgins, & Rothstein, 2009). Two sensitivity analyses tested whether the exclusion of low quality (with risk of bias) studies, or the removal of any one study, influenced the results.

3. Results

Fig. 1 shows an overview of the study search and selection process. Forest plots for random-effects meta-analysis are presented in Fig. 2. The search was performed in June 2014 and yielded 2149 unique articles from five databases. The majority of articles ($n = 2092$) were excluded after screening. Major reasons for exclusion were: absence of PTSD diagnosis in study sample ($n = 374$), no veteran or active soldier sample ($n = 511$), not a psychotherapy study, or psychotherapy did not target PTSD, or PTSD measurements were not included ($n = 844$), secondary analysis (including reviews and meta-analyses), books (chapters), or protocols ($n = 166$), and studies investigating a psychotherapy that was not considered first-choice, or with unspecified treatment content ($n = 142$). The database search identified 55 eligible studies. Two additional studies were added after screening the reference lists of all eligible studies, resulting in 57 reporting on 69 eligible samples.

Table 1 describes the data collected from each study. The studies were almost exclusively from North-American origin (93%). The remaining four studies originated from Australia ($n = 2$), Israel ($n = 1$), and Portugal ($n = 1$). Most studies consisted of either ET or CPT therapy (90%). The CAPS and PTSD Checklist (PCL) were the primary PTSD outcome measures in 86% of the studies. Most studies had an observational design (67%), whilst a third (33%) had a randomised controlled trial (RCT) design. The majority of interventions delivered psychotherapy in an individual format (58%) and in an outpatient setting (65%). 17% were treated in an inpatient setting and another 17% had an unknown treatment setting. Some studies reported very large effect sizes (max. 3.1), whereas other studies reported a worsening of symptoms after treatment (min. $-.46$). Most studies involved veterans (88%) instead of active duty soldiers (12%). The average amount of patients per study was 104 patients ($SD = 246$), with $n = 5$ as the lowest number of patients, and $n = 1888$ as the highest number of patients in a study. For additional details the reader is referred to a supplementary table (Appendix B). The quality of each included study is summarised in Appendix C, almost half (48%) of the studies were considered of high quality with a low overall risk of bias, 22% were of moderate quality, and 23% of low quality. The pooled effect size for all interventions was $g = 1.12$ (95% CI, .98–1.25; see Fig. 2).

3.1. Univariate predictors

The predictive utility of several categorical variables was examined by means of subgroup analyses (Table 2 and Fig. 3). Interventions that solely consisted of a group-only therapy format fared significantly worse compared with interventions that consisted of—or included—individual psychotherapy ($g = .63$ vs. $g = 1.22$; $p < .001$). The individual therapy format did not differ significantly from a combination (individual and group) format ($g = 1.17$ vs. $g = 1.40$; $p = .26$). The results demonstrated significant differences ($p < .001$) between treatment interventions, with CPT ($g = 1.33$) and ET ($g = 1.06$) yielding greater effect sizes than EMDR ($g = .38$) and SMT ($g = .16$). These results show that patients treated with CPT or ET had greater PTSD symptom reductions compared to those treated with EMDR and SMT. As expected, non-random treatment allocation was associated with a higher effect size compared to random treatment allocation ($g = 1.27$ vs. $g = .68$; $p < .001$), showing that patients that were randomly allocated to a guideline recommended PTSD intervention experienced fewer treatment gains (i.e., lower effect size) compared to patients that participated in observational studies. There were no significant group differences regarding type of treatment delivery, treatment setting, intent-to treat vs. completer analyses, measurement instrument and measurement method.

Meta-regression analyses (Table 3) identified the number of trauma-focused sessions ($\beta = .51$; $p < .001$) as a positive predictor, indicating that each subsequent trauma-focused session further decreased PTSD symptom severity. PTSD symptom severity did not predict treatment outcome. After visual inspection of the pretreatment symptom severity scatterplot, a quadratic expression between symptom severity and treatment outcome was added to the linear expression. The quadratic regression expression of pretreatment severity ($\beta = -.29$; $p = .01$) negatively predicted treatment outcome, indicating that patients with relatively low and high PTSD symptom severity levels benefited less from treatment than patients with moderate symptom severity levels. Demographic data and the number of treatment sessions did not predict treatment outcome.

3.2. Multivariate predictors

The significant univariate predictors were further assessed whilst controlling for interference from confounding study characteristics variables. Treatment allocation was the only significant predictor and therefore the only study characteristic we controlled for (Table 4). Therapy format proved a significant categorical predictor in the previous subgroup analysis. It was dummy coded (group-only vs. individual or combination therapy format) and reanalysed as a continuous predictor. This enabled us to compare the effects of therapy format on treatment outcome with other continuous predictors and control for confounding variables. The same strategy was employed for treatment type. Each intervention was dummy coded against ET as reference group.

Multivariate meta-regression analyses revealed the number of trauma-focused sessions ($\beta = .40$; $p < .01$) as a positive predictor of treatment effect, meaning that each subsequent trauma-focused sessions decreased PTSD symptoms (i.e., increased treatment effect size). Group-only therapy format ($\beta = -.40$; $p < .001$) was a negative treatment predictor, indicating that patients treated in a group therapy format benefitted less from therapy than patients treated in an individual therapy format or in a combination (individual and group) format. The quadratic expression of pretreatment PTSD symptom severity ($\beta = -.29$; $p < .01$) was a negative outcome predictor, illustrating that patients with relatively low and high PTSD symptom severity levels experienced less symptom decrease compared to patients with moderate severity levels (Fig. 4). The SMT intervention ($\beta = -.26$; $p < .05$) negatively predicted treatment outcome compared to ET (dummy reference group), indicating that patients that were treated with SMT

experienced less PTSD symptom reduction compared to ET therapy. EMDR ($\beta = -.12$; $p = .26$) no longer predicted treatment outcome after controlling for allocation, indicating that EMDR was equally effective as ET (dummy reference group) in reducing PTSD symptoms.

3.3. Heterogeneity, publication bias and sensitivity analysis

There was evidence of heterogeneity ($p(Q) = .00$) with a high dispersion of the observed variance ($I^2 = 96\%$). These findings validated

the usage of the random-effects model and the search for covariates to explain the observed dispersion. The Egger test did not indicate a possible publication bias ($t = 1.38$, $df = 67$, p (1-tailed) = .09). Sensitivity analysis showed that exclusion of $n = 20$ (29%) studies that were judged to run a risk of bias did not impact the study results. The sensitivity analyses were completed by recalculating the pooled effect outcomes after removal of any one study from the total meta-analysis to examine the influence of each individual study on the overall effect estimate, the highest and lowest pooled effect sizes ranged between

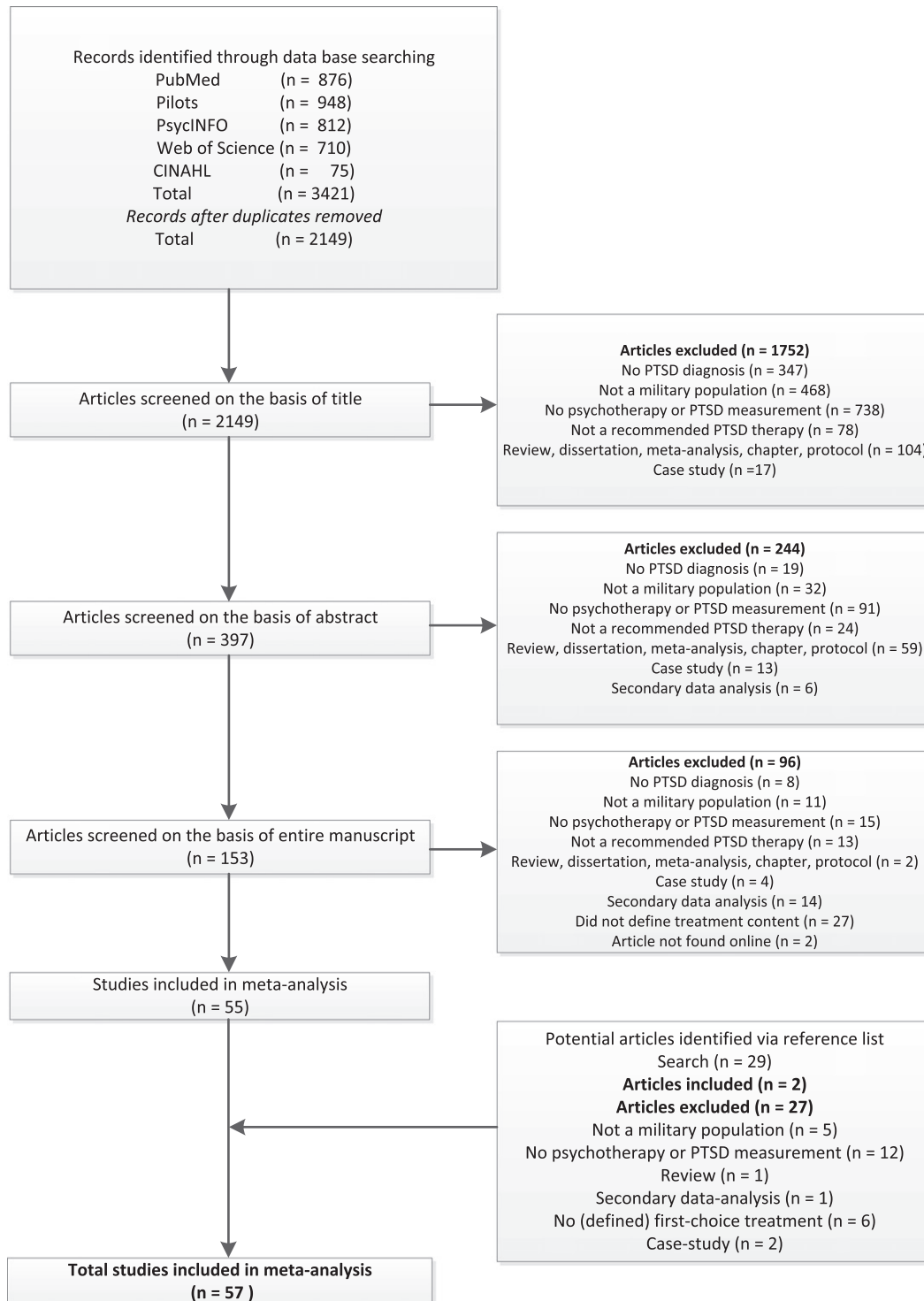


Fig. 1. Flowchart study selection.

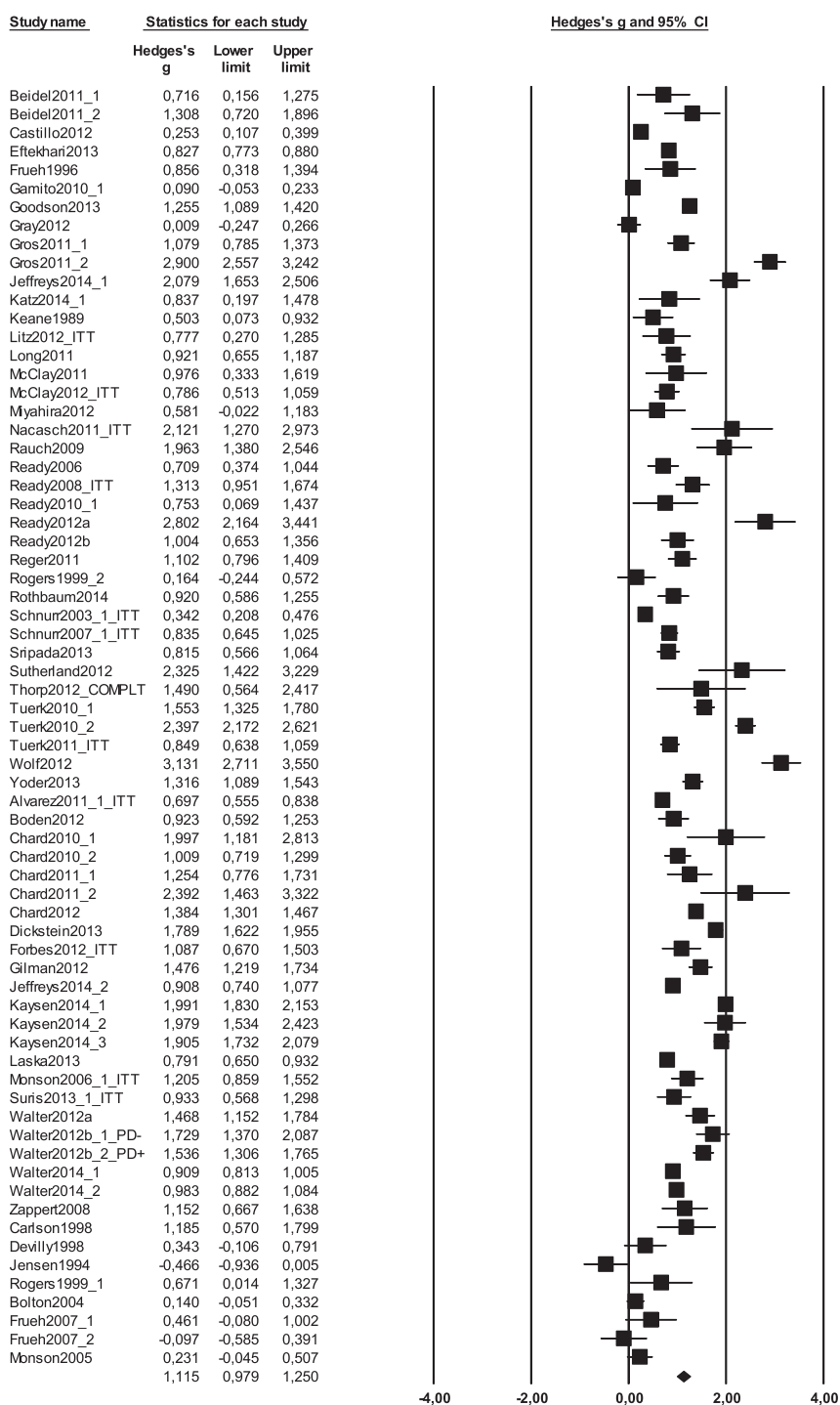


Fig. 2. Forest plot for PTSD treatment efficacy (pre vs. post).

1.14 [95% CI, 1.00–1.27] and 1.08 [95% CI, .95–1.22]. This indicated that the influence of each individual study on the pooled effect size was small.

4. Discussion

The present meta-analysis investigated PTSD psychotherapy outcome predictors for veterans and soldiers. An individual or combination (group and individual) therapy format, (prolonged) ET and CPT interventions as well as the number of trauma-focused therapy sessions predicted increased treatment effectiveness. In contrast, group-only

therapy, EMDR and SMT interventions, negatively impacted treatment effectiveness. EMDR was however no longer associated with decreased treatment effectiveness after controlling for a random or non-random treatment allocation. High and low pretreatment PTSD severity levels predicted lower treatment gains compared with moderate pretreatment PTSD severity levels (Fig. 4).

SMT interventions were less effective compared to ET and CPT interventions, whilst the results for EMDR were mixed compared to ET and CPT interventions. SMT might be less effective because it does not particularly target maladaptive trauma-related cognitions, or activate fear memory structures that allow for habituation and modification of

Table 1
Data collected from included meta-analysis studies.

		N	%
Intervention	ET	38	55
	CPT	24	35
	EMDR	4	6
	SMT	3	4
Instrument	CAPS	31	45
	PCL	28	41
	Other	10	14
Sample	Min range	5	
	Max range	1888	
Allocation	Random	23	33
	Non-random	46	67
Analysis	ITT	29	42
	Completer	36	52
Setting	Inpatient	12	17
	Outpatient	45	65
Modality	Individual	40	58
	Group	14	20
	Combination	12	17
No. of sessions	Mean	14	
	Min range	1	
	Max range	47	
No. of trauma-focused sessions	Mean	7.5	
	Min range	0	
	Max range	13	
Pretreatment symptom severity (%)	Mean	64	
	Min range	42	
	Max range	81	
ES (Hedges g)	Mean	1.1	
	Min range	−.46	
	Max range	3.1	

Note. Intervention: ET = Exposure therapy; CPT = Cognitive processing therapy; EMDR = Eye movement and reprocessing therapy; SMT = Stress management therapy. Instrument: CAPS = Clinician-Administered PTSD Scale; PCL = PTSD Checklist. Analysis: ITT = Intent-to-treat analysis. Modality: Individual = Individual therapy; Group = Group therapy; Combination = Group therapy combined with individual therapy.

the pathological fear structures. Both ET and CPT are based on cognitive and emotional processing theories (Ehlers & Clark, 2000; Rauch & Foa, 2006), using proven therapy elements, such as exposure. It is presently unclear why EMDR might be less effective than ET and CPT. Unlike exposure therapies, EMDR therapy uses free association techniques that often only briefly access details of traumatic memories, instead of repetitive exposure to traumatic memories. Experimental studies showed that the underlying mechanism of EMDR did not seem to be based on habituation (e.g., Leer, Engelhard, Altink, & Van den Hout, 2013), and would therefore be less suited for promoting habituation and symptom reduction compared exposure-based therapies (McGuire, Lee, & Drummond, 2014; Rogers & Silver, 2002). Alternatively, the inferior EMDR results might be attributed to study design characteristics. Non-random allocations are known to overestimate effect sizes (Schulz, Chalmers, Hayes, & Altman, 1995), whereas all EMDR studies used a 'superior' random allocation design. After controlling for treatment allocation, EMDR no longer predicted a negative treatment outcome compared to ET. Therefore, EMDR might be as effective as ET and CPT. It is recommended to test both hypotheses mentioned above using well-designed and controlled studies that directly compare EMDR with CPT and ET for veterans and soldiers.

Group therapy is a popular and recommended treatment format for traumatised veterans (The management of post-traumatic stress Working Group, 2010), despite insufficient evidence regarding its efficacy (IOM, 2008). The present meta-analysis demonstrated that a group-only format performed significantly worse than an individual or combined treatment format. It is expected that group size limits the amount of exposure time to one's own traumatic experiences. Most patients did not receive more than one or two personal exposure sessions within group therapy and spent the majority of exposure time listening to the traumatic stories of fellow veterans. Listening to the traumatic content of others might be less effective in activating

Table 2
Univariate subgroup analyses.

Variables	p	Mean ES	n
<i>Treatment characteristics</i>			
Intervention	.001		
CPT		1.33	23
Exposure		1.06	38
EMDR		.38	4
SMT		.16	3
Treatment setting	.70		
Outpatient		1.10	45
Inpatient		1.20	12
Treatment modality	.01		
Combination ^a		1.40	11
Individual therapy		1.17	41
Group therapy		.63	14
Treatment delivery	.16		
Face to face		1.14	57
Internet/telehealth		.82	3
Virtual reality		.73	8
<i>Study characteristics</i>			
Allocation	.001		
Non-Random		1.27	46
Random		.68	23
Analysis	.96		
Completer		1.09	36
Intent-to-treat		1.08	29
PTSD instrument	.17		
CAPS		1.19	31
PCL		1.07	28
Other		.75	10
Measurement method	.22		
Questionnaire		1.00	35
Interview		1.18	34

Note. n = Number of studies. Mean ES = Mean effect size (Hedges g).

^a Combination therapy = Group and individual therapy combined.

and habituating one's own traumatic memories. Another explanation could be that within-group tensions or sociodynamics deter from the expected therapy results (Battegay, 1977). For example, anger—a common issue among veterans with PTSD—can provoke counter-aggression from other group members, and discussions with the group leader that challenge the therapeutic progress (Stone, 2009). Traumatic experiences that evoke intense feelings of shame or guilt are also expected to be problematic for patients in a group format because they make patients become self-conscious, feel exposed, or fear judgement instead from their peers (Lee, Scragg, & Turner, 2001). Shame or guilt-ridden patients must likely overcome higher anxiety thresholds before feeling sufficiently safe to share their thoughts, feelings and experiences in group therapy compared to individual therapy.

A combination therapy format was found to be as effective as an individual-only format. All combination therapy programmes provided individual trauma-focused therapy, unlike the group-only formats that offered collective trauma-focused therapy. The combination formats often used the group therapy component to target other non-trauma focused themes, such as providing psychoeducation, social support, or emotional-regulation to address social isolation, impaired social functioning, and anger management issues. These issues can have detrimental effects for PTSD treatment outcome (Evans et al., 2009, 2010; Forbes et al., 2002, 2003, 2008; Lloyd et al., 2014; Owens et al., 2008). We believe group therapy might augment trauma-focused therapy if used in conjunction with individual trauma-focused therapy. These combination formats had the highest combined effect size, though no significant difference in effect size was found with the individual formats that reported a somewhat lower combined effect size. Interested readers are referred to the supplementary table (Appendix B) for an overview of the therapy format of each study.

The present results bridge the gap between conflicting findings regarding pretreatment symptom severity (Forbes et al., 2003;

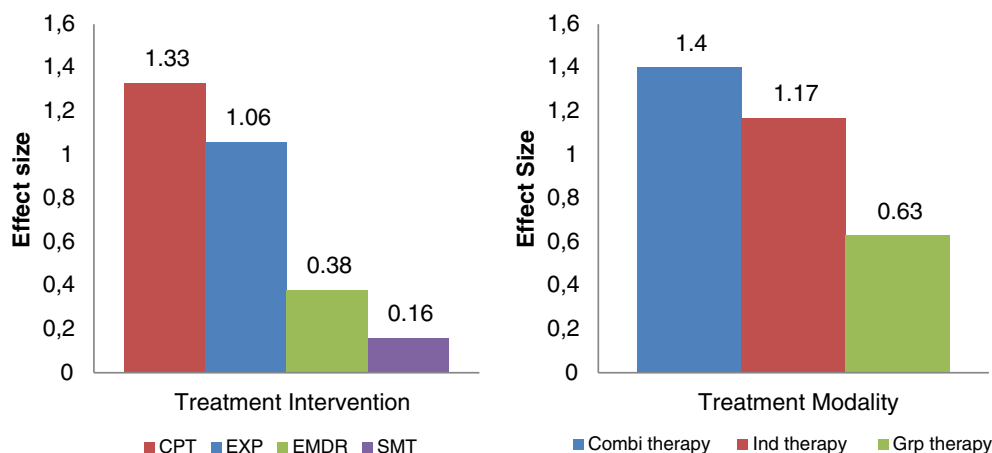


Fig. 3. Univariate analyses of treatment effect size (Hedges' g) for treatment interventions and treatment modalities.

Perconte & Griger, 1991). At moderate severity levels, patients appeared to receive the most benefit from recommended therapies, whilst low and high severity levels predicted lower treatment gains. Relatively low severity levels might reflect a state of underengagement that does not sufficiently activate the fear structure to enable optimal habituation and PTSD symptom reduction (Rauch & Foa, 2006). Conversely, patients with progressively severe symptoms become increasingly overwhelmed (overengagement) by the fear-related emotional intensity of their traumatic memories, and are unable to voluntarily cognitively inhibit and disengage from re-experiencing threatening intrusive memories (Aupperle, Melrose, Stein, & Paulus, 2012; Rubin, Boals, & Berntsen, 2008). The emotional intensity obstructs habituation to decrease anxiety levels, whilst the distracting nature of threatening stimuli could impair attention regulation and performance at the cost of therapeutic suggestions (Aupperle et al., 2012). Alternatively, increasing severity levels could cause a gradual loss in adaptive abilities (Davidson et al., 2012; Moore, Varra, Michael, & Simpson, 2010), resulting in mental defeat, which is a negative outcome predictor (Ehlers et al., 1998; Kleim & Ehlers, 2009). Higher PTSD severity levels are also indicative of multiple life and (post-) deployment stressors

among military personnel (Smid, Kleber, Rademaker, Van Zuiden, & Vermetten, 2013). Multiple (traumatic) stressors suggest a cumulative burden on survivors that complicates treatment compared to single traumatic events. Previous traumatic events moreover sensitised survivors to respond more strongly to subsequent stressors that impair recovery.

Unlike the total number of sessions, only the number of trauma-focused sessions patients received predicted treatment improvement. These results contribute to the growing evidence that PTSD interventions need to focus on the traumatic content in order to be the most effective (e.g., Bisson, Roberts, Andrew, Cooper, & Lewis, 2013). It also highlights the importance of treatment attendance to decrease PTSD symptoms. Treatment attendance was previously identified by Tarrier, Sommerfield, Pilgrim, and Faragher (2000) as one of the strongest predictors of lower PTSD treatment gains.

The different modes of delivery appeared equally effective as face-to-face therapy. The demographic variables age, gender, ethnicity, marital, work, and military status, did not appear to play a part in PTSD treatment efficacy in soldiers and veterans, suggesting that recommended PTSD interventions are equally effective across these demographic groups. Though it must be noted that ethnicity was operationalised for only three major minority groups in the United

Table 3
Univariate regression analyses.

Variables	β	R ²	n
<i>Patient characteristics</i>			
Age	-.17	3%	67
Male gender	.05	3%	65
Caucasian	-.05	0%	57
Afro-American	.03	0%	48
Hispanic	.25	6%	32
Divorced	-.29	8%	24
Unemployed	.12	2%	25
Veteran status	.10	1%	66
Pretreatment symptom severity	.06	0%	67
Pretreatment symptom severity ²	-.29*	8%	67
<i>Treatment characteristics</i>			
No. of sessions	.19	4%	68
No. of trauma-focused sessions	.51**	26%	43

Note. Age = Age in years; Male gender = % of males versus females; Caucasian = % belonging to a Caucasian ethnicity; Afro-American = % belonging to an Afro-American ethnicity; Hispanic = % belonging to a Hispanic ethnicity; Divorced = % divorced; Unemployed = % unemployed; Veteran status = % veterans versus active duty; Pretreatment symptom severity = Pretreatment PTSD symptom severity based on total questionnaire score expressed as a %; No. of sessions = Number of therapy sessions; No. of trauma-focused sessions = Number of trauma-focused therapy sessions; R² = Explained variance; n = Number of studies.

* p < .05.
** p < .01.
*** p < .001.

Table 4
Multivariate regression analyses of significant univariate predictors with 'treatment allocation as covariate.

Variables	β	R ²	ΔR^2	n
<i>Patient characteristics</i>				
Pretreatment symptom severity ²	-.29**	27%	9%	67
<i>Treatment characteristics</i>				
Group therapy format	-.40***	35%	17%	66
No. of trauma-focus sessions	.40**	37%	19%	43
CPT vs Exposure	.17	23%	5%	68
EMDR vs Exposure	-.12	21%	3%	68
SMT vs Exposure	-.26*	27%	9%	68

Note. No. of trauma-focused sessions = Number of trauma-focused therapy sessions. Group therapy format = Dummy coded variable group versus individual therapy and combination therapy. Pretreatment symptom severity = Pretreatment PTSD symptom severity based on total questionnaire score expressed as a %. CPT vs Exposure, EMDR vs Exposure and SMT vs Exposure are dummy variables of the categorical variable 'Intervention'. R² = explained variance. ΔR^2 = the change in R² values after subtracting explained variance from control variable 'Allocation'. n = Number of studies.

* p < .05.
** p < .01.
*** p < .001.

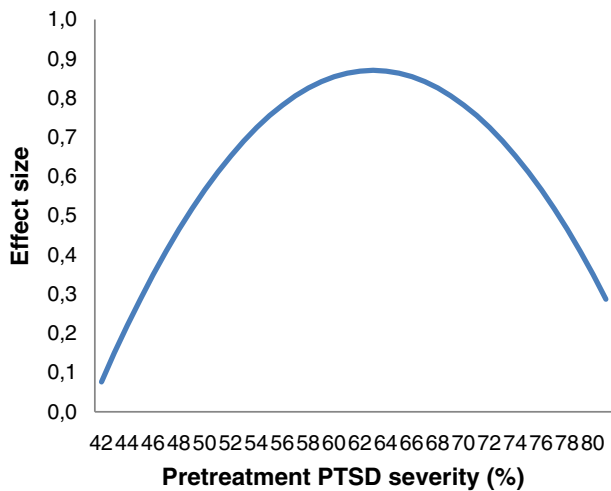


Fig. 4. Graph of quadratic regression of pretreatment PTSD symptom severity level as percentages on effect size (Hedges' *g*), whilst controlling for 'treatment allocation'.

States and in a manner that might not grasp the dynamics surrounding the concept of ethnicity, such as the phase of cultural adaptation (e.g., Knipscheer & Kleber, 2006).

4.1. Strengths and limitations

The present study is the first to gather predictive information from recommended PTSD interventions. The meta-analyses were in accordance with PRISMA guidelines (Moher, Liberati, Tetzlaff, & Altman, 2009); we performed a thorough search that minimised publication and language bias, and assessed the quality of each included study to increase the reliability of the results. Medication use is a common practice for veterans with PTSD with over 65% receiving SSRI/SNRIs (Abrams, Lund, Bernardy, & Friedman, 2013). This number roughly reflects the percentage on medication (75%) in the included meta-analysis studies and strengthens the generalisability of our findings for the clinical practice. Medication use was not investigated in the present study due to insufficient reported data. In general, medication use can be expected to have a small positive augmenting effect on treatment compared to a large psychotherapy effect on treatment outcome (Watts et al., 2013). The present study has a number of limitations. Our meta-analysis is mainly based on findings among veterans from the U.S.A. The possibility of generalizing our results to other countries remains an issue for future research. Furthermore, all meta-analyses risk ecological fallacy and the current study is not exempt from this risk (Reade, Delaney, Bailey, & Angus, 2008). The exploratory nature of the present study did not correct for multiple hypothesis testing and could risk type-I errors because it was considered more important to detect possible predictors instead of using stringent criteria that may fail to detect significant predictors. We did not examine follow-up data because only 18 studies provided data. The loss of more than two thirds of the available studies was considered an unacceptable loss in statistical power. The quality of the included studies varied, but was considered adequate based on a quality assessment; the results were robust after performing the sensitivity analysis excluding low quality studies. Only four studies examined EMDR and three studies examined SMT for veterans with PTSD, which could obscure the results. Nevertheless, the findings did not encourage SMT interventions for traumatised veterans and did not provide clear indications regarding the suitability of EMDR. It should be noted that SIT is a specific form of SMT that has been recommended by the VA-DoD guidelines (The management of post-traumatic stress Working Group, 2010), but has not been sufficiently studied for veterans and soldiers with PTSD.

4.2. Clinical implications and conclusion

Veterans are best served using individual-based, or a combination of individual-based and group-based psychotherapy, to target PTSD. Group-only therapy formats should not be used to target PTSD. Exposure-based therapies, such as (prolonged) ET and CPT, are preferred above SMT. Though we might err on the side of caution, our results do not yet support EMDR as a recommended therapy for veterans (see also Albright & Thyer, 2010; IOM guidelines, 2008).

Patients with relatively low and high PTSD symptom severity levels appear at greater risk of treatment stagnation. This finding stresses the importance for therapists to maintain a proper therapeutic window: a psychological midpoint between inadequate and overwhelming activation of trauma-related emotion during treatment (Briere & Scott, 2014). There are no interventions that specifically target high levels of PTSD severity, however, these levels are indicative of greater and more diverse impairment (Wolf et al., 2014). Currently, most PTSD experts recommend phase-based or sequenced therapy approaches that target a diversity (e.g., personality changes) of symptoms that clinically correlate with PTSD and that are often referred to as complex PTSD (e.g., Cloitre et al., 2012). Whether such approaches are more effective than immediate trauma-focused treatment remains a matter of debate. These findings highlight the need to develop interventions that target this poor outcome group since these patients place a considerable cost and burden on the health care system in terms of on-going needs for care, as well as associated disability benefits and work productivity loss (Engel et al., 1999; Sayer et al., 2010; Wald & Taylor, 2009).

Current advances in magnetic resonance imaging (MRI) scan abilities combined with longitudinal study designs allow researchers to connect psychoneurobiological information to treatment outcome (e.g., Kennis et al., 2015). There is definitely a need to examine the neurobiological pathways of high symptomatology patients against moderate and low symptomatology patients for a better understanding of the neural underpinnings of treatment resistant veterans.

Therapists are further advised to discuss the beneficial effects of treatment attendance during trauma-focused therapy and discuss the dangers of therapy avoidance regarding decreases in treatment gains.

In conclusion, the current results were derived from a veteran and active military population and this should be taken into account when generalising beyond the current PTSD population. Nonetheless, the identified predictors may play an important role with respect to the enhancement of psychotherapies among other traumatised populations that face violent traumatic events and likely receive similar interventions in comparable therapeutic environments (e.g., police officers and victims of violent crimes). We urge researchers to test the identified predictors in other trauma populations in order to optimise recommended PTSD psychotherapies.

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Contributors

Each author contributed to the article in the following manner: Study concept and design: J.F.G. Haagen, G.E. Smid, J.W. Knipscheer and R.J. Kleber. Study protocol and literature searches: J.F.G. Haagen and G.E. Smid. Statistical analysis: J.F.G. Haagen and G.E. Smid. First draft: J.F.G. Haagen. Study supervision: J.W. Knipscheer and R.J. Kleber. All authors contributed to and have approved the final manuscript.

Conflict of interest

All authors declare that they have no conflicts of interest.

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