

# Meta-Analysis of the Efficacy of Treatments for Posttraumatic Stress Disorder

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**ABSTRACT**

**Objective:** Posttraumatic stress disorder (PTSD) is an important mental health issue in terms of the number of people affected and the morbidity and functional impairment associated with the disorder. The purpose of this study was to examine the efficacy of all treatments for PTSD.

**Data Sources:** PubMed, MEDLINE, PILOTS, and PsycINFO databases were searched for randomized controlled clinical trials of any treatment for PTSD in adults published between January 1, 1980, and April 1, 2012, and written in the English language. The following search terms were used: *post-traumatic stress disorders, posttraumatic stress disorder, PTSD, combat disorders, and stress disorders, post-traumatic.*

**Study Selection:** Articles selected were those in which all subjects were adults with a diagnosis of PTSD based on DSM criteria and a valid PTSD symptom measure was reported. Other study characteristics were systematically collected. The sample consisted of 137 treatment comparisons drawn from 112 studies.

**Results:** Effective psychotherapies included cognitive therapy, exposure therapy, and eye movement desensitization and reprocessing ( $g = 1.63, 1.08, \text{ and } 1.01$ , respectively). Effective pharmacotherapies included paroxetine, sertraline, fluoxetine, risperidone, topiramate, and venlafaxine ( $g = 0.74, 0.41, 0.43, 0.41, 1.20, \text{ and } 0.48$ , respectively). For both psychotherapy and medication, studies with more women had larger effects and studies with more veterans had smaller effects. Psychotherapy studies with wait-list controls had larger effects than studies with active control comparisons.

**Conclusions:** Our findings suggest that patients and providers have a variety of options for choosing an effective treatment for PTSD. Substantial differences in study design and study participant characteristics make identification of a single best treatment difficult. Not all medications or psychotherapies are effective.

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Many treatments for posttraumatic stress disorder (PTSD) have been developed over the past 2 decades.<sup>1,2</sup> The treatments include a variety of psychotherapies, medications, and somatic and complementary therapies. The most commonly studied types of psychotherapy are cognitive-behavioral therapies (CBTs), such as prolonged exposure,<sup>3,4</sup> cognitive processing therapy,<sup>5,6</sup> and cognitive therapy,<sup>7,8</sup> along with eye movement desensitization and reprocessing.<sup>9,10</sup> Most of the research has focused on individual treatment, although there have been some studies of group-based treatment as well.<sup>11,12</sup> The most commonly studied medications are antidepressants, particularly selective serotonin reuptake inhibitors (SSRIs). Atypical antipsychotic medications also have been studied relatively often, although to a far lesser extent than antidepressants.<sup>13,14,15</sup>

The development of practice guidelines has followed the emergence of these treatments for PTSD. However, despite the existence of practice guidelines,<sup>16</sup> questions persist regarding how to most effectively treat patients with PTSD.<sup>17</sup> Comprehensive reviews describing the efficacy of PTSD treatments (including both medications and psychotherapy) differ in terms of their scope, methods, and conclusions. No single guideline or review is considered to be definitive. Van Etten and Taylor's meta-analysis<sup>18</sup> is often cited, but it includes no studies published after 1997; most studies of PTSD treatment have been published since then. A report by the Institute of Medicine largely focused on the goal to "note limitations in the evidence base and make suggestions for further research."<sup>19(p3)</sup> This conclusion provides little guidance for clinicians, who must rely upon current evidence in selecting treatments for PTSD. Several reviews<sup>16,20–28</sup> focused only on psychotherapy. Other reviews<sup>2,16,29–31</sup> focused only on the effectiveness of medication.

We sought to address the gaps in reviews of the PTSD treatment literature by conducting a meta-analysis of all randomized controlled clinical trials for PTSD. We used broad inclusion criteria and a treatment categorization system designed to allow comparisons across clinically relevant treatment groupings, such as whether a cognitive-behavioral treatment was cognitively or behaviorally oriented. Our aim was to inform clinicians about effective treatment options and thus lead to more informed decisions about treatment.

**DATA SOURCES AND SEARCH STRATEGIES**

We searched PubMed, MEDLINE, PILOTS, PsycINFO, and the Cochrane databases for articles published between January 1, 1980, and April 1, 2012. For PubMed and MEDLINE, we used the search terms *post-traumatic stress disorders, posttraumatic stress disorder, PTSD, combat disorders, and stress disorders, post-traumatic.* We limited the results to articles indexed by a thesaurus term as a clinical trial or those that included the terms *treatment trial, randomized, or controlled trial* in their title or abstract. We searched the entire Cochrane database by hand. For PILOTS, we used the thesaurus terms *clinical trial* and *adults* and limited our search to English language publications since

- A large number of effective treatments exist for posttraumatic stress disorder (PTSD), including psychotherapies and medications.
- No single treatment is most effective or the preferred treatment for PTSD.

1980.<sup>32</sup> In addition, we systematically reviewed references of all included studies as well as previous review articles and meta-analyses in order to locate additional references.

### STUDY SELECTION

Included studies had to (1) be a clinical trial in which participants were randomly assigned to 1 or more active treatments and to a control group; (2) involve only adult participants (age 18 and older), all of whom met PTSD diagnostic criteria in the *Diagnostic and Statistical Manual of Mental Disorders*, Third Edition; Third Edition, Revised; or Fourth Edition (*DSM-III*, *DSM-III-R*, *DSM-IV*); and (3) present pretreatment and posttreatment measures of PTSD symptoms.

### Classification of Treatment Type

Three authors (B.V.W., M.J.F., and P.P.S.) developed a hierarchy of treatment types to classify studies. After reviewing descriptions of the intervention and other details, we classified each study into its smallest group of similar treatment comparisons. The reviewers were able to reach consensus on all classifications.

The most basic classification was modality (psychotherapy, somatic therapy, and pharmacotherapy). If there was more than 1 study in a category and the category included heterogeneous approaches, we continued to refine the categorization. Somatic treatments were divided into 2 categories: acupuncture and transcranial magnetic stimulation. We created a more detailed hierarchy for psychotherapy and medication.

Psychotherapy was first categorized into general types: CBT, eye movement desensitization and reprocessing, psychodynamic psychotherapy, hypnotherapy, self-help, biofeedback, and group psychotherapy. These classifications were based on the theoretical underpinning of the therapy. The CBT category was then divided into primarily cognitive, primarily exposure, mixed cognitive and exposure, skills-based, and desensitization. The primarily cognitive category grouped psychotherapies in which the focus and the majority of sessions was spent identifying and challenging dysfunctional thoughts and emotions. Similarly, the primarily exposure grouping was made up of psychotherapies in which the focus and majority of sessions were devoted to in vivo or imaginal exposure to feared stimuli. Skills-based therapies applied a variety of techniques to teach new skills to patients with PTSD. Often this involved developing skills to manage stressful situations. It was usually the case that some amount

of skills training, cognitive therapy, and exposure were present in each type of CBT; however, our classification was based on the approach used in most sessions. If a significant focus was placed on more than 1 of these approaches (cognitive, exposure, or skills), we classified the treatment as mixed. The cognitive, exposure, and mixed categories were further divided into clinically meaningful types, eg, primarily exposure was divided into prolonged exposure, simulator exposure (virtual reality), narrative exposure therapy, and other types of exposure. These subgroups included very similar treatment approaches that typically used the same treatment manual.

Similarly, we categorized medications by primary classes: antidepressants, atypical antipsychotics, mood stabilizers,  $\alpha$ -adrenergic agents, and benzodiazepines. Antidepressants were further classified by mechanism of action into venlafaxine (a serotonin-norepinephrine reuptake inhibitor), SSRIs, tricyclic antidepressants, monoamine oxidase inhibitors, and other antidepressants (bupropion, mirtazapine, and nefazodone). Types of SSRIs included paroxetine, fluoxetine, sertraline, and citalopram. Types of atypical antipsychotics included risperidone and olanzapine. Types of antiadrenergic agents included the  $\alpha_1$  antagonist (prazosin) and  $\alpha_2$  agonist (guanfacine) agents.

### Classification of Study Characteristics

Two authors (B.V.W. and L.M.) independently assessed studies for eligibility and rated study characteristics. Initially, these authors reviewed 60 studies separately. Because the assessments showed excellent interrater reliability ( $\kappa = 0.94$ ), each remaining article was reviewed by 1 of the 2 reviewers.

Studies were characterized in terms of the following variables: (1) type of control condition (wait list, drug placebo, psychotherapy control); (2) status of providers, participants, and assessors, with regard to blinding; (3) handling of dropouts (completer analysis, last observation carried forward, or a method robust to the effect of missing data); (4) percentage of veteran participants; and (5) percentage of female participants. Psychotherapy control included any type of intervention designed to control for the nonspecific benefits of treatment. Methods robust to missing data included multiple imputation and random-effects models. Each study's design and participant characteristics were coded and transformed into categorical values to be examined as effect size moderators as follows: type of control condition (wait list, drug placebo, or psychotherapy control), blinding (none, assessor only, or double), handling of dropouts (completer analysis, last observation carried forward, or robust method), percentage of veteran participants (none, 1%–24%, 25%–49%, 50%–74%, 75%–100%), and gender/percentage of female participants (none, 1%–24%, 25%–49%, 50%–74%, 75%–100%).

### Data Extraction

Two authors (B.V.W. and L.M.) divided the articles to extract data. Each author checked the other's work to ensure accuracy. The primary outcome was change in the

PTSD symptom measure. If more than 1 PTSD measure was used in a study, we extracted data according to a hierarchy developed prior to the data extraction. Interviews such as the Clinician-Administered PTSD Scale<sup>33</sup> or PTSD Symptom Scale-Interview Version<sup>34</sup> were used if available. If not, we used participant self-report measures such as the PTSD Checklist<sup>35</sup> or PTSD Symptom Scale.<sup>36</sup> We recorded the mean and SD of pretreatment and posttreatment measures for the treatment group(s) and the control group. If multiple posttreatment assessments were completed, we used the first assessment performed after the end of treatment. Additionally, we recorded the number of participants starting and completing the study and accounted for in the posttreatment assessment. If necessary information was missing, we contacted authors to obtain it. We excluded studies for which needed information could not be obtained (either because authors failed to reply or because they did not have the information).

### Statistical Analysis

The primary outcome used to calculate the effect size was a continuous measure of PTSD symptom severity. Effect sizes and pooled estimates of effects for the studies were calculated with the Comprehensive Meta-Analysis software package.<sup>37</sup> We calculated effect size as the between-groups difference in pretreatment-posttreatment change using Hedges *g* correction for small samples.<sup>38</sup> We used the pooled pretreatment SD of the treatment and control groups because we were unable to obtain the posttreatment SD for more than 14% (19) of the potentially eligible articles. Kulinskaya et al<sup>39</sup> recommend using the pretreatment SD when assessing change relative to pretreatment values.

Random-effects models were used in all cases. Heterogeneity was evaluated with a *Q* statistic and *I*<sup>2</sup> statistic.<sup>40</sup> These 2 complementary statistics evaluate whether the effect sizes in a group are homogeneous (*Q*) and the amount of heterogeneity present (*I*<sup>2</sup>).<sup>41</sup>

If a study had more than 1 possible control group for comparison (which occurred in 23 studies), we used the most active control group available, according to the following hierarchy: (1) active treatment or placebo (for drug studies), (2) nonspecific comparison treatment such as treatment as usual, or (3) wait-list control.

We performed a linear regression to examine the effect of moderator variables on outcome (PTSD symptoms). The dependent variable was the effect size of each study. The independent variables were each of the moderator variables described above. We performed analyses for psychotherapy studies alone and medication studies alone. We had attempted to combine both types of studies in a single analysis, but, because medication and psychotherapy studies varied substantially in characteristics that could influence the effect size (such as type of comparison group and type of blinding), those comparisons were not statistically reliable. All analyses were performed by using Comprehensive Meta-Analysis software package.<sup>39</sup>

The possibility of publication bias was examined by using the funnel plot technique.<sup>42</sup> Effect sizes are plotted

as a function of sample size; smaller studies are typically expected to be less precise than larger studies.<sup>43</sup> However, regardless of sample size or precision, the plot is expected to be symmetrical about the estimated overall effect size. If it is not, this suggests bias, which can be positive or negative. For example, an absence of smaller effect sizes would suggest that the overall effect size derived from published trials overestimates the true effect size.

## RESULTS

The search strategy yielded more than 450 citations. Review of abstracts for the 252 unique citations eliminated 121 studies (Figure 1). We examined the remaining 131 in greater detail, excluding 8 because they did not require a PTSD diagnosis, 4 because they examined pediatric populations, 3 because they did not include a PTSD measure, and 4 because the primary outcome data were not available in the article or from multiple contact attempts with the authors.

The remaining 112 studies were included in the meta-analysis.<sup>3-15,44-142</sup> They contained data from 137 separate comparisons because 21 studies compared more than 1 treatment with a control group (46 comparisons). The effect size for all comparisons combined was  $g=0.81$  (95% CI, 0.71–0.91), with a range from  $-0.85$  to  $3.60$ . In 54 comparisons (39%), the intervention did not differ significantly from the control group.

### Comparisons Among Treatment Types

When divided into the 3 broadest categories (Figure 2), the effect sizes for each of these categories differed significantly from control: psychotherapy ( $g=1.14$ ), somatic treatments ( $g=1.24$ ), and medications ( $g=0.42$ ). The effect size for psychotherapy was larger than the effect size for medication ( $Z=2.76$ ,  $P<.001$ ). The effect size for somatic treatments did not differ from the effect sizes for either psychotherapy ( $Z=1.10$ ,  $P<.26$ ) or medication ( $Z=0.91$ ,  $P<.41$ ).

In examining the primary categories of psychotherapy, several trends emerged. First, the vast majority of comparisons (72%) involved CBT. This category also had the largest effect size ( $g=1.26$ ). The next largest category in terms of both number of studies and effect size was eye movement desensitization and reprocessing ( $g=1.01$ ). One category, resilience therapy, showed a large effect size ( $g=1.26$ ) in a single recent trial. Two categories, hypnotherapy and psychodynamic psychotherapy, had moderate effects based on a single clinical trial (both published in the same article over 20 years ago). For 3 psychotherapies, there were small to medium effect sizes, with CIs that included 0, indicating that they did not differ from controls: group psychotherapy, self-help/self-guided, and biofeedback. However, the effectiveness of group therapy differed by approach. There was a moderate-sized and statistically significant effect for interpersonal group therapy and a small, nonsignificant effect for cognitive-behavioral group therapy.

The subcategories of CBT varied in both the extent they were studied and evidence of effectiveness. Primarily cognitive therapy, primarily exposure therapy, and mixed

CBT therapies accounted for most of the studies and had the largest effect sizes ( $g = 1.08$ – $1.63$ ). Stress inoculation therapy and desensitization were less often studied ( $g = 0.73$ – $1.37$ ). Primarily cognitive therapy was composed of 2 categories, with similar large effects ( $g = 1.63$ – $1.69$ ). The primarily exposure category consisted of 4 subcategories with large effects ( $g = 0.80$ – $1.38$ ): prolonged exposure (the most often studied protocol), exposure using a simulation device, narrative exposure therapy, and other primarily exposure therapies. The therapies that combined 2 or more forms of CBT had large significant effects ( $g = 1.02$ – $1.52$ ).

There were 2 types of somatic comparisons. Acupuncture was examined in a single trial that showed a large effect ( $g = 1.28$ ). There were 4 trials of repetitive transcranial magnetic stimulation showing a large but nonsignificant effect ( $g = 1.23$ ).

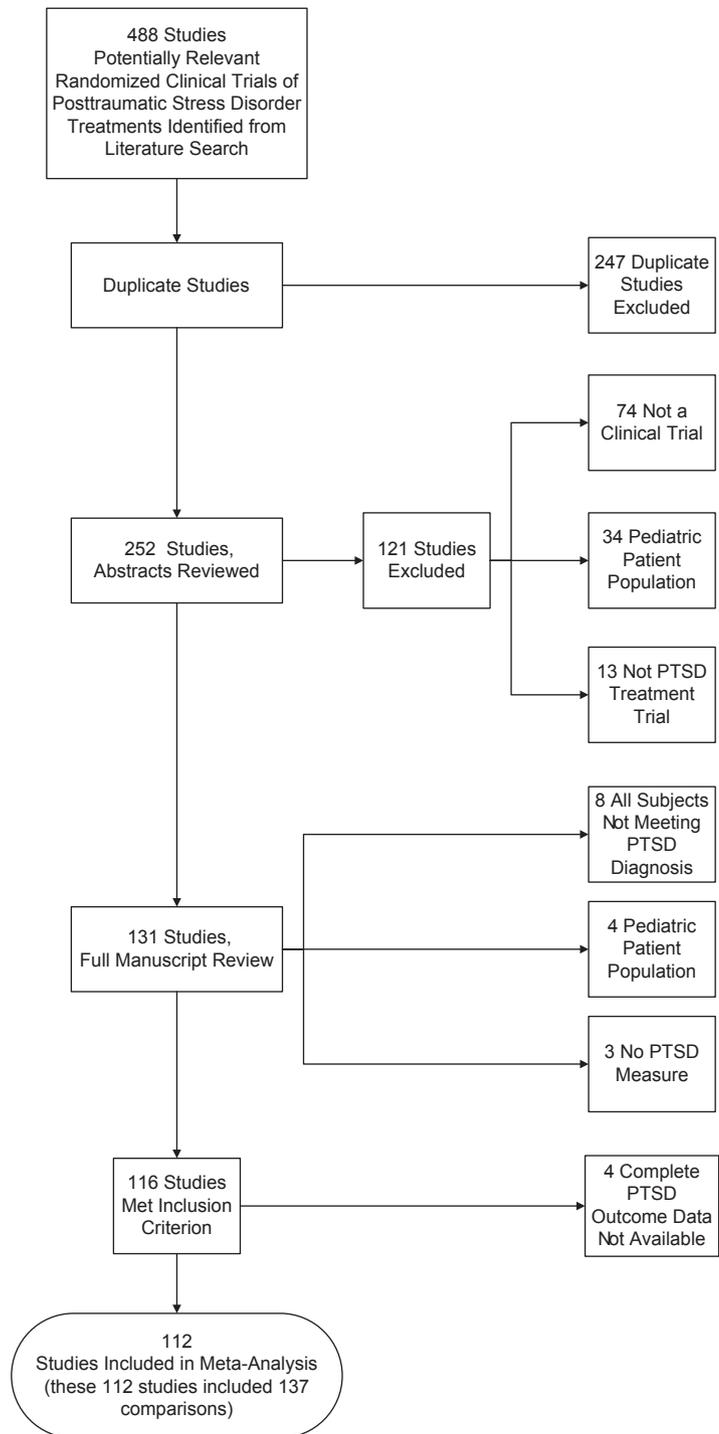
The 2 major categories of medication that were most often studied had the largest effects. The antidepressant category included 32 studies with a combined significant effect size of  $g = 0.43$ . The atypical antipsychotic category included 9 studies with a combined significant effect size of  $g = 0.36$ . The other major medication categories—anticonvulsants, benzodiazepines, and  $\alpha$ -adrenergic drugs—did not differ statistically from placebo.

Among antidepressants, only SSRIs and venlafaxine, both of which had medium effects, were superior to placebo. The effect sizes for SSRIs varied substantially, ranging from significant effects for paroxetine ( $g = 0.74$ ), fluoxetine ( $g = 0.43$ ), and sertraline ( $g = 0.41$ ) to a nonsignificant negative effect for citalopram ( $g = -0.71$ ) that was based on a single study. Tricyclic antidepressants, monoamine oxidase inhibitors, bupropion, nefazodone, and mirtazapine had small nonsignificant effects. In the atypical antipsychotic category, only risperidone, which had a medium effect, was superior to placebo. Risperidone's effect varied somewhat depending on study design; a single comparison using risperidone as monotherapy had an estimated effect size of  $g = 0.95$ , whereas a pooled group of 6 studies using risperidone as augmentation had an effect size of  $g = 0.31$ . Both monotherapy and augmentation had a statistically significant effect. No other anticonvulsant separated from placebo.

### Effect of Moderator Variables

Table 1 presents the results of our moderator analyses. For the psychotherapy studies, participant gender and

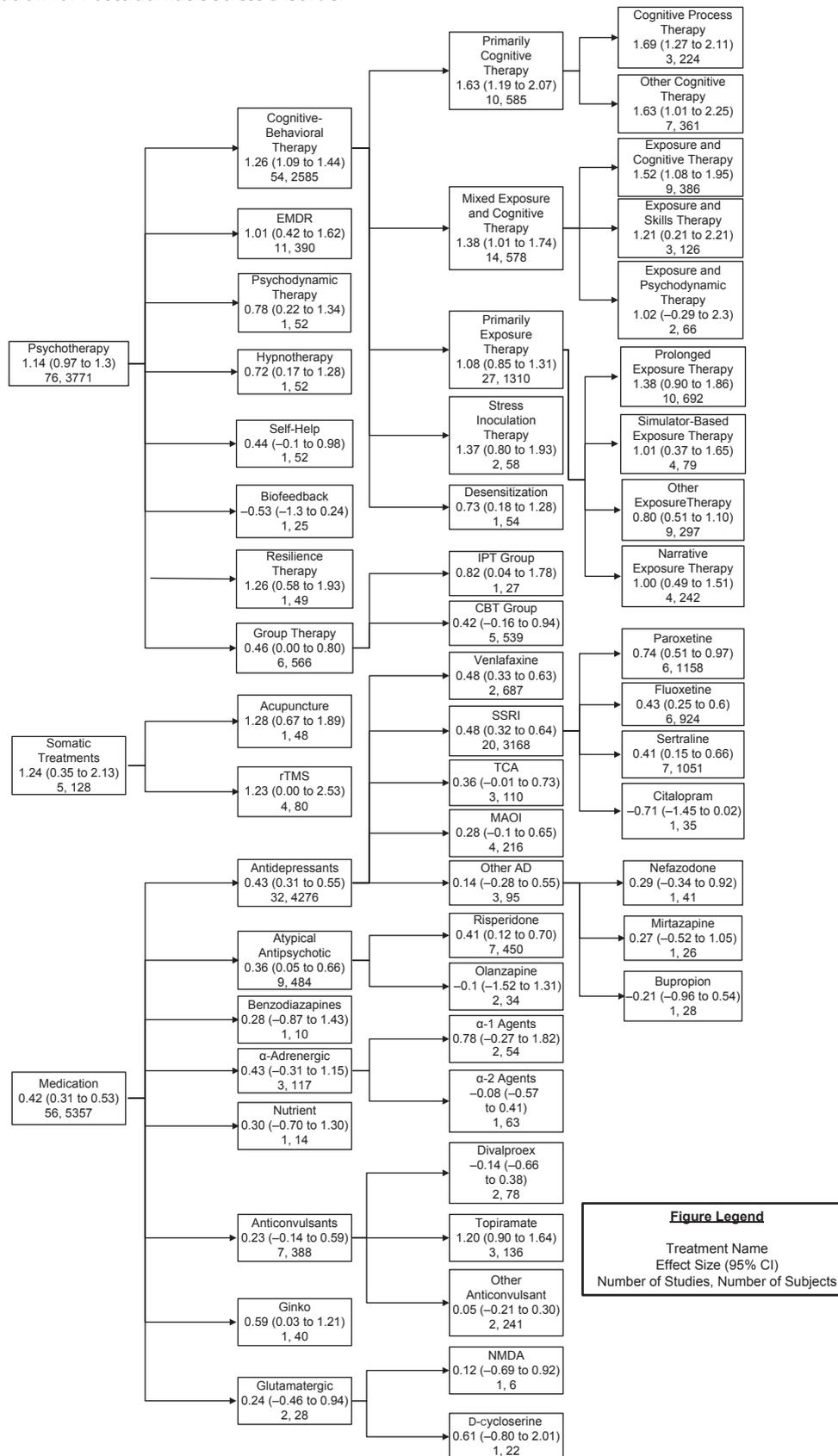
**Figure 1. Flow Diagram of Study Identification and Selection**



Abbreviation: PTSD = posttraumatic stress disorder.

veteran's status as well as type of control group used and method of handling missing data had a substantial effect on outcome. Studies with more women or fewer veterans had larger effects. Studies with wait-list controls had larger effects than studies with more active control comparisons. For medication, it was not possible to examine the effects of type of blinding or comparison group because all studies used the

**Figure 2. Effect Sizes, 95% CIs, and Sample Size for Studies of Psychotherapy, Somatic Therapy, and Medication for Posttraumatic Stress Disorder**



Abbreviations: AD = antidepressant, CBT Group = cognitive-behavioral group therapy, EMDR = eye movement desensitization and reprocessing, IPT Group = interpersonal group therapy, MAOI = monoamine oxidase inhibitor, NMDA = N-methyl-D-aspartate, rTMS = repetitive transcranial magnetic stimulation, SSRI = selective serotonin reuptake inhibitor, TCA = tricyclic antidepressant.

**Table 1. Regression Analyses Examining Predictors of Effect Size as a Function of Study Characteristics for Medication and Psychotherapy Studies**

Characteristic	Medication (n = 55)			Psychotherapy (n = 75)		
	$\beta$	SE	P	$\beta$	SE	P
Percentage of women <sup>a</sup>	.06	.02	.001	.12	.02	<.001
Percentage of veterans <sup>a</sup>	.06	.03	.04	.27	.03	<.001
Control comparison	...	...	...	.56	.06	<.001
Blinding	...	...	...	.11	.08	.16
Missing data	.006	.06	.91	.29	.04	<.001

<sup>a</sup>Coded as none, 1%–24%, 25%–49%, 50%–74%, and 75%–100%.

Abbreviation: SE = standard error.

Symbol: ... = not included in analyses for medication because of lack of variation among these studies.

same design. As in the psychotherapy studies, medication studies with more women had larger effects, and those with more veterans had smaller effects. There was considerable overlap between studies having more women and fewer veterans, but we lacked power to explore this association in either the psychotherapy or medication analyses.

Although it was not possible to directly compare effect sizes between studies of medication and psychotherapy using meta-regression (because the most important study characteristics are confounded between those 2 groups of treatments), exploratory analyses indicated that type of comparison group may not fully explain the larger effect size for psychotherapy studies. The effect size for wait-list controlled psychotherapy studies ( $d = 1.26$ ; 95% CI, 1.08–1.45) was larger than the effect size for medication studies ( $d = 0.42$ ; 95% CI, 0.31–0.54 [ $Z = 2.31$ ,  $P < .01$ ]). However, the effect size for psychotherapy studies with active comparison groups ( $d = 0.92$ ; 95% CI, 0.65–1.18) also differed from the effect size for medication studies ( $Z = 1.52$ ,  $P < .03$ ).

### Tests for Heterogeneity and Publication Bias

The overall value for  $Q$  was 669.95 and for  $I^2$  was 80.12 ( $P < .001$ ), indicating significant heterogeneity among all studies. For the treatment categories, the mean value for  $Q$  was 8.88 and for  $I^2$  was 32.51, indicating significant ( $P < .001$ ) heterogeneity and supporting the use of random effects modeling in the analysis.

According to our funnel plot analysis, 24 of the 135 effect sizes (18%) in our meta-analysis were larger than expected: 20 of the 75 psychotherapy comparisons (27%), 3 of the 55 medication comparisons (5%), and 1 of the 5 somatic comparisons (20%). This finding suggests that the observed effect size for psychotherapy may be optimistically biased.

## DISCUSSION

Our meta-analysis demonstrates that there are a large number of effective treatments for PTSD. Those with the largest amount of evidence include various types of CBT, eye movement desensitization and reprocessing, antidepressants (specifically venlafaxine and SSRIs), risperidone, and topiramate. In addition, several treatments

that have been evaluated in only 1 or 2 studies were effective: psychodynamic therapy, hypnotherapy, skills-based CBT, desensitization, ginkgo, and acupuncture. The effect size for group therapy failed to reach a conventional level of statistical significance, but the effectiveness of group therapy differed by approach. There was a moderate-sized and statistically significant effect for group interpersonal therapy, and a small, nonsignificant effect for cognitive-behavioral group therapy.

It is difficult to attribute any difference in estimated effect sizes to the therapeutic approach alone, as the studies differed in other important ways that could affect effect size. Despite the necessary cautions, we can offer general descriptive judgments about the relative effects of these treatments. Like others (eg, Bisson et al,<sup>22</sup> Bradley et al<sup>1</sup>), we found that CBT and eye movement desensitization and reprocessing were the most often-studied types of psychotherapy. Both were effective. There were no differences among types of CBT emphasizing cognitive restructuring, exposure, or blending the 2. Thus, the findings support the recommendation of CBT and eye movement desensitization and reprocessing as effective psychotherapies for PTSD.<sup>17</sup> The single study showing the effectiveness of acupuncture suggests the usefulness of this approach for treating PTSD, although the finding needs to be replicated in order to determine the robustness of the effect.

Our findings diverged from a previous review of medications for PTSD (Stein et al<sup>2</sup>) that recommended only SSRIs, most likely because of the rapid proliferation of new research regarding pharmacologic treatment of PTSD. Antidepressants (venlafaxine and SSRIs) and the atypical antipsychotics were the most often-studied types of medications. Both were effective, but not all types of either medication had similar effects. Citalopram was not effective, unlike the other SSRIs, and only risperidone was effective among the atypical antipsychotics. In addition, topiramate demonstrated efficacy in a pooled analysis of 3 studies. This finding is particularly notable since no other anticonvulsant was effective. Although these results are based on a limited number of small studies, the heterogeneity within classes suggests that clinicians should not necessarily consider findings for a single agent as a “class effect.” The issue of prior patient treatment and response also appears important. The issue of prior treatment response is highlighted by risperidone’s larger effect as monotherapy in contrast to use as an augmentation, when participants have had an inadequate response to another agent. More research is needed regarding the ideal sequencing of medication treatment for PTSD.

Our findings suggest the possibility of publication bias in the psychotherapy literature, with psychotherapy studies being more likely to be published when the results were positive (and less likely when their results were negative). This potential may exist because psychotherapy trials (average no. = 50.1) were smaller than medication trials (average no. = 102.3), making it harder to publish negative results. Whatever the reason, our findings indicate that the effect size for the psychotherapy treatments literature may

be inflated to some degree. We cannot say with certainty how much.

Effects were larger in studies with a higher proportion of women and in studies with a lower proportion of veterans. A previous meta-analysis of psychotherapy also has found that effect sizes were smaller in studies of veterans.<sup>1</sup> We urge caution in drawing any definitive conclusions about the possibility that existing treatments are less beneficial for veterans or for men because the studies and samples in these studies differ in a number of ways that could affect outcome. Moreover, effect in veterans appears to differ by treatment setting, with studies conducted in US Veterans Affairs tending to have less treatment response. More carefully controlled research is needed in order to determine whether veteran status or gender affect treatment outcome.

Methodological factors such as type of control group must be considered when comparing treatments.<sup>143</sup> We found that type of comparison strongly affected the effect size of psychotherapy studies, with wait-list control being associated (as expected) with larger effects. However, type of control group may not fully explain the difference between psychotherapy and medication. The effect sizes for both wait-list and active control studies differed from the effect size for medication. Thus, on the basis of our findings, it appears that psychotherapy may be more effective than medication for the treatment of PTSD. Again, we urge caution in drawing definitive conclusions about this difference given the heterogeneity within types of psychotherapy and medications, as well as other differences between medication and psychotherapy studies that possibly could explain the findings. This statement is further amplified by our findings involving possible positive publication bias in psychotherapy studies compared to medication studies. Direct comparisons between the most effective psychotherapies and the most effective medications are needed.

Several limitations must be considered. Although we examined important factors that could influence effect size, other such factors might be operating. Also, use of moderators at the individual study level, not at the individual participant level, is standard for meta-analysis, but it does not account for the underlying distribution and correlation of the moderators at the participant level and should be viewed with caution. Some treatments currently used to treat PTSD have not been studied in randomized trials (eg, acceptance and commitment therapy, couple and family therapy) or have not received adequate study (eg, different types of group psychotherapy). It is not possible to draw conclusions about these treatments. Only future research can determine which other treatments are effective. We excluded studies if some participants did not meet full criteria for PTSD. Thus, our findings may not apply to patients with subsyndromal PTSD symptoms. Another limitation is that we report only on PTSD outcomes and not on other important outcomes, such as comorbid symptoms, functioning, dropout, side effects, and remission. The lack of consistently reported data on most other outcomes limited the number of comparisons available. Furthermore, definitions of remission varied substantially,

making comparisons on that important outcome across studies difficult. Lastly, because it was necessary to rely on the descriptions of psychotherapy from published articles, we cannot be assured in all cases whether these treatments were delivered as described. Only 19 of the studies (25%) reported fidelity ratings based on independent review of audio or video recordings of therapy sessions.

Fifteen years ago, a comprehensive review of the literature identified only 15 controlled clinical trials of treatments for PTSD.<sup>18</sup> We found considerable growth in the evidence regarding effective treatments for PTSD. Many effective treatments exist. It was not possible to identify a single “best” treatment. Our belief is that selection between effective treatments is better guided by important real differences in the characteristic of the treatments, rather than selection based on small differences in the reported effectiveness. Ultimately, other factors, such as access, acceptability, and patient preference, should exert strong and appropriate influence over the choice of treatment.

**Drug names:** bupropion (Wellbutrin, Aplenzin, and others), citalopram (Celexa and others), divalproex (Depakote and others), fluoxetine (Prozac and others), guanfacine (Intuniv, Tenex, and others), mirtazapine (Remeron and others), olanzapine (Zyprexa and others), paroxetine (Paxil, Pexeva, and others), prazosin (Minipress and others), risperidone (Risperdal and others), sertraline (Zoloft and others), topiramate (Topamax and others), venlafaxine (Effexor and others).

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