Running head: A GUIDE TO PTSD GUIDELINES

A Guide to Guidelines for the Treatment of Posttraumatic Stress Disorder in Adults: An Update

J. L. Hamblen,<sup>1,2</sup> S. B. Norman,<sup>1,3</sup> J. Sonis,<sup>4</sup> A. Phelps,<sup>5</sup> J. Bisson,<sup>6</sup> V. Delgado Nunes,<sup>7</sup> O. Megnin-Viggars,<sup>7,8</sup>, D. Forbes,<sup>5</sup> D. Riggs,<sup>9,10</sup> & P. P. Schnurr<sup>1,2</sup>

- 1. National Center for PTSD, White River Junction, Vermont
- 2. Department of Psychiatry, Geisel School of Medicine at Dartmouth, Hanover, NH
- 3. University of California, San Diego School of Medicine, Department of Psychiatry, San Diego, CA
- 4. Departments of Social Medicine and Family Medicine, University of North Carolina at Chapel Hill School of Medicine
- 5. Phoenix Australia, Centre for Posttraumatic Mental Health, Department of Psychiatry, University of Melbourne, Melbourne, Australia
- 6. Cardiff University School of Medicine, Cardiff University, United Kingdom
- 7. National Guideline Alliance, Royal College of Obstetricians and Gynaecologists, London
- 8. Research Department of Clinical, Educational & Health Psychology, University College London
- 9. Department of Medical and Clinical Psychology, Uniformed Services University of the Health Sciences, Bethesda MD
- 10. Center for Deployment Psychology

#### **Author Note**

Correspondence concerning this article should be addressed to Jessica Hamblen, National Center for PTSD (116D), VA Medical Center, 215 North Main Street, White River Junction, VT, 05009. E-mail: <a href="Jessica.L.Hamblen@Dartmouth.edu">Jessica.L.Hamblen@Dartmouth.edu</a>. We wish to thank Juliette Harik, National Center for PTSD for her comments on multiple drafts. The NICE guideline referred to in this article was produced by the National Guideline Alliance (NGA) for the National Institute for Health and Care Excellence (NICE). The APA guideline was developed by the American Psychological Association (APA) PTSD Treatment Guideline Development Panel and adopted as APA Policy by the Council of Representatives on February 24, 2017. The Australian Guidelines were produced by Phoenix Australia Centre for Posttraumatic Mental Health. The views expressed in this article are those of the authors and not necessarily those of the APA, Department Veterans Affairs, Department of Defense, International Society for Traumatic Stress Studies, Phoenix Australia Centre for Posttraumatic Mental Health or NICE.

#### **Abstract**

Clinical practice guidelines (CPGs) are used to support clinicians and patients in diagnostic and treatment decision-making. Along with patients' preferences and values, and clinicians' experience and judgment, practice guidelines are a critical component to ensure patients are getting the best care based on the most updated research findings. Most CPGs are based on systematic reviews of the treatment literature. Although most reviews are now restricted to randomized controlled trials, others may consider non-randomized effectiveness trials. Despite a reliance on similar procedures and data, methodological decisions and the interpretation of the evidence by the guideline development panel can result in different recommendations. In this paper we will describe key methodological points for five recently released CPGs on the treatment of PTSD in adults and highlight some of the differences in both the process and subsequent recommendations.

Clinical Impact Statement:

Question: What are the primary posttraumatic stress disorder treatment recommendations across the various PTSD clinical practice guidelines?

Findings: All of the guidelines gave the highest overall recommendations to trauma-focused psychotherapies (usually including Eye Movement Desensitization and Reprocessing) and all agreed that Selective Serotonin Reuptake Inhibitors (either specific ones or the whole class) were the most effective medications.

Meaning: There is general consistency across the PTSD clinical practice guidelines.

Next Steps: Clinical practice guideline recommendations need to be disseminated to clinicians and, along with patient preferences, used to guide treatment decision-making.

Keywords: posttraumatic stress disorder, evidence-based treatment, clinical practice guideline

# A Guide to Guidelines for the Treatment of Posttraumatic Stress Disorder in Adults: An Update

Choice is an integral component in the process of treating physical and mental health conditions—first, about whether any treatment will be pursued, and second, the nature of the treatment(s) that will be used. In the optimal scenario, the decision is informed by scientific evidence, a clinician's experience and training, and a patient's preferences and values. These three elements meet the definition of an evidence-based practice provided by the Presidential Task Force on Evidence-Based Practice (American Psychological Association; APA, 2006).

Clinical practice guidelines (CPGs) are intended to facilitate choice. The National Academy of Medicine (formerly called the Institute of Medicine; IOM, 2011) defines CPGs as "statements that include recommendations intended to optimize patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options (p. 4)." Although they make recommendations for how a given problem should be treated, guidelines are not mandates: "Rather than dictating a one-size-fits-all approach to patient care, CPGs are able to enhance clinician and patient decision-making by clearly describing and appraising the scientific evidence and reasoning (the likely benefits and harms) behind clinical recommendations, making them relevant to the individual patient encounter (p. 1)." Guidelines support, but do not dictate, decision-making.

Since the initial formalization of the diagnostic criteria for posttraumatic stress disorder (PTSD) in the *Diagnostic and Statistical Manual (DSM)-III* (American Psychiatric Association, 1980), guidelines for treating PTSD have been developed and revised as the evidence on treatment has evolved. In 2011, a seminal report by the IOM (2011) significantly changed the

criteria for developing trustworthy guidelines. According to the report, guidelines should (1) be based on a systematic review of evidence; (2) be developed by experts from multiple disciplines and include stakeholder input; (3) take patient subgroups and preferences into consideration; (4) be based on a transparent process that reduces bias and conflict of interest; (5) provide ratings of the quality of evidence and strength of outcomes; and (6) be revised in order to maintain currency as new evidence emerges. One of the most significant implications of these recommendations is the emphasis on evidence, rather than clinical consensus, as a basis for making recommendations.

In 2010, Forbes and colleagues (Forbes et al., 2010) published a "guide to guidelines" in order to synthesize the recommendations and help readers understand the similarities and differences among the then available guidelines. This article is an update to that guide, focusing on recent guidelines from the American Psychological Association (APA, 2017), the International Society for Traumatic Stress Studies (ISTSS, 2018), the National Institute for Health and Care Excellence (NICE, 2018), the Phoenix Australia Centre for Posttraumatic Mental Health (Phoenix Australia, 2013), and the US Departments of Veterans Affairs and Defense (VA/DoD, 2017). The aim of this article is to review, compare, and contrast the methodologies and recommendations of these five clinical practice guidelines for PTSD (see Table 1) with the goal of helping clinicians make decisions about the use of the recommended treatments.

## **PTSD Clinical Practice Guideline Methodologies**

Of the guidelines reviewed, two were from professional associations, the APA and ISTSS (which is international). The other three were developed by national organizations, spanning three continents. Phoenix Australia (formerly the Australian Centre for Posttraumatic Mental

Health) is a non-profit organization that collaborates with the Departments of Veterans' Affairs and Defence in Australia. NICE is a public organization that creates national guidance on physical and mental health services and social care in the United Kingdom. And, the VA/DoD guideline was a collaborative effort between two US governmental agencies. In earlier guidelines, some recommendations were made based on consensus expert opinion, rather than a reliance on evidence. This changed dramatically in the recently completed guidelines reviewed here resulting in some changes in the recommendations. For example, in the VA/DoD guideline, the reliance on evidence for making recommendations reduced the number of recommendations from 213 in the 2010 document to 40 in the 2017 update.

## **Scope of Review**

Table 2 includes the basic characteristics of the five guidelines, including the scope of each. Four guidelines were updates (NICE was a partial update) to previous versions while one, the APA guideline, was a new addition. There was considerable consistency in methodology across the guidelines, likely due to the IOM report and standards (IOM, 2011). For example, each guideline was overseen by a multidisciplinary panel of identified experts and there was a transparent process for the selection of panel members. Efforts were also taken to minimize conflicts of interests (COIs) in members; each of the guidelines required members to disclose financial COIs that had the potential to affect their evaluation of the evidence. All except the VA/DoD guideline required the disclosure of intellectual COIs in which a member's point of view might affect the ability to judge evidence regarding a particular treatment method and make recommendations. The APA guideline took the strictest approach to COI. While other guidelines required members to declare their COIs, APA stated that "no panel members were to be singularly identified with particular interventions nor were they to have significant known

financial conflicts that would compromise their ability (or appearance thereof) to weigh evidence fairly." (APA, 2017, p. 19). In essence, this meant that developers of specific PTSD treatments were not members of the APA guideline panel.

Each guideline process began with the identification of a series of key questions (a process known as "scoping") that the guideline members (and in the case of ISTSS, its members) agreed were most relevant to their constituents. These questions became the focus of the evidence review and the basis for generating recommendations. A guideline would therefore not necessarily make a recommendation about group versus individual treatment unless the comparative effectiveness of group versus individual treatment for PTSD was queried as a key question.

All five guidelines received input from individuals with PTSD on these key questions. Forbes and colleagues (2010) make no mention of this type of input in the previous guidelines. Individuals with PTSD had more involved roles in the development of the Phoenix guideline, for which they also provided feedback on the recommendations, and the APA and NICE guidelines, for which they were full voting committee members. Each guideline also provided an opportunity for external review. Typically, the guideline was posted on the internet for several weeks during which comments from reviewers (professionals and interested members of the general public) were accepted. An exception was ISTSS, which was only open to comments from its own members.

In most cases (APA, ISTSS, Phoenix, and VA/DoD), an external independent evidence review was conducted to inform each key question. If the key question was an update from a previous recommendation, the evidence review was typically limited to only those studies published since the previous guideline. APA based its evidence review on Jonas et al. (2013)

and then updated the search to include new articles published between 2012 and June 2016, but did not rate the new trials for risk of bias or conduct new meta-analyses. The group then rated the likelihood that the recommendation would change since 2013 based on the new evidence published after the Jonas et al. review. NICE conducted a partial update in which evidence from the 2005 guideline was carried forward and updated, and new reviews with unrestricted dates up to January, 2018 were added. For each key question a detailed search strategy using a specific methodology (e.g., Cochrane) was developed to identify all relevant articles. Information about the specific search strategies are available in each guideline.

## **Study Characteristics**

Once key questions were identified, studies pertinent to each question were gathered. For characteristics of the studies see Table 3. Identified studies that met specified criteria were included in the evidence review. Slight differences in search methodology and inclusion/exclusion criteria can have substantive effects on the final recommendations. For example, whereas all five guidelines relied heavily on randomized controlled trials (RCTs), some also included systematic reviews (SRs) of RCTs. The VA/DoD guideline prioritized SRs, which can cause challenges for evidence review as they may not include all the outcomes of interest, or they may classify treatment type in a manner that is inconsistent with how individual studies were classified in the guideline. The NICE and VA/DoD guidelines were the only ones to restrict inclusion of RCTs to those that included a minimum number of participants. Specifically, trials with fewer than 10 participants per arm were excluded. Although this could result in a failure to include potentially relevant studies, it helped to protect against undue influence given that small trials are more likely to be published if they find positive effects (Song, Hooper, & Loke, 2013).

There was also variability across the guidelines in defining the degree to which study participants had to meet criteria for PTSD. For example, the VA/DoD guideline required that for a study to be included in the evidence review, at least 80% of participants had to meet criteria for PTSD. The systematic review that APA used as its evidence base did not restrict RCTs based on the percentage of participants who met PTSD criteria; however, all included studies had > 75% who met criteria for diagnosis. Only ISTSS specified that PTSD be diagnosed by structured or clinician interview. Thus, even guidelines that ask the same key questions may result in differing recommendations due to differences in which studies were included.

Finally, differences in how primary and secondary treatment outcomes were operationalized can also influence recommendations. Although all of the guidelines prioritized PTSD symptom severity, the VA/DoD required that PTSD was measured by either the Clinician Administered PTSD Scale (Weathers, Blake, Schnurr, Kaloupek, Marx, & Keane, 2013) or another validated structured clinical interview to assess symptoms. This is important because (1) self-reported changes in PTSD are typically larger than clinician ratings (e.g., Krystal et al., 2016; Raskind et al., 2018; Resick et al., 2017; Schnurr et al., 2007) and (2) the guidelines reviewed different studies and study outcomes in their evidence reviews. Another major difference was that whereas all the guidelines considered harms and adverse events, only APA and NICE considered these as a primary outcome. Thus, APA and NICE recommendations may have been more likely than the other guidelines to downgrade a treatment due to harms and adverse events.

## **Evaluations that Determine the Direction and Strength of Recommendations**

For each guideline, the evidence review relied on specific, previously published criteria to evaluate the quality of individual studies from different organizations: Agency for Healthcare

Research and Quality (AHRQ, 2008; APA), Cochrane (Higgins & Green, 2011; ISTSS and NICE), National Health and Medical Research Council (NHMRC, 2011; Phoenix) and U.S. Preventative Services Task Force (USPSTF, 2015; VA/DoD). Each evidence review had a formal system for evaluating study quality (see Table 4). Despite using different methodologies, there was general consensus across the guidelines on what these ratings took into account, even if they used different wording. For example, each considered selection, attrition, and detection biases. For four out of the five guidelines, the complete evidence review is publicly available to download; the VA/DoD guideline provides a briefer evidence table that includes the study references for each recommendation.

After evaluating individual studies, the review groups evaluated the overall body of evidence for each key question. Again, there was considerable consistency across the guidelines in regard to the criteria used to make the rating. Three guidelines (ISTSS, NICE, and VA/DoD,) used Grading of Recommendations Assessment, Development and Evaluation (GRADE; Andrews et al., 2013), APA used the AHRQ Methods Guide for Comparative Effectiveness Reviews (Viswanathan et al., 2012) which is based on GRADE, and Phoenix used NHMRC procedures (NHMRC, 2011). Examples of the criteria used to make the overall rating were risk of bias, consistency, directness, and precision. Risk of bias, as noted above, includes adequacy of randomization, differential attrition, and measurement bias. Consistency is the degree to which study findings are the same across the body of evidence. Directness is the degree to which the tested intervention compares to the primary interest. Precision has to do with the confidence interval associated with the estimate of the effect where a tighter confidence interval indicates a more precise effect.

Based on these factors, the overall body of evidence for each key question was rated as high, moderate, low, or very low (see Table 5). High quality evidence means that what is known about the effect of the treatment in question is not likely to change with the addition of more research, thus patients and providers can have the most confidence or trust in the evidence. Moderate quality evidence means additional research could change the estimate of the effect, so patients and providers can have some, although not full, confidence in the research. Low or very low quality is when there is uncertainty in the effect.

Once the quality of the evidence was determined, each guideline also considered other relevant factors as part of determining the strength of the evidence before making specific recommendations. Such factors included the balance of desirable and undesirable outcomes (including harms and adverse events), patient values and preferences, generalizability of a treatment to subgroups, feasibility and acceptability. For example, an effective treatment might receive a lower recommendation if it has serious side effects. A treatment that could be delivered by video teleconferencing might receive a higher rating if committee members had reason to believe patients would prefer the flexibility of not having to travel to the clinic or provider for treatment. Only one guideline, NICE, directly considered the cost-effectiveness of treatments.

## **Grading the Strength of the Recommendation**

The last step in the process was determining a recommendation and developing a statement that included a specification of the strength of the recommendation. In order to make the recommendations comparable across the different guidelines for the purpose of this review, we (the authors<sup>1</sup>) developed a common nomenclature to describe the strength of the

-

<sup>&</sup>lt;sup>1</sup> Authors included members from each of the represented guidelines

recommendations across guidelines (see Table 6). We also made decisions about how to align the various levels across the guidelines since some guidelines had more levels than others. APA, NICE and VA/DoD had only two levels to choose from and recommendations could be either for or against. In contrast, ISTSS had four levels (two of which could be for or against) and Phoenix had four levels, as well as a clinical recommendation. This meant that ISTSS and Phoenix had more opportunity to make recommendations about treatments for which there was a lower level of support. Four of the five guidelines (all but NICE) also allowed for a formal insufficient evidence recommendation. Given the variability in levels and naming conventions, in some cases what we categorized as "moderate" was rated as "weak" by the specific guideline, but weak does not equate with low evidence. It is also important not to confuse strength of recommendation with strength of evidence available to make that recommendation. For example, ISTSS recommended several medications as low effect interventions because strong evidence was found that they were beneficial to people with PTSD but the magnitude of symptom change was lower than for the strongly recommended psychological treatments.

## **PTSD Clinical Practice Guideline Recommendations**

Although there are many consistencies in recommendations across the five guidelines, the variability in key questions and methodology resulted in some differences. Below we summarize the primary PTSD treatment recommendations across guidelines and highlight key similarities and differences. We also present recommendations on group, couples, internet-based, complementary and integrated, and non-pharmacologic biological treatments as a primary treatment for PTSD. We do not present recommendations on prevention, Acute Stress Disorder, assessment, or specific PTSD symptoms. We also do not include recommendations related to children, adolescents, or families. The APA, Phoenix and VA/DoD guidelines also include

narrative descriptions summarizing the recommendations. The ISTSS guideline will have an accompanying book with chapters dedicated to the recommended treatments. The NICE guideline did not include accompanying summaries.

# Treatment Initiation Recommendations for Individual Psychotherapies and Pharmacotherapies

A new addition to some of the clinical practice guidelines were recommendations that focused on prioritizing the use of some types of treatment over other types (see Table 7a). Three out of five guidelines had specific recommendations to deliver trauma-focused psychotherapies over pharmacotherapies (NICE, Phoenix, and VA/DoD). This is different from separate recommendations that give higher ratings to one treatment over another. For example, in the VA/DoD guideline, both specific trauma-focused psychotherapies and specific pharmacotherapies were given the highest recommendation, but the guideline also recommended these trauma-focused psychotherapies over the pharmacotherapies. Similarly, although some medications were given a stronger recommendation than some non-trauma-focused treatments, the VA/DoD guideline specified that there was insufficient evidence to recommend whether to deliver an individual non-trauma-focused psychotherapy or medications in cases where an individual trauma-focused psychotherapy was not available or preferred or was not effective. It should be noted that the two guidelines that did not have treatment prioritization recommendations (APA and ISTSS) still gave stronger ratings to trauma-focused treatments than they did to medications. Due to methodological differences between psychotherapy trials and medication trials that might influence treatment effect magnitude (Huhn et al., 2014), the APA committee did not believe there was sufficient evidence, in the absence of head-to-head trials, to

support prioritizing psychotherapy over medications. However, the APA guideline did include comparative effectiveness recommendations (although they are not presented in this manuscript).

# **Individual Psychotherapy Recommendations for PTSD**

Recommendations related to psychotherapy for PTSD are included in Table 7b. All five guidelines gave a strong recommendation to trauma-focused psychotherapies (TFTs). In some cases, the guidelines elected to recommend the overall category of TFTs, while in others they named the treatments they were recommending. In either case all included Prolonged Exposure therapy (PE), Cognitive Processing Therapy (CPT) and trauma-focused cognitive behavioral therapy (TF-CBT) and some include other trauma-focused treatments as well. Four of the five guidelines also gave Eye Movement Desensitization and Reprocessing (EMDR) a strong recommendation. The exception was the APA guideline, which gave EMDR a moderate rating<sup>2</sup>.

There was less consistency in ratings across other psychotherapies. Among traumafocused therapies the VA/DoD guideline gave a strong recommendation to Brief Eclectic
Psychotherapy, which was rated as moderate by APA and insufficient by ISTSS. The VA/DoD
guideline also gave a strong recommendation to Narrative Exposure Therapy (NET) which was
rated as moderate by both APA and ISTSS, and to written narrative exposure which was not
specified at all in other guidelines. APA gave a strong recommendation to general cognitive
behavioral therapy (CBT), but a closer look at which treatments were included in this category
suggests that the majority of these studies were in fact TF-CBTs.

Three of the guidelines (VA/DoD, Phoenix, and ISTSS) provided non-trauma-focused options at various levels of support. The VA/DoD guideline gave a moderate recommendation to

<sup>&</sup>lt;sup>2</sup> EMDR was rated as having moderate strength of evidence for loss of PTSD diagnosis; however, loss of PTSD diagnosis was considered an important, but not critical outcome, by the APA panel for all recommendation decisions for all treatments.

Stress Inoculation Training (SIT), Present-Centered Therapy (PCT) and Interpersonal Psychotherapy. The Phoenix guideline gave a low recommendation to non-trauma-focused treatments such as SIT and suggested only using them when non-trauma-focused treatments have been tried. ISTSS gave a moderate recommendation to CBT without a trauma focus and PCT.

Three of the guidelines (APA, ISTSS, VA/DoD) provided insufficient recommendations for certain treatments, indicating that there is not enough research to support their use for the treatment of PTSD at this time. These included popular treatments such as Seeking Safety, Dialectical Behavior Therapy, Acceptance and Commitment Therapy, and Skills Training in Affect and Interpersonal Regulation. This does not mean that the treatments were ineffective, but rather that there was insufficient evidence to show they were effective for treating PTSD at this time. NICE reviewed a long list of additional psychotherapies but did not make any formal insufficient recommendations.

# Pharmacotherapy Recommendations for PTSD

As seen in Table 7c there was general agreement as to which medications were most effective for treating PTSD. Guidelines that named medications (APA, ISTSS, and VA/DoD) supported the use of sertraline, paroxetine, fluoxetine and venlafaxine. The Phoenix guideline recommended the class of selective serotonin reuptake inhibitors (SSRIs), while the NICE guideline named SSRIs (and cited sertraline as an example) as well as venlafaxine. There was less consistency, however, in the strength of those pharmacotherapy recommendations. Across the guidelines, the most effective medications were ranked as a strong recommendation by only one guideline (VA/DoD), a moderate by two (APA and NICE), and a low by two (ISTSS and Phoenix). The lack of agreement among the guidelines may be due to differences in estimated

treatment effect sizes and confidence intervals based on the RCTs that were included in the meta-analyses and differences in how strongly the guidelines weighted harms (e.g., side effects).

Only two guidelines (NICE and VA/DoD) offered second line pharmacotherapy recommendations. The VA/DoD guideline included nefazodone, imipramine, and phenelzine. The NICE guideline also gave a moderate recommendation for antipsychotics (with risperidone cited as an example) following non-response to other drug or psychological treatments, but only as an augmentation to psychological therapies and in the context of disabling symptoms and behaviors. The ISTSS guideline also gave an emerging recommendation to quetiapine. The VA/DoD guideline was the only one that made specific recommendations against a pharmacotherapy (see Table 7c for a complete list). Strong "against" recommendations were generally due to negative results and/or harmful side effects. Three of the guidelines made a recommendation to note which medications had insufficient evidence. Although NICE did not make a formal insufficient recommendation, the guideline committee considered a long list of additional medications for which they determined there was not sufficient evidence to support. APA also considered some medications for which they chose not to make a formal recommendation.

#### Other Recommendations for PTSD

Three of the five guidelines (ISTSS, Phoenix, and VA/DoD) assessed group treatments (see Table 7d). The ISTSS guideline provided a range of recommendations from a moderate recommendation for group CBT with a trauma-focus to an emerging recommendation for combined group and individual CBT with a trauma focus. They also gave group interpersonal therapy, group stabilizing treatment, and group supportive counselling insufficient recommendations. The Phoenix guideline gave a low recommendation for group CBT (with or

without a trauma-focus) but only as an adjunct to treatment. The VA/DoD guideline gave a moderate recommendation but only as compared to no treatment at all, based on a literature review showing that group was less effective than individual therapy. Although the NICE guideline found limited evidence in support of trauma-focused group therapy, a formal recommendation was not made because group was not determined to be clinically or cost effective.

Only two guidelines made recommendations regarding couples therapy (see Table 7d). The VA/DoD guideline gave both trauma-focused and non-trauma focused couples therapy an insufficient recommendation. The ISTSS guideline, however, gave trauma-focused couples therapy an emerging recommendation.

There was moderate consistency across guidelines with respect to internet-based interventions (see Table 7d). Three guidelines (ISTSS, NICE and VA/DoD) gave a moderate recommendation for internet-based interventions that included therapist support. The Phoenix guideline gave a low recommendation but did not require the support of a therapist.

With respect to complementary and integrated health interventions, there was the greatest support for acupuncture. The ISTSS guideline gave acupuncture an emerging recommendation, the Phoenix guideline gave it a very low recommendation, and the VA/DoD guideline gave it an insufficient recommendation as a primary treatment for PTSD. The NICE guideline considered exercise and acupuncture but did not make a formal recommendation.

Finally, three of the guidelines considered non-pharmacologic biological treatments. The NICE and VA/DoD guidelines gave an insufficient recommendation to repetitive transcranial magnetic stimulation (rTMS). The VA/DoD guideline also gave electroconvulsive shock

therapy, hyperbaric oxygen, stellate ganglion, and vagal nerve stimulation insufficient recommendations. ISTSS gave TMS an emerging recommendation.

#### **Discussion and Conclusion**

The goal of this review was to compare and contrast methodologies and recommendations across five recently published PTSD clinical practice guidelines. It is clear that since the previous round of clinical practice guidelines for PTSD, there is now a more rigorous approach to guideline development methodology and that the field is making progress by moving towards evidence-based guidelines. The IOM (2011) report in 2011 had an impact on both defining what a clinical practice guideline is and the methods used in their development. In fact, many guidelines are moving toward using the exact same methodology. For example, the majority of the guidelines reviewed here used GRADE to assess the strength of evidence for making recommendations. As a result, the recommendations across the PTSD guidelines were fairly consistent.

All of the guidelines gave the highest recommendations to trauma-focused psychotherapies (including EMDR in 4 of the 5 guidelines) and all agreed that SSRIs (either specific ones or the whole class) were the most effective medications. All except APA agreed that the best psychotherapies were more effective than the best medications; the APA panel concluded that comparative effectiveness could not be assessed in the absence of head-to-head trials. These recent guidelines were the first ones to make recommendations regarding how to prioritize treatment modalities relative to each other. All of the ones that had recommendations regarding prioritization recommended trauma-focused therapy over medication. These recommendations were based on meta-analyses because there were so few head-to-head comparisons of a single medication with a single psychotherapy. Future guidelines may be able

to base recommendations regarding how to prioritize treatments on studies that directly compare different evidence-based treatment modalities to one and other.

Perhaps the biggest methodological difference among the guidelines was whether they recommended treatments by name (e.g., PE), type (e.g., trauma-focused therapy), or both. Each guideline committee had to make a decision as to whether the trauma-focused treatments were similar enough that they should be recommended as a class rather than individually. If the core components of the treatments were thought to be what makes them effective (e.g., exposure and cognitive restructuring) then recommending the class of treatments (e.g., cognitive behavioral therapy) may make sense. The VA/DoD guideline based its definition of "trauma-focused" on Schnurr (2017; i.e., "any therapy that uses cognitive, emotional, or behavioral techniques to facilitate processing a traumatic experience and in which the trauma focus is a central component of the therapeutic process). However, the committee also chose to list those specific treatments for which there was the strongest support. The NICE guideline also recommended individual trauma-focused CBT interventions as a class but listed some specific interventions as examples of that class.

The same issue arose with medications. Recommendations for a class of medications implied that all medications within the class had both similar efficacy and similar side effect profiles. Some guidelines determined that those criteria were met and recommended the class of SSRIs while others named only specific SSRIs given evidence of varying levels of efficacy within the class (e.g., Watts et al., 2013).

There was variability in the support of some treatments such as BEP, NET, and IPT, where some guidelines gave them strong recommendations and others gave them weak or emerging/insufficient recommendations. Group treatments, as well as some other popular

treatments such as SS and ACT, received little support across the guidelines (except in the ISTSS guideline which gave group treatment with a trauma focused a moderate recommendation).

Couples treatments and TMS received emerging/insufficient recommendations. Acupuncture was the most supported CAM intervention, but received either a very low recommendation or an emerging/insufficient recommendation. Finally, therapist guided internet-based interventions received mostly moderate recommendations; the Phoenix guideline gave it a low recommendation but this was likely due to fact that their literature review did not include RCTs after 2011.

Given the increasing number of treatment options, how does a clinician choose among the most effective treatment options, especially in a situation when providers may lack training and competency in these treatments? Several of the guidelines specifically recommended shared decision making (SDM). In SDM, the patient and provider work together to review treatment options to determine which treatment best meets the patient's needs and preferences. Part of that process involves not only a discussion about which treatments are most effective, but also whether they can be provided, and where they can be accessed, and any harms or burdens associated with them. Thus, patients are making an informed choice about what treatments may work best for them and may even choose a treatment that does not have the highest level of support. New comparative effectiveness trials will also be useful in helping clinicians and patients make treatment decisions. Clinicians may also make choices based on which of the treatments they have training in and resources to deliver. Ideally, CPGs are used to inform policy and resource allocation to make the most highly recommended treatments available. However, in the short term, or in a situation where there are multiple effective options, not all may be available.

Clinicians often desire more specific information about what treatments work for the patients they see in clinical practice based on a concern that research participants do not fully resemble clinical populations. Many of the RCTs included in the evidence reviews were based on diverse and complex patients and are therefore generalizable to a wide range of patients. Thus, the guidelines generally support the use of these treatments with all patients and should not be limited to only those with PTSD and no other comorbidities or complexities. In fact, the NICE and VA/DoD guidelines had a specific recommendation stating that the presence of co-occurring disorders should not prevent patients from receiving recommended treatments. A limitation, however, is that the guidelines are unable to make specific recommendations about whether some treatments work best for different subgroups of patients because few trials performed subgroup analyses or were powered to do so. In addition, some providers may also be concerned that trauma-focused interventions in particular may interfere with the therapeutic alliance. A recent meta-analysis, however, confirmed that while there is a positive relationship between alliance and outcome, this effect was not moderated by type of intervention (Fluckiger, Del Re, Wampold, & Horvath, 2018).

It is notable that there are so many PTSD practice guidelines. How does a clinician determine which guideline to use? In some cases, clinicians may choose based on the constituency of which they are a part. For example, if they work in the VA, they may follow the VA/DoD guideline, whereas if they are in Australia, they may defer to the Phoenix guideline. It is worth asking if in fact all are needed. Considerable resources are put forth in conducting the evidence reviews, making the recommendations, and writing the guidelines. And almost as soon as the guidelines are released, the process of updating begins. Is there a better way? Perhaps in the future, different entities and organizations would do better to collaborate on producing joint

guidelines. While it is likely that each organization will want to continue to produce its own guideline, the National Center for PTSD has recently committed to producing a public database of all PTSD treatment studies that might make it easier to identify the relevant literature and conduct the evidence review. When completed it will be available at <a href="https://www.ptsd.va.gov">www.ptsd.va.gov</a>.

Although treatment guidelines have existed for a long time now, many providers are not aware that they exist. One survey of 463 community providers in Texas found that only half were aware of any clinical practice guideline for PTSD (Finley, Noel, et al., 2018). In a related study, while half of providers reported using an evidence-based treatment for PTSD, far fewer said they used the core components of those treatments, suggesting they are not delivering them with fidelity (Finley, Mader, et al., 2018). For practice guidelines to be useful, they need to be widely disseminated and training and support are required for providers to deliver the treatments with fidelity.

Several limitations of clinical practice guidelines have already been mentioned. For example, the guidelines are limited by the original scoping questions and the current literature. Few trials exist that examine how the treatments respond with various subgroups or how the treatments compare to one another. Recommendations on emerging interventions are also limited because of the lack of available randomized controlled trials, but that does not mean these interventions are ineffective. Of note, ISTSS in particular made specific recommendations for treatments with emerging evidence as a way to recognize them. There are also new treatments being developed and new delivery mechanisms (such as telehealth and internet) being evaluated to determine if they are effective. Given that the literature is always growing, it is important that guidelines are updated regularly. For example, the VA/DoD guidelines are intended to be updated every five years.

In closing, we, as authors of this review and members of the various clinical practice guideline committees, want to end by revisiting the goal of CPGs, which should drive practice and may or may not support the practices that clinicians are already delivering. But they are also not policies in and of themselves and should not blindly be followed. Instead, CPGs should support clinicians and patients in diagnostic and treatment decision-making. They provide critical information about the effectiveness of specific treatments based on rigorous methodology and should be used as a starting place for a conversation about treatment choice. Along with patients' preferences and values, and clinicians' experiences, practice guidelines are a critical component to ensure patients receive the best care possible.

### References

- Agency for Healthcare Research and Quality, US. (2008). *Methods guide for effectiveness and comparative effectiveness reviews*. Rockville, MD: U.S. Government Printing Office.
- American Psychiatric Association (1980). *Diagnostic and statistical manual of mental disorders*, *DSM-III*. Washington, DC: Author.
- American Psychological Association-Presidential Task Force on Evidence-Based Practice (2006). Evidence-based practice in psychology. *American Psychologist*, 61, 271-285 doi:10.1037/0003-066X.61.4.271
- American Psychological Association (2017). Clinical practice guideline for the treatment of posttraumatic stress disorder (PTSD) in adults. Washington, DC: Author.
- Andrews, J. C., Schünemann, H. J., Oxmand, A. D., Pottie, K., Meerpohl, J. J., Coello, P. A., ...

  Guyatt, G. (2013). GRADE guidelines: 15. Going from evidence to recommendationdeterminants of a recommendation's direction and strength. *Journal of Clinical Epidemiology*, 66, 726-735. doi:10.1016/j.jclinepi.2013.02.003
- 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.
- Finley, E. P., Mader, M., Haro, E. K., Noël, P. H., Bernardy, N., Rosen, C. S., . . . Pugh, M. J. V. (2018). Use of guideline-recommended treatments for PTSD among community-based providers in Texas and Vermont: Implications for the Veterans Choice Program. *Journal of Behavioral Health Services and Research*. doi:10.1007/s11414-018-9613-z

- Finley, E. P., Noël, P. H., Lee, S., Haro, E., Garcia, H., Rosen, C., ... Pugh, J. A. (2018).

  Psychotherapy practices for veterans with PTSD among community-based providers in Texas. *Psychological Services*, *15*, 442–452. doi:10.1037/ser0000143
- Fluckiger, C., Del Re, A. C. Wampold, B. E. & Horvath, A. O. (2018). The alliance in adult psychotherapy: A meta-analytic synthesis. *Psychotherapy*, *55*, 316-340. doi:10.1037/pst0000172
- Forbes, D., Creamer, M., Bisson, J. L., Cohen, J. A., Crow, B. E., Foa, E. B., . . . Ursano, R. J. (2010). A guide to guidelines for the treatment of PTSD and related conditions. *Journal of Traumatic Stress*, 23, 537-552. doi:10.1002/jts.20565
- Higgins, J. P. & Green, S. (Eds.) (2011). Cochrane handbook for systematic reviews of interventions version 5.1.0. The Cochrane Collaboration, 2011. Retrieved from www.handbook.cochrane.org.
- Huhn, M., Tardy, M., Spineli, L. M., Kissling, W., Förstl, H., Pitschel-Walz, G., ... Leucht, S.
  (2014). Efficacy of pharmacotherapy and psychotherapy for adult psychiatric disorders:
  A systematic overview of meta-analyses. *JAMA Psychiatry*, 71, 706-715.
  doi:10.1001/jamapsychiatry.2014.112
- Institute of Medicine (2011). *Clinical practice guidelines we can trust*. Washington, DC: The National Academies Press.
- International Society for Traumatic Stress Studies (2018). ISTSS PTSD prevention and treatment guidelines: Methodology and recommendations. Retrieved from:

  www.istss.org/getattachment/Treating-Trauma/New-ISTSS-Prevention-and-Treatment-Guidelines/ISTSS\_PreventionTreatmentGuidelines\_FNL.pdf.aspx

- Jonas D. E., Cusack, K., Forneris, C. A., Wilkins, T. M., Sonis, J., Middleton, J. C., ... Gaynes, B. N. (2013). *Psychological and pharmacological treatments for adults with Posttraumatic Stress Disorder (PTSD). Comparative effectiveness review no. 92.* (Report No. 13-EHC011-EF.112) Rockville, MD: Agency for Healthcare Research and Quality. Retrieved from: <a href="https://www.effectivehealthcare.ahrq.gov/reports/final.cfm">www.effectivehealthcare.ahrq.gov/reports/final.cfm</a>.
- Krystal, J. H., Pietrzak, R. H., Rosenheck, R. A., Cramer, J. A., Vessicchio, J. C., Jones, K. M., ... Veterans Affairs Cooperative Study Group (2016). Sleep disturbance in chronic military-related PTSD: Clinical impact and response to adjunctive risperidone in the Veterans Affairs Cooperative Study #504. *Journal of Clinical Psychiatry*, 77, 483-491. doi:10.4088/JCP.14m09585
- National Health and Medical Research Council (2000). How to review the evidence: Systematic identification and review of the scientific literature. Canberra, AU: Author.
- National Health and Medical Research Council (2011). *Procedures and requirements for meeting the 2011 NHMRC standard for clinical practice guidelines*. Melbourne, AU: Author.
- National Institute for Health and Clinical Practice (2018). *Guideline for post-traumatic stress disorder*. London, EN: Author.
- Phoenix Australia Centre for Posttraumatic Mental Health (2013). Australian guidelines for the treatment of acute stress disorder and posttraumatic stress disorder. Melbourne, AU: Author.
- Raskind, M. A., Peskind, E. R., Chow, B., Harris, C., Davis-Karim, A., Holmes, H. A., ... Huang, G. D. (2018). Trial of prazosin for post-traumatic stress disorder in military

- veterans. New England Journal of Medicine, 378, 507-517. doi:10.1056/NEJMoa1507598
- Resick, P. A., Wachen, J. S., Dondanville, K. A., Pruiksma, K. E., Yarvis, J. S., Peterson, A. L., ... Young-McCaughan, S. (2017). Effect of group vs individual Cognitive Processing Therapy in active-duty military seeking treatment for posttraumatic stress disorder: A randomized clinical trial. *JAMA Psychiatry*, 74, 28-36. doi:10.1001/jamapsychiatry.2016.2729
- Schnurr, P. P. (2017) Focusing on trauma-focused psychotherapy for posttraumatic stress disorder. *Current Opinion in Psychology*, *14*, 56-60. doi:10.1016/j.copsyc.2016.11.005
- Schnurr, P. P., Friedman, M. J., Engel, C. C., Foa, E. B., Shea, M. T., Chow, B. K., . . .

  Bernardy, N. C. (2007). Cognitive behavioral therapy for posttraumatic stress disorder in women: A randomized controlled trial. *Journal of the American Medical Association*, 29, 820-830. doi:10.1001/jama.297.8.820
- Song, F., Hopper, L., & Loke, Y. (2013). Publication bias: What is it? How do we measure it?

  How do we avoid it? *Open Access Journal of Clinical Trials*, 5, 71-81.

  doi:10.2147/OAJCT.S34419
- U.S. Preventive Services Task Force (2015). *U.S. preventive services task force procedure*manual. Rockville, MD: U.S. Dept. of Health & Human Services, Agency for Healthcare

  Research and Quality. Retrieved from: <a href="https://www.uspreventiveservicestaskforce.org/">https://www.uspreventiveservicestaskforce.org/</a>
- Viswanathan, M., Ansari, M. T., Berkman, N. D., Chang, S., Hartling, L., McPheeters, L. M., . . . Treadwell, J. R. (2012). Assessing the risk of bias of individual studies in systematic reviews of health care interventions. In *Methods guide for comparative effectiveness*

- *reviews*. Rockville, MD: Agency for Healthcare Research and Quality. Retrieved from: https://www.ncbi.nlm.nih.gov/books/NBK91433/
- Watts, B. V., Schnurr, P. P., Mayo, L. Young-Xu, Y., Weeks, W. B., & Friedman, M. J. (2013).

  Meta-analysis of the efficacy of treatments for posttraumatic stress disorder. *Journal of Clinical Psychiatry*, 74, 541-550. doi:10.4088/JCP.12r08225
- Weathers, F., Blake. D., Schnurr, P. P. Kaloupek, D., Marx, B., & Keane, T. (2013). The clinician-administered PTSD scale for DSM-5 (CAPS-5). Retrieved from: https://www.ptsd.va.gov

Table 1

The Five Most Recent Clinical Practice Guidelines for Posttraumatic Stress Disorder

Author, Date	Guideline Name	URL
American Psychological	Clinical Practice Guideline for the	https://www.apa.org/ptsd-guideline/ptsd.pdf
Association, 2017	Treatment of PTSD in Adults	
International Society for	ISTSS Posttraumatic Stress Disorder	https://www.istss.org/getattachment/Treating-
Traumatic Stress	Prevention and Treatment	Trauma/New-ISTSS-Prevention-and-Treatment-
Studies, 2018	Guidelines: Methodology and	Guidelines/ISTSS_PreventionTreatmentGuidelines_FNL.p
	Recommendations	<u>df.aspx</u>
National Institute for	Post-traumatic Stress Disorder:	https://www.nice.org.uk/guidance/ng116/resources/posttra
Health and Care	Management (update)	umatic-stress-disorder-pdf-66141601777861
Excellence, 2018		
Phoenix Australia, 2013	Australian Guidelines for the	https://www.phoenixaustralia.org/wp-
	Treatment of Acute Stress Disorder	content/uploads/2015/03/Phoenix-ASD-PTSD-
	and Posttraumatic Stress Disorder	<u>Guidelines.pdf</u>
Department of Veterans	Clinical Practice Guideline for the	https://www.healthquality.va.gov/guidelines/MH/
Affairs/Department of	Management of Posttraumatic Stress	ptsd/VADoDPTSDCPGFinal012418.pdf
Defense, 2018	Disorder and Acute Stress Disorder	

Table 2
Scope of Review

	APA, 2017	ISTSS, 2018	NICE, 2018	Phoenix, 2013	VA/DoD, 2018
Type of review	New	Update from 2005	Update from 2005	Update from 2007	Update from 2010
Country	United States	International	United Kingdom	Australia	United States
Focus of review	Key questions	Key questions	Key questions	Key questions	Key questions
Developed by	Multidisciplinary panel	Multidisciplinary panel	Multidisciplinary panel	Multidisciplinary panel	Multidisciplinary panel
Selection of panel members	Chair and members selected by the Advisory Steering Committee of APA	Identified by Chair of ISTSS Guidelines Committee and approved by ISTSS Board of Directors	NICE committee members recruited through an application process	Core development group selected by co-chairs     Multidisciplinary reference group nominated by professional associations	Chairs selected by VA and DoD     Panel members selected by chairs
Type of conflict of interest considered	Financial and intellectual	Financial and intellectual	Financial and intellectual	Financial and intellectual	Financial
Involvement of people with PTSD	Voting panel members	Provided input on key questions	Voting panel members	Provide input on key questions and recommendations (non- voting)	Provided input on key questions
Community involvement	Public comments (60 days)	Comment by ISTSS members and ISTSS Board (4 weeks)	Registered stakeholder review during public consultation period (6 weeks)	Public comments (6 weeks)	Public comments (about 3 weeks)
Time period covered and who conducted the review	Agency for Healthcare Research and Polity (AHRQ) (Jonas et a., 2013) covering 1980-June 2013. AHRQ review supplemented by updated search conducted by panel sub-group, 2013-2016	• 1980-March 2018 • Previous reviews updated with new searches covering January 2008 to March 2018	1980-January 2018 (September 2017 for qualitative reviews)     Previous updated with new search covering 2005-2018	• 1996-October 2011 • Previous reviews updated with new searches covering 2005 to 2011 (unless new question and then 1996-2011)	• 1980-March 2016 • Previous reviews updated with new search covering 2009 to 2016

Table 3
Study Characteristics

	APA, 2017	ISTSS, 2018	NICE, 2018	Phoenix, 2013	VA/DoD, 2018
Nature of studies examined	Primarily systematic reviews of RCTS and individual RCTs     Key questions related to harms and patient preferences included other study designs as well as consideration of consumer and clinician experience	RCTs	Primarily systematic reviews of RCTs and individual RCTs     One question allowed qualitative and mixed methods studies	Primarily systematic reviews of RCTs and individual RCTs     If fewer than two RCTs other study designs were included	Primarily systematic reviews of RCTs and individual RCTs (N>20)     One key question allowed cohort study.
English language studies only	Yes	Yes	Yes	Yes	Yes
Study Treatment Target	PTSD	Prevention, ASD, and PTSD	Prevention, ASD, PTSD, family members and care givers of those with PTSD	Prevention, ASD, and PTSD	Prevention, ASD, and PTSD
Patient, Population, or Problem	Adults with PTSD	Adults with ASD or PTSD (>70% dx via structured or clinician interview), and adolescents and children (with full or partial PTSD)	Adults, adolescents, children with PTSD diagnosis or above threshold on a validated scale	Adults with ASD or PTSD (>70% dx), adolescents and children	Adults with ASD or PTSD (>80% dx)
Target Interventions	Psychological     Pharmacological	Psychological Pharmacological Non-pharmacologic biologic Complementary and integrative health Other	Psychological Pharmacological Non-pharmacologic biologic Complementary and integrative health Psychosocial Technology based Support for family and caregivers	Psychological     Pharmacological     Repeated transcranial magnetic stimulation     Psychosocial rehabilitation     Acupuncture     School based	Psychological     Pharmacological     Non-pharmacologic     biologic     Complementary and integrative health     Collaborative care/integrated care     Technology based
Comparison Interventions	Any	Any	Any	Any	Any
Primary Outcomes of Interest	PTSD symptom severity     Other: serious harms or adverse events	PTSD symptom severity	• PTSD symptom severity • Other: adverse events (retention/dropout rate), loss of diagnosis/remission, findings from qualitative studies	PTSD symptom severity	PTSD symptom severity (based on CAPS or other validated structured clinical interview)

					• Other: adverse events, retention/dropout rate, loss of diagnosis/remission
Secondary Outcome of Interest	APA	Loss of diagnosis/remission     Other: comorbid symptoms, quality of life, functional status, adverse events	• Other: comorbid symptoms, dissociative symptoms, quality of life, functional status	PTSD diagnosis     Other: symptom change, functional status, and tolerability	• Other: comorbid symptoms, dissociative symptoms, functional status
Setting	All	All	All	All	All

Note. APA = American Psychological Association; ASD = Acute Stress Disorder; ISTSS = International Society for Traumatic Stress Studies; NICE = National Institute for Health and Care Excellence; PTSD = Posttraumatic Stress Disorder; RCT = Randomized Controlled Trials; VA/DoD = Department of Veterans Affairs and Department of Defense.

Table 4: Criteria for Evaluating Study Quality

APA, 2017	ISTSS, 2018	NICE, 2018	Phoenix, 2013	VA/DoD, 2018
AHRQ Methods Guide for	Cochrane Collaboration Tool	Cochrane Collaboration Tool	National Health and Medical	U.S. Preventative Services Task
Comparative Effectiveness	(Higgins et al., 2011)	(Higgins & Green, 2011)	Research Council (NHMRC,	Force Method (USPSTF, 2015)
Reviews (Viswanathan et al.,			2000)	·
2012)			,	
Comparable groups	Random sequence generation	Random sequence generation	Comparable groups	Initial assembly of comparable
Adequate randomization	(selection bias)	(selection bias)	Adequate randomization	groups:
Allocation concealment	Allocation concealment	Allocation concealment	Allocation concealment	<ul> <li>For RCTs: adequate</li> </ul>
Comparable groups at	(selection bias)	(selection bias)	Masking of outcome assessor	randomization, including first
baseline	Masking of participants and	Masking of participants and	assessment	concealment and whether
Masked assessment	personnel (performance bias)	personnel (performance bias)	<ul> <li>Masking of providers</li> </ul>	potential confounders were
Masked providers	Masking of outcome	Masking of outcome	<ul> <li>Masking of patients</li> </ul>	distributed equally among
Masked patients	assessment (detection bias)	assessment (detection bias)	• Intention to treat is used	groups
Overall attrition	Incomplete outcome data	Incomplete outcome data	Overall attrition	Maintenance of comparable
Differential attrition	(attrition bias)	(attrition bias)		groups (includes attrition, cross-
<ul> <li>Intention to treat is used</li> </ul>	Selective reporting (reporting	Selective reporting (reporting)		overs, adherence,
Appropriate methods for	bias)	bias)		contamination)
handling missing data	Other bias	Other bias		Important differential loss to
Reliable and valid measures				follow up or overall high loss to
Treatment fidelity based on				follow up
independent raters				Measurements: equal, reliable,
				and valid (includes masking of
				outcome assessment)
				Clear definition of
				interventions
				All important outcomes
				considered
				Analysis: adjustment for
				potential confounders for cohort
				studies or intention-to-treat
				analysis for RCTs

Note. AHRQ = Agency for Healthcare Research and Quality, APA = American Psychological Association, ISTSS = International Society for Traumatic Stress Studies, NICE = National Institute for Health and Care Excellence, VA/DoD = Department of Veterans Affairs and Department of Defense.

Table 5

Evaluating the Body of Evidence

	APA, 2017	ISTSS, 2018	NICE, 2018	Phoenix, 2013	VA/DoD, 2018
High Quality	Further research is <u>verv</u> <u>unlikely</u> to change confidence in the estimate of effect	Further research is <u>very</u> <u>unlikely</u> to change confidence in the estimate of effect	Further research is <u>very</u> <u>unlikely</u> to change confidence in the estimate of effect	Body of evidence can be trusted to guide practice	Further research is <u>very</u> <u>unlikely</u> to change confidence in the estimate of effect
Moderate Quality	Further research <u>may</u> change our confidence in the estimate of the effect and <u>may</u> change the estimate	Further research is <u>likely</u> to have important impact on our confidence in the estimate of effect and <u>may</u> change the estimate	Further research is <u>likely</u> to have important impact on our confidence in the estimate of effect and <u>may</u> change the estimate	Body of evidence can be trusted to guide practice in most situations	Further research is <i>likely</i> to have important impact on our confidence in the estimate of effect and <i>may</i> change the estimate
Low Quality	Further research is <i>likely</i> to change confidence in the estimate of the effect and is <i>likely</i> to change the estimate	Further research is <u>very likely</u> to have an important impact on confidence in the estimate of effect and is <u>likely</u> to change the estimate	Further research is <u>very likely</u> to have an important impact on confidence in the estimate of effect and is <u>likely</u> to change the estimate	Body of evidence provides some support for recommendation(s) but care should be taken in its application	Further research is <u>very likely</u> to have an important impact on confidence in the estimate of effect and is <u>likely</u> to change the estimate
Very Low Quality	Any estimate of effect is very uncertain	Any estimate of effect is very uncertain	Any estimate of effect is very uncertain	Body of evidence is weak and recommendation(s) must be applied with caution	Any estimate of effect is very uncertain

Table 6

Grading Strength of Recommendation

	APA, 2017	ISTSS, 2018	NICE, 2018	Phoenix, 2013	VA/DoD, 2018
Strong Recommendation	Strong for/against (or "We recommend/recommend against offering this option")	A Strong for/against recommendation	Should be offered ("Offer/Do not offer")	Grade A	Strong for/against (or "We recommend/recommend against offering this option")
Moderate Recommendation	Weak for/against (or "We suggest /suggest against offering this option")	A standard for/against recommendation	Could be offered ("Consider/Do not consider")	Grade B	Weak for/against (or "We suggest /suggest against offering this option")
Low Recommendation	Not applicable	Intervention with low effect	Not applicable	Grade C	Not applicable
Very Low Recommendation	Not applicable	Not applicable	Not applicable	Grade D	Not applicable
Insufficient Recommendation	No recommendation for or against (or "There is insufficient evidence")	Insufficient Evidence to Recommend	Not applicable: Recommend more research where insufficient evidence was found	Consensus Points: used when a research question was asked of the data, but no evidence was forthcoming	No recommendation for or against (or "There is insufficient evidence")
Emerging Recommendation	Not applicable	Intervention with emerging evidence	Not applicable	Not applicable	Not applicable
Clinical Recommendation	Not applicable	Not applicable	Not applicable	Good Practice Points: used when the research question was not asked, often because the working party was confident that no evidence existed	Not applicable

Note. In order to make comparisons across the recommendations, the authors developed their own strength of recommendation categories.

Note. APA = American Psychological Association; ISTSS = International Society for Traumatic Stress Studies; NICE = National Institute for Health and Care Excellence; VA/DoD = Department of Veterans Affairs and Department of Defense.

Table 7a. Treatment Prioritization Recommendations for Individual Psychotherapies and Pharmacotherapies for PTSD

	APA, 2017	ISTSS, 2018	NICE, 2018	Phoenix, 2013	VA/DoD, 2018	APA, 2017
Strong Recommendation	71171, 2017	15155, 2010	Recommend individual, manualized trauma-focused CBT or EMDR (latter for non-combat-related trauma only) over other psychological, or pharmacological, interventions for the primary treatment of established PTSD	Thocha, 2013	778 505, 2010	We recommend individual, manualized trauma-focused psychotherapy over other pharmacologic and nonpharmacologic interventions for the primary treatment of PTSD     When individual trauma-focused psychotherapy is not readily available or not preferred, we recommend pharmacotherapy or individual non-trauma-focused psychotherapy. With respect to pharmacotherapy and non-trauma-focused psychotherapy, there is insufficient evidence to recommend one over the other
Moderate Recommendation			Consider CBT interventions targeted at specific symptoms such as sleep disturbance or anger only if the person is unable or unwilling to engage in a traumafocused intervention or has residual symptoms are a traumafocused intervention     Consider medications only if person has a preference for drug treatment, or as second-line	Drug treatments for PTSD should not be preferentially used as a routine first treatment for adults, over trauma-focused cognitive behavioral therapy or Eye Movement Desensitization and Reprocessing		

augmentation treatment for disabling symptoms		
and behaviors		

Note. In order to make comparisons across the recommendations, the authors created their own strength of recommendation categories. Only rows for which there were recommendations were included in the table. In addition, the APA guideline offers recommendations based on comparative effectives such as a strong recommendation that clinicians offer either prolonged exposure or prolonged exposure plus cognitive restructuring when both are being considered and that clinician offer either venlafaxine ER or sertraline when both are being considered.

Table 7b

Individual Psychotherapy Recommendations for PTSD

	APA, 2017	ISTSS, 2018	NICE, 2018	Phoenix, 2013	VA/DoD, 2018
Strong Recommendation	Cognitive behavioral therapy     Prolonged exposure therapy     Cognitive processing therapy     Cognitive therapy	Trauma-focused cognitive behavioral therapy (undifferentiated)     Prolonged Exposure     Cognitive Processing Therapy     Cognitive Therapy     Eye Movement Desensitization and Reprocessing	Trauma-focused cognitive behavioral interventions     Cognitive Processing Therapy     Cognitive therapy for PTSD     Narrative exposure therapy     Prolonged Exposure     Eye Movement Desensitization and Reprocessing (more than 3 months after non-combatrelated trauma)	Trauma-focused cognitive behavioral interventions     Eye Movement Desensitization and Reprocessing	Prolonged Exposure     Cognitive Processing     Therapy     Eye Movement     Desensitization and     Reprocessing     Specific cognitive     behavioral therapies for     PTSD     Brief Eclectic     Psychotherapy     Narrative Exposure     Therapy     Written narrative exposure
Moderate Recommendation	Brief Eclectic     Psychotherapy     Eye Movement     Desensitization and     Reprocessing     Narrative Exposure     Therapy	Cognitive behavioral therapy without a trauma focus     Narrative Exposure Therapy     Present-Centered Therapy	Eye Movement Desensitization and Reprocessing (1-3 months after non-combat-related trauma)		Interpersonal     Psychotherapy     Present-Centered Therapy     Stress Inoculation     Training
Very Low Recommendation	Not applicable	Not applicable	Not applicable	Where symptoms have not responded to a range of trauma-focused interventions, evidence-based non-trauma-focused psychological interventions (such as stress inoculation training) should be considered	Not applicable
Insufficient Recommendation	Relaxation     Seeking Safety	Brief Eclectic     Psychotherapy     Dialogical Exposure     Therapy     Emotional freedom     techniques     Interpersonal     psychotherapy	Not applicable		Acceptance and Commitment Therapy     Dialectical Behavior Therapy     Seeking Safety     Skills Training in Affect and Interpersonal Regulation     Supportive counselling

		Observed and experimental integration     Psychodynamic psychotherapy     Psychoeducation     Relaxation training     REM desensitization     Supportive counselling			
Emerging Recommendation	Not applicable	Single session cognitive behavioral therapy     Reconsolidation of traumatic memories     Virtual reality therapy     Written Exposure Therapy	Not applicable	Not applicable	Not applicable

Note. In order to make comparisons across the recommendations, the authors created their own strength of recommendation categories. Only rows for which there were recommendations were included in the table.

Table 7c

Pharmacotherapy Recommendations for PTSD

	APA, 2017	ISTSS, 2018	NICE, 2018	Phoenix, 2013	VA/DoD, 2018
Strong Recommendation For					Fluoxetine     Paroxetine     Sertraline     Venlafaxine
Moderate Recommendation For	Fluoxetine     Paroxetine     Sertraline     Venlafaxine		Selective serotonin reuptake inhibitors (such as sertraline)     Venlafaxine     Antipsychotics, such as risperidone (in addition to psychological therapies and only if they have disabling symptoms and behaviors and symptoms have not responded to other drug or psychological treatments)		Nefazodone     Imipramine     Phenelzine
Low Recommendation For	Not applicable	<ul><li>Fluoxetine</li><li>Paroxetine</li><li>Sertraline</li><li>Venlafaxine</li></ul>	Not applicable	Selective serotonin reuptake inhibitors	Not applicable
Emerging Recommendation	Not applicable	Quetiapine	Not applicable	Not applicable	Not applicable
Moderate Recommendation Against				Not applicable	Amitriptyline     Citalopram     Lamotrigine     Olanzapine     Other atypical     antipsychotics (except for risperidone, which is a Strong Against)     Prazosin (for the global symptoms of PTSD)     Quetiapine     Topiramate
Strongest Recommendation Against				Not applicable	Benzodiazepines     D-cycloserine     Divalproex     Guanfacine

				Hydrocortisone
				Ketamine
				Risperidone
				Tiagabine
Insufficient	Risperidone	Amitriptyline	Not applicable	Bupropion
Recommendation	Topiramate	Brofaromine		Buspirone
		• Divalproex		Cyproheptadine
		Ganaxolone		Desipramine
		Imipramine		Desvenlafaxine
		Ketamine		Doxepin
		Lamotrigine		• D-serine
		Mirtazapine		Duloxetine
		Neurokinin-1 Antagonist		Escitalopram
		Olanzapine		Eszopiclone
		Phenelzine		Fluvoxamine
		Tiagabine		Hydroxyzine
		Topiramate		Levomilnacipran
				Mirtazapine
				Nortriptyline
				Razodone
				Vilazodone
				Vortioxetine
				• Zaleplon
				• Zolpidem

Note. In order to make comparisons across the recommendations, the authors created their own strength of recommendation categories. Only rows for which there were recommendations were included in the table.

Table 7d

Other Recommendations for PTSD

	APA, 2017	ISTSS, 2018	NICE, 2018	Phoenix, 2013	VA/DoD, 2018
Group	Not addressed	Moderate recommendation:     Group cognitive behavioral therapy with a trauma focus     Emerging Recommendation:     Combined group plus individual with a trauma focus     Insufficient recommendation:     Group interpersonal therapy, group stabilizing treatment, group supportive counselling		Low Recommendation: Group cognitive behavioral therapy (trauma-focused or non-trauma-focused) may be provided as adjunctive to, but not be considered an alternative to, individual trauma-focused therapy	Moderate recommendation: Group therapy over no treatment     Insufficient recommendation: There is insufficient evidence to recommend using one type of group therapy over any other
Couples	Not addressed	Emerging Recommendation: Couples CBT with a trauma focus	Insufficient recommendation: Cognitive-behavioral conjoint therapy	Not addressed	Insufficient recommendation: Trauma-focused or non-trauma- focused couples therapy
Internet-based	Not addressed	Moderate recommendation: Guided internet-based trauma- focused CBT	Moderate recommendation: Guided internet-based trauma- focused CBT	Low Recommendation: Internet-based trauma-focused CBT as an alternative to treatment	Moderate recommendation: Guided internet-based CBT as an alternative to no treatment
Complementary and Integrative Health	Not addressed	Emerging Recommendation:     Acupuncture, neurofeedback,     somatic experiencing,     Saikokeishikankyoto, somatic     experiencing, and yoga     Insufficient recommendation:     Attentional bias modification,     electroacupuncture,     hypnotherapy, Mantram     Repetition, group Mindfulness     Based Stress Reduction, group     music therapy, nature adventure     therapy and physical exercise	Insufficient recommendation: Acupuncture, arts therapies, biofeedback, exercise, meditation or mindfulness- based stress reduction (MBSR), neurofeedback and yoga.	Very Low Recommendation: Acupuncture for people who have not responded to trauma- focused psychological therapy or pharmacotherapy	Insufficient recommendation: Acupuncture or any complementary and integrative health practice, such as meditation (including mindfulness), yoga, and mantram meditation
Non- Pharmacologic Biological	Not addressed	Emerging Recommendation: Transcranial Magnetic Stimulation	Insufficient recommendation: Repetitive transcranial magnetic stimulation		Insufficient recommendation: Repetitive transcranial magnetic stimulation, electroconvulsive therapy, hyperbaric oxygen therapy, stellate ganglion block, and vagal nerve stimulation.

Note. In order to make comparisons across the recommendations, the authors created their own strength of recommendation categories.

Note. APA = American Psychological Association; ISTSS = International Society for Traumatic Stress Studies; NICE = National Institute for Health and Care Excellence; VA/DoD = Department of Veterans Affairs and Department of Defense.