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CLINICAL GUIDELINE

The Management of Posttraumatic Stress Disorder and Acute Stress Disorder: Synopsis of the 2023 U.S. Department of Veterans Affairs and U.S. Department of Defense Clinical Practice Guideline

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Description: The U.S. Department of Veterans Affairs (VA) and Department of Defense (DoD) worked together to revise the 2017 VA/DoD Clinical Practice Guideline for the Management of Posttraumatic Stress Disorder and Acute Stress Disorder. This article summarizes the 2023 clinical practice guideline (CPG) and its development process, focusing on assessments and treatments for which evidence was sufficient to support a recommendation for or against.

Methods: Subject experts from both departments developed 12 key questions and reviewed the published literature after a systematic search using the PICOTS (population, intervention, comparator, outcomes, timing of outcomes measurement, and setting) method. The evidence was then evaluated using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) method. Recommendations were made after consensus was reached; they were based on quality and strength of evidence and informed by other factors, including feasibility and patient perspectives. Once the draft was peer reviewed by an external group of experts and their inputs were incorporated, the final document was completed.

Recommendations: The revised CPG includes 34 recommendations in the following 5 topic areas: assessment and diagnosis, prevention, treatment, treatment of nightmares, and treatment of posttraumatic stress disorder (PTSD) with co-occurring conditions. Six recommendations on PTSD treatment were rated as strong. The CPG recommends use of specific manualized psychotherapies over pharmacotherapy; prolonged exposure, cognitive processing therapy, or eye movement desensitization and reprocessing psychotherapy; paroxetine, sertraline, or venlafaxine; and secure video teleconferencing to deliver recommended psychotherapy when that therapy has been validated for use with video teleconferencing or when other options are unavailable. The CPG also recommends against use of benzodiazepines, cannabis, or cannabis-derived products. Providers are encouraged to use this guideline to support evidence-based, patient-centered care and shared decision making to optimize individuals' health outcomes and quality of life.

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Approximately 7 in 10 U.S. adults will experience a traumatic event, such as sexual or physical assault, war-zone exposure, a serious accident, or a disaster, at some point in their lifetime (1). Exposure can lead to substantial problems, especially posttraumatic stress disorder (PTSD), a condition with symptoms that persist for more than 1 month after exposure and cause clinically significant distress or functional impairment. Acute stress disorder (ASD) can occur during the first 30 days after traumatic exposure. Individuals with occupationally related exposure, such as military personnel exposed to combat in a war zone, are at increased risk for both ASD and PTSD, making these conditions particularly relevant to the U.S. Department of Veterans Affairs (VA) and the U.S. Department of Defense (DoD). However, civilians also experience PTSD: Its lifetime prevalence in the U.S. general population is 4% in men and 8% in women (1).

The VA/DoD Evidence-Based Practice Work Group was established in 2004 to advise the VA/DoD Health Executive Committee "on the use of clinical and epidemiological evidence to improve the health of the population" across the Veterans Health Administration and Military Health System by facilitating development and dissemination of clinical practice guidelines (CPGs) for the VA and DoD populations (2). In 2017, VA and DoD published a CPG for PTSD and ASD. Following recommendations for best practices in guideline development (3), the Evidence-Based Practice Work Group initiated the update of the 2017 VA/DoD CPG for PTSD and ASD in January 2022. This article summarizes the revised guideline (4), released in 2023, focusing on assessments and treatments for which evidence was sufficient to permit a recommendation for or against.

See also:

Web-Only
Supplement

GUIDELINE DEVELOPMENT PROCESS

The Evidence-Based Practice Work Group sets the criteria and procedures for development of all VA/DoD CPGs, based on the standards put forth by the National Academy of Medicine (3). Leadership from the VA and DoD selected a multidisciplinary group of experts within their respective departments to serve on the Work Group for PTSD and ASD, including specialists in psychology, psychiatry, primary care, pharmacy, nursing, and social work (**Supplement Table 1**, available at Annals.org); 2 members from each department served as champions (leaders). Financial, intellectual, and other potential conflicts of interest were assessed at the outset of the process. As a result, one of the initial champions, who had an identified financial conflict, was replaced and served as a member only; they did not participate in discussion or decision making for topics related to their conflict. The process also required disclosure of any new conflicts at the beginning of each discussion, but none were disclosed. A focus group of service members and veterans is conducted for all VA/DoD CPGs to gain the patient perspective on having a particular disorder and on assessment and treatment. An external contractor experienced in guideline development, The Lewin Group, coordinated all activities.

The Work Group first developed 12 key questions using the PICOTS (population, intervention, comparator, outcomes, timing of outcomes measurement, and setting) framework (**Supplement Table 2**, available at Annals.org). The questions addressed the effectiveness and safety of treatments of ASD and PTSD, in both individual and group settings and via technological methods, and the accuracy of methods for assessing PTSD. The questions guided an evidence review that included evidence from 1 January 2016 through 1 May 2022 and was done by an independent third party, ECRI, which searched Embase, Medline, PubMed, PsycInfo, and gray literature sources (Part 2 of the **Supplement**, available at Annals.org). The Work Group examined the evidence identified through this review as well as evidence reviewed for the 2017 CPG for PTSD and ASD. To be included, a study had to have been published in English and, for studies of treatment, have at least 80% of participants with PTSD (or an acute reaction) and a follow-up of at least 1 month.

The Work Group developed recommendations using GRADE (Grading of Recommendations Assessment, Development and Evaluation) (5), which requires that recommendations are based on evidence using 4 domains: confidence in the quality of the identified studies; balance of desirable and undesirable outcomes; patient values and preferences; and other considerations, as appropriate (for example, resource use, equity, acceptability, feasibility, and subgroup considerations). Military status of research participants was a particular consideration given that effects are typically smaller in studies of service members and veterans than in studies of civilians (6). For systematic reviews and meta-analyses, the quality of evidence was based on the quality of included studies as rated by the review authors; see Appendix A, Section B, of the full guideline (4) for details.

Per GRADE, recommendations can be *strong* ("We recommend . . ."") or *weak* ("We suggest . . ."), and *for* or *against*. Evidence can also be rated as *neither for nor against* ("There is insufficient evidence to recommend for or against") if the evidence is limited or mixed, precluding a recommendation. A draft of the guideline was sent to external experts for peer review; revisions were made on the basis of the feedback received to complete the final version described here.

The 2023 CPG for PTSD and ASD reflects a more rigorous application of the GRADE methodology than the 2017 version. The Work Group used clinician-rated PTSD symptoms, which permit blinded assessment, as the critical outcome for making recommendations on treatments. Patient-reported symptoms, other clinical outcomes, and safety were important outcomes to inform recommendations. Therefore, compared with the 2017 version, recommendations in the 2023 version are more directly linked to confidence in the quality of the evidence on an outcome critical to clinical decision making (**Supplement Table 3**, available at Annals.org). Also, in the 2017 version, trauma-focused psychotherapies were evaluated as a class. In the 2023 version, the evidence on each trauma-focused psychotherapy was reviewed independently, consistent with how evidence was reviewed for pharmacotherapies—that is, by medication rather than by class.

SUMMARY OF RECOMMENDATIONS

The **Table** contains a complete list of recommendations. Part 2 of the **Supplement** contains algorithms for assessment and treatment.

Assessment and Diagnosis

The CPG suggests screening for PTSD using the Primary Care PTSD Screen for the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5; recommendation 1), a 5-item questionnaire that performs well in detecting a DSM-5 PTSD diagnosis (7). The evidence consisted of 2 studies conducted in veterans using VA care (7, 8), including 1 study of more than 400 VA primary care patients (7). Both study samples were predominantly White male veterans. Studies in other populations (for example, women and persons of other genders, active-duty service members, and samples with greater racial or ethnic diversity) are necessary to establish cut point scores appropriate for the population. For example, 1 of the 2 included studies found that the optimal cut point was the same for men and women but performed less well for women (7). No potential harms were identified in the systematic evidence review. Patient values and preferences varied because some patients do not like completing screening measures.

Table. Evidence-Based Clinical Practice Recommendations, With Strength and Category

Number	Recommendation	Strength*	Category†
Assessment and diagnosis of PTSD			
1	When screening for PTSD, we suggest using tde Primary Care PTSD Screen for DSM-5.	Weak for	Reviewed, new/replaced
2	For confirmation of the diagnosis of PTSD, we suggest using a validated, structured, clinician-administered interview, such as the CAPS-5 or PSSI-5.	Weak for	Reviewed, new/replaced
3	To detect changes in PTSD symptom severity over time, we suggest the use of a validated instrument, such as the PTSD Checklist for DSM-5, or a structured clinician-administered interview, such as the CAPS-5.	Weak for	Reviewed, new/replaced
Prevention of PTSD: selective prevention			
4	For the prevention of PTSD among individuals who have been exposed to trauma, there is insufficient evidence to recommend for or against psychotherapy or pharmacotherapy in the immediate posttrauma period.	Neither for nor against	Not reviewed, amended
Prevention of PTSD: indicated prevention			
5	For the prevention of PTSD among patients diagnosed with ASD, we suggest trauma-focused cognitive behavioral psychotherapy.	Weak for	Reviewed, new/replaced
6	For the prevention of PTSD among patients diagnosed with acute stress reaction/ASD, there is insufficient evidence to recommend for or against any pharmacotherapy.	Neither for nor against	Reviewed, new/replaced
Treatment of PTSD: treatment selection			
7	We recommend individual psychotherapies, listed in recommendation 8, over pharmacologic interventions for the treatment of PTSD.	Strong for	Reviewed, new/replaced
Treatment of PTSD: psychotherapy			
8	We recommend the following individual, manualized, trauma-focused psychotherapies for the treatment of PTSD: CPT, EMDR, or PE.	Strong for	Reviewed, new/replaced
9	We suggest the following individual, manualized psychotherapies for the treatment of PTSD: Ehlers CT, PCT, or WET.	Weak for	Reviewed, new/replaced
10	There is insufficient evidence to recommend for or against the following individual psychotherapies for the treatment of PTSD: accelerated resolution therapy, adaptive disclosure, acceptance and commitment therapy, brief eclectic psychotherapy, dialectical behavior therapy, emotional freedom techniques, impact of killing, interpersonal psychotherapy, narrative exposure therapy, PE in primary care, psychodynamic therapy, psychoeducation, reconsolidation of traumatic memories, seeking safety, stress inoculation training, skills training in affective and interpersonal regulation, skills training in affective and interpersonal regulation in primary care, supportive counseling, thought field therapy, trauma-informed guilt reduction, or trauma management therapy.	Neither for nor against	Reviewed, new/replaced
11	There is insufficient evidence to recommend using individual components of manualized psychotherapy protocols over, or in addition to, the full therapy protocol for the treatment of PTSD.	Neither for nor against	Reviewed, not changed
12	There is insufficient evidence to recommend for or against any specific manualized group therapy for the treatment of PTSD.	Neither for nor against	Reviewed, new/replaced
13	There is insufficient evidence to recommend using group therapy as an adjunct to the primary treatment of PTSD.	Neither for nor against	Reviewed, new/replaced
14	There is insufficient evidence to recommend for or against the following couples therapies for the treatment of PTSD: behavioral family therapy, structured approach therapy, or cognitive behavioral conjoint therapy.	Neither for nor against	Reviewed, not changed
Treatment of PTSD: pharmacotherapy			
15	We recommend paroxetine, sertraline, or venlafaxine for the treatment of PTSD.	Strong for	Reviewed, new/replaced
16	There is insufficient evidence to recommend for or against amitriptyline, bupropion, buspirone, citalopram, desvenlafaxine, duloxetine, escitalopram, eszopiclone, fluoxetine, imipramine, mirtazapine, lamotrigine, nefazodone, olanzapine, phenelzine, pregabalin, rivastigmine, topiramate, or quetiapine for the treatment of PTSD.	Neither for nor against	Reviewed, new/replaced
17	There is insufficient evidence to recommend for or against psilocybin, ayahuasca, dimethyltryptamine, ibogaine, or lysergic acid diethylamide for the treatment of PTSD.	Neither for nor against	Reviewed, new/added
18	We suggest against divalproex, guanfacine, ketamine, prazosin, risperidone, tiagabine, or vortioxetine for the treatment of PTSD.	Weak against	Reviewed, new/replaced
19	We recommend against benzodiazepines for the treatment of PTSD.	Strong against	Reviewed, new/replaced
20	We recommend against cannabis or cannabis derivatives for the treatment of PTSD.	Strong against	Reviewed, amended

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Table–Continued

Number	Recommendation	Strength*	Category†
Treatment of PTSD: augmentation therapy			
21	There is insufficient evidence to recommend for or against the combination or augmentation of psychotherapy (recommendations 8 and 9) or medications (recommendation 15) with any psychotherapy or medication for the treatment of PTSD (see recommendation 22 for antipsychotic medications and recommendation 23 for MDMA).	Neither for nor against	Reviewed, new/replaced
22	We suggest against aripiprazole, asenapine, brexpiprazole, cariprazine, iloperidone, lumateperone, lurasidone, olanzapine, paliperidone, quetiapine, risperidone, or ziprasidone for augmentation of medications for the treatment of PTSD.	Weak against	Reviewed, new/replaced
23	There is insufficient evidence to recommend for or against MDMA-assisted psychotherapy for the treatment of PTSD.	Neither for nor against	Reviewed, new/added
Treatment of PTSD: nonpharmacologic biological treatments			
24	There is insufficient evidence to recommend for or against the following somatic therapies for the treatment of PTSD: capnometry-assisted respiratory therapy, hyperbaric oxygen therapy, neurofeedback, NightWare, repetitive transcranial magnetic stimulation, stellate ganglion block, or transcranial direct current stimulation.	Neither for nor against	Reviewed, new/replaced
25	We suggest against electroconvulsive therapy or vagus nerve stimulation for the treatment of PTSD.	Weak against	Reviewed, new/replaced
Treatment of PTSD: complementary, integrative, and alternative approaches			
26	We suggest mindfulness-based stress reduction for the treatment of PTSD.	Weak for	Reviewed, new/replaced
27	There is insufficient evidence to recommend for or against the following mind–body interventions for the treatment of PTSD: acupuncture, cognitively-based compassion training–veteran version, creative arts therapies (e.g., music, art, dance), guided imagery, hypnosis or self-hypnosis, loving kindness meditation, mantram repetition program, mindfulness-based cognitive therapy, other mindfulness trainings (e.g., integrative exercise, mindfulness-based exposure therapy, brief mindfulness training), relaxation training, somatic experiencing, tai chi or qigong, transcendental meditation, or yoga.	Neither for nor against	Reviewed, new/replaced
28	There is insufficient evidence to recommend for or against the following interventions for the treatment of PTSD: recreational therapy, aerobic or non-aerobic exercise, animal-assisted therapy (e.g., canine, equine), or nature experiences (e.g., fishing, sailing).	Neither for nor against	Reviewed, new/replaced
Treatment of PTSD: technology-based treatment			
29	We recommend secure video teleconferencing to deliver treatments in recommendations 8 and 9 when that therapy has been validated for use with video teleconferencing or when other options are unavailable.	Strong for	Reviewed, new/replaced
30	There is insufficient evidence to recommend for or against mobile apps or other self-help–based interventions for the treatment of PTSD.	Neither for nor against	Reviewed, new/added
31	There is insufficient evidence to recommend for or against facilitated, internet-based cognitive behavioral therapy for the treatment of PTSD.	Neither for nor against	Reviewed, new/replaced
Treatment of nightmares			
32	We suggest prazosin for the treatment of nightmares associated with PTSD.	Weak for	Reviewed, amended
33	There is insufficient evidence to recommend for or against the following treatments of nightmares associated with PTSD: imagery rehearsal therapy; exposure, relaxation, and rescripting therapy; imaging rescripting and reprocessing therapy; or NightWare.	Neither for nor against	Reviewed, new/added
Treatment of PTSD with co-occurring conditions			
34	We suggest that the presence of co-occurring substance use disorder and/or other disorder(s) not preclude treatments in recommendations 8 and 9 for PTSD.	Weak for	Reviewed, new/replaced

ASD = acute stress disorder; CAPS-5 = Clinician-Administered PTSD Scale for DSM-5; CPT = cognitive processing therapy; CT = cognitive therapy; EMDR = eye movement desensitization and reprocessing; MDMA = 3,4-methylenedioxymethamphetamine; PCT = present-centered therapy; PE = prolonged exposure; PSSI-5 = PTSD Symptom Scale Interview for DSM-5; PTSD = posttraumatic stress disorder; WET = written exposure therapy.
* Strength of recommendation can be strong or weak, for or against. Strength can also be rated as neither for nor against if evidence does not permit a recommendation. See Table 4 in the full guideline (4) for details.
† Category of recommendation can be reviewed (new/added, new/replaced, not changed, amended, or deleted) or not reviewed (not changed, amended, or deleted). See Table 5 in the full guideline (4) for more details.

The CPG suggests using a validated, structured, clinician-administered interview, such as the Clinician-Administered PTSD Scale for DSM-5 (CAPS-5) (9) or PTSD Symptom Scale Interview for DSM-5 (PSSI-5) (10), to diagnose PTSD (recommendation 2). The recommendation is based on 2 studies demonstrating the diagnostic validity of the CAPS-5 (9, 11) and 1 study of the PSSI-5 (10) (included in the evidence review for the 2017 CPG but not included in the current evidence review or affecting the strength of this recommendation).

The latter study found good convergent validity between PSSI-5 and CAPS-5 total scores and moderate correspondence between CAPS-5 and PSSI-5 diagnoses. The benefits of clinician-administered interviews outweighed the potential harms. Although some patients may experience distress when asked to describe traumatic events and associated symptoms, this risk is generally outweighed by the value of an appropriate diagnosis for treatment planning. Patient values and preferences may vary because some patients might find detailed assessments inconvenient or invasive. The Work Group recognized that structured, clinician-administered interviews can be resource-intensive and time-consuming, often require specialized training and competency, and therefore may not be routinely feasible in clinical settings.

For assessing symptom change, the CPG suggests use of validated instruments (recommendation 3), such as the PTSD Checklist for DSM-5 (12) or a structured, clinician-administered interview (for example, CAPS-5) (9), on the basis of 2 studies in veteran samples (13, 14). The evidence is further supported by prior research (included in the evidence review for the 2017 CPG but not affecting the strength of this recommendation) that found correspondence in longitudinal scores in the DSM-IV versions of these 2 instruments (15). Although no studies on sensitivity to change for the PSSI-5 were found in the evidence review, prior research (included in the evidence review for the 2017 CPG but not the current evidence review) supports its validity and applicability for measuring symptom change (10). The benefits of monitoring symptom change outweighed the potential harms. Patient values and preferences may vary because some patients might find assessments inconvenient or invasive whereas others may appreciate the value of systematically tracking progress.

Selective and Indicated Prevention of PTSD

Prevention of PTSD is important because service members and veterans may be exposed not only to combat in a war zone but also to other traumatic events during or after military service. Unfortunately, the evidence was insufficient to make a recommendation for using psychotherapy or pharmacotherapy in the immediate posttrauma period to prevent PTSD in traumatized persons (recommendation 4). Evidence was also insufficient to make a recommendation for using pharmacotherapy to prevent PTSD in persons with ASD (recommendation 6). However, the CPG suggests trauma-focused cognitive behavioral therapy to prevent PTSD in persons with ASD (recommendation 5). No specific protocol was identified, but 1 systematic review (with 9 studies, 4 of which had the critical outcome of clinician-rated PTSD) found that patients with ASD who received brief, trauma-focused cognitive behavioral therapy, including cognitive restructuring and exposure, had reduced PTSD symptom severity at 3- to 6-month follow-up compared with those who received supportive counseling or were on a waitlist (16). The body of evidence had some limitations, including small sample sizes, risk of bias, and lack of studies in service members or veterans. However, the benefits of reduced symptoms and lower rates of subsequent diagnosis of PTSD outweighed the potential harms and burdens (such as time required to attend psychotherapy sessions).

Treatment Selection

Three psychotherapies (recommendation 8) and 3 pharmacotherapies (recommendation 15) are recommended for treating PTSD. When both treatment methods are available and feasible, the CPG recommends the psychotherapies over the pharmacotherapies (recommendation 7). The Work Group based the recommendation on 2 systematic reviews included in the 2017 version of the CPG (17, 18) and 1 newer systematic review and network meta-analysis (19). The reviews found that trauma-focused psychotherapies impart greater improvement on core PTSD symptoms than pharmacotherapies and that these improvements persist longer. These findings held true even in a meta-analysis of medications and psychotherapies in which the only psychotherapy studies included had used active comparison treatments, such as present-centered therapy (PCT), as opposed to waitlists or usual care (17).

In making this recommendation, the Work Group considered several factors in addition to the apparent differences in the magnitude of change associated with the 2 treatment methods. First, although the risks for adverse effects or negative reactions vary across individual patients, they are generally more likely to occur with pharmacologic treatments than with psychotherapies (recommendation 15 and Appendix B in the full guideline) (4). Second, the positive effects of medication treatment often diminish over time and are lost when medications are withdrawn (17). The body of evidence had some limitations, including few direct comparisons and studies with small sample sizes. The benefits of using psychotherapy over pharmacotherapy slightly outweighed the potential harms, which were considered minimal. Patient values and preferences varied largely, with some patients expressing a strong preference for one method or the other, but most patients seem to prefer psychotherapy over pharmacotherapy, even when psychotherapy is trauma-focused (20–23).

Psychotherapy

The 2017 CPG for PTSD and ASD recommended trauma-focused therapies that use 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. After reviewing the evidence on specific psychotherapies, the 2023 CPG Work Group recommended the following 3 trauma-focused psychotherapies (recommendation 8) on the basis of evidence of efficacy from 6 systematic reviews (24–29): cognitive processing therapy (CPT) with

or without a trauma account, eye movement desensitization and reprocessing (EMDR), and prolonged exposure (PE). The body of evidence had some limitations, including no studies of EMDR in active-duty service members and few studies of EMDR in veterans. The benefits of CPT, EMDR, and PE in improving the critical outcome of clinician-rated PTSD symptoms and other important outcomes outweighed the potential harms (such as adverse events), which were small.

In addition to recommending CPT, EMDR, and PE, the CPG suggests Ehlers cognitive therapy (CT), PCT, and written exposure therapy (WET) on the basis of evidence from 2 systematic reviews and 1 individual study (24, 30, 31) (recommendation 9). Regarding patient preferences, PCT might be more acceptable than trauma-focused treatments because it does not require talking about trauma. In addition, PCT has lower dropout rates than trauma-focused treatments (32). The body of evidence had some limitations, including no studies of Ehlers CT and only 1 study of WET in military populations. All studies of CT and WET were done by the respective treatment developers, which might limit generalizability of findings because of potential allegiance bias. No studies compared PCT with an active control, although there were multiple comparisons with active treatment. The benefits of Ehlers CT, PCT, and WET in improving the critical outcome of clinician-rated PTSD symptoms and other important outcomes outweighed the potential harms (for example, of adverse events), which were small.

The Work Group found insufficient evidence to make a recommendation about other psychotherapies (recommendation 10) based on 6 systematic reviews and meta-analyses and 2 randomized controlled trials (RCTs) (24, 33–38), because either there were few studies of a treatment with the critical outcome of clinician-rated PTSD or the efficacy of a treatment was inconsistent across studies. (Recommendations 11 to 14 refer to additional psychotherapies for which evidence was inconsistent.)

Pharmacotherapy

The CPG recommends paroxetine, sertraline, and venlafaxine (recommendation 15) on the basis of a systematic review that included 6 trials of paroxetine, 6 trials of sertraline, and 2 trials of venlafaxine (39). This recommendation is a change from the 2017 CPG, which also recommended fluoxetine on the basis of older systematic reviews (17, 40). The more recent review (39) found no benefit of fluoxetine for clinician-rated PTSD in a single trial. Fluoxetine is now categorized as having insufficient evidence for or against its use.

The body of evidence had limitations, including risk of bias and concerns about study quality and high heterogeneity. Generalizability to military populations may be limited because there were only 2 studies in veterans (1 of which was negative) and no studies of service members. However, the Work Group determined that the benefits of treatment with paroxetine, sertraline, and venlafaxine outweighed the small potential harm of adverse events. Patient values and preferences may vary because of differing attitudes about use of medications.

Evidence was rated as insufficient for a large group of medications (recommendation 16), including several changes from the 2017 CPG based on more rigorous application of GRADE criteria and 2 new systematic reviews (39, 41), as well as consideration of the evidence reviewed for the 2017 CPG (17, 40). Most notably, olanzapine and quetiapine (previously *weak against*) and phenelzine (previously *weak for*) are now classified as *neither for nor against*.

The Work Group found that evidence was insufficient to recommend for or against the use of psychedelics (such as psilocybin) for the treatment of PTSD (recommendation 17); the Combination and Augmentation section below discusses 3,4-methylenedioxymethamphetamine (MDMA)–assisted psychotherapy. No studies meeting search criteria were identified, and these agents cannot be legally prescribed in the United States outside a research study. In addition, these agents might have adverse effects, risks, or both that are currently unknown (and adverse events have been anecdotally reported).

Recommendation 18 suggests against divalproex, guanfacine, ketamine, prazosin, risperidone, tiagabine, and vortioxetine for the overall treatment of PTSD on the basis of 3 systematic reviews and 1 RCT (39, 41–43) (see recommendation 32 on prazosin for nightmares). The 2017 CPG recommended against risperidone and neither for nor against vortioxetine. The *weak against* recommendation for ketamine in the 2017 CPG was maintained in the 2023 version, supported by an additional negative trial (44). The body of evidence had limitations, including a lack of evidence of effectiveness. Thus, the Work Group determined that the benefits of these medications were outweighed by the harms, which include multiple potential side effects and risks associated with increased blood pressure and heart rate. Patient values and preferences are likely to vary because of the different considerations for each medicine, including the level of evidence for an effect on PTSD symptoms, side effect profiles, and potential benefits for alternative uses.

The CPG recommends against benzodiazepines on the basis of a lack of evidence of benefits and the presence of known harms (recommendation 19). A systematic review (39) included a single negative trial that, along with evidence from the 2017 CPG for PTSD and ASD (45), found that benzodiazepines are associated with misuse, decreased effectiveness of recommended PTSD treatments, and adverse cognitive changes, especially in the elderly.

The CPG also recommends against cannabis or cannabis derivatives for the treatment of PTSD (recommendation 20) because of the lack of well-designed RCTs and potentially serious side effects associated with cannabis use in 4 systemic reviews (46–49). Evidence from

1 randomized, double-blind, crossover study that did not meet inclusion criteria for the CPG review because of insufficient length of follow-up (and therefore did not affect the strength of this recommendation) indicated no difference in change in PTSD symptom severity between active cannabis concentrations and placebo (50).

Combination and Augmentation

Evidence was insufficient to recommend for or against the combination of evidence-based medications or psychotherapies to enhance treatment outcomes in PTSD (recommendation 21). This largely reflects the scarcity of studies examining combination treatments, but also findings of a systematic review (51) and individual studies (52–56). Similarly, with the exception of atypical antipsychotic medications, evidence (40, 42) was insufficient to support augmenting recommended or suggested psychotherapy or medication treatment with other non–PTSD-indicated medication (recommendation 21). The CPG suggests against atypical antipsychotic medications because of lack of demonstrated benefit and known harms (recommendation 22). Only 3 atypical antipsychotic medications—risperidone, aripiprazole, and olanzapine—have been evaluated for augmenting medication treatment in PTSD (42, 57, 58). For these and other atypical antipsychotic medications for which no studies exist, there are known serious risks, including weight gain, hyperlipidemia, diabetes mellitus, QTc prolongation, and extrapyramidal side effects (59).

The Work Group found insufficient evidence to recommend for or against MDMA-assisted psychotherapy for the treatment of PTSD (recommendation 23). A systematic review of 5 RCTs found benefit for improving clinician-rated PTSD (42), but the evidence had limitations: relatively few total participants ($n = 176$), few veterans or active-duty service members, and differing control conditions that affected adequacy of blinding. The MDMA-assisted psychotherapy protocol (three 8-hour medication sessions staffed by 2 therapists and 12 weekly 90-minute psychotherapy sessions) would be challenging to implement in current VA and DoD (and other) health care systems.

Nonpharmacologic Biological Treatments

The Work Group found the evidence insufficient to make a recommendation on a range of somatic treatments, including capnometry-assisted respiratory therapy, hyperbaric oxygen therapy, neurofeedback, NightWare, repetitive transcranial magnetic stimulation, stellate ganglion block, and transcranial direct current stimulation (recommendation 24). For most treatments, evidence was mixed or had methodological limitations. No RCTs studied clinician-rated PTSD severity for NightWare or transcranial direct current stimulation. No new studies were identified to support the efficacy of electroconvulsive therapy or vagus nerve stimulation for the treatment of PTSD, so the Work Group used the assessment of the evidence from the 2017 CPG for PTSD and ASD, a meta-analysis and 2 RCTs (60–62), to make a *weak against* recommendation (recommendation 25). Given the lack of efficacy data, the potential harms of electroconvulsive therapy and vagus nerve stimulation (such as risks associated with general anesthesia and, for vagus nerve stimulation, surgery) outweighed the potential benefits.

Complementary, Integrative, and Alternative Approaches

The CPG suggests mindfulness-based stress reduction for treating PTSD (recommendation 26) on the basis of a systematic review including 5 RCTs that used the critical outcome of clinician-rated PTSD (63). Three of these RCTs involved veterans and showed that mindfulness-based stress reduction outperformed present-centered group therapy (64, 65) or usual care (66). Evidence was insufficient to make a recommendation for all other mind–body interventions or alternative practices (recommendations 27 and 28).

Technology

Technology, such as mobile apps and video teleconferencing, can increase access to mental health care. The CPG recommends video teleconferencing to deliver the psychotherapies with *strong* or *weak for* recommendations that have been validated for telehealth delivery (recommendation 29). Three RCTs reviewed as part of the 2017 CPG for PTSD and ASD (67–69), plus a systematic review and 2 additional RCTs identified in the current evidence review (70–72), suggest that delivery of CPT and PE via video teleconferencing is noninferior to face-to-face delivery. The Work Group determined that the benefits outweighed the potential for harm from lack of treatment if patients cannot receive in-person treatment. However, patient values and preferences vary because some patients might prefer in-person care. Evidence was insufficient to make a recommendation for or against other technological methods, such as mobile apps (recommendations 30 and 31).

Treatment of Nightmares

In addition to examining the effects of interventions on overall PTSD severity, the Work Group examined the effects on nightmares, a core symptom of PTSD. Although the CPG suggests against using prazosin to treat PTSD symptoms, the evidence supports a *weak for* recommendation for prazosin to treat nightmares (recommendation 32), as demonstrated by 2 systematic reviews and 1 RCT (73–75). Insufficient evidence exists to recommend for or against imagery rehearsal therapy, exposure relaxation and rescripting therapy, imaging rescripting and reprocessing therapy, or NightWare (recommendation 33).

Treatment of PTSD With Co-occurring Conditions

In recommendation 34, the CPG suggests that the presence of comorbid psychiatric disorders not prevent

delivery of the psychotherapies listed in recommendations 8 and 9. Evidence from 5 systematic reviews (36, 76–79) and 11 individual studies (80–90) showed that persons with comorbid conditions, including substance use disorders, can tolerate and benefit from evidence-based individual PTSD treatments, such as PE and CPT. The evidence included both standard treatments of PTSD and integrated treatments that address comorbidity (83). Evidence from 2 systematic reviews (76, 77) and 4 individual studies (85, 86, 88, 89) showed that the presence of comorbid conditions does not alter the effectiveness of these treatments. The evidence indicates that the presence of comorbid conditions should not delay PTSD treatment because, for adults diagnosed with PTSD, treatment safety and effectiveness do not seem to be altered by the presence of comorbid conditions. The body of evidence had limitations, including small sample sizes and high dropout rates, although the benefits of treating PTSD in patients with comorbid conditions outweighed the potential harms. Therefore, the CPG suggests that the presence of co-occurring substance use disorder or other disorders not preclude psychotherapies that received a *strong* or *weak for* recommendation.

Providers may consult other VA/DoD guidelines for recommendations on the treatment of comorbid conditions in PTSD. For example, although the 2023 CPG for PTSD and ASD suggests against the use of ketamine for PTSD, the 2022 VA/DoD CPG for major depressive disorder recommends ketamine for treatment-resistant cases (91). Because PTSD is highly comorbid with major depressive disorder in both veterans and service members, ketamine might be considered for treating depression in patients with both conditions.

Research Recommendations

During development of the CPG, the Work Group identified topics needing additional research. The greatest priorities are studies of comparative effectiveness and those that evaluate strategies to enhance treatment outcomes. Also, studies of active-duty service members are needed, especially for medication and complementary and integrative health interventions. Use of active control conditions is a cross-cutting need for research on psychedelics; somatic treatments, such as stellate ganglion block and transcranial magnetic stimulation; and novel treatments, such as complementary and integrative health interventions.

Regarding comparative effectiveness, both head-to-head and meta-analytic comparisons are needed. More attention needs to be paid to generalizability of findings to subgroups based on gender, sexuality, race, ethnicity, age, and other patient characteristics. Research is also needed on enhancing treatment outcomes and on precision mental health to help determine the optimal treatment for a given patient using biomarkers, patient characteristics, and social determinants of health.

For psychotherapy, a key topic is how to enhance the feasibility of delivery (for example, brief treatments for primary care settings), as well as engagement and retention. Given the limited number of recommended and suggested medications for PTSD and the recommendation of psychotherapy over medication as a frontline strategy, research is needed to expand knowledge about effective medications, including novel medications, trials longer than 12 weeks, and durability of outcomes after medication treatment discontinuation.

Discussion

The recommendations in the 2023 CPG for PTSD and ASD offer patients and providers a range of pharmacologic and nonpharmacologic options for managing PTSD, whereas guidance on managing ASD is limited and that on prevention is lacking. The strong recommendations in the 2017 CPG for PTSD and ASD were largely consistent with recommendations in the other guidelines (92). For example, 3 of the 5 guidelines (including VA/DoD) recommended trauma-focused psychotherapy over medication. Four (including VA/DoD) recommended trauma-focused psychotherapy, but 1 did not recommend EMDR for military personnel and 1 gave EMDR a weaker rating than it gave to other therapies. The 2023 CPG's approach of reviewing psychotherapies individually makes it differ from these other guidelines because fewer psychotherapies are recommended or suggested, but this approach is consistent with that taken in the American Psychological Association's guideline (92).

When using the 2023 CPG for PTSD and ASD, providers are encouraged to consider its strengths and limitations. Strengths include a rigorous process of guideline development that is based on best practice recommendations, including use of GRADE criteria, careful attention to potential conflicts of interest, and a standardized process that is used for the development of all VA/DoD CPGs. Limitations include a lack of evidence to inform generalizing recommendations to gender, racial, ethnic, sexual, and other subgroups. Because the Work Group considered military status information when making recommendations, some recommendations might have differed had military status not been considered. However, a lack of data on veterans or service members alone did not alter any recommendations. Providers can use the CPG for treating military and nonmilitary patients.

The psychotherapies recommended or suggested for treating PTSD are most feasible in mental health settings with specially trained providers, but the guideline is relevant to providers in other settings. For example, primary care providers could use the Primary Care PTSD Screen for DSM-5 (7) to screen for PTSD and the PTSD Checklist for DSM-5 (12) to monitor symptom change. They could also prescribe medications for PTSD and nightmares. Depending on the setting, arranging for

telehealth delivery of recommended psychotherapy might be possible. Providers can also use the information on treatments for which the evidence is insufficient to educate patients and inform decision making and to counsel patients on use of treatments that are not recommended (cannabis and benzodiazepines).

Clinical practice guidelines are intended to promote the delivery of evidence-based care, but they are not mandates that define required care. The VA/DoD CPGs encourage providers to engage in evidence-based practice, using knowledge of the evidence base along with a patient-centered approach and shared decision making (93). Treatment goals and plans should be based on patient capabilities, needs, and preferences. We suggest that providers use this guideline to support communication to improve the quality of care and enhance clinical outcomes for their patients.

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