

Posttraumatic Stress Disorder
Prevention and Treatment Guidelines

Methodology and Recommendations



International Society
for Traumatic Stress Studies

1. Introduction

1.1. The updated ISTSS PTSD Prevention and Treatment Guidelines Methodology and Recommendations, and Position Papers on Complex PTSD are available to download through the ISTSS website, along with the evidence summaries that generated the recommendations. These documents are key components of the updated Guidelines; the final component, the third edition of *Effective Treatments for PTSD*, is due to be published at the end of 2019 and will focus on providing practitioners with more detailed guidance on the use of the recommendations and position papers to inform clinical practice.

1.2. This document includes the recommendations and describes the methodology used to develop them. Important issues that should be considered when interpreting the recommendations, and translating them into practice, are highlighted. It was decided to publish the recommendations and position papers in advance of the book as they represent a comprehensive and up-to-date synthesis of high quality research evidence that is likely to help practitioners in their work. It is, however, important to highlight that the *Effective Treatments for PTSD* book will provide the detailed narrative required to assist practitioners to make fully informed decisions about the applicability of the recommendations to specific clinical situations.

2. Methodology Overview

2.1. The recommendations and position papers were developed through a rigorous process that was overseen by the ISTSS Guidelines Committee. The methodology involved the development of scoping questions and undertaking systematic reviews to identify randomized controlled trials (RCTs) that could answer them. Meta-analyses were then conducted with usable data from included studies, and the results used to generate recommendations for prevention and treatment interventions. A definition of clinical importance and an algorithm for determining the recommendation level of a given intervention (see below) were agreed upon before the meta-analyses were undertaken.

2.2. Given the limited resources available, it was not possible to commission new comprehensive systematic reviews in every area. It was, however, possible to develop a robust and replicable process that systematically gathered and considered the RCT evidence currently available for any intervention in a standardized manner. A process adapted from approaches taken by the Australian Centre for Posttraumatic Mental Health¹ (now Phoenix Australia–Centre for Posttraumatic Mental Health), the Cochrane Collaboration², the United Kingdom’s National Institute for Health and Care Excellence (NICE)³, and the World Health Organisation (WHO)⁴ was used.

2.3. The Committee agreed on general scoping questions in a PICO (Population, Intervention, Comparator, Outcomes) format (e.g., “For adults with PTSD, do psychological treatments, when compared to treatment as usual, waiting list or no treatment, result in a clinically important reduction of symptoms, improved functioning/quality of life, presence of disorder, or adverse effects?”) for the prevention and treatment of PTSD in children, adolescents and adults. Prior to finalization, the committee sought and integrated feedback from the ISTSS membership around these scoping questions.

2.4. High quality systematic reviews developed through the Cochrane Collaboration, NICE and the WHO were identified that addressed the scoping questions. RCTs from these reviews were used as the basis of the evidence to be considered and re-evaluated according to the criteria agreed for the ISTSS Treatment Guidelines. Existing reviews were supplemented with additional systematic searches for more recent RCTs and by asking experts in the field and the ISTSS membership to determine if there were any missing studies.

2.5. The evidence for each of the scoping questions was summarized and its quality assessed using the Cochrane Collaboration’s risk of bias rating toolⁱ (to assess for potential methodological concerns within identified studies) and the GRADEⁱⁱ system (i.e., the level of confidence that the estimate of the effect of an intervention is correct). The evidence summaries and quality assessments were then used to generate draft recommendations using the algorithm described below. The draft recommendations were posted on the ISTSS website during August and September 2018, for a period of consultation by ISTSS members. Feedback was incorporated before the recommendations were finalized and approved by the ISTSS Board in October 2018.

ⁱThe Cochrane Collaboration’s risk of bias criteria² determine low, uncertain or high risk ratings for: Random sequence generation (selection bias); Allocation concealment (selection bias); Blinding of participants and personnel (performance bias); Blinding of outcome assessment (detection bias); Incomplete outcome data (attrition bias); Selective reporting (reporting bias); and Other bias

ⁱⁱGRADE Working Group Grades of Evidence⁵

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

3. Scoping Questions

3.1. Following consultation with the ISTSS membership and reference groups of practitioners and non-practitioner consumers, the ISTSS Guidelines Committee proposed 20 scoping questions that were passed by the ISTSS Board (See Appendix 1). Inclusion of separate scoping questions on treatments for complex presentations of PTSD for children, adolescents and adults was considered. Concerns were, however, raised that due to definitional issues and the virtual absence of studies specifically designed to answer possible scoping questions on treatments for complex presentations of PTSD, their inclusion would be unlikely to provide clear answers.

3.2. It was concluded that, rather than systematically reviewing the evidence for the treatment of complex presentations of PTSD, it would likely be more beneficial to undertake a narrative review of the current situation with respect to Complex PTSD, what it is, and how it should be defined to enable the development of an evidence base of how best to treat it. Facilitated by the publication of the ICD-11 diagnosis of Complex PTSD during the course of the Committee's operation, position papers (one for children and adolescents, and one for adults) were developed that consider the current issues around Complex PTSD and make recommendations to facilitate further research. The position papers were drafted by members of the ISTSS Guidelines Committee and consulted on with the rest of the Committee, the ISTSS Board and the ISTSS membership before being finalized.

4. Systematic reviews and meta-analyses

4.1. New systematic searches were undertaken by the Cochrane Collaboration for the period 1 January 2008 to 31 March 2018, using their comprehensive search strategies, to identify RCTs of any intervention designed to prevent or treat PTSD. Additional RCTs were identified through consultation with experts in the field, including the ISTSS Board and the entire ISTSS membership.

4.2. The new searches identified 5,500 potential new studies. These and the studies included in existing systematic reviews were assessed against the inclusion criteria agreed upon for the ISTSS Guidelines. The inclusion criteria were designed to focus on reduction in symptoms of PTSD as the primary outcome and differed slightly for early intervention and treatment studies (i.e., as opposed to early interventions studies, treatment studies required a defined severity of PTSD symptoms to be included).

4.3. The inclusion criteria for early intervention studies were:

- Any randomised controlled trial (including cluster and cross-over trials) evaluating the efficacy of interventions aimed at preventing, treating or reducing symptoms of PTSD.
- Study participants have been exposed to a traumatic event as specified by PTSD diagnostic criteria for DSM-III, DSM-III-R, DSM-IV, DSM-5, ICD-9, ICD-10 or ICD-11.
- Intervention is not provided pre-trauma.
- Intervention begins no later than 3 months after the traumatic event.
- Eligible comparator interventions for psychosocial interventions: waitlist, treatment as usual, symptom monitoring, repeated assessment, other minimal attention control group or an alternative psychological treatment.
- Eligible comparator interventions for pharmacological interventions: placebo, other pharmacological or psychosocial intervention.
- The RCT is not solely a dismantling study.
- Study outcomes include a standardised measure of PTSD symptoms (either clinician-administered or self-report).
- No restriction on the basis of severity of PTSD symptoms or the type of traumatic event.
- Individual, group and couple interventions.
- No minimum sample size.
- Only studies published in English.
- Unpublished studies eligible.

4.4. The inclusion criteria for treatment studies were:

- Any randomised controlled trial (including cluster and cross-over trials) evaluating the efficacy of psychological interventions aimed at reducing symptoms of PTSD.
- For adults, at least 70% of participants required to be diagnosed with PTSD according to DSM or ICD criteria by means of a structured interview or diagnosis by a clinician.
- For children and adolescents, at least 70% diagnosed with partial or full DSM or ICD PTSD by means of a structured interview or diagnosis by a clinician (partial PTSD is defined as at least one symptom per cluster and presence of impairment), or score above a standard cut-off of a validated self-report measure.
- No restrictions on the basis of comorbidity, but PTSD required to be the primary diagnosis.
- Eligible comparator interventions for psychosocial interventions: waitlist, treatment as usual, symptom monitoring, repeated assessment, other minimal attention control group or an alternative psychological treatment.
- Eligible comparator interventions for pharmacological interventions: placebo, other pharmacological or psychosocial intervention.
- The RCT is not solely a dismantling study.
- Duration of PTSD symptoms required to be three months or more.
- No restriction on the basis of severity of PTSD symptoms or the type of traumatic event.

- Individual, group and couple interventions.
- No minimum sample size.
- Only studies published in English.
- Unpublished studies eligible.

4.5. A total of 361 RCTs fulfilled the criteria for inclusion in the meta-analyses undertaken. Studies that fulfilled the inclusion criteria were further scrutinised to determine if data were available to use in the meta-analyses, and to assess risk of bias according to the Cochrane Collaboration criteria. If sufficient data were not available, requests were made to authors for data that could be used. A total of 327 (91%) of the included RCTs provided data that were included in the meta-analyses. The classification and grouping of the interventions included is described in Appendix 2. The final meta-analyses and reference lists of all eligible studies can be found on the ISTSS website.

5. Definition of Clinical Importance

5.1. In order to generate recommendations from the results of the meta-analyses, the following definition of clinical importance was developed and agreed upon:

5.1.1. PTSD symptom change was the primary outcome measure and other outcomes (e.g., diagnosis, functioning, other symptom change, tolerability) were considered as secondary outcome measures.

5.1.2. The clinically important definition was based on both magnitude of change and strength/quality of evidence.

5.1.3. Informed by previous work in this area (e.g., the UK NICE guidelines for PTSD development group³), to be rated clinically important, an intervention delivered three or more months after the traumatic event had to demonstrate an effect size, calculated as the standardized mean difference (SMD), for continuous outcomes of >0.8 (<0.65 relative risk for binary outcomes) for wait list control comparisons, >0.5 for attention control comparisons (no meaningful treatment, but same dosage of time/same number of sessions with a therapist), >0.4 for placebo control comparisons and >0.2 for active treatment control comparisons.

5.1.4. To be rated clinically important, an early intervention started within three months of the traumatic event had to demonstrate an effect size for continuous outcomes of >0.5 for wait list control comparisons (< 0.8 relative risk for binary outcomes).

5.1.5. If there was only one RCT, an intervention was not normally recommended as clinically important. Non-inferiority RCT evidence alone was not enough to recommend an intervention as clinically important.

5.1.6. Unless there was a GRADE quality of evidence rating of high or moderate, consideration was given to downgrading the strength of recommendation made with respect to clinical importance.

5.1.7. The primary analysis for a particular question included data from all included studies. When available, this was clinician rated; when not, self-report was included. In addition, an analysis was also considered of only studies with clinician rated data. The combination of these two analyses was considered along with the GRADE ratings and risk of bias ratings to determine the strength of recommendation.

5.1.8. The 95% confidence interval range had to completely exclude the thresholds for the strongest level of recommendation (e.g. lower confidence interval of >0.8 for waiting list control comparisons of treatments).

6. Recommendation Setting

6.1. An algorithm was developed to allow the systematic and objective agreement of recommendations after scrutiny of the meta-analyses pertaining to individual scoping questions. Consideration was given to magnitude of change, strength/quality of evidence and any other important factors (e.g., adverse effects).

6.2. Five different levels of recommendation were possible. A '*Strong*' recommendation was made for/against interventions with at least reasonable quality of evidence and the highest certainty of effect. A '*Standard*' recommendation was made when there was at least reasonable quality of evidence and lower certainty of effect. An '*Intervention with Low Effect*' recommendation was made for interventions with at least reasonable quality of evidence and high certainty of a low level of effect. An '*Emerging Intervention*' recommendation was made for interventions with lower quality of evidence and/or certainty of effect. An '*Insufficient Evidence to Recommend*' recommendation was made when there was an absence of evidence of effectiveness or ineffectiveness.

6.3. The following criteria had to be met for a *Strong Recommendation*:

Quality - GRADE rating better than low or mean less than three for red rated risk of bias criteria for the meta-analysis on which results are based on. (If the mean number of high-risk of bias criteria is three or more, a sensitivity analysis excluding the high-risk studies was undertaken and used as the primary meta-analysis if the effectiveness criterion was met.)

Effectiveness - Results met the clinical importance definition for the primary outcome. Alternatively, results showed strong evidence of equivalence (in head-to-head trials) to an intervention that met the clinical importance definition. If the only results pertained to a single RCT, over 300 participants per arm were required.

Other Factors - No other factors identified resulted in the Committee recommending against a strong recommendation.

6.4. The following criteria had to be met for a *Standard Recommendation*:

Quality - GRADE rating better than low or mean less than three for red rated risk of bias criteria for the meta-analysis on which results were based on. (If the mean number of high-risk of bias criteria was three or more, a sensitivity analysis excluding high-risk studies was undertaken and used as the primary meta-analysis if the effectiveness criterion was met.)

Effectiveness - Results did not meet the clinical importance definition for the primary outcome but the mean difference/relative risk was greater than the threshold. If the results pertained to a single RCT, over 100 participants per arm were required.

Other Factors - No other factors resulted in the Committee recommending against a standard recommendation.

6.5. The following criteria had to be met for an *Intervention with Low Effect Recommendation*:

Quality - GRADE rating better than low or mean less than three for red rated risk of bias criteria for the meta-analysis on which results are based on. (If the mean number of high-risk of bias criteria is three or more, a sensitivity analysis excluding high-risk studies was undertaken and used as the primary meta-analysis if the effectiveness criterion was met.)

Effectiveness - Results did not meet the clinical importance definition for the primary outcome and the mean difference/relative risk was less than the threshold. If the results pertained to a single RCT, over 300 participants per arm were required.

Other Factors - No other factors resulted in the Committee recommending against an intervention with low effect recommendation.

6.6. *Intervention with Emerging Evidence* was used if the quality criteria for a strong, standard or low effect recommendation were not met but the results and 95% CIs were better than the control condition. If the results pertained to a single RCT, at least 20 participants per arm were required and there had to be no other factors that resulted in the Committee recommending against an emerging intervention recommendation.

6.7. *Insufficient Evidence to Recommend* was used for all interventions when the primary meta-analysis results did not meet the clinical importance definition for the primary outcome and the 95% CIs overlapped with the point of no difference to the control condition.

6.8. Example of Recommendation Generated:

Scoping Question: “For adults with PTSD, do pharmacological treatments when compared to placebo result in a clinically significant reduction of symptoms, improved functioning/ quality of life, presence of disorder, or adverse effects?”

Recommendation: Drug X is recommended for the treatment of adults with posttraumatic stress disorder.

Strength of recommendation: Standard

7. ISTSS Member Consultation

7.1. ISTSS members were consulted at various points of the process. Initially they were asked to comment on the scoping questions and methodology. They were also asked to consider reference lists of eligible studies to determine if studies were missing. Finally, they were asked to review the initial draft evidence summaries and recommendations, check them for any apparent inaccuracies and to consider the following questions:

- a. Have the agreed “rules” been applied consistently and appropriately with respect to the levels of recommendation made?
- b. Are any studies missing?
- c. Are there any apparent inaccuracies in the position papers?

8. Key Points to Consider in Interpreting the Recommendations

8.1. As a result of resource constraints, the focus was on the prevention and treatment of PTSD rather than other conditions/outcomes. The primary outcome measure for all the scoping questions was a continuous measure of PTSD symptoms.

8.2. The scoping questions selected did not cover all questions of relevance to the traumatic stress field and resulted in key elements of the evidence base not being considered. For example, community and school-based interventions for populations in conflict zones that did not occur within three months of a traumatic event were not included and studies focusing on co-morbidity were not included, unless PTSD was the primary diagnosis.

8.3. Studies that did not meet the strict inclusion criteria were not considered. This included a number of high quality, innovative studies such as dismantling RCTs and RCTs that focused on different ways of delivering the same intervention (e.g., face-to-face or telemedicine delivery).

8.4. The recommendations are primarily based on efficacy as determined by meta-analyses of RCTs. RCT evidence of effect is very important and should strongly influence clinical decision making, but it should not dictate it. It is important to remember the maxim, “*Absence of evidence does not mean absence of effect*” and that “*Good healthcare professionals use both individual clinical expertise and the best available external evidence, and neither alone is enough*”.⁶

8.5. The studies included in the meta-analyses cover heterogeneous settings and populations. These and other factors, for example, variation in therapist competence, differences between grouped interventions, and the number of sessions/dosage delivered, mean that care should be taken in interpreting recommendations and determining their implications for clinical practice. These issues will be covered in detail in the *Effective Treatments for PTSD* book.

8.6. It is possible for pharmacological, psychological and other forms of intervention to cause adverse effects and to be less tolerated by some individuals than others. Although there was no reason found to downgrade the level of recommendation for any intervention, it cannot be assumed that they will be appropriate for all PTSD sufferers.

8.7. Whatever the recommendation, interventions should only be delivered after a thorough assessment of individuals’ needs and, where possible, a discussion between the individual (and/or caregivers) and therapist with clear information about the evidence base, potential benefits and risks to allow informed decision-making and the development of a co-produced intervention plan.

9. References

1. Australian Centre for Posttraumatic Mental Health. *Australian Guidelines for the Treatment of Adults with Acute Stress Disorder and Posttraumatic Stress Disorder*. Melbourne, Australia: Author; 2007.
2. Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from <http://handbook.cochrane.org>.
3. National Institute for Health and Clinical Excellence. Post-traumatic stress disorder. London: Royal College of Psychiatrists and The British Psychological Society; 2005.
4. World Health Organization. Guidelines for the management of conditions specifically related to stress. Geneva: WHO; 2013.
5. GRADE website. <http://www.gradeworkinggroup.org>. Accessed 22 October, 2018.
6. Sackett D, Rosenberg W, Gray J, Haynes R, Richardson W. Evidence based medicine: what it is and what it isn't. *BMJ*, 1996;312(7023), 71-72.

ISTSS Guidelines PTSD Prevention and Treatment Recommendations

The ISTSS Guidelines Recommendations should be used with an understanding of the methodology and the key points to consider in interpretation described above. The recommendations for specific early interventions and treatments are listed under summaries of the relevant scoping questions. The recommendations are grouped according to the five different levels of strength of recommendation possible (*Strong, Standard, Low Effect, Emerging Evidence, and Insufficient Evidence to Recommend*). For an intervention or treatment to be listed there must have been at least one randomised controlled trial that was included in at least one of the meta-analyses undertaken to answer the relevant scoping questions. The recommendations were generated with the information available to the ISTSS Guidelines Committee on 10 October 2018; as more knowledge becomes available it is likely that the level of some of the recommendations will change.

Children and Adolescents

Early Psychosocial Intervention

Summary of Relevant Scoping Questions: *For children and adolescents within the first three months of a traumatic event, do psychosocial interventions when compared to intervention as usual, waiting list, no intervention or other psychosocial interventions, result in a clinically important reduction/prevention of symptoms, improved functioning/ quality of life, presence of disorder, or adverse effects?*

Early Preventative Interventionsⁱⁱⁱ

Intervention with Emerging Evidence - *Self-directed Online*

Psychoeducation for Caregivers and Children* and *Self-directed Online

Psychoeducation for Children within the first three months of a traumatic event have emerging evidence of efficacy for the prevention of clinically relevant post-traumatic stress symptoms in children and adolescents.

Intervention with Emerging Evidence NOT to Recommend - *Individual*

Psychological Debriefing within the first three months of a traumatic event has emerging evidence of increasing the risk of clinically relevant post-traumatic stress symptoms in children and adolescents.

Insufficient Evidence to Recommend - There is insufficient evidence to recommend ***Brief CBT-T*** or ***Self-directed Online Psychoeducation for Caregivers only***.

ⁱⁱⁱ Targeted at unscreened or minimally screened populations

Pharmacological Treatment

Summary of Relevant Scoping Questions: *For children and adolescents with clinically relevant post-traumatic stress symptoms, do pharmacological treatments when compared to placebo, other pharmacological or psychosocial interventions result in a clinically important reduction of symptoms, improved functioning/ quality of life, presence of disorder, or adverse effects?*

Insufficient Evidence to Recommend - There is insufficient evidence to recommend **Sertraline** for the treatment of children and adolescents with clinically relevant post-traumatic stress symptoms.

Non-psychological and Non-pharmacological Treatment

Summary of Relevant Scoping Questions: *For children and adolescents with clinically relevant post-traumatic stress symptoms, do non-psychological and non-pharmacological treatments/interventions when compared to treatment as usual, waiting list, no treatment or other treatments result in a clinically important reduction of symptoms, improved functioning/ quality of life, presence of disorder, or adverse effects?"*

Insufficient Evidence to Recommend - There is insufficient evidence to recommend **Mind Body Skills** or **Trauma-focused Expressive Art Therapy** for the treatment of children and adolescents with clinically relevant post-traumatic stress symptoms.

Adults

Early Psychosocial Intervention

Summary of Relevant Scoping Questions: *For adults within the first three months of a traumatic event, do psychosocial interventions when compared to intervention as usual, waiting list, no intervention or other psychosocial interventions, result in a clinically important reduction/prevention of symptoms, improved functioning/ quality of life, presence of disorder, or adverse effects?”*

Single Session Interventions

Intervention with Emerging Evidence - *Group 512 PM* and *Single-session EMDR* within the first three months of a traumatic event have emerging evidence of efficacy for the prevention and treatment of PTSD symptoms in adults.

Insufficient Evidence to Recommend - There is insufficient evidence to recommend ***Group Debriefing, Group Education, Group Stress Management, Heart Stress Counselling, Individual Debriefing, Individual Psychoeducation/Self-help, Reassurance, Single-session Computerised Visuospatial Task, or Trauma-Focused Counselling*** within the first three months of a traumatic event for the prevention or treatment of PTSD symptoms in adults.

Multiple Session Prevention Interventions^v

Intervention with Emerging Evidence - *Brief Dyadic Therapy*, and *Self-guided Internet Based Intervention* within the first three months of a traumatic event have emerging evidence of efficacy for the prevention of PTSD symptoms in adults.

Insufficient Evidence to Recommend - There is insufficient evidence to recommend ***Brief IPT, Brief Individual Trauma Processing Therapy, Brief Parenting Intervention Following Premature Birth, Collaborative Care, Communication Facilitator in an Intensive Care Setting, Intensive Care Diaries in an Intensive Care Context, Nurse-led Intensive Care Recovery Program, Supported Psychoeducational Intervention, or Telephone-based CBT***, within the first three months of a traumatic event for the prevention of PTSD symptoms in adults.

^v Targeted at unscreened or minimally screened populations

Multiple Session Early Treatment Interventions^{vi}

Standard Recommendation - CBT-T, Cognitive Therapy and **EMDR** within the first three months of a traumatic event are recommended for the treatment of PTSD symptoms in adults.

Intervention with Low Effect - Stepped/Collaborative Care within the first three months of a traumatic event is recommended as a low effect treatment of PTSD symptoms in adults.

Intervention with Emerging Evidence - Internet-based Guided Self-help and **Structured Writing Intervention** within the first three months of a traumatic event have emerging evidence of efficacy for the treatment of PTSD symptoms in adults.

Insufficient Evidence to Recommend - There is insufficient evidence to recommend **Behavioural Activation, Computerized Neurobehavioural Training, Internet Virtual Reality Therapy, Supportive Counselling, or Telephone-based CBT-T** within the first three months of a traumatic event for the treatment of PTSD symptoms in adults.

Early Pharmacological Intervention

Summary of Relevant Scoping Questions: *For adults within the first three months of a traumatic event, do pharmacological interventions when compared to placebo, other pharmacological or psychosocial interventions result in a clinically important reduction/prevention of symptoms, improved functioning/ quality of life, presence of disorder, or adverse effects?*

Intervention with Emerging Evidence - Hydrocortisone within the first three months of a traumatic event has emerging evidence of efficacy for the prevention of PTSD symptoms in adults.

Insufficient Evidence to Recommend - There is insufficient evidence to recommend **Docosahexaenoic Acid, Escitalopram, Gabapentin, Oxytocin** or **Propranolol** within the first three months of a traumatic event for the prevention or treatment of PTSD symptoms in adults.

^{vi} Provided to individuals with emerging traumatic stress symptoms

Psychological Treatment

Summary of Relevant Scoping Questions: For adults with PTSD, do psychological treatments when compared to treatment as usual, waiting list, no treatment or other psychological treatments result in a clinically important reduction of symptoms, improved functioning/ quality of life, presence of disorder, or adverse effects?

Strong Recommendation - Cognitive Processing Therapy, Cognitive Therapy, EMDR, Individual CBT with a Trauma Focus (undifferentiated)^{vii}, and Prolonged Exposure are recommended for the treatment of adults with PTSD.

Standard Recommendation - CBT without a Trauma Focus, Group CBT with a Trauma Focus, Guided Internet-based CBT with a Trauma Focus, Narrative Exposure Therapy, and Present Centred Therapy are recommended for the treatment of adults with PTSD.

Interventions with Emerging Evidence - Couples CBT with a Trauma Focus, Group and Individual CBT with a Trauma Focus, Reconsolidation of Traumatic Memories, Single Session CBT, Written Exposure Therapy, and Virtual Reality Therapy have emerging evidence of efficacy for the treatment of adults with PTSD.

Insufficient Evidence to Recommend - There is insufficient evidence to recommend **Brief Eclectic Psychotherapy for PTSD, Dialogical Exposure Therapy, Emotional Freedom Techniques, Group Interpersonal Therapy, Group Stabilising Treatment, Group Supportive Counselling, Interpersonal Psychotherapy, Observed and Experimental Integration, Psychodynamic Psychotherapy, Psychoeducation, Relaxation Training, REM Desensitisation, or Supportive Counselling** for the treatment of adults with PTSD.

Pharmacological Treatment

Scoping Question: For adults with PTSD, do pharmacological treatments when compared to placebo, other pharmacological or psychosocial interventions result in a clinically important reduction of symptoms, improved functioning/ quality of life, presence of disorder, or adverse effects?

Interventions with Low Effect - Fluoxetine, Paroxetine, Sertraline and Venlafaxine are recommended as low effect treatments for adults with PTSD.

Interventions with Emerging Evidence - Quetiapine has emerging evidence of efficacy for the treatment of adults with PTSD.

Insufficient Evidence to Recommend - There is insufficient evidence to recommend **Amitriptyline, Brofaromine, Divalproex, Ganaxolone, Imipramine, Ketamine, Lamotrigine, Mirtazapine, Neurokinin-1 Antagonist, Olanzapine, Phenelzine, Tiagabine or Topiramate** for the treatment of adults with PTSD.

^{vii} The *Individual CBT with a Trauma Focus (undifferentiated)* recommendation is made from a meta-analysis of all studies meeting the CBT-T definition provided in appendix 2.

Non-psychological and Non-pharmacological Treatment

Summary of Relevant Scoping Questions: For adults with PTSD, do non-psychological and non-pharmacological treatments/interventions when compared to treatment as usual, waiting list, no treatment or other treatments result in a clinically important reduction of symptoms, improved functioning/ quality of life, presence of disorder, or adverse effects?

Intervention with Emerging Evidence - Acupuncture, Neurofeedback, Saikokeishikankyoto, Somatic Experiencing, Transcranial Magnetic Stimulation, and Yoga have emerging evidence of efficacy for the treatment of adults with PTSD.

Insufficient Evidence to Recommend - There is insufficient evidence to recommend **Attentional Bias Modification, Electroacupuncture, Group Mindfulness Based Stress Reduction Group Music Therapy, Hypnotherapy, Mantram Repetition, Mindfulness Based Stress Reduction, Nature Adventure Therapy** or **Physical Exercise** for the treatment of adults with PTSD.

Scoping Questions

1.	For children and adolescents within the first three months of a traumatic event, do psychosocial interventions when compared to intervention as usual, waiting list or no intervention, result in a clinically important reduction/prevention of symptoms, improved functioning/ quality of life, presence of disorder, or adverse effects?"
2.	For children and adolescents within the first three months of a traumatic event, do psychosocial interventions when compared to other psychosocial interventions result in a clinically important reduction/prevention of symptoms, improved functioning/ quality of life, presence of disorder, or adverse effects?"
3.	For adults within the first three months of a traumatic event, do psychosocial interventions when compared to intervention as usual, waiting list or no intervention, result in a clinically important reduction/prevention of symptoms, improved functioning/ quality of life, presence of disorder, or adverse effects?"
4.	For adults within the first three months of a traumatic event, do psychosocial interventions when compared to other psychosocial interventions result in a clinically important reduction/prevention of symptoms, improved functioning/ quality of life, presence of disorder, or adverse effects?"
5.	For children and adolescents within the first three months of a traumatic event, do pharmacological interventions when compared to placebo result in a clinically important reduction/prevention of symptoms, improved functioning/ quality of life, presence of disorder, or adverse effects?"
6.	For children and adolescents within the first three months of a traumatic event, do pharmacological interventions when compared to other pharmacological or psychosocial interventions result in a clinically important reduction/prevention of symptoms, improved functioning/ quality of life, presence of disorder, or adverse effects?"
7.	For adults within the first three months of a traumatic event, do pharmacological interventions when compared to placebo result in a clinically important reduction/prevention of symptoms, improved functioning/ quality of life, presence of disorder, or adverse effects?"
8.	For adults within the first three months of a traumatic event, do pharmacological interventions when compared to other pharmacological or psychosocial interventions result in a clinically important reduction/prevention of symptoms, improved functioning/ quality of life, presence of disorder, or adverse effects?"
9.	For children and adolescents with clinically relevant post-traumatic stress symptoms, do psychological treatments when compared to treatment as usual, waiting list or no treatment, result in a clinically important reduction of symptoms, improved functioning/ quality of life, presence of disorder, or adverse effects?"
10.	For children and adolescents with clinically relevant post-traumatic stress symptoms, do psychological treatments when compared to other psychological treatments, result in a clinically important reduction of symptoms, improved functioning/ quality of life, presence of disorder, or adverse effects?"
11.	For adults with PTSD, do psychological treatments when compared to treatment as usual, waiting list or no treatment, result in a clinically important reduction of symptoms, improved functioning/ quality of life, presence of disorder, or adverse effects?"
12.	For adults with PTSD, do psychological treatments when compared to other psychological treatments, result in a clinically important reduction of symptoms, improved functioning/ quality of life, presence of disorder, or adverse effects?"

13.	For children and adolescents with clinically relevant post-traumatic stress symptoms, do pharmacological treatments when compared to placebo result in a clinically important reduction of symptoms, improved functioning/ quality of life, presence of disorder, or adverse effects?
14.	For children and adolescents with clinically relevant post-traumatic stress symptoms, do pharmacological treatments when compared to other pharmacological or psychosocial interventions result in a clinically important reduction of symptoms, improved functioning/ quality of life, presence of disorder, or adverse effects?”
15.	For adults with PTSD, do pharmacological treatments when compared to placebo result in a clinically important reduction of symptoms, improved functioning/ quality of life, presence of disorder, or adverse effects?”
16.	For adults with PTSD, do pharmacological treatments when compared to other pharmacological or psychosocial interventions result in a clinically important reduction of symptoms, improved functioning/ quality of life, presence of disorder, or adverse effects?”
17.	For children and adolescents with clinically relevant post-traumatic stress symptoms, do non-psychological and non-pharmacological treatments/interventions when compared to treatment as usual, waiting list or no treatment, result in a clinically important reduction of symptoms, improved functioning/ quality of life, presence of disorder, or adverse effects?”
18.	For children and adolescents with clinically relevant post-traumatic stress symptoms, do non-psychological and non-pharmacological treatments/interventions when compared to other treatments, result in a clinically important reduction of symptoms, improved functioning/ quality of life, presence of disorder, or adverse effects?”
19.	For adults with PTSD, do non-psychological and non-pharmacological treatments/interventions when compared to treatment as usual, waiting list or no treatment, result in a clinically important reduction of symptoms, improved functioning/ quality of life, presence of disorder, or adverse effects?”
20.	For adults with PTSD, do non-psychological and non-pharmacological treatments/interventions when compared to other treatments, result in a clinically important reduction of symptoms, improved functioning/ quality of life, presence of disorder, or adverse effects?”

Classification and Grouping of Interventions

Various interventions have been studied for the prevention and treatment of PTSD and it is vital that similar and different interventions are grouped in a meaningful way for appropriate meta-analyses to be undertaken. The ISTSS Guidelines Committee, therefore, agreed to group interventions into categories that would be widely recognised as separate by the traumatic stress community and allow discrimination between different types of intervention.

Individual meta-analyses were undertaken for all pharmacological treatments identified. Psychological and other interventions for the prevention and treatment of PTSD can be divided into those with a trauma focus and those without a trauma focus, and into those delivered to individuals, couples or groups, but greater granularity is required to maximise the accuracy and usefulness of prevention and treatment recommendations. When sufficient studies were available, the principle that interventions should be grouped according to their broad theoretical base (e.g. CBT-T, EMDR, Psychodynamic Therapy) was used. Sub-groups were then developed if there was good evidence that a more homogenous grouping could be created that was based on a specific, well defined intervention that would be widely recognised as a discrete intervention by individuals working in the field (e.g. Prolonged Exposure, Cognitive Processing Therapy).

Early Interventions

The following groupings/subgroupings were agreed for early interventions:

A. Interventions with a Trauma Focus

1. Brief Eye Movement Desensitisation and Reprocessing (EMDR) - EMDR is a standardised, eight-phase, trauma-focused therapy, involving the use of bilateral physical stimulation (eye movements, taps or tones). Targeted traumatic memories are considered in terms of an image, the associated cognition, the associated affect and body sensation. These four components are then focused on as bilateral physical stimulation occurs. It is hypothesised that EMDR stimulates the individual's own information processing in order to help integrate the targeted memory as an adaptive contextualised memory. Processing targets involve past events, present triggers and adaptive future functioning. EMDR at times uses restricted questioning related to cognitive processes paired with bilateral stimulation to unblock processing.

2. Brief Individual Trauma Processing Therapy - This sub-group consisted of a number of brief therapies - lasting two or more sessions - that were theoretically diverse but shared similar core treatment components. These included: psychoeducation and therapist directed reliving of the index trauma to promote elaboration of the trauma memory and help to contextualise or reframe aspects of the experience.

3. Cognitive Behavioural Therapy with a Trauma Focus (CBT-T) – CBT-T includes all therapies that aim to help PTSD sufferers and those displaying early traumatic stress symptoms by addressing and changing their thoughts, beliefs and/or behaviour. Typically, CBT-T involves homework and includes psycho-education, exposure work, cognitive work and more general relaxation/stress management; the relative contribution of these elements varies between different forms of CBT-T.

4. Debriefing – The debriefing interventions are single-session and based on critical incident stress debriefing; individuals are asked to provide detailed facts of what happened, their thoughts, reactions and symptoms before being provided with psychoeducation about symptoms and how to deal with them.

5. Group 512PM – Group 512 PM is based on debriefing but supplemented with cohesion training exercises, for example playing games that need team co-operation.

6. Internet Virtual Reality Therapy – This involves CBT-T delivered through a virtual reality therapy room, rather than face-to-face.

7. Nurse-led Intensive Care Recovery Program – This intervention, based on several models, involved delivery of a nurse led psychological intervention aimed at developing a narrative about the individual's admission and stay on an intensive care unit.

8. Stepped/Collaborative Care (SCC) – SCC involves the provision of flexible and modular interventions based on needs identified through screening and direct assessment. Individuals may be offered a range of different psychological interventions based on identified need. Intervention is normally CBT based, but sometimes based on other psychological approaches (e.g. motivational interviewing) and may include components of case management and prescription of pharmacological intervention.

9. Structured Writing Therapy (SWT) – SWT involves individuals undertaking guided homework based writing assignments about their trauma experience and their thoughts and feelings. SWT does not involve the teaching or practice of cognitive therapy based techniques.

10. Telephone-based CBT-T – CBT-T delivered by telephone, rather than face-to-face.

B. Interventions without a Trauma Focus

1. Behavioural Activation (BT) - BT aims to help the individual to learn to manage negative feelings through activity planning. Core features of the intervention include psychoeducation, behavioural analysis, activity planning, goal identification, trouble shooting, homework and relapse prevention.

2. Brief Dyadic Therapy - This sub-group consisted of brief CBT based therapies delivered dyadically with the aim of improving communication and fostering a shared approach to addressing psychological and practical difficulties.

3. Brief Interpersonal Psychotherapy (IPT) - IPT focuses on individuals' social and interpersonal functioning and helps patients develop skills in social interactions and social support mobilisation. The focus is on current interpersonal encounters rather than past trauma.

4. Brief Parenting Intervention - This intervention is delivered following premature birth, primarily focused on supporting the interaction between the neonate and mother.

5. Cognitive Therapy - This includes a variety of non-trauma focused techniques commonly used in generic CBT, including, but not limited to: stress management, emotional stabilisation, relaxation training, breathing retraining, positive thinking and self-talk, assertiveness training, thought stopping and stress inoculation training. Cognitive therapy does not involve exposure to trauma memories with the aim of undertaking reprocessing.

6. Communication Facilitator in an Intensive Care Setting - This approach involves intervention aimed at trying to understand the needs of patients and their families in an intensive care setting and active liaison between clinicians and patients and family members in order to improve communication and expectations.

7. Computerised Neurobehavioral Training - this intervention aims to teach participants skills in order to improve neurocognitive functioning through an online program. Participants are encouraged to practice new skills through regular practice.

8. Computerised Visuospatial Task - This involves playing a computer game (e.g. Tetris) to disrupt consolidation of trauma memories.

9. Intensive Care Diaries - This approach is based on the provision of post discharge diary feedback to patients admitted to intensive care units to help promote an understanding of events that occurred during their admission.

10. Self-guided Internet-based Intervention – This approach uses internet-based programmes to treat PTSD sufferers using CBT approaches. Use of the intervention is self-directed.

11. Supportive Counselling (SC) – SC involves active, empathic listening to the patient who is usually provided with unconditional positive regard. The therapist helps the patient to explore and clarify issues, may provide advice, reflect and confirm appropriate reactions, and introduce problem-solving techniques. SC has been used as a non-trauma focused control condition in several trials and focused attention to the index trauma event is usually avoided.

12. Supported Psychoeducational Intervention – This intervention involves the provision of psychoeducational information, normally in booklet or leaflet form, with follow-up guidance, typically by telephone, aimed at reinforcing use of the psychoeducational material.

13. Telephone-based CBT – CBT delivered by telephone, rather than face-to-face.

Treatment Interventions

The following groupings/subgroupings were agreed for treatment interventions:

A. Psychological Interventions with a Trauma Focus

1. Cognitive Behavioural Therapy with a Trauma Focus (CBT-T) – CBT-T includes all therapies that aim to help PTSD sufferers by addressing and changing their thoughts, beliefs and/or behaviour. Typically, CBT-T involves homework and includes psycho-education, exposure work, cognitive work and more general relaxation/stress management; the relative contribution of these elements varies between different forms of CBT-T.

For children and adolescents, separate meta-analyses were undertaken for CBT-T delivered to child/adolescent only, child/adolescent and caregiver, and caregiver only. TF-CBT is a specific, phase-based model of CBT-T delivered to child/adolescent and caregiver. The first phase includes affect regulation skills and the second phase processing of the trauma narrative. Gradual exposure is incorporated into all components to enhance the child's/adolescent's and caregiver's mastery of trauma reminders. Caregivers are included, when possible, throughout treatment to support the child's/adolescent's practice and mastery of skills and to enhance positive parenting and parental support.

For adults, the following therapies have been included in meta-analyses as sub-groups of CBT-T for individuals or couples (there were not enough RCTs of different types of group therapy to allow meaningful sub-group analyses):

a. Brief Eclectic Psychotherapy for PTSD (BEPP) – BEPP draws on elements of CBT-T and psychodynamic therapy, including the relationship between the patient and the therapist. It includes exposure to traumatic memories, therapeutic letter writing and consideration of how the individual has been affected by their experience(s). BEPP usually ends with a farewell ritual.

b. Cognitive Therapy for PTSD (CT-PTSD) – CT-PTSD focuses on the identification and modification of negative appraisals and behaviours that lead the PTSD sufferer to overestimate current threat (fear). It also involves modification of beliefs related to other aspects of the experience and how the individual interprets their behaviour during the trauma (e.g. issues concerning guilt and shame).

c. Cognitive Processing Therapy (CPT) – The main focus of CPT is on the evaluation and modification of problematic thoughts that have developed following the traumatic experience(s). For example, using cognitive techniques to challenge typical thoughts of PTSD, that the individual is to blame for their trauma or that the world is now unsafe. An optional component of CPT is the development of a detailed written narrative account of the trauma.

d. Internet-based CBT-T – Internet-based CBT-T uses internet-based programmes to treat PTSD sufferers using CBT-T approaches. A therapist who has less contact with the patient than in traditional face-to-face CBT-T often guides internet-based CBT-T.

e. Narrative Exposure Therapy (NET) – NET allows PTSD sufferers to describe and develop a coherent, chronological, autobiographical narrative of their life that includes their traumatic experiences (a testimony). The therapist facilitates emotional processing through the use of cognitive-behavioural techniques. A modified version (KidNET) has been developed for children.

f. Prolonged Exposure (PE) – The primary focus of PE is to help the PTSD sufferer to confront their traumatic memories using a verbal narrative technique that involves detailed recounting of the traumatic experience that is then recorded and listened to on a repeated basis with the goal of habituation. In addition, real-life repeated exposure to avoided and fear-evoking situations, that are now safe but associated with the trauma, is undertaken, again with the aim of habituation.

g. Reconsolidation of Traumatic Memories (RTM) – RTM involves activation of a traumatic memory and then a procedure that includes imagining a black and white movie of the event, dissociated from its content, and re-winding it when fully-associated over two seconds. This is designed to change the perspective from which the memory is recalled.

h. Virtual Reality Therapy (VRT) – VRT involves the PTSD sufferer being exposed to a computer-generated virtual reality that is representative of the individual's traumatic experience(s). A therapist is present and regulates the amount of exposure according to the patient's response. The aim is to achieve habituation.

i. Written Emotional Disclosure (WED) – WED involves the PTSD sufferer writing about their traumatic experience(s) based on the belief that suppressed thoughts and emotions maintain PTSD symptoms and accessing, expressing and processing them will be beneficial.

2. Dialogical Exposure Therapy (DET) – DET uses CBT techniques (with and without a trauma focus) and a Gestalt based exposure method (chair work) in a dialogical framework. Supported by the therapist, the individual enters into a dialogue with aspect of the traumatic experience.

3. Emotional Freedom Techniques (EFT) – EFT is a trauma-focused intervention that involves recalling a traumatic event and pairing it with a statement of self-acceptance. This is verbally repeated whilst energy meridians used in acupuncture are stimulated using finger taps rather than needles.

4. Eye Movement Desensitisation and Reprocessing (EMDR) – EMDR is a standardised, eight-phase, trauma-focused therapy, involving the use of bilateral physical stimulation (eye movements, taps or tones). Targeted traumatic memories are considered in terms of an image, the associated cognition, the associated affect and body sensation. These four components are then focused on as bilateral physical stimulation occurs. It is hypothesised that EMDR stimulates the individual's own information processing in order to help integrate the targeted memory as an adaptive contextualised memory. Processing targets involve past events, present triggers and adaptive future functioning. EMDR at times uses restricted questioning related to cognitive processes paired with bilateral stimulation to unblock processing.

5. Observed and Experiential Integration (OEI) – OEI involves alternately covering and uncovering the eyes (“switching”) and the eyes tracking different locations in the visual field (“glitch-work”) while experiencing a disturbing thought, feeling or memory. It also includes observation of differences between the two eyes' perceptions.

6. Rapid Eye Movement Desensitization (REM-D) – REM-D initially involves conditioning soothing images with a calming piece of music. Individuals then wear glasses during sleep that detect rapid eye movements (as would occur during dreams) and activate playing of the same piece of music for a period of 30 seconds with the aim of desensitization during nightmares.

B. Psychological and Other Interventions without a Trauma Focus

1. Acupuncture – Acupuncture involves the insertion of fine needles at specific points on the body (acupressure points) to reduce symptoms of PTSD.

2. Attentional Bias Modification (ABM) – ABM is a treatment designed for the management of anxiety disorders based on the finding that patients with anxiety disorders selectively attend to threatening information. It involves computer-based training to keep attention away from threatening information.

3. CBT Without a Trauma Focus – This includes a heterogeneous group of therapies that use a variety of non-trauma focused techniques commonly used in generic CBT, including, but not limited to: stress management, emotional stabilisation, relaxation training, breathing retraining, positive thinking and self-talk, assertiveness training, thought stopping and stress inoculation training.

4. Hypnotherapy – Hypnotherapy uses hypnosis to induce an altered state of consciousness before undertaking therapeutic work.

5. Interpersonal Psychotherapy (IPT) – IPT is an attachment-based treatment that focuses on current interpersonal problems and the resolution of these to improve symptoms.

6. Mantram Repetition – This involves repeating a holy word(s) or phrase(s).

7. Metacognitive therapy (MT) – MT involves a focus on metacognition, the aspect of cognition that controls our thinking and conscious experience. MC aims to change unhelpful thinking patterns that may be maintaining symptoms by addressing the metacognitive beliefs that give rise to them.

8. Mind Body Skills – Mind body skills include various techniques, including mindfulness, meditation, guided imagery, expressive drawing and writing, self-hypnosis and biofeedback.

9. Mindfulness Based Stress Reduction (MBSR) – MBSR aims to help individuals experience traumatic-memories without significant distress by facilitating acceptance of them. MBSR includes meditation practice, mindful awareness practice and its application to real-life situations.

10. Neurofeedback – Neurofeedback involves real-time displays of brain activity that are used to help individuals train (self-regulate) their brain activity.

11. Parent-child Relationship Enhancement – Parent-child relationship enhancement describes therapies that use different techniques, e.g. play, with a primary focus to improve parent-child relationships.

12. Present Centred Therapy (PCT) – PCT is designed to target daily challenges that PTSD sufferers encounter as a result of their symptoms. It includes psychoeducation about the impact of PTSD symptoms, the development of effective strategies to deal with day-to-day challenges and homework to practice newly developed skills.

13. Psychodynamic Therapy – Psychodynamic therapy uses psychoanalytic theories and practices to help individuals understand and resolve their problems by increasing awareness of their inner world and its influences over current and past relationships.

14. Psychoeducation – Psychoeducation provides individuals with information about traumatic stress reactions, PTSD and how to manage them.

15. Saikokeishikankyoto – This is a traditional Japanese herbal medicine.

16. Somatic Experiencing – This involves a focus on perceived body sensations and to learn how to regulate these with the aim of resolving symptoms.

17. Stepped Care CBT-T – This is an intervention developed for children with the introduction of a first step (before therapist-led CBT-T) of parent-led treatment supported by a therapist and web-based materials. If children require more treatment they then receive CBT-T.

18. Supportive/Non-directive Counselling (SC) – SC involves active, empathic listening to the patient who is usually provided with unconditional positive regard. The therapist helps the patient to explore and clarify issues, may provide advice, reflect and confirm appropriate reactions, and introduce problem-solving techniques.

19. Transcranial Magnetic Stimulation (TMS) – TMS uses magnetic fields to stimulate nerve cells in targeted areas of the brain. It is usually given in a repetitive manner and is non-invasive.

20. Yoga – Yoga is an integrative practice of body postures, breathing and meditation. It aims to increase present-focused attention and awareness and to facilitate mindfulness and acceptance.

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