



Acute Stress Disorder, Posttraumatic Stress Disorder and Complex PTSD

Methodology

A flow chart on page five of Chapter 1 provides a pictorial summary of the steps taken to develop the guideline recommendations. The purpose of this chapter is to provide details of the methods used in the systematic review of evidence that underpins the guideline recommendations, and outline the use of the GRADE Evidence to Decision (EtD) framework to develop recommendations. Full details of the research studies included in the systematic review, summaries of the evidence for each research question, and the rationale behind recommendations, are provided in the MAGICApp online platform.

Approach to the systematic review

The evidence review that informed these Guidelines comprised the following:

1. Existing systematic reviews of the evidence conducted by the International Society for Traumatic Stress Studies (ISTSS) for their 2018 PTSD Prevention and Treatment Guidelines (research published up to 10 October 2018)
2. An update of the ISTSS systematic reviews to identify and incorporate new trials published subsequent to the last search (conducted by Phoenix Australia; research published up to 6 June 2019)
3. A systematic review of evidence addressing an additional question on pre-incident preparedness (conducted by Phoenix Australia; research published up to 6 June 2019)
4. Preparation of GRADE evidence profiles, in which a summary of findings from the body of evidence for each clinical question and an assessment of the certainty of evidence for each critical outcome was presented.

The methodology for these evidence reviews is outlined in Figure 1, Chapter 1 and described in more detail below. For completeness, the description of the systematic review methods as reported in the ISTSS guidelines is appended (Appendix 1).

Formulating clinical questions and determining outcomes

The Guideline Development Group (GDG) formed for the current guideline, discussed and agreed to use the clinical questions from the recently completed ISTSS evidence review. In reviewing the questions, the GDG identified pre-incident preparedness as a priority question that had not been included in the ISTSS evidence review and agreed that this should be addressed in the Australian guidelines. The GDG also considered whether to specify questions for a systematic review of evidence on treatments for Complex PTSD (CPTSD) for adults, and children and adolescents. However, the GDG decided against this because there is currently no direct evidence about the treatment of people with CPTSD. Instead a chapter (Chapter

7) is included on considerations for the care of people with CPTSD, current issues and future research. The chapter is informed by research, but not based on a systematic review.

Across all questions, two outcomes (PTSD symptom severity and diagnosis) were prioritised as being critical for making recommendations about prevention and treatment of PTSD in the ISTSS guideline. The Guideline Development Group (GDG) for the current guideline agreed that these outcomes were critical for decision making and of importance to the expected end users of the guideline.

In line with recommendations in the Guideline, evidence was reviewed separately for adults, and for children and adolescents for each of the following:

- pre-incident preparedness
- intervention within the first 3 months of a traumatic event
- treatment for those with clinically relevant post-traumatic stress symptoms

Psychosocial, pharmacological and non-psychosocial and non-pharmacological interventions were considered.

Criteria for selecting studies

For each clinical question, criteria for selecting studies ('eligibility criteria') were specified using the Population, Interventions, Comparators, and Outcomes (PICO) framework. The final list of 22 questions is presented in Table 1 below and a summary of PICO criteria are provided in Table 2.

Table 1: Clinical questions

Pre-incident preparedness

- Q 1: For children and adolescents exposed to trauma do pre-incident preparedness interventions improve outcomes compared to no pre-incident preparedness interventions?
- Q 2: For adults exposed to trauma, do pre-incident preparedness interventions improve outcomes compared to no pre-incident preparedness interventions?

For CHILDREN AND ADOLESCENTS within the first three months of a traumatic event:

- Q 3: do psychosocial interventions, when compared to intervention as usual, waiting list, no intervention, or other treatment, result in a clinically important improvement of outcomes?
- Q 4: do psychosocial interventions, when compared to other psychosocial interventions, result in a clinically important improvement of outcomes?
- Q 5: do pharmacological interventions, when compared to placebo, or other pharmacological or psychosocial interventions, result in a clinically important improvement of outcomes?
- Q 6: do pharmacological interventions, when compared to other pharmacological or psychosocial interventions, result in a clinically important improvement of outcomes?

For CHILDREN AND ADOLESCENTS with PTSD:

- Q 7: do psychological treatments, when compared to treatment as usual, waiting list, or no treatment, result in a clinically important improvement of outcomes?
- Q 8: do psychological treatments, when compared to other psychological treatments, result in a clinically important improvement of outcomes?
- Q 9: do pharmacological treatments, when compared to placebo or other treatments, result in a clinically important improvement of outcomes?
- Q 10: do pharmacological treatments, when compared to other pharmacological or psychosocial interventions, result in a clinically important improvement of outcomes?
- Q 11: do non-psychological and non-pharmacological treatments/interventions, when compared to treatment as usual, waiting list, no treatment, or other treatment, result in a clinically important improvement of outcomes?
- Q 12: do non-psychological and non-pharmacological treatments/interventions, when compared to other treatments, result in a clinically important improvement of outcomes?

For ADULTS within the first three months of a traumatic event:

- Q 13: do psychosocial interventions, when compared to intervention as usual, waiting list, or no intervention, result in a clinically important improvement of outcomes?
- Q 14: do psychosocial interventions, when compared to other psychosocial interventions, result in a clinically important improvement of outcomes?
- Q 15: do pharmacological interventions, when compared to placebo or other pharmacological or psychosocial interventions, result in a clinically important improvement of outcomes?
- Q 16: do pharmacological interventions when compared to placebo or other pharmacological or psychosocial interventions result in a clinically important improvement of outcomes?

For ADULTS with PTSD:

- Q 17: do psychological treatments, when compared to treatment as usual, waiting list, or no treatment, result in a clinically important improvement of outcomes?
- Q 18: do psychological treatments, when compared to other psychological treatments, result in a clinically important improvement of outcomes?
- Q 19: do pharmacological treatments, when compared to placebo, result in a clinically important improvement of outcomes?
- Q 20: do pharmacological treatments, when compared to other pharmacological or psychosocial interventions, result in a clinically important improvement of outcomes?
- Q 21: do non-psychological and non-pharmacological treatments/interventions, when compared to treatment as usual, waiting list or no treatment, result in a clinically important improvement of outcomes?
- Q 22: do non-psychological and non-pharmacological treatments/interventions, when compared to other treatments, result in a clinically important improvement of outcomes?

Studies were screened on title and abstract by two independent reviewers against the eligibility criteria, which were consistent with the inclusion criteria used in the ISTSS Guidelines, to determine eligibility for a full-text assessment. Studies meeting the eligibility criteria or for which eligibility criteria remained unclear were included in full text screening. Screening at the title and abstract level was performed independently by both reviewers. Any disagreements were resolved by discussion. Full-text assessment was also performed independently by both reviewers. Disagreement were resolved by discussion.

Table 2: PICO eligibility criteria

	Pre-incident preparedness	Early intervention	Treatment
Types of studies	Any randomised controlled trial (including cluster and cross-over trials)	Any randomised controlled trial (including cluster and cross-over trials) <ul style="list-style-type: none"> - not solely a dismantling study - no minimum sample size - unpublished studies were eligible Exclusions: <ul style="list-style-type: none"> - editorials, letters to the editor, reviews, dissertations, and protocol papers 	
Types of participants	Adults or children/adolescents 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.		Adults: <ul style="list-style-type: none"> - 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 Children and adolescents: <ul style="list-style-type: none"> - 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 PTSD diagnosis <ul style="list-style-type: none"> - Duration of PTSD symptoms required to be three months or more - No restrictions on the basis of comorbidity, but PTSD required to be the primary diagnosis. - No restriction on the basis of severity of PTSD symptoms or the type of traumatic event.
Types of interventions	Pre-incident preparedness interventions delivered before trauma exposure, aimed at preventing symptoms of PTSD	Any intervention aimed at preventing, treating or reducing symptoms of PTSD which <ul style="list-style-type: none"> - was not provided pre-trauma, and - began no later than 3 months after the traumatic event. Eligible interventions included: <ul style="list-style-type: none"> - psychosocial prevention (e.g., psychological 	Any psychological interventions aimed at reducing symptoms of PTSD <ul style="list-style-type: none"> - Delivered by any mode, including to individuals, groups or couples Eligible interventions included <ul style="list-style-type: none"> - psychosocial (e.g. cognitive processing therapy) - pharmacological treatments - non-psychosocial and non-pharmacological treatments (e.g., mindfulness-based stress reduction)

		debriefing, psychoeducation) - psychosocial treatment (e.g. brief trauma-focussed CBT) - pharmacological treatment	
Types of comparators	Other pre-incident preparedness interventions or no pre-incident preparedness intervention	For psychosocial interventions: - waitlist, treatment as usual, symptom monitoring, repeated assessment, other minimal attention control group - alternative psychological treatment. For pharmacological interventions: - placebo - other pharmacological intervention - psychosocial intervention.	
Types of outcomes	Critical: ASD or PTSD symptom change Important: ASD or PTSD diagnosis Excluded: does not report data on PTSD symptoms or PTSD diagnosis		

Across all questions, the following additional eligibility criteria were used:

- Date of publication - All studies included in these Guidelines were published within the dates of the search, that is, January 2008 to 6 June 2019.
- Language - All included studies were published in English.

Search methods

Literature sources

For the ISTSS systematic reviews, systematic reviews developed through the Cochrane Collaboration, the UK National Institute for Health and Care Excellence (NICE) and the World Health Organisation (WHO) were identified. RCTs from these reviews were used as the initial set of studies and re-evaluated by the ISTSS review team. Searches were conducted by the ISTSS team to update the identified systematic reviews, in addition to asking experts in the field to identify missing studies. The ISTSS searches were then updated by Phoenix Australia for the period of October 2018 to 6 June 2019. In addition, searching was conducted for the two new scoping questions between the period of 2008 and 6 June 2019. These searches were conducted in the CENTRAL (Cochrane), Medline, PSYCInfo, and PILOTS databases.

Search strategy

The ISTSS systematic reviews, the updates to these reviews, and the searches for the two new questions involved the same search strategy. The search terms 'PTSD', 'posttrauma*', 'post-trauma*', 'post trauma*', 'combat disorder*', 'stress disorder*' were used to be as broad as possible and ensure that all relevant RCTs were captured.

Data extraction and analysis

Evidence tables were used to guide the extraction of data from the individual studies and summarise results. Two researchers independently extracted data from included studies.

Studies that fulfilled the inclusion criteria were further scrutinised to determine if data were available to use in the meta-analyses. If sufficient data were not available, requests were made to authors for data that could be used. All available data addressing specific scoping questions were meta-analyzed using Revman (Version 5.3) software (The Nordic Cochrane Centre, 2014)¹ using a fixed-effects model where statistical heterogeneity, as indicated by I^2 , was less than 30%, where heterogeneity was > 30% or higher, a random-effects model was used.

Appraisal of individual studies: risk of bias assessment

Individual studies were summarised and appraised independently by two people using version one of the Cochrane Collaboration's risk of bias tool² Inter-rater reliability was calculated and disagreements were resolved by discussion. Assessment involved judging whether there was a low, uncertain or high risk of bias for each of the following domains: 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.

Assessment of the certainty of the body of evidence

The Grading of Recommendations, Assessment, Development and Evaluations (GRADE) system was used to assess the certainty of the evidence base.³ The GRADE rating provides an indication of confidence in the estimates of the effect of an intervention.⁴ Evidence from RCTs starts at high certainty and may be downgraded for serious or very serious concerns relating to each of the following domains.

1. **Risk of bias:** based on the overall risk of bias (methodological limitations) of the trials contributing to each result. For the purpose of grading the evidence, an overall judgement of risk of bias was first made across studies for each risk bias domain, and then across domains. This judgment considered the extent to which studies at high or unclear risk of bias influenced the meta-analysis (i.e. weight).
2. **Indirectness:** the extent to which the PICO characteristics of the body of evidence adequately address the clinical questions (PICO) for the guideline.
3. **Imprecision:** whether the confidence interval includes both appreciable benefit and harm (or vice versa) and whether the optimal information size was met (based on a rule of thumb of >400 participants for continuous outcomes; > 300 events for binary). Judgments of appreciable benefit (or harm) were based on the thresholds below.
4. **Inconsistency:** the extent to which there is unexplained inconsistency in results across studies. Judgements were based on visual inspection of data (overlap in confidence intervals, the direction and magnitude of effect) and statistical measures and tests of heterogeneity.
5. **Publication bias:** The likelihood of small study effect or other evidence of publication bias.

A body of evidence is rated as being of high quality (i.e., further research is very unlikely to change our confidence in the estimate of effect), moderate quality (i.e., further research is likely to have an important impact on our confidence in the estimate effect and may change the estimate), low quality (i.e., 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) or very low quality (i.e., we are very uncertain about the estimate).

The following thresholds were used for judging the clinical importance of effects on symptom severity (reported as standardised mean difference or risk ratio) and for judging imprecision:

- for interventions delivered 3 or more months post trauma, >0.8 for waitlist comparisons, >0.5 for treatment attention control comparisons, >0.4 for placebo control comparisons and >0.2 for active treatment control comparisons for continuous outcomes and <0.65 for binary outcomes
- for interventions delivered within 3 months, >0.5 for treatment comparisons and >0.2 for prevention comparisons for continuous outcomes and <0.8 for binary outcomes
- for the pre-incident preparedness, 0.2 for any control comparison

Evidence profiles reporting relative and absolute effects, the GRADE of evidence for each outcome, and the rationale for GRADE judgements were prepared in MAGICApp.

Development of recommendations

The GRADE Evidence to Decision (EtD) framework was used by the Guideline Development Group (GDG) to develop recommendations. The framework, as implemented in MAGICApp, prompts guideline developers to consider the following criteria for each intervention option.

- **The balance of benefits and harms.** The GDG considered whether the balance between desirable and undesirable effects favoured the intervention, and whether the effects were clinically important.
- **The certainty of evidence.** The GDG judged the overall certainty of evidence across the critical outcomes. In general, strong recommendations were underpinned by high or moderate certainty evidence.
- **Patients' values and preferences.** The GDG considered whether all patients would feel that the desirable effects of the intervention outweighed the harms. Input from the consumer representatives on the GDG informed discussion during the GDG meeting and the summary of values and preferences presented in MAGICApp.
- **Resources, equity, acceptability and feasibility.** The GDG considered each of these factors in relation to the implementation of each intervention. Funding and access to services were key considerations. Implications for special populations are considered in Chapter 9.

Recommendations for or against each intervention were made by the GDG after considering each of these criteria. The strength of each recommendation (strong or conditional) was determined and worded in accordance with GRADE guidelines (see MAGICApp for interpretation of strong and conditional recommendations). Decisions were made through consensus and key considerations are presented in MAGICApp.

Limitations of the review

This systematic review of the treatments for ASD and PTSD is limited by the following factors. The review:

- does not cover questions pertaining to an assessment of some additional multi-component treatments versus other multi-component treatments or versus placebo/waitlist for the populations under review
- does not assess levels of evidence lower than randomised controlled trials
- does not provide a comprehensive review of potential safety issues (i.e., studies too small to detect many adverse events, particularly rare adverse events) – this is of particular relevance to the section on pharmacological treatments

These Guidelines were based in part on the ISTSS Guidelines, which have their own limitations. In updating these Guidelines, some of these limitations must be acknowledged, despite the use of a near-identical methodology.

- Some studies that potentially met the inclusion criteria may have been missed.
- Effect sizes were calculated on the difference in post-treatment scores between the groups, the assumption being that randomisation negated any potential baseline differences between the groups. This assumption may be valid for large trials but is not necessarily correct for small trials.

Appendix 1: Methodology used for the ISTSS Guidelines

The following information has been extracted from the ISTSS Guidelines methodology and development process paper.⁵

Methodology overview

The ISTSS Guidelines recommendations were developed through a rigorous process that was overseen by the ISTSS Guidelines Committee. Scoping questions were developed and systematic reviews were undertaken to identify relevant RCTs. Meta-analyses were then conducted with usable data from included studies, and the results were used to generate recommendations for prevention and treatment interventions.

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 standardised manner. A process adapted from approaches taken by the Australian Centre for Posttraumatic Mental Health⁶ (now Phoenix Australia–Centre for Posttraumatic Mental Health), the Cochrane Collaboration,² the United Kingdom’s National Institute for Health and Care Excellence (NICE),⁷ and the World Health Organization (WHO)⁸ was used.

General scoping questions were agreed on by the Committee 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 improvement of outcomes?”) for the prevention and treatment of PTSD in children, adolescents, and adults. Prior to finalisation, the committee sought and integrated feedback from the ISTSS membership around these scoping questions.

High-quality systematic reviews developed through the Cochrane Collaboration, NICE, and the WHO were identified that addressed the scoping questions except those pertaining to non-psychological and non-pharmacological interventions. 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 (Bisson, Andrew, Roberts, Cooper, & Lewis, 2013;⁹ Hoskins et al., 2015;¹⁰ Lewis, Roberts, Bethell, & Bisson, 2015;¹¹ NICE, 2018b;¹² Roberts, Kitchiner, Kenardy, & Bisson, 2009;¹³ Rose, Bisson, Churchill, Wessely, 2005;¹⁴ Sijbrandij, Kleiboer, Bisson, Barbui, & Cuijpers, 2015¹⁵) 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. New systematic reviews were undertaken for the non-psychological and non-pharmacological scoping questions. The Cochrane Collaboration Mental Health Disorders Group completed additional searches, using their comprehensive search strategies to identify RCTs of any intervention designed to prevent or treat PTSD.

The evidence for each of the scoping questions was summarised and its certainty assessed by two researchers 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).

Systematic reviews and meta-analyses

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.

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 prior to the additional searches being undertaken. 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).

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 three 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.

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.

ⁱⁱ GRADE Working Group Grades of Evidence⁵

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

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

Low certainty: 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 certainty: We are very uncertain about the estimate.

- 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.

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 or 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.

A total of 361 RCTs fulfilled the criteria for inclusion in the meta-analyses undertaken.

Two researchers independently extracted data from included studies. 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 final meta-analyses and reference lists of all eligible studies can be found on the ISTSS website.

References

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Appendix 2: PICOs and selection criteria

Pre-incident preparedness

PICO 1

For children and adolescents exposed to trauma, do pre-incident preparedness interventions improve outcomes compared to no pre-incident preparedness interventions?

Selection criteria

Population	Children and adolescents exposed to trauma, including the subgroup with ASD
Intervention	Pre-incident preparedness intervention
Comparator	No pre-incident preparedness intervention Other pre-incident preparedness intervention
Primary outcome	Symptoms of ASD or PTSD
Secondary outcome	PTSD diagnosis

PICO 2

For adults exposed to trauma, do pre-incident preparedness interventions improve outcomes compared to no pre-incident preparedness interventions?

Selection criteria

Population	Adults exposed to trauma, including the subgroup with ASD
Intervention	Pre-incident preparedness intervention
Comparator	No pre-incident preparedness intervention Other pre-incident preparedness intervention
Primary outcome	Symptoms of ASD or PTSD
Secondary outcome	PTSD diagnosis

For CHILDREN AND ADOLESCENTS

Early psychosocial interventions

PICO 3

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 treatment, result in a clinically important improvement of outcomes?

Selection criteria

Population	Children and adolescents within the first three months post traumatic event
Intervention	Psychosocial interventions
Comparator	Intervention as usual Waiting list or no intervention Other treatment
Primary outcome	ASD or PTSD symptom change
Secondary outcome	ASD or PTSD diagnosis

PICO 4

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 improvement of outcomes?

Selection criteria

Population	Children and adolescents within the first three months post traumatic event
Intervention	Psychosocial interventions
Comparator	Other psychosocial interventions
Primary outcome	ASD or PTSD symptom change
Secondary outcome	ASD or PTSD diagnosis

Early pharmacological interventions

PICO 5

For children and adolescents within the first three months of a traumatic event, do pharmacological interventions, when compared to placebo, or other pharmacological or psychosocial interventions, result in a clinically important improvement of outcomes?

Selection criteria

Population	Children and adolescents within the first three months post traumatic event
Intervention	Pharmacological interventions
Comparator	Placebo Other pharmacological or psychosocial interventions
Primary outcome	ASD or PTSD symptom change
Secondary outcome	ASD or PTSD diagnosis

PICO 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 improvement of outcomes?

Selection criteria

Population	Children and adolescents within the first three months post traumatic event
Intervention	Pharmacological intervention
Comparator	Other pharmacological or psychosocial interventions
Primary outcome	ASD or PTSD symptom change

Psychological treatment for PTSD

PICO 7

For children and adolescents with clinically relevant posttraumatic stress symptoms, do psychological treatments, when compared to treatment as usual, waiting list, or no treatment, result in a clinically important improvement of outcomes?

Selection criteria

Population	Children and adolescents with clinically relevant posttraumatic stress symptoms
Intervention	Psychological treatment
Comparator	Treatment as usual Wait list or no treatment
Primary outcome	PTSD symptom change

PICO 8

For children and adolescents with clinically relevant posttraumatic stress symptoms, do psychological treatments, when compared to other psychological treatments, result in a clinically important improvement of outcomes?

Selection criteria

Population	Children and adolescents with clinically relevant posttraumatic stress symptoms
Intervention	Psychological treatments
Comparator	Other psychological treatments
Primary outcome	PTSD symptom change

Pharmacological treatments for PTSD

PICO 9

For children and adolescents with clinically relevant posttraumatic stress symptoms, do pharmacological treatments, when compared to placebo or other treatments, result in a clinically important improvement of outcomes?

Selection criteria

Population	Children and adolescents with clinically relevant posttraumatic stress symptoms
Intervention	Pharmacological treatment
Comparator	Placebo Other treatment
Primary outcome	PTSD symptom change

PICO 10

For children and adolescents with clinically relevant posttraumatic stress symptoms, do pharmacological treatments, when compared to other pharmacological or psychosocial interventions, result in a clinically important improvement of outcomes?

Selection criteria

Population	Children and adolescents with clinically relevant posttraumatic stress symptoms
Intervention	Pharmacological treatment
Comparator	Other pharmacological or psychosocial interventions
Primary outcome	PTSD symptom change

Non-psychological and non-pharmacological treatments/interventions:

PICO 11

For children and adolescents with clinically relevant posttraumatic stress symptoms, do non-psychological and non-pharmacological treatments/interventions, when compared to treatment as usual, waiting list, no treatment, or other treatment, result in a clinically important improvement of outcomes?

Selection criteria

Population	Children and adolescents with clinically relevant posttraumatic stress symptoms
Intervention	Non-psychological and non-pharmacological treatments
Comparator	Treatment as usual Waiting list or no treatment Other treatment
Primary outcome	PTSD symptom change

PICO 12

For children and adolescents with clinically relevant posttraumatic stress symptoms, do non-psychological and non-pharmacological treatments/interventions, when compared to other treatments, result in a clinically important improvement of outcomes?

Selection criteria

Population	Children and adolescents with clinically relevant posttraumatic stress symptoms
Intervention	Non-psychological and non-pharmacological treatments
Comparator	Other treatments
Primary outcome	PTSD symptom change

For ADULTS

Early psychosocial interventions

PICO 13

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 improvement of outcomes?

Selection criteria

Population	Adults within the first three months post traumatic event
Intervention	Psychosocial interventions
Comparator	Intervention as usual Waiting list or no intervention
Primary outcome	ASD or PTSD symptom change
Secondary outcome	ASD or PTSD diagnosis

PICO 14

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 improvement of outcomes?

Selection criteria

Population	Adults within the first three months post traumatic event
Intervention	Psychosocial interventions
Comparator	Other psychosocial interventions
Primary outcome	ASD or PTSD symptom change
Secondary outcome	ASD or PTSD diagnosis

Early pharmacological interventions

PICO 15

For adults within the first three months of a traumatic event, do pharmacological interventions, when compared to placebo result in a clinically important improvement of outcomes?

Selection criteria

Population	Adults within the first three months post traumatic event
Intervention	Pharmacological intervention
Comparator	Placebo
Primary outcome	ASD or PTSD symptom change

PICO 16

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 improvement of outcomes?

Selection criteria

Population	Adults within the first three months post traumatic event
Intervention	Pharmacological intervention
Comparator	Other pharmacological or psychosocial interventions
Primary outcome	ASD or PTSD symptom change

Psychological treatment for PTSD

PICO 17

For adults with PTSD, do psychological treatments, when compared to treatment as usual, waiting list, or no treatment, result in a clinically important improvement of outcomes?

Selection criteria

Population	Adults with PTSD
Intervention	Psychological treatment
Comparator	Treatment as usual Wait list or no treatment
Primary outcome	PTSD symptom change

PICO 18

For adults with PTSD, do psychological treatments, when compared to other psychological treatments, result in a clinically important improvement of outcomes?

Selection criteria

Population	Adults with PTSD
Intervention	Psychological treatments
Comparator	Other psychological treatments
Primary outcome	PTSD symptom change

Pharmacological treatments

PICO 19

For adults with PTSD, do pharmacological treatments, when compared to placebo, result in a clinically important improvement of outcomes?

Selection criteria

Population	Adults with PTSD
Intervention	Pharmacological treatment
Comparator	Placebo
Primary outcome	PTSD symptom change

PICO 20

For adults with PTSD, do pharmacological treatments, when compared to other pharmacological or psychosocial interventions, result in a clinically important improvement of outcomes?

Selection criteria

Population	Adults with PTSD
Intervention	Pharmacological treatment
Comparator	Other pharmacological or psychosocial interventions
Primary outcome	PTSD symptom change

Non-psychological and non-pharmacological treatments/interventions:

PICO 21

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 improvement of outcomes?

Selection criteria

Population	Adults with PTSD
Intervention	Non-psychological and non-pharmacological treatments
Comparator	Treatment as usual Waiting list or no treatment
Primary outcome	PTSD symptom change

PICO 22

For adults with PTSD, do non-psychological and non-pharmacological treatments/interventions, when compared to other treatments, result in a clinically important improvement of outcomes?

Selection criteria

Population	Adults with PTSD
Intervention	Non-psychological and non-pharmacological treatments
Comparator	Other treatments
Primary outcome	PTSD symptom change