Comparative efficacy for different age groups of psychological or psychosocial treatments on post-traumatic stress disorder: protocol for systematic review, meta-analysis and meta-regression analysis

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ABSTRACT

Introduction It remains unknown whether psychological or psychosocial treatments for post-traumatic stress disorder (PTSD) have comparable effects across the life span. This study aims at comparing the effects of psychological/psychosocial treatments for PTSD between different age groups of youth, early-middle adults and late adults.

Methods and analysis A systematic search will be conducted among thirteen electronic databases, including Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, PsycINFO, EMBASE, ERIC, PubMed, SCOPUS, Web of Science, Published International Literature on Traumatic Stress, China National Knowledge Infrastructure Database, the Wanfang database, the Chinese Scientific Journal Database (VIP Database) and ProQuest Dissertations and Theses, from inception to 15 May 2022. Electronic searches will be supplemented by a comprehensive grey literature search in Conference proceedings and trial registries. Randomised controlled trials (RCTs) comparing psychological or psychosocial treatments for PTSD with control conditions in all age groups will be included. The primary outcome is the between-treatments efficacy for PTSD that refers to the outcomes of the RCTs included in the meta-analysis. Effect sizes will be calculated for all comparisons and pooled with a fixed effects model or a random effects model. Differences in the efficacy of psychological/psychosocial therapies for PTSD across the age groups will be examined by stratified analyses and meta-regression analyses.

Ethics and dissemination Data used in this study will be anonymised. These data will not be used for other purposes than research. Authors who supply the data will be acknowledged. The authors declare that no conflicts of interest exist. The findings of this study will be disseminated through briefing reports, publications and presentations. Trial registration number CRD42022334305.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This is the first study to compare the efficacy of psychological or psychosocial treatments for post-traumatic stress disorder (PTSD) across the life span.
⇒ This is the largest systematic review and meta-analysis of psychological or psychosocial treatments for PTSD ever conducted.
⇒ Only randomised controlled trials will be included to allow more realistic and rigorous results.
⇒ Subgroup and sensitivity analyses will be conducted to identify potential factors that influence the efficacy of psychological or psychosocial treatments between different age groups.
⇒ This study will be limited by not examining the differences in long-term efficacy of psychological or psychosocial treatments across the life span because of the small number of studies.

INTRODUCTION

Trauma is a global issue.1 The World Mental Health Survey, conducted by the WHO in 24 countries, showed that approximately 70% of the global population experienced at least one lifetime traumatic event, such as witnessing death or serious injury, the death of loved one, being mugged, accident and life-threatening illness.2 Although most people who experience trauma will recover over time, a proportion of them will develop post-traumatic stress disorder (PTSD). The cross-national lifetime prevalence of PTSD was 5.6% among the trauma exposed, with prevalence rates ranging from 0.5% to 14.5%.3 The lifetime prevalence of PTSD in the global population was 3.9%, high-income countries (5.0%) had twice the proportion of PTSD cases as upper-middle-income (2.3%)
and lower-middle-income countries (2.1%). PTSD is estimated to result in 3.6 days of lost productivity per month. A meta-analysis of war survivors showed that PTSD was associated with approximately three million disability-adjusted life-years. If left untreated, PTSD will significantly increase the risk of chronic physical disease, co-occurring mental illnesses and mortality, and it will accelerate ageing. More seriously, the adverse effects of PTSD could be transmitted intergenerationally. This presents a serious burden of public health on society.

A variety of interventions for PTSD have been developed, including pharmacological treatments, psychological/psychosocial treatments and non-pharmacological non-psychological treatments. Among these treatments, trauma-focused psychological therapies are recommended as first-line treatments for PTSD by several clinical guidelines. Meta-analyses comparing the efficacy of pharmacological and psychological interventions for PTSD showed that psychological therapies were more effective than pharmacological treatments for adults and children. A conceptual review also showed that psychological/psychosocial treatments could significantly reduce PTSD symptoms and other trauma-related symptoms, such as anxiety, depression and social functioning, among children and adolescents, adults and older adults. Meta-analyses showed that the psychological interventions can produce medium to large effect sizes for PTSD.

Although the effectiveness of psychological/psychosocial therapies on the treatment of PTSD have been examined, it remains unknown whether the efficacy of psychological/psychosocial therapies is the same across age groups. Up to the present time, most studies have been conducted to address the efficacy of treatments among children and adolescents, or older adults separately. The efficacy of the treatments among different age groups are not compared. A few studies have begun to address this issue. For example, the results of a meta-analysis study showed that trauma-focused cognitive-behavioural therapy (CBT) was regarded as ‘level 1’ intervention for school-age children and adolescents (ages 6–18), but the rating of its efficacy for preschoolers (ages 3–6) was ‘level 2’. The finding of this study suggests that there may be differences in efficacy of a psychotherapy across the age groups. However, to our knowledge, no meta-analysis study focuses on the differences of efficacy of psychological/psychosocial interventions on PTSD among patients across the life span.

It may be necessary to rank the efficacy of psychological/psychosocial therapies for youth, early-middle adults or late adults who suffer from PTSD. First, if differences in the efficacy of psychological/psychosocial therapies across the age groups can be found, this may suggest that different procedures or treatment processes may be needed to reduce PTSD symptoms for patients at different ages. This may also suggest that different underlying mechanisms are involved in the treatment of PTSD patients at different ages. Second, identifying differences in the efficacy of psychological/psychosocial therapies across the age groups may help clinicians to understand better the therapeutic potential of these therapies. This may also help the clinicians to select treatments that are best for patients at an age group.

This study is designed to conduct a systematic review and meta-analysis of psychological/psychosocial therapies for PTSD to examine whether the efficacy of these treatments varies due to patients’ ages. A database of these therapies for treating patients who suffer from PTSD regardless of their age will be established. As a result, the efficacy of these treatments across the life span can be examined objectively and accurately.

OBJECTIVES AND HYPOTHESES

The first objective of this study is to assess the efficacy of psychological/psychosocial therapies for PTSD. Based on the findings of previous studies, this study hypothesises that psychological/psychosocial treatments show medium to large effect sizes for PTSD.

Second, this study aims at assessing whether there are significant differences in the efficacy of psychological/psychosocial therapies for PTSD across different age groups of youth, early-middle adults and late adults. Based on findings of previous studies, the hypothesis in this study is that there are significant differences in the efficacy of psychological/psychosocial therapies for PTSD across different age groups.

Third, this study aims at examining the relationship between the mean age of study population and effect sizes. It hypothesises that the mean age is a significant predictor of the effect sizes.

METHODS

The methodology for this study was developed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension statement. This study was registered in the PROSPERO (registration number: CRD4202234305). It will be conducted from 21 May 2022 to 21 May 2024.

Patients and public involvement

No patient involved.

Types of studies

Only RCTs (including cluster RCTs) will be included. Studies that do not include quantitative PTSD measurements in the pretest and post-test will be excluded.

Types of participants

Inclusion criteria

Individuals of any age who meet the criteria for PTSD will be included in this study. Both male participants and female participants will be included. Clinical guidelines suggest that treatment decisions should be based on...
symptom severity and functional impairment rather than the presence of clinical PTSD diagnosis. Therefore, a broad range of criteria will be used to determine the inclusion of participants. Both of the following types of participants will be included: (1) Full PTSD, as diagnosed according to validated screening/severity measures or clinical diagnosis based on international classifications (Diagnostic and Statistical Manual of Mental Disorders or the International Classification of Diseases); (2) Subthreshold/partial PTSD, defined as patients who have experienced psychological trauma and report some subsequent PTSD symptoms, but not meeting all diagnostic criteria for PTSD.

This study will include participants who are diagnosed with comorbid psychiatric disorders, but their primary diagnosis should be PTSD. The comorbid psychiatric disorders include: comorbid depression, anxiety disorders, attention deficit and hyperactivity disorder, oppositional defiant disorder, comorbid personality disorders, substance abuse, etc. Sensitivity analyses will be conducted to assess the impact of comorbid psychiatry disorders on the pooled effect size by removing one study at a time that included participants with comorbid psychiatric disorders.

**Exclusion criteria**
Participants who are diagnosed with acute stress disorder will be excluded.

**Types of interventions**

**Inclusion criteria**
All psychological and psychosocial therapies for PTSD will be included. Psychological and psychosocial therapies will be considered as one intervention in this study. The psychological and psychosocial therapies in this study are defined primarily based on National Institute for Health and Care Excellence guidelines.

Psychological treatments included:

- Trauma-focused CBTs, including cognitive therapy, narrative exposure therapy, exposure therapy/prolonged exposure, virtual reality exposure therapy, imagery rehearsal therapy, mindfulness-based cognitive therapy and narrative exposure therapy.
- Non-trauma-focused CBT, including stress inoculation training.
- Psychologically focused debriefing (including single session debriefing).
- Hypnotherapy.
- Psychodynamic therapies, including traumatic incident reduction.
- Counselling, including non-directive/supportive/person-centred counselling.
- Human givens therapy.
- Combined somatic and cognitive therapies, including thought field therapy and emotional freedom technique.
- Parent training/family interventions, including behavioural family therapy (such as Child and Family Traumatic Stress Intervention).
- Couple interventions, including cognitive–behavioural conjoint therapy.
- Play therapy.
- Psychosocial treatments included:

Comparators

The comparators included the waitlist, non-treatment, treatment as usual, placebo and other active interventions.

**Types of outcome measures**

**Primary outcomes**
Between-treatments efficacy at post-treatment for PTSD, as measured with end-point scores of PTSD.
symptom severity rating scales that are completed by a child, parent, clinician or teacher. First, if more than one measurement was reported in one study, the results of the measurement with better psychometric properties will be selected as the primary outcome. Second, if PTSD measurement was reported by more than one rater in a study, self-rated measures were preferred to calculate the effect size because these measures tended to result in more conservative effect size. Then parent-rated, clinician-rated or teacher-rated measures would be considered. In addition, the rating scales will be individually identified, and categorised in clinician-administrated, self-report or assisted administration (including parent-rated and teacher-rated measures). Subgroup analysis will be used to examine the impact of raters’ categories on the primary outcome.

Secondary outcomes
- Between-treatments efficacy at follow-up, as measured with the scores of PTSD scales at the point of follow-up (up to 6 months).

Data from participants who received follow-up treatment (eg, continued psychological/psychosocial treatment or intensive treatment) after the intervention will be excluded from subsequent analyses. If studies report follow-up outcomes at multiple time points, outcomes at 3 and 6 months of follow-up will be primarily extracted to compare the effect sizes of therapies within the same follow-up period, respectively.
- Between-treatments efficacy for anxiety symptoms, as measured with the post-treatment scores on anxiety symptom severity rating scales.
- Between-treatments efficacy for depression symptoms, as measured with the post-treatment scores on depression symptom severity rating scales.
- Between-treatments efficacy for behavioural problems for youth, as measured with post-treatment scores.
- Between-treatments efficacy for psychosocial functioning, as measured with post-treatment scores.

Search strategy
In this study, the following online databases will be searched: Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, PsycINFO, EMBASE, ERIC, PubMed, SCOPUS, Web of Science, Published International Literature on Traumatic Stress. Chinese databases will include China National Knowledge Infrastructure Database (CNKI), the Wanfang database and the Chinese Scientific Journal Database (VIP Database). No restrictions are placed on publication type. Conference proceedings will be searched in the Conference Proceedings Citation Index using Web of Science. Dissertations and theses published in ProQuest and China National Knowledge Infrastructure Database (CNKI) will also be searched. International trials registers, such as WHO International Clinical Trials Registry Platform and ClinicalTrials.gov will be searched for ongoing trials. All studies cited in relevant review articles will be included. The review will examine all studies published until 15 May 2022. The database will be updated before publication. Search will be restricted to articles in English or Chinese.

Two researchers who do research on PTSD and two university librarians who are experts on systematic review will form a search team. The search terms are discussed by the search team. Three search terms are identified: PTSD, treatment and RCT. Then, the search team are divided into two groups, and each group includes one researcher and one librarian. For each online database, the two groups design independently the search strategy and conduct a preliminary search. The search results are recorded. Subsequently, the search team compares the differences between these two groups’ search results (eg, whether the number of these two groups’ search records are equal and whether the search results are relevant to the review). If there are any inconsistency, the research team discuss the differences between search strategies to reach consensus. The full search strategy for the database of PubMed is presented in online supplemental appendix 1.

Study selection and data extraction
Selection of trials
Two researchers will screen the articles’ titles and/or abstracts independently. They will then retrieve the full text of these articles and assess these articles independently based on the inclusion and exclusion criteria. The inter-rater reliability of these two researchers will be calculated to examine their consistency. They will discuss the differences between their judgements to reach consensus on this issue. If the consensus on the inclusion of an article cannot be reached, a third researcher will discuss with these two researchers to reach consensus.

Data extraction
Two researchers will independently extract data using a standardised data extraction form. To ensure consistency between these two researchers, a calibration exercise will be conducted prior to starting the extraction. The reliability of these two researchers’ data extraction will be assessed. The discrepancies between their judgements will be resolved through their discussions. If consensus cannot be reached between them, a third researcher will discuss with these two researchers to reach consensus. Missing or additional data will be requested from original authors, if needed. The extracted data are the following:
- Study characteristics, including title, first author, publication year, publication type, publication journal, location and sponsor.
- Patient characteristics, including mean age, age categories, diagnostic criteria for PTSD, type of trauma, severity of PTSD symptoms, comorbidities and the number, gender, marital status, identity (such as people in military, medical workers), cultural background and education of participants, family involvement etc.
Outcome measures, including mean scores, measurement, outcome raters for each predefined outcome, time(s) of outcome measurement, data analysis methodology (eg, intention-to-treat or completers only sample), effect size, etc.

Risk of bias assessment
Quality of included studies will be assessed by using the Cochrane Collaboration tool for assessing risk of bias (V.5.1.0). The risk of bias will be rated as ‘low risk’, ‘high risk’ or ‘unclear’ in the following domains: (1) random sequence generation (selection bias); (2) allocation concealment (selection bias); (3) binding of participants and personnel (performance bias); (4) binding of outcome assessment (detection bias); (5) incomplete outcome data (attrition bias); (6) selective reporting (reporting bias) and (7) other sources of bias.46

Two researchers will assess the quality of all studies independently. The inter-rater reliability of these two researchers’ assessing the risk of bias will also be calculated. Any difference between their judgements will be discussed. If they cannot resolve the discrepancies between their judgements, a third researcher will be involved. The authors of this study will calculate graphical representations of potential bias within studies and across studies using RevMan V.5.3.

Missing data
The authors of this study will attempt to contact the authors of the primary studies to request the missing data. If there is no reply, interpolation approach will be used according to the type of data missing at random. Subsequently, the authors will conduct a sensitivity analysis by removing one study at a time to determine the robustness of the impact of the study with high bias in missing data.47

Assessment of statistical heterogeneity
Statistical heterogeneity will be assessed with forest plots, I² statistics and its 95% CI. $I^2 \geq 50\%$ indicates high heterogeneity. In addition, the $I^2$ and $H^2$ statistics$^{48}$ will also be calculated to estimate the heterogeneity of the study. When heterogeneity is identified, subgroup analysis and sensitivity analysis will be conducted to explore the possible sources of heterogeneity. If the heterogeneity is considerable, systematic review rather than meta-analysis will be conducted.

Data synthesis
Included studies will be analysed with meta-analysis method if the data can be analysed in quantitative analyses. When quantitative analyses are not appropriate, such as, considerable clinical heterogeneity, insufficient number of included studies or insufficiency in outcome reporting, systematic review instead of meta-analysis will be conducted.47

Statistical analysis
First, the age of participants will be examined in different ways: (1) calculating the mean age of the participants; (2) categorising the studies into seven specific age categories: preschool children (mean age is below 6 years); children (6–13 years); adolescents (13–18 years); young adults (mean age between 18 and 24); adults (mean age above 24); older adults (mean age above 55); older elderly (mean age above 75); (3) clustering these seven categories into three main age categories: youth (preschool children, children and adolescents); early-middle adults (young adults and middle-aged adults) and late adults (older adults and older elderly).

Subsequently, the authors will calculate the effect size for the difference in PTSD symptoms between two groups at the post-test. For continuous data, the authors will use the mean differences when all trials measured the outcome on the same scale.47 If some studies measured the outcome based on different scales, the standardised mean difference (Hedge’s g) will be used. This is calculated as dividing the difference in mean outcomes between groups with SD of outcome among participants.49

For dichotomous outcome, the authors will calculate risk ratios and convert it to Hedge’s g using Comprehensive Meta-Analysis 3.3070 (CMA). If neither of the above was reported in studies, Hedge’s g will be calculated by using other statistics (such as t values or p values) in CMA.47 Hedge’s g can be conservatively interpreted by Cohen (1988), with 0.2 indicating small, 0.5 indicating moderate and 0.8 indicating large.40

Finally, when heterogeneity is low, a fixed-effect model will be used to pool the overall effect sizes. Otherwise, a random effect model will be used. Stratified analyses will be used to compare differences in effect sizes across age categories (eg, seven age categories and three age categories). In addition, meta-regression analyses will be used to analyse the relationship between mean age and effect sizes of studies.

Assessment of publication bias
Publication bias will be assessed by examining funnel plots on primary outcome measures. The Egger’s test$^{51}$ will be used to test whether the bias is significant. In addition, Duval and Tweedie’s trim and fill procedure$^{52}$ will be used in CMA to estimate the corrected effect size when publication bias is taken into account.$^{47,53}$

Subgroup analysis
If data are available, meta-regressions will be used to assess the impact of potential moderators on the primary outcome:

- Mean age.
- Males versus females.
- With family involvement versus without family involvement (including caregiver involvement and couple involvement).
Full PTSD versus subthreshold/partial PTSD.
Psychological therapy versus psychosocial therapy.
Clinician-administrated results versus self-report results versus assisted administration results.

Sensitivity analysis
Sensitivity analysis will be performed by removing one study at a time to analyse the impact of individual studies on the pooled effect size.47
Studies in which participants had comorbid psychiatric disorders.
Studies in which intervention included less than three sessions.
Studies with high levels of missing data.
Studies with high risk of bias.
Studies conducted in clinical settings.
Studies in specific groups (eg, veterans, studies in war area).

DISCUSSION
This systematic review, meta-analysis and meta-regression analysis will compare the efficacy of psychological or psychosocial interventions for PTSD across the life span. To our knowledge, this is the first systematic review, meta-analysis and meta-regression analysis of psychological/psychosocial trials for PTSD across age groups. It is also the largest systematic review, meta-analysis and meta-regression analysis of PTSD psychological/psychosocial treatments ever conducted. The authors of this study expect that the findings will assist researchers and clinicians to understand better the therapeutic potential of psychological/psychosocial treatments. The authors of this study also expect that the findings will support clinicians in treatment selection.

There are some limitations in the present protocol. First, the differences in long-term efficacy of psychological/psychosocial treatments across the life span will not be examined because of the small number of relevant studies. Second, trials in which patients with comorbidity were enrolled will not be excluded in this study because PTSD commonly co-occurs with other psychiatric comorbidities. Although this will enhance the generalisability of the findings in this study, it will increase the risk of bias for outcomes.

REFERENCES

ETHICS AND DISSEMINATION
Data used in this study will be anonymised. These data will not be used for other purposes than research. Authors who supply the data will be acknowledged. The authors declare that no conflicts of interest exist. The findings of this study will be disseminated through briefing reports, publications and presentations.

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