TECHNICAL COMMENTARY

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POST-TRAUMATIC STRESS DISORDER LIBRARY

All therapies in low- and middle-income countries

Introduction

Many people living in low- or middle-income countries are exposed to adversities, including conflict and war. PTSD is prevalent in such communities. In developing countries, most people with PTSD do not receive adequate care due to insufficient mental health services and challenges in implementing evidence-based interventions that are adapted to their specific needs. Non-specialist health workers and other professionals such as teachers, may have an important role to play in delivering mental health care in these settings.

Method

We have included only systematic reviews (systematic literature search, detailed methodology with inclusion/exclusion criteria) published in full text, in English, from the year 2010 that report results separately for people with PTSD. Reviews were identified by searching the databases MEDLINE, EMBASE, and PsycINFO. When multiple copies of review topics were found, only the most recent and comprehensive review was included. We prioritised reviews with pooled data for inclusion.

Review reporting assessment was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist that describes a preferred way to present a meta-analysis[1]. Reviews with less than 50% of items checked have been excluded from the library. Note that early reviews may have been guided by less stringent reporting checklists than the PRISMA, and that some reviews may have been limited by journal guidelines.

Evidence was graded using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group approach where high quality evidence such as that gained from randomised controlled trials (RCTs) may be downgraded to moderate or low if review and study quality is limited, if there is inconsistency in results, indirect comparisons, imprecise or sparse data and high probability of reporting bias. It may also be downgraded if risks associated with the intervention or other matter under review are high. Conversely, low quality evidence such as that gained from observational studies may be upgraded if effect sizes are large or if there is a dose dependent response. We have also taken into account sample size and whether results are consistent, precise and direct with low associated risks (see end of table for an explanation of these terms)[2]. The resulting table represents an objective summary of the available evidence, although the conclusions are solely the opinion of staff of NeuRA (Neuroscience Research Australia).

Results

We found seven systematic reviews that met our inclusion criteria[3-9].

- Moderate to low quality evidence found large improvements in PTSD symptoms, depression, and anxiety for up to four weeks following treatment with psychological therapies in adults exposed to humanitarian crises. There were smaller, but significant improvements for up to 6 months.
- There were also improvements in children in these settings, particularly in children aged 15-18 years, in non-displaced children, and in children living in smaller households (<6 members). Functioning, hope, coping, and social support also improved, although only improvements in functioning helped improvements in PTSD symptoms. There were no significant improvements in depression and anxiety immediately post-treatment and at follow up (≥6 weeks).
- Moderate quality evidence found a large improvement in PTSD symptoms with active psychological treatments following treatment and at follow-up (up to 24 months) in child and adult survivors of mass violence in low- and middle-income countries. The effects were smaller, but remained significant, when

Margarete Ainsworth Building, Barker Street, Randwick NSW 2031. Phone: 02 9399 1000. Email: info@neura.edu.au

compared to control conditions. Depression and functioning also improved.

- For non-specialist lay health worker interventions, moderate to low quality evidence found a small improvement in PTSD symptoms in adults (counselling plus psychoeducation), and a large improvement in PTSD symptoms in children by 6 months post-treatment (school-based groups). Functioning and depression, but not anxiety, also improved in children and adolescents.
- Moderate quality evidence found no differences in PTSD symptoms following psychological therapies between women exposed to intimate partner violence and women not exposed to intimate partner violence in low- and middle-income countries. Only anxiety improved in exposed women.

Margarete Ainsworth Building, Barker Street, Randwick NSW 2031. Phone: 02 9399 1000. Email: info@neura.edu.au

Keynejad RC, Hanlon C, Howard LM

Psychological interventions for common mental disorders in women experiencing intimate partner violence in low-income and middle-income countries: a systematic review and meta-analysis

The Lancet Psychiatry 2020; 7: 173-90

View review abstract online

Comparison	**Effectiveness of psychological therapies (various) for PTSD symptoms in women exposed vs. women not exposed to intimate partner violence in low- and middle-income countries.**
Summary of evidence	**Moderate quality evidence (large sample, inconsistent, precise, indirect) found no differences in PTSD symptoms between women exposed to intimate partner violence and women not exposed to intimate partner violence in low- and middle-income countries.**
PTSD symptoms	
Pre-post-treatment analysis showed no differences in PTSD symptoms compared to women not exposed to intimate partner violence; 8 studies, N = 1,436, SMD = 0.14, 95%CI -0.06 to 0.33, $p > 0.05$, $I^2 = 43\%$, $p = 0.027$ Only anxiety showed improvements.	
Consistency in results‡	Inconsistent
Precision in results§	Precise
Directness of results‖	Indirect; mixed treatment conditions

Morina N, Malek M, Nickerson A, Bryant RA

Meta-analysis of interventions for posttraumatic stress disorder and depression in adult survivors of mass violence in low- and middle-income countries

Depression and Anxiety 2017; 34: 679-91

View review abstract online

Comparison	**Effectiveness of active psychological therapies (mostly individual therapies given by people with an average of 9 days**

	treatment) vs. control conditions (various) for adult survivors of mass violence in low- and middle-income countries.
Summary of evidence	**Moderate quality evidence (large sample, inconsistent, mostly precise, indirect) found a large effect that active psychological treatments improved PTSD symptoms following treatment and at follow-up (up to 24 months). These effects were smaller when compared to control conditions. Depression and functioning also improved.**
PTSD symptoms	
18 RCTs, N = 3,058 *Active treatments for PTSD yielded a large effect pre-post treatment;* 16 RCTs, g = 1.29, 95%CI 0.99 to 1.59, $p < 0.05$, I^2 = 92% *There was also a large pre-post treatment effect at follow-up (1-24 months);* 14 RCTs, g = 1.75, 95%CI 1.17 to 2.32, $p < 0.05$, I^2 not reported *There was a small to medium-sized effect at post-treatment when compared to control conditions;* 15 RCTs, g = 0.39, 95%CI 0.24 to 0.55, $p < 0.05$, I^2 = 44% *There was a large pre-post treatment effect at follow-up when compared to control conditions;* 10 RCTs, g = 0.93, 95%CI 0.56 to 1.31, $p < 0.05$, I^2 not reported The effects were similar when active treatments were compared to waitlist controls. Depression and functioning also improved with treatment.	
Consistency in results	Inconsistent
Precision in results	Mostly precise
Directness of results	Indirect; mixed treatment and/or control conditions

Morina N, Malek M, Nickerson A, Bryant RA

Psychological interventions for post-traumatic stress disorder and depression in young survivors of mass violence in low- and middle-income countries: meta-analysis

British Journal of Psychiatry 2017; 210: 247-54

View review abstract online

Comparison	**Effectiveness of active psychological therapies (various) vs. control conditions (various) for young survivors of mass violence in low- and middle-income countries.**

Summary of evidence	**Moderate quality evidence (large sample, inconsistent, mostly precise, indirect) found a large improvement in PTSD symptoms with active psychological treatments following treatment and at follow-up (up to 12 months). These effects were smaller when compared to control conditions. Depression and functioning also improved.**
PTSD symptoms	
Active treatments for PTSD yielded a large effect pre-post treatment; 22 RCTs, N = 4,512, g = 1.15, 95%CI 0.82 to 1.48, $p < 0.05$, I^2 = 97% *There was also a large pre-post treatment effect at follow-up (3-12 months);* 16 RCTs, g = 1.28, 95%CI 0.98 to 1.57, $p < 0.05$, I^2 not reported *There was a medium-sized effect at post-treatment when compared to control conditions;* 16 RCTs, g = 0.57, 95%CI 0.27 to 0.88, $p < 0.05$, I^2 = 95% *There was a small pre-post treatment effect at follow-up when compared to control conditions;* 9 RCTs, g = 0.23, 95%CI 0.05 to 1.41, $p < 0.05$, I^2 not reported The effects were similar when active treatments were compared to waitlist controls. Depression and functioning also improved with treatment.	
Consistency in results	Inconsistent
Precision in results	Mostly precise
Directness of results	Indirect; mixed treatment and/or control conditions

Purgato M, Gastaldon C, Papola D, van Ommeren M, Barbui C, Tol WA

Psychological therapies for the treatment of mental disorders in low- and middle-income countries affected by humanitarian crises

Cochrane Database of Systematic Reviews 2018; 7: CD011849

View review abstract online

Comparison	**Effectiveness of psychological therapies (trauma-focussed or supportive therapies, EMDR, CBT, interpersonal psychotherapy) vs. control conditions (usual care, waitlist, or no treatment) for PTSD symptoms in adults and children exposed to humanitarian crises.**
Summary of evidence	**Moderate to low quality evidence (large samples, inconsistent, mostly precise, indirect) found large improvements in PTSD**

	symptoms, depression, and anxiety post-treatment with psychological therapies, medium-sized improvements for up to 4 months and smaller improvements for up to 6 months post-treatment.
PTSD symptoms	
A large effect showed significant improvement in PTSD symptoms with psychological therapies between 0-4 weeks after treatment; Adults: 16 RCTs, N = 1,272, SMD = -1.07, 95%CI -1.34 to -0.79, $p < 0.00001$, $I^2 = 78\%$ Children and adolescents: 3 RCTs, N = 130, SMD = -1.56, 95%CI -3.13 to 0.01, $p = 0.052$, $I^2 = 93\%$ *At 1-4 months follow-up, a medium-sized effect showed significant improvement in PTSD symptoms with psychological therapies;* Adults: 18 RCTs, N = 1,660, SMD = -0.49, 95%CI -0.68 to -0.31, $p < 0.00001$, $I^2 = 61\%$ *At 6 months follow-up, a small to medium-sized effect showed significant improvement in PTSD symptoms with psychological therapies;* Adults: 5 RCTs, N = 400, SMD = -0.37, 95%CI -0.61 to -0.14, $p = 0.0019$, $I^2 = 0\%$ Depression, anxiety, functioning and quality of life also improved with psychological therapies.	
Risks	Drop-out rates were similar across groups.
Consistency in results	Mostly inconsistent.
Precision in results	Mostly precise.
Directness of results	Indirect; mixed treatment and/or control conditions

Purgato M, Gross AL, Betancourt T, Bolton P, Bonetto C, Gastaldon C, Gordon J, O'Callaghan P, Papola D, Peltonen K, Punamaki RL, Richards J, Staples JK, Unterhitzenberger J, van Ommeren M, de Jong J, Jordans MJD, Tol WA, Barbui C

Focused psychosocial interventions for children in low-resource humanitarian settings: a systematic review and individual participant data meta-analysis

The Lancet Global Health 2018; 6: e390-e400

View review abstract online

Comparison	**Effectiveness of focussed psychosocial therapies vs. waitlist for PTSD symptoms in children and adolescents (0-18 years) in low-resource humanitarian settings.** **Interventions included a youth readiness intervention, creative play, a mind-body skills group program, class-based**

Margarete Ainsworth Building, Barker Street, Randwick NSW 2031. Phone: 02 9399 1000. Email: info@neura.edu.au

	interventions, a family focused intervention, teaching recovery techniques, a sport for development intervention, and emotional writing and positive writing.
Summary of evidence	**Moderate to low quality evidence (large samples, inconsistent, precise, indirect) found small improvements in PTSD symptoms, but not depression and anxiety, post-treatment and at follow up (≥6 weeks) with psychosocial therapies. Most improvements were found in children aged 15-18 years, in non-displaced children, and in children living in smaller households (<6 members). Functioning, hope, coping, and social support also improved.**
PTSD symptoms	
A small effect showed significant improvement in PTSD symptoms with psychological therapies between 0-4 weeks after treatment; 8 RCTs, N = 2,355, SMD = -0.33, 95%CI -0.52 to -0.14, p = 0.0006, I^2 = 80% *At ≥6 weeks follow-up, a small effect was found;* 6 RCTs, N = 1,808, SMD = -0.21, 95%CI -0.42 to -0.01, $p < 0.05$, I^2 = 78% There was a stronger improvement in PTSD symptoms in children aged 15–18 years, in non-displaced children, and in children living in smaller households (<6 members). Functioning, hope, coping, and social support also improved with psychological therapies. There were no significant differences between psychological therapies and waitlist in depression or anxiety symptoms.	
Consistency in results	Inconsistent
Precision in results	Precise
Directness of results	Indirect; mixed treatment conditions

Purgato M, Tedeschi F, Betancourt TS, Bolton P, Bonetto C, Gastaldon C, Gordon J, O'Callaghan P, Papola D, Peltonen K, Punamaki RL, Richards J, Staples JK, Unterhitzenberger J, de Jong J, Jordans MJD, Gross AL, Tol WA, Barbui C

Mediators of focused psychosocial support interventions for children in low-resource humanitarian settings: analysis from an Individual Participant Dataset with 3,143 participants

Journal of Child Psychology and Psychiatry, and Allied Disciplines 2019; 07: doi.org/10.1111/jcpp.13151

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Comparison	**Factors associated with how psychosocial therapies are effective for children and adolescents (0-18 years) in low-resource humanitarian settings.**
Summary of evidence	**Moderate to low quality evidence (large samples, indirect) found functioning ability was a significant mediator for focused psychosocial interventions on PTSD symptoms. There were no mediating effects of coping, hope, or social support.**
Factors associated with improvements in PTSD symptoms	
Functioning was the strongest mediator for focused psychosocial interventions on PTSD symptoms; 6 RCTs, N = 1,877, β = -0.087 There were no mediating effects of coping, hope, or social support.	
Consistency in results	Not reported
Precision in results	Not reported
Directness of results	Indirect; mixed treatment conditions

van Ginneken N, Tharyan P, Lewin S, Rao GN, Meera SM, Pian J, Chandrashekar S, Patel V

Non-specialist health worker interventions for the care of mental, neurological, and substance-abuse disorders in low- and middle-income countries

Cochrane Database of Systematic Reviews: 2013; CD009149

View review abstract online

Comparison	**Effectiveness of non-specialist, lay health worker interventions (group or individual counselling with or without psychoeducation) vs. standard care for adults and children with PTSD in low- and middle-income countries.**
Summary of evidence	**Moderate to low quality evidence (medium to large samples, some inconsistency and imprecision, indirect) found a small improvement in PTSD symptoms in adults, and a large improvement in PTSD symptoms in children, after non-specialist health worker interventions (~6 months post-treatment). Functioning and depression symptoms also improved in children (small effects), with no differences in anxiety symptoms.**

PTSD symptoms	
There was a small effect of improved PTSD symptoms in adults after non-specialist health worker interventions by 6 months post-treatment; 3 RCTs, N = 223, SMD = -0.36, 95%CI -0.67 to -0.05, p = 0.02, I^2 = 22% *There was a large effect of improved PTSD symptoms in children after non-specialist health worker interventions within 6 months post-treatment (mostly in groups, school-based);* 3 RCTs, N = 298, SMD = -0.89, 95%CI -1.49 to -0.03, p < 0.01, I^2 = 79% *There was no significant difference with Classroom-Based Intervention (a specific, manual-based intervention including elements of creative-expressive therapy, co-operative play, and CBT);* 3 RCTs, N = 1,090, MCD = -0.56, 95%CI -2.82 to 1.70, p = 0.63, I^2 = 82% Functioning and depression was improved in children after any non-specialist intervention within 6 months post-treatment (small effects), however there was no difference in anxiety symptoms.	
Consistency in results	Consistent for adults, inconsistent for children.
Precision in results	Precise for adults, imprecise for children.
Directness of results	Indirect; mixed treatment conditions

Explanation of acronyms

β = beta coefficient, CBT = cognitive behavioural therapy, CI = confidence interval, CrI = credible interval, *d* or *g* = Cohen's d and Hedges' g, standardised mean difference, EMDR = eye movement desensitisation and reprocessing, I^2 = the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance), LOR = log odds ratio, MCD = mean change difference, N = number of participants, SMD = standardised mean difference, p = statistical probability of obtaining that result, vs. = versus

Explanation of technical terms

* Bias has the potential to affect reviews of both RCT and observational studies. Forms of bias include; reporting bias – selective reporting of results; publication bias - trials that are not formally published tend to show less effect than published trials, further if there are statistically significant differences between groups in a trial, these trial results tend to get published before those of trials without significant differences; language bias – only including English language reports; funding bias - source of funding for the primary research with selective reporting of results within primary studies; outcome variable selection bias; database bias - including reports from some databases and not others; citation bias - preferential citation of authors. Trials can also be subject to bias when evaluators are not blind to treatment condition and selection bias of participants if trial samples are small[10].

† Different effect measures are reported by different reviews.

Prevalence refers to how many existing cases there are at a particular point in time. Incidence refers to how many new cases there are per population in a specified time period. Incidence is usually reported as the number of new cases per 100,000 people per year. Alternatively some studies present the number of new cases that have accumulated over several years against a person-years denominator. This denominator is the sum of individual units of time that the persons in the population are at risk of becoming a case. It takes into account the size of the underlying population sample and its age structure over the duration of observation.

Reliability and validity refers to how accurate the instrument is. Sensitivity is the proportion of actual positives that are correctly identified (100% sensitivity = correct identification of all actual positives) and specificity is the proportion of negatives that are correctly identified (100% specificity = not identifying anyone as positive if they are truly not).

Weighted mean difference scores refer to mean differences between treatment and comparison groups after treatment (or occasionally pre to post treatment) and in a randomised trial there is an assumption that both groups are comparable on this measure prior to treatment. Standardised mean differences are divided by the pooled standard deviation (or the standard deviation of one group when groups are homogenous) that allows results from different scales to be combined and compared. Each study's mean difference is then given a weighting depending on the size of the sample and the variability in the data. Less than 0.4 represents a small effect, around 0.5 a medium effect, and over 0.8 represents a large effect[10].

Odds ratio (OR) or relative risk (RR) refers to the probability of a reduction (< 1) or an increase (> 1) in a particular outcome in a treatment group, or a group exposed to a risk factor, relative to the comparison group. For example, a RR of 0.75 translates to a reduction in risk of an outcome of 25% relative to those not receiving the treatment or not exposed to the risk factor. Conversely, a RR of 1.25 translates to an increased risk of 25% relative to those not receiving treatment or not having been exposed to a risk factor. A RR or OR of 1.00 means there is no difference between groups. A medium effect is considered if RR > 2 or < 0.5 and a large effect if RR > 5 or < 0.2[11]. lnOR stands for logarithmic OR where a lnOR of 0 shows no difference between groups. Hazard ratios measure the effect of an explanatory variable on the hazard or risk of an event.

Correlation coefficients (eg, r) indicate the strength of association or relationship

Margarete Ainsworth Building, Barker Street, Randwick NSW 2031. Phone: 02 9399 1000. Email: info@neura.edu.au

between variables. They can provide an indirect indication of prediction, but do not confirm causality due to possible and often unforseen confounding variables. An r of 0.10 represents a weak association, 0.25 a medium association and 0.40 and over represents a strong association. Unstandardised (*b*) regression coefficients indicate the average change in the dependent variable associated with a 1 unit change in the independent variable, statistically controlling for the other independent variables. Standardised regression coefficients represent the change being in units of standard deviations to allow comparison across different scales.

‡ Inconsistency refers to differing estimates of effect across studies (i.e. heterogeneity or variability in results) that is not explained by subgroup analyses and therefore reduces confidence in the effect estimate. I^2 is the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance) - 0% to 40%: heterogeneity might not be important, 30% to 60%: may represent moderate heterogeneity, 50% to 90%: may represent considerable heterogeneity and over this is considerable heterogeneity. I^2 can be calculated from Q (chi-square) for the test of heterogeneity with the following formula[10];

$$I^2 = \left(\frac{Q - df}{Q}\right) \times 100\%$$

§ Imprecision refers to wide confidence intervals indicating a lack of confidence in the effect estimate. Based on GRADE recommendations, a result for continuous data (standardised mean differences, not weighted mean differences) is considered imprecise if the upper or lower confidence limit crosses an effect size of 0.5 in either direction, and for binary and correlation data, an effect size of 0.25. GRADE also recommends downgrading the evidence when sample size is smaller than 300 (for binary data) and 400 (for continuous data), although for some topics, these criteria should be relaxed[12].

‖ Indirectness of comparison occurs when a comparison of intervention A versus B is not available but A was compared with C and B was compared with C that allows indirect comparisons of the magnitude of effect of A versus B. Indirectness of population, comparator and/or outcome can also occur when the available evidence regarding a particular population, intervention, comparator, or outcome is not available and is therefore inferred from available evidence. These inferred treatment effect sizes are of lower quality than those gained from head-to-head comparisons of A and B.

Margarete Ainsworth Building, Barker Street, Randwick NSW 2031. Phone: 02 9399 1000. Email: info@neura.edu.au

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Margarete Ainsworth Building, Barker Street, Randwick NSW 2031. Phone: 02 9399 1000. Email: info@neura.edu.au