TECHNICAL COMMENTARY

NeuRA
Discover. Conquer. Cure.
POST-TRAUMATIC STRESS DISORDER LIBRARY

Remission

Introduction

Remission and recovery are generally achieved when there are long-term symptom improvements and subsequent improvements in overall functioning. While many people fully recover from PTSD over time, some do not, with symptoms continuing and fluctuating over time.

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 reviews were found, only the most recent version 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 four systematic reviews that met our inclusion criteria[3-6].

- Moderate to high quality evidence found around 44% of adults who were not receiving treatment remitted from PTSD within seven years post-trauma. Rates were highest in the first five months and in people exposed to natural disasters rather than physical disease.
- Moderate to high quality evidence found a 53% reduction in prevalence rates and a corresponding improvement in PTSD symptoms between one and six months post trauma exposure in children and adolescents, with little change between six months and one year.
- Moderate quality evidence found around 53-63% of people treated with cognitive behavioural therapy for PTSD remitted after treatment or at follow-up.

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

Hiller RM, Meiser-Stedman R, Fearon P, Lobo S, McKinnon A, Fraser A, Halligan SL

Research Review: Changes in the prevalence and symptom severity of child post-traumatic stress disorder in the year following trauma - a meta-analytic study

Journal of Child Psychology and Psychiatry, and Allied Disciplines 2016; 57: 884-98

View review abstract online

Comparison	**Rates of PTSD diagnosis and symptoms over time in children and adolescents aged 5-18 years exposed to trauma.** **Most studies recruited children after accidental injury, while three studies included children who had experienced an assault, and three studies were natural disaster samples.**
Summary of evidence	**Moderate to high quality evidence (large sample, mostly inconsistent and precise, direct) found a reduction in prevalence rates and an improvement in PTSD symptoms between one and six months post trauma, with little change after 6 months.**

Prevalence and symptom reductions over time

28 studies, N = 3,910

Point prevalence

1 month: 18 studies, 21%, 95%CI 16% to 28%

3 months: 16 studies, 15%, 95%CI 10% to 22%

6 months: 17 studies, 12%, 95%CI 9% to 16%

1 year: 11 studies, 11%, 95%CI 7% to 17%

Prevalence reduction

1 to 3 months: 6 studies, 17%, 95%CI 3% to 55%

3 to 6 months: 7 studies, 32%, 95%CI 14% to 56%

1 to 6 months: 9 studies, 53%, 95%CI 43% to 63%

3 months to 1 year: 6 studies, 34%, 95%CI 21% to 49%

Symptom severity reduction

1 to 3 months: 6 studies, $d = 0.37$, 95%CI 0.18 to 0.57, $p < 0.05$

1 to 6 months: 7 studies, $d = 0.44$, 95%CI 0.29 to 0.58, $p < 0.05$

3 to 6 months: 5 studies, $d = 0.27$, 95%CI 0.17 to 0.38, $p < 0.05$

3 months to 1 year: 4 studies, $d = 0.21$, 95%CI 0.00 to 0.41, $p = 0.05$

Older samples were associated with a lower prevalence reduction between 3 and 6 months. There were no moderating effects of sex or PTSD measurement (self-report vs. diagnostic interview).

Consistency in results‡	Mostly inconsistent
Precision in results§	Mostly precise
Directness of results‖	Direct

Morina N, Wicherts JM, Lobbrecht J, Priebe S

Remission from post-traumatic stress disorder in adults: a systematic review and meta-analysis of long-term outcome studies

Clinical Psychology Review 2014; 34: 249-55

View review abstract online

Comparison	**Long-term rates of remission in adults with PTSD, with the majority not receiving treatment.**
Summary of evidence	**Moderate to high quality evidence (large sample, inconsistent, precise, direct) found around 44% of adults remitted from PTSD within seven years post-trauma. Rates were highest in the first five months and in people exposed to natural disasters rather than physical disease.**

Rates of remission over time
Around 44.0% of participants spontaneously remitted from PTSD from 3.5 to 7 years post-trauma; 42 studies, N = 81,642, ES = 0.75, 95%CI 0.68 to 0.83, I^2 = 97% Studies with the baseline assessment conducted within the first five months post-trauma were more likely to have reported higher remission rates than baseline assessments made after five months (51.7% vs. 36.9%). Studies with participants exposed to a natural disaster reported higher remission rates than studies with participants exposed to a physical disease (60% vs. 31.4%).

Consistency in results	Inconsistent
Precision in results	Precise
Directness of results	Direct

NeuRA Discover. Conquer. Cure.
POST-TRAUMATIC STRESS DISORDER LIBRARY

Remission

Springer KS, Levy HC, Tolin DF

Remission in CBT for adult anxiety disorders: A meta-analysis

Clinical Psychology Review 2018; 61: 1-8

View review abstract online

Comparison	**Rates of remission in adults with PTSD after treatment with cognitive behavioural therapy (CBT).**
Summary of evidence	**Moderate quality evidence (unclear sample size, inconsistent, appears precise, direct) found around 53-63% of people treated with CBT for PTSD remitted after treatment or at follow-up.**
Rates of remission over time	
ITT analysis Post-treatment: 20 studies, N not reported, remission = 53.3%, 95%CI 45.3% to 61.1%, I^2 = 88% Follow-up: 13 studies, N not reported, remission = 54.8%, 95%CI 44.7% to 64.4%, I^2 = 88% Completer analysis Post-treatment: 23 studies, N not reported, remission = 62.8%, 95% 52.1% to 72.3%, I^2 = 91% Follow-up: 17 studies, N not reported, remission = 63.5%, 95%CI 48.7% to 76.1%, I^2 = 93%	
Consistency in results	Inconsistent
Precision in results	Appears precise
Directness of results	Direct

Explanation of acronyms

CI = confidence interval, *d* = Cohen's d standardised mean difference, ES = effect size, I^2 = the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance), N = number of participants, *p* = statistical probability of obtaining that result, vs. = versus

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

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[7].

† 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[7].

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[8]. 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

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[7];

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

§ 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[9].

‖ 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

References

1. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMAGroup (2009): Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *British Medical Journal* 151: 264-9.
2. GRADEWorkingGroup (2004): Grading quality of evidence and strength of recommendations. *British Medical Journal* 328: 1490.
3. Hiller RM, Meiser-Stedman R, Fearon P, Lobo S, McKinnon A, Fraser A*, et al.* (2016): Research Review: Changes in the prevalence and symptom severity of child post-traumatic stress disorder in the year following trauma - a meta-analytic study. *Journal of Child Psychology and Psychiatry, and Allied Disciplines* 57: 884-98.
4. Morina N, Wicherts JM, Lobbrecht J, Priebe S (2014): Remission from post-traumatic stress disorder in adults: a systematic review and meta-analysis of long term outcome studies. *Clinical Psychology Review* 34: 249-55.
5. Steinert C, Hofmann M, Leichsenring F, Kruse J (2015): The course of PTSD in naturalistic long-term studies: high variability of outcomes. A systematic review. *Nordic Journal of Psychiatry* 69: 483-96.
6. Springer KS, Levy HC, Tolin DF (2018): Remission in CBT for adult anxiety disorders: A meta-analysis. *Clinical Psychology Review* 61: 1-8.
7. CochraneCollaboration (2008): Cochrane Handbook for Systematic Reviews of Interventions. Accessed 24/06/2011.
8. Rosenthal JA (1996): Qualitative Descriptors of Strength of Association and Effect Size. *Journal of Social Service Research* 21: 37-59.
9. GRADEpro (2008): [Computer program]. Jan Brozek, Andrew Oxman, Holger Schünemann. *Version 32 for Windows*