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Introduction

For a person to be diagnosed with PTSD, at least one stressor is required. Stressors as determined by the latest version of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) include being exposed to threatened death, actual or threatened serious injury, or actual or threatened sexual violence. Examples are direct exposure, witnessing the trauma, or learning that a relative or close friend was exposed to a trauma. Stressors can also be encountered in the course of professional duties. This summary table presents the evidence for risk of PTSD in people exposed to the loss of a loved one.

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-analysis¹. 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 (<u>GRADE</u>) 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 five systematic reviews that met our inclusion criteria³⁻⁷.

- Moderate to low quality evidence found the prevalence of PTSD in mothers ranged from 23% to 49.1% within 3 months post-loss, from 0.6% to 37% between 3 months and 12 months post-loss, and from 3.3% to 15.2% by 18 years post-loss. In fathers, prevalence of PTSD ranged from 5% to 8.4% between 7 weeks and 18 years post-loss.
- Moderate to high quality evidence found an increased risk of PTSD in bereaved people after exposure to any trauma compared to non-bereaved people after exposure to any trauma.
- Moderate quality evidence found the incidence of PTSD following an earthquake in bereaved individuals was around 39% compared to around 20% for individuals who were not bereaved.
- Moderate quality evidence found that 19.1% of people who were bereaved due to homicide met criteria for lifetime PTSD, and 5.2% met criteria for current PTSD. Homicidally bereaved people were more likely than non-homicidally bereaved people

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to report past-year PTSD symptoms. Twice as many parents whose children were murdered met PTSD criteria two years post loss compared to parents who lost their child due to accident or suicide. There were no differences in PTSD symptoms between homicidally bereaved people and victims of physical or sexual assault.

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Christiansen DM

Posttraumatic stress disorder in parents following infant death: A systematic review

Clinical Psychology Review 2017; 51: 60-74

View review abstract online

| Comparison | PTSD in parents following infant loss. |
|---|---|
| Summary of evidence | Moderate to low quality evidence (unclear sample size, appears inconsistent and imprecise, direct) found the prevalence of PTSD in mothers ranged from 23% to 49.1% within 3 months post-loss, from 0.6% to 37% between 3 months and 12 months post-loss, and from 3.3% to 15.2% by 18 years post-loss. In fathers, prevalence of PTSD ranged from 5% to 8.4% between 7 weeks and 18 years post-loss. |
| PTSD in parents after infant loss | |
| | Mothers |
| <3 months post-loss: 5 studies, prevalence ranged from 23% to 49.1% | |
| 3-12 months post-loss: 6 studies, prevalence ranged from 0.6% to 37% | |
| Up to 18 years post-loss: 3 studies, prevalence ranged from 3.3% to 15.2% | |
| | <u>Fathers</u> |
| 7 weeks to 18 ye | ears post-loss: 2 studies, prevalence ranged from 5% to 8.4% |
| | ng effects from whether the death occurred prior to, during, or following s gestational age consistently associated with PTSD severity. |
| Consistency in results | Appears inconsistent |
| Precision in results | Appears imprecise |
| Directness of results | Direct |

Dai W, Chen L, Lai Z, Li Y, Wang J, Liu A

The incidence of post-traumatic stress disorder among survivors after earthquakes: a systematic review and meta-analysis

BMC Psychiatry 2016; 16: 188

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| Comparison | PTSD after earthquakes in bereaved vs. not bereaved individuals. |
|--|---|
| Summary of evidence | Moderate quality evidence (large sample, inconsistent, imprecise, direct) finds the incidence of PTSD after an earthquake in bereaved individuals is around 39% compared to around 20% for individuals who are not bereaved. |
| Bereavement after earthquakes | |
| 46 studies, N = 76,101 | |
| The incidence of PTSD after earthquake was higher in bereaved than non-bereaved individuals; | |
| Bereaved: 39.10%, 95%CI 25.74% to 53.33% | |
| Not bereaved: 19.92%, 95%CI 10.89% to 30.83% | |
| Consistency in results | Authors report these data are inconsistent. |
| Precision in results | Appears imprecise |
| Directness of results | Direct |

Tang B, Deng Q, Glik D, Dong J, Zhang L

A Meta-Analysis of Risk Factors for Post-Traumatic Stress Disorder (PTSD) in Adults and Children after Earthquakes

International Journal of Environmental Research and Public Health 2017; 14: 1537

View review abstract online

| Comparison | PTSD after earthquakes in bereaved vs. not bereaved adults and | |
|---|---|--|
| | children. | |
| Summary of evidence | Moderate quality evidence (large sample, inconsistent, imprecise, direct) found medium-sized effects of increased risk of PTSD after earthquakes in bereaved adults and children than in non-bereaved adults and children following earthquakes. | |
| Bereavement after earthquakes | | |
| | 15 studies, N = 22,931 | |
| Adults and children who e | xperienced bereavement were more likely to have PTSD than those who were not bereaved (medium-sized effect); | |
| А | Adults: OR = 2.49, 95%Cl 2.04 to 3.04, $l^2 = 71\%$ | |
| Children: OR = 2.24, 95%Cl 1.95 to 2.56, l^2 not reported | | |

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| Consistency in results | Inconsistent for adults. |
|------------------------|--------------------------|
| Precision in results | Imprecise |
| Directness of results | Direct |

Trickey D, Siddaway AP, Meiser-Stedman R, Serpell L, Field AP

| A meta-analysis of risk factors for post-traumatic stress disorder in |
|---|
| children and adolescents |

Clinical Psychology Review 2012; 32: 122-38

View review abstract online

| Comparison | PTSD after exposure to any trauma involving bereavement vs. exposure to any trauma without bereavement. | |
|---|--|--|
| Summary of evidence | Moderate to high quality evidence (unclear sample size, consistent, precise, direct) found a small association between bereavement after exposure to any trauma and increased risk of PTSD. | |
| Bereavement after any trauma | | |
| A small association was found between bereavement and increased risk of PTSD; | | |
| 4 studies, N not reported, r = 0.22, 95%CI 0.12 to 0.32, p < 0.001, Qp > 0.05 | | |
| Consistency in results | Consistent | |
| Precision in results | Precise | |
| Directness of results | Direct | |

van Denderen M, de Keijser J, Kleen M, Boelen PA

Psychopathology among homicidally bereaved individuals: a systematic review

Trauma Violence and Abuse 2015; 16: 70-80

View review abstract online

| Comparison | PTSD in bereaved people. |
|---------------------|--|
| Summary of evidence | Moderate quality evidence (mostly large samples, direct) found |

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| | homicidally bereaved individuals were more likely than non- homicidally bereaved victims to report past-year PTSD symptoms. 19.1% of people who were homicide bereaved met criteria for lifetime PTSD, and 5.2% met current PTSD criteria. Twice as many parents whose children were murdered met PTSD criteria two years post loss compared to parents who lost their child due to accident or suicide. There were no differences by five years post loss. There were also no differences in PTSD symptoms between homicidally bereaved and victims of physical or sexual assault. |
|--|--|
| Bereavement after homicide | |
| 1 study (N = 1,753) found that homicidally bereaved victims were more likely than non-homicidally bereaved victims to report past-year PTSD symptoms (OR = 1.88). | |
| 1 study (N = 12,500) found 19.1% of people who were homicide bereaved met criteria for lifetime PTSD, and 5.2% met current PTSD criteria. | |
| 1 study (N = 171) found twice as many parents whose children were murdered met PTSD criteria two years post loss compared to parents who lost their child due to accident or suicide. There were no differences by five years post loss. | |
| 1 study (N = 120) found no difference in PTSD between the homicidally bereaved and victims of physical or sexual assault. | |
| Consistency in results | Unable to assess; no measure of consistency is reported. |
| Precision in results | Unable to assess; no measure of precision is reported. |
| Directness of results | Direct |

Explanation of acronyms

CI = confidence interval, I^2 = the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance), N = number of participants, OR = odds ratio, Q = test for heterogeneity, vs. = versus

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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 small⁸.

† 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 effect⁸.

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 < 0.2^9 . InOR stands for logarithmic OR where a InOR 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

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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 а strona 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 the other independent for 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. I² 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 heterogeneity. considerable l² can be calculated from Q (chi-square) for the test of heterogeneity with the following formula⁸;

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

§ 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 relaxed¹⁰.

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 Β. Indirectness versus 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-tohead comparisons of A and B.

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