**Manuscript:** **How safe are psychological interventions for adult PTSD? A meta-analysis on the incidence and relative risk of deterioration, adverse events and serious adverse events**

**Supplement 1: PRISMA-P checklist**

**Supplement 2: Search string used for systematic literature search.**

**Supplement 3: References of related reviews and meta-analyses scrutinized as part of the systematic literature search.**

**Supplement 4: Trial characteristics of included trials.**

**Supplement 5: References of included trials.**

**Supplement 6: Incidence and relative risk of pre-to-posttreatment deterioration (top) and pre-to-follow-up deterioration (bottom) – extended Table version.**

**Supplement 7: Moderator results – incidences of pre-to-posttreatment deterioration.**

**Supplement 8: Publication bias and outlier checks.**

**Supplement 9: Moderator results – incidences of pre-to-posttreatment adverse events.**

**Supplement 10: Moderator results – incidences of pre-to-posttreatment serious adverse events.**

**Supplement 11: Risk of bias assessment.**

**Supplement 1: PRISMA-P checklist**

|  |  |  |  |
| --- | --- | --- | --- |
| **Section/topic**  | **#** | **Checklist item**  | **Reported on page #**  |
| **TITLE**  |  |
| Title  | 1 | Identify the report as a systematic review, meta-analysis, or both.  | 1 |
| **ABSTRACT**  |  |
| Structured summary  | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.  | 2 |
| **INTRODUCTION**  |  |
| Rationale  | 3 | Describe the rationale for the review in the context of what is already known.  | 3 |
| Objectives  | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).  | 4 |
| **METHODS**  |  |
| Protocol and registration  | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.  | 4 |
| Eligibility criteria  | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.  | 4 |
| Information sources  | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.  | 4-5 |
| Search  | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.  | 4 & Supplement 2 |
| Study selection  | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).  | 4  |
| Data collection process  | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.  | 5 |
| Data items  | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.  | 5-6 |
| Risk of bias in individual studies  | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.  | 5 |
| Summary measures  | 13 | State the principal summary measures (e.g., risk ratio, difference in means).  | 6 |
| Synthesis of results  | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I2) for each meta-analysis.  | 7 |
| Risk of bias across studies  | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).  | 6-7 |
| Additional analyses  | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.  | 6-7 |
| **RESULTS**  |  |
| Study selection  | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.  | 8 & Fig. 1 |
| Study characteristics  | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.  | 8 (summary)Supplement 4 (per trial) |
| Risk of bias within studies  | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).  | Supplement 11 |
| Results of individual studies  | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.  | Supplement 8 |
| Synthesis of results  | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency.  | 8-13 & Table 1-3 & Supplement 6 |
| Risk of bias across studies  | 22 | Present results of any assessment of risk of bias across studies (see Item 15).  | 8 & Supplement 7+9 |
| Additional analysis  | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).  | Table 1-3 & Supplement 6-10 |
| **DISCUSSION**  |  |
| Summary of evidence  | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).  | 13-14 |
| Limitations  | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).  | 15 |
| Conclusions  | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research.  | 14-15 |
| **FUNDING**  |  |
| Funding  | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.  | 17 |

*From:*  Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

**Supplement 2: Search string used for systematic literature search.**

|  |  |
| --- | --- |
| Databases | Search Terms |
| MEDLINE and PsycINFO | ( TI ( ptsd OR ptss OR post-traumatic stress OR posttraumatic stress OR post-traumatic syndrome OR posttraumatic syndrome) OR AB ( ptsd OR ptss OR post-traumatic stress OR posttraumatic stress OR post-traumatic syndrome OR posttraumatic syndrome ) OR SU ( ptsd OR ptss OR post-traumatic stress OR posttraumatic stress OR post-traumatic syndrome OR posttraumatic syndrome ) ) AND ( TI ( treatment\* OR intervention\* OR therap\* OR psychotherap\* OR exposure OR counse\*ing OR trial\* ) OR AB ( treatment\* OR intervention\* OR therap\* OR psychotherap\* OR exposure OR counse\*ing OR trial\* ) OR SU ( treatment\* OR intervention\* OR therap\* OR psychotherap\* OR exposure OR counse\*ing OR trial\* ) ) |
| PTSDpubs | (ptsd OR ptss OR post-traumatic stress OR posttraumatic stress OR post-traumatic syndrome OR posttraumatic syndrome) AND (treatment\* OR intervention\* OR therap\* OR psychotherap\* OR exposure OR counse\*ing OR trial\*) |
| Web of Science | ALL=( ptsd OR ptss OR post-traumatic stress OR posttraumatic stress OR post-traumatic syndrome OR posttraumatic syndrome ) AND ALL=( treatment\* OR intervention\* OR therap\* OR psychotherap\* OR exposure OR counse\*ing OR trial\* ) |
| Note that the search string contains APA thesaurus/MeSH search terms (i.e., “posttraumatic stress”, “treatment”, “intervention”, “psychotherapy”, “exposure” and “counseling” as well as additional terms (e.g., “post-traumatic stress”, “PTSD”, “trial”, “therapy”) in case a particular trial was not registered under these APA thesaurus/MeSH search terms. |

**Supplement 3: References of related reviews and meta-analyses scrutinized as part of the systematic literature search.**

**1** Althobaiti S, Kazantzis N, Ofori-Asenso R, Romero L, Fisher J, Mills KE et al. Efficacy of interpersonal psychotherapy for post-traumatic stress disorder: A systematic review and meta-analysis. *J Affect Disord* 2020; **264**: 286–94.

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| Supplement 4: Trial characteristics of included trials. |
| Publication, conditions/category,(number & length of sessions) | Number of completers at posttreatment assessment | Assessment of deterioration | Assessment of adverse events | % fulfilling PTSD diagnosis at baseline | Outcome measure | Country | Mean age (SD or range) | Longest follow-up in months | Treatment format | Stat. analysis | % female | Type of trauma | Quality sum score (out of 8) |
| Andersen et al., 20211 TF-CBT/TF-CBT (10 sessions, 60 – 90 min.) SPT /non-tf-Other (10 sessions, 60 min.) | 4346 | n.a. | Serious adverse events (unspecified) | 100 | CAPS | Australia and Denmark | 39.71 (13.3)44.49 (11.6) | 12 | IndividualIndividual | Compl. | 73.672 | Motor vehicle accident | 7 |
| Blanchard et al., 20032 CBT/TF-CBT (10 sessions, n.r.) SPT/non-tf-Other (10 sessions, n.r.) WL/PCC | 272724 | n.a. | Adverse events (moving from no depression to depression and from no GAD to GAD from pre-to-posttreatment) | 77.7877.7887.50 | CAPS | USA | 40.60 (11.00)40.60 (13.10)42.10 (10.90) | 3 | IndividualIndividual | ITT | 787863 | Motor vehicle accident | 6 |
| Bohus et al., 20133 DBT-PTSD/TF-CBT (23 sessions, 45 min.)  TAU/ACC (n.r.) | 3434 | Pre-to-follow-up increase in CAPS (liberal) | Serious adverse events (suicide attempts) | 100 | CAPS | Germany | 35.14 (10.60)36.71 (9.84) | 3 | IndividualIndividual | ITT | 100 | Childhood sexual abuse | 7 |
| Bormann et al., 20134 MM/non-tf-Other (6 sessions, 90 min.) TAU/ACC | 6670 | n.a. | Adverse events (unspecified) | 100 | CAPS | USA |  57.00 (10.10) | r.b.i. | GroupIndividual | ITT | 3 | Combat | 6 |
| Brom et al., 20175 SE/non-tf-Other (15 sessions, 60 min.) WL/PCC | 2830 | n.a. | Adverse events (unspecified) | 100 | CAPS | Israel | 40.51 (13.05) | r.b.i. | Individual | Compl. | 4657 | Multiple types | 7 |
| Bryant et al., 20116 CBT/TF-CBT (8 sessions, 60 min.)  TAU/ACC (8 sessions, n.r.)  | 1612 | n.a. | Adverse events (unspecified) | 100 | PSS-I | Thailand | 42.30 (6.30)43.9 (11.9) | 3 | IndividualIndividual | ITT | 10091 | Terror | 5 |
| Bryant et al., 20197 CBT long/TF-CBT (12 sessions, 90 min.) WL/PCC | 2727 | n.a. | Serious adverse events (any signs of psychiatric crisis such as imminent suicidal risk or need for acute protection) | 100 | CAPS | Australia | 44.7 (10.7)43.4 (7.8) | r.b.i. | Individual | Compl. | 1229 | Multiple types | 4 |
| Buhmann et al., 20168 TF-CBT/TF-CBT (16 sessions, n.r.) WL/PCC | 5248 | n.a. | Serious adverse events (e.g., emergency psychiatric admission) and adverse vents (unspecified) reported separately | 100 | HTQ | Denmark | 46.00 (8.00)47.00 (8.00) | n.a. | Individual | Compl. | 4239 | Mass conflict | 6 |
| Butollo et al., 20169 DET/tf-Other (24 sessions, n.r.)  CPT/TF-CBT (24 sessions, n.r.)  | 4859 | Reliable change index (PDS, conservative) | Adverse events (significant worsening in GSI and BSI as defined by reliable change index) | 100 | PDS | Germany | 37.99 (12.10)33.67 (10.30) | 6 | IndividualIndividual | ITT | 6568 | Multiple types | 7 |
| Chard 200510 CPT/TF-CBT (17 sessions à 90 min. group +  10 sessions à 60 min. individual)  MA/PCC (17 phone-calls à 5-10 min.) | 2828 | Pre-to-post increase in CAPS | n.a. | 100 | CAPS | USA | 32.77 (8.87) | r.b.i. | CombiIndividual | Compl. | 100 | Childhood sexual abuse | 6 |
| Cloitre et al., 200211 STAIR/TF-CBT (16 sessions, 8 à 60 min. + 8 à 90 min.) WL/PCC | 2224 | Pre-to-post increase in CAPS (liberal) | n.a. | 100 | CAPS | USA | 34.00 (7.22) | r.b.i. | Individual | Compl. | 100 | Childhood sexual and/or physical abuse | 5 |
| Cloitre et al., 201012 STAIR/TF-CBT (16 sessions, 90 min.) Skills comparator/ACC (n.r.) | 2526 | ≥ 1 SD pre-to-post increase in CAPS OR absolute pre-to-post increase in CAPS of ≥ 7 points (conservative) | n.a. | 100 | CAPS | USA | 33.20 (n.r.)37.10 (n.r.) | 6 | IndividualIndividual | ITT | 100 | Childhood sexual and/or physical abuse | 8 |
| Davis et al., 202013 HYP/non-tf-Other (16 sessions, 90 min.) WLP/ACC (16 sessions, 90 min.) | 7070 | n.a. | Adverse events (unspecified) | 100 | CAPS | USA | 49.9 (12.6)51.2 (13.3) | 7 | GroupGroup | Compl. | 34 | Multiple types | 6 |
| Duffy et al., 200714 CBT/TF-CBT (12 sessions, n.r.)  WL/PCC | 2029 | Pre-to-post increase in PDS (liberal) | n.a. | 100 | PDS | Northern Ireland | 44.1 (11.3)43.7 (12.3) | r.b.i. | Individual | ITT | 3445 | Terror | 7 |
| Ehlers et al., 201415 Standard CT/TF-CBT (12 sessions, 20h in total)  EFST/non-tf-Other (12 sessions, 20h in total) WL/PCC  | 312730 | Absolute pre-to-post increase in CAPS or PDS of ≥ 10 points or 6,15 points, respectively (conservative) | Adverse events (significant increases indissociation,suicidal intent, or hyperarousal) | 100 | CAPS | UK | 41.50 (11.70)37.80 (9.90)36.80 (10.50) | 10 | IndividualIndividual | ITT | 585760 | Multiple types | 8 |
| Ertl et al., 201116 NET/TF-CBT (8 sessions, 90-120 min.)  SC/ACC (8 sessions, 90-120 min.) WL/PCC | 26a24a28a | Absolute pre-to-post increase in CAPS of ≥ 15 points (conservative) | n.a. | 100 | CAPS | Uganda | 18.66 (3.77)18.32 (4.30)18.07 (3.55) | 12 | IndividualIndividual | Compl. | 556843 | Various types including childhood soldier victimization | 6 |
| Foa et al., 201817 massed PE/TF-CBT (10 sessions, 90 min.) PCT/non-tf-Other (10 sessions, 90 min.) MA/PCC (4 sessions, 10-15 min.) | 938840 | n.a. | Serious adverse events (e.g., suicide attempt) and adverse events (unspecified) reported separately | 100 | PSS-I | USA | 32.65 (7.54) 32.54 (7.45)32.70 (7.68) | 6 | IndividualIndividual | ITT | 15155 | Combat | 8 |
| Forbes et al., 201218 CPT/TF-CBT (12 sessions, 60 min.) TAU/ACC (n.r.) | 2423 | n.a. | Adverse events (unspecified) | 100 | CAPS | Australia | 53.13 (13.97)53.62 (13.33) | 3 | IndividualIndividual | ITT | 70 | Combat | 7 |
| Ford et al., 201119 TARGET/tf-Other (12 sessions, 50 min.)  PCT/non-tf-Other (12 sessions, n.r.)  WL/PCC  | 343535 | CAVE: n.r. for WL. Absolute pre-to-post increase in CAPS of ≥ 7 points (conservative) | Serious adverse events (unspecified) | 807487 | CAPS | USA | 30.70 (6.90) | r.b.i. | IndividualIndividual | ITT | 100100100 | Multiple types | 6 |
| Ford et al., 201320 TARGET/tf-Other (12 sessions, 75 min.)  SGT/non-tf-Other (12 sessions, 75 min.)  | 3834 | Absolute pre-to-post increase in CAPS of ≥ 7 points (conservative) | Serious adverse events (requiring crisis care) | 8274 | CAPS | USA | 34.60 (8.60)38.00 (7.80) | n.a. | IndividualGroup | Compl. | 100100 | Multiple types | 6 |
| Galovski et al., 201221 MCPT/TF-CBT (4-18 sessions, n.r.) SMDT/PCC (n.r.) | 3837 | n.a. | Adverse events (unspecified) | 100 | CAPS | USA | 39.80 (11.74) | r.b.i. | Individual | ITT | 69 | Sexual or physical assault | 8 |
| Ghafoori et al., 201722 PE/TF-CBT (12 sessions, 60-90 min.) PCT/non-tf-Other (12 sessions, 60-90 min.)  | 4724 | n.a. | Adverse events (unspecified) | 100 | PCL-5 | USA | 35.10 (12.80)35.30 (10.40) | n.a. | IndividualIndividual | ITT | 8383 | Physical assault and other types | 6 |
| Gray et al., 201923 RTM/TF-CBT (3 sessions, 120 min.) WL/PCC | 3633 | n.a. | Serious adverse events (need for emergency treatment) | 100 | PSS-I | USA | 48.60 (13.30) | r.b.i. | Individual | ITT | 0 | Combat and other types | 7 |
| Gray et al., 202124 RTM/TF-CBT (3 sessions, ≤120 min.) WL/PCC | 1415 | n.a. | Adverse events (unspecified) | 100 | PSS-I | USA | n.r.n.r. | r.b.i. | Individual | ITT | 100 | Multiple types | 6 |
| Ivarsson et al., 201425 iCBT/TF-CBT (8 sessions, 28 min. of contact  to therapists on average) SC/ACC (n.r.) | 2629 | Reliable change index (IES-R, conservative) | n.a. | 100 | IES-R | Sweden | 44.80 (11.20)47.20 (12.20) | r.b.i. | Individual | ITT | 7787 | Multiple types | 8 |
| Johnson et al., 201126 HOPE/TF-CBT (12 sessions, 60-90 min.) TAU/ACC (n.r.) | 3434 | n.a. | Serious adverse events (unspecified) | 88.6085.70 | CAPS | USA | 32.55 (8.00) | 6 | IndividualGroup | Compl. | 100 | IPV | 5 |
| Johnson et al., 201627 HOPE/TF-CBT (16 sessions, 60 min.) TAU/ACC (n.r.) | 2625 | 50% pre-to-post increase in CAPS (conservative) | Incidence not reported separately for groups | 93.3096.70 | CAPS | USA | 33.30 (10.48) 33.20 (10.39) | 6 | IndividualGroup | Compl. | 100 | IPV and other types | 6 (Post + FU1)5 (FU2) |
| Johnson et al., 202028 HOPE/TF-CBT (16 sessions, 50– 60 min.) PCT+/non-tf-Other (16 sessions, 50– 60 min.) | 6577 | n.a. | Serious adverse events (unspecified) | 100 | CAPS | USA | 34.34 (9.46)35.87 (8.78) | 12 | IndividualIndividual | Compl. | 100 | IPV | 6 |
| Kearney et al., 202129 CPT-C/TF-CBT (12 sessions, 90 min.) LKM/non-tf-Other (12 sessions, 90 min.) | 5763 | Absolute pre-to-post increase in CAPS of ≥ 20 points (conservative) | Adverse events (increase of 2 PROMIS scores on PHQ-9) | 100 | CAPS | USA | 56.1 (13.7)58.2 (12.5) | 6 | GroupGroup | ITT | 16 | Multiple types | 8 |
| Kelly et al., 202130 CPT/TF-CBT (12 sessions, 90 min.) Trauma-Sensitive Yoga/non-tf-Other (10  sessions, 60 min.) | 2038 | n.a. | Adverse events (unspecified) | 100 | CAPS | USA | 48.38 (11.1) | 3 | GroupGroup | Compl. | 100 | Military Sexual Trauma | 5 (Post) 4 (FU) |
| Lang et al., 201931 CM/non-tf-Other (10 sessions, 90 min.) VC/ACC (10 sessions, 90 min.) | 1414 | n.a. | Adverse events (unspecified) | 100 | CAPS | USA | 49.10 (14.50) | n.a. | GroupGroup | Compl. | 25 | Combat | 5 |
| Langkaas et al., 201732 PE/TF-CBT (10 sessions, 90-120 min.) IR/tf-Other (10 sessions, 90-120 min.) | 3031 | Reliable change index (PSS-I, conservative) | n.a. | 100 | PSS-I | Norway | 45.20 (9.70) | 12 | IndividualIndividual | ITT | 58 | Multiple types | 8 |
| Lehavot et al., 202133 DESTRESS-WV/TF-CBT (16 sessions, n.r.)  Phone monitoring/ACC (9 sessions, 15 min.) | 4348 | Reliable change index (PCL-5, conservative) | n.a. | 100 | PCL-5 | USA | 49.9 (11.3)48.9 (12.2) | 6 | Individual | ITT | 100 | Multiple types | 7 |
| Lely et al., 201934 NET/TF-CBT (11 sessions, 90 min.) PCT/non-tf-Other (11 sessions, 90 min.) | 1512 | Absolute pre-to-post increase in CAPS of ≥ 10 points (conservative) | n.a. | 100 | CAPS | NL | 62.65 (5.89)62.47 (6.24) | 4 | IndividualIndividual | ITT | 2827 | Multiple types | 7 |
| Lewis et al., 201735 iCBT/TF-CBT (n.r.) WL/PCC | 1527 | n.a. | Adverse events (unspecified) | 100 | CAPS | UK | 39.29 (12.70) | 3 | Individual | ITT | 60 | Multiple types | 7 |
| Littleton et al., 201636 FSTTP/tf-Other (n.r.) iPSY-EDU/ACC (n.r.) | 2328 | Reliable change index (PSS-I, conservative) | Adverse events (significant worsening of depression or anxiety as defined by reliable change index) | 100 | PSS-I | USA | 22 (18-42) | 3 | IndividualIndividual | Compl. | 100 | Rape and other IPV | 6 (Post) 5 (FU1) |
| Litz et al., 202137 CPT-C/TF-CBT (12 sessions, 60 min.) AD/non-tf-Other (6-8 sessions, 90 min.) | 3337 | Reliable change index (CAPS, conservative) | Serious adverse events (e.g., suicide attempt) and adverse events (e.g., increased psychiatric symptoms) reported separately | 100 | CAPS | USA | 30.30 (6.43)29.80 (6.39) | r.b.i. | IndividualIndividual | Compl. | 8 | Combat | 6 |
| Markowitz et al., 201538 IPT/non-tf-Other (14 sessions, 50 min.) PE/TF-CBT (10 sessions, 90 min.) RT/ACC (10 sessions, 90 min.)  | 383630 | n.a. | Adverse events (worsening of comorbid symptoms such as depression) | 100 | CAPS | USA | 41.00 (9.10)47.50 (10.60)34.80 (5.10) | 3 | IndividualIndividualIndividual | ITT | 705588 | Multiple types | 7 |
| Mitchell et al., 201439 YI/non-tf-Other (12 sessions, 75 min.)  WL/PCC | 1412 | n.a. | Adverse events (unspecified) | 7171 | PCL | USA | 44.37(12.37) | 1 | Group | ITT | 100100 | Multiple types | 5 |
| Monson et al., 200640 CPT/TF-CBT (12 sessions, n.r.) WL/PCC | 2427 | Reliable change index (CAPS, conservative) | Serious adverse events (unspecified) | 100 | CAPS | USA | 54.00 (6.30) | 1 | Individual | ITT | 6,713,3 | Combat | 7 |
| Monson et al., 201241 CBCT/TF-CBT (15 sessions, n.r.) WL/PCC | 1619 | n.a. | Serious adverse events (severe intimate aggression) | 100 | CAPS | USA & Canada | 40.40 (11.30)33.80 (10.50) | r.b.i. | Couple | ITT | 6585 | Multiple types | 7 |
| NCT0060781542 CPT/TF-CBT (12 sessions, 65 min.) PCT/non-TF-PIs (12 sessions, 65. min) | 4336 | n.a. | Adverse events and serious adverse events (unspecified) | 100 | CAPS | USA | 29.50 (7.11)32.11 (7.85) | 12 | IndividualIndividual | ITT | 00 | Combat | 5 |
| Neuner et al., 201043 NET/TF-CBT (5-17 sessions, 120 min.) TAU/ACC (n.r.) | 1416 | Reliable change index (PDS, conservative) | n.a. | 100 | PDS | Germany (refugees) | 31.10 (7.80)31.60 (7.70) | 6 | IndividualIndividual | ITT | 3131 | Physical torture and other types | 7 |
| Nidich et al., 201844 PE/TF-CBT (12 sessions, 90 min.) TMed/non-tf-Other (12 sessions, 90 min.) HE/ACC (12 sessions, 90 min.) | 575356 | n.a. | Serious adverse events (e.g., drug overdose, psychiatric hospitalization) | 100 | CAPS | USA | 48.50 (15.60)46.40 (14.30)46.20 (16.40) | n.a. | IndividualIndividualIndividual | ITT | 181815 | Combat | 7 |
| Niles et al., 201245 t-MBSR/non-tf-Other (8 sessions; 2 f2f à 45 min., 6 tele à 20 min.) t-PSY-EDU/ACC (8 sessions; 2 f2f à 45 min., 6  tele à 20 min.) | 1314 | Absolute pre-to-post increase in CAPS or PCL-M of ≥ 20 points or 10 points, respectively (conservative) | Adverse events (unspecified) | 100 | CAPS (post)PCL-M (FU) | USA | 52.00 (13.00) | 1.50 | IndividualIndividual | Compl. | 0 | Combat or mass violence | 5 |
| Reger et al., 201646 PE/TF-CBT (10 sessions, 90-120 min.) WL/PCC | 3247 | Reliable change index (CAPS, conservative) | n.a. | 100 | CAPS | USA | 30.89 (7.09)30.39 (6.45) | r.b.i. | Individual | ITT | 42 | Nonsexualassault | 8 |
| Resick et al., 201547 gCPT/TF-CBT (12 sessions, 90 min.) gPCT/non-tf-Other (12 sessions, 90 min.) | 5351 | Absolute pre-to-post increase in PSS-I of ≥ 15 points (conservative) | Serious adverse events (e.g., suicide attempt) and adverse events (e.g., increased depression severity) reported separately | 100 | PSS-I | USA | 31.80 (7.30)32.40 (7.90) | 12 | GroupGroup | ITT | 78 | Combat and other types | 6 |
| Robjant et al., 201948 NET/TF-CBT (6 sessions á 90-120 min.  individual, 6 sessions á 90-120 group) TAU/ACC (n.r.) | 4344 | Reliable change index (PSS-I, conservative) | Adverse events (significant worsening of depression defined by reliable change index) | 100 | PSS-I | DRC | 18 (16-25)18 (16-25) | 9 | CombiIndividual | Compl. | 100 | Child soldiers | 7 |
| Schnurr et al., 200749 PE/TF-CBT (10 sessions, 90 min.) PCT/non-tf-Other (10 sessions, 90 min.) | 120126 | n.a. | Serious adverse events (suicide attempt, death, psychiatric hospitalization) | 100 | CAPS | USA | 44.60 (9.39)44.90 (9.47) | 6 | IndividualIndividual | ITT | 100 | Sexual Trauma and other types | 7 |
| Suris et al., 201350 CPT/TF-CBT (12 sessions, n.r.) PCT/non-tf-Other (12 sessions, n.r.) | 5234 | n.a. | Serious adverse events (e.g., suicide attempt by overdose) | 100 | CAPS | USA | 44.60 (10.50)48.40 (8.20) | 12 | IndividualIndividual | Compl. | 8388 | Military Sexual Trauma | 7 |
| Taylor et al., 200351PE/TF-CBT (8 sessions, 90 min.)EMDR/EMDR (8 sessions, 90 min.)RT/ACC (8 sessions, 90 min.) | 151515 | Pre-to-post increase in CAPS (liberal) | n.a. | 100 | CAPS | Canada | 37.00 (10.00) | 3 | IndividualIndividualIndividual | ITT | 75 | Multiple types | 6 |
| ter Heide et al., 201652EMDR/EMDR (9 sessions, 3x60+6x90 min.)TAU/ACC (12 sessions, 60 min.) | 3231 | Absolute pre-to-post increase in CAPS of ≥ 10 points (conservative) | Severe adverse events (e.g., suicide attempts) | 100 | CAPS | NL | 43.10 (10.70)39.80 (11.90) | 3 | IndividualIndividual | Compl | 1739 | Multiple types | 7 |
| van den Berg et al., 201553EMDR/EMDR (8 sessions, 90 min.)PE/TF-CBT (8 sessions, 90 min.) WL/PCC | 444739 | n.a. | Severe adverse events (unspecified) | 100 | CAPS | NL | 40.40 (11.30)42.60 (10.30)40.30 (9.70) | 6 | IndividualIndividual | ITT | 555751 | Multiple types | 8 |
| van Gelderen et al., 202054 3MDR/EMDR (6 sessions, 70-90 min.) NTCC/ACC | 1920 | Reliable change index (CAPS, conservative) | Serious adverse events (e.g., suicidal intent) | 100 | CAPS | NL | 42.41 (9.80)41.93 (9.12) | r.b.i. | IndividualIndividual | ITT | 4.50 | Multiple types | 7 |
| Wells et al., 201555 MCT/non-tf-Other (8 sessions, 60 min.) PE/TF-CBT (8 sessions, 60 min.) WL/PCC | 101010 | Reliable change index (IES, conservative) | n.a. | 100 | IES | UK | 40.60 (11.90)40.50 (10.90)42.70 (18.50) | 3 | IndividualIndividual | Compl. | 363640 | Multiple types | 6 |
| Zoellner et al., 201756 IE + Placebo/TF-CBT (5 sessions, 50 min.) WL/PCC | 1510 | n.a. | Adverse events (unspecified) | 100 | PSS-I | USA | 37.50 (12.40) | 3 | Individual | ITT | 71 | Multiple types | 6 |

Abbreviations: AD = Adaptive Disclosure; BSI = Brief Symptom Inventory; CAPS = Clinician-Administered PTSD Scale; CBCT = Cognitive-Behavior Couple Therapy; CBT = Cognitive-Behavioral Therapy; CBT long = trial involved an ordinary (i.e., long) version and a massed version (i.e., brief) of CBT delivery; CM = Compassion Meditation; Compl. = Completer analysis; CPT = Cognitive-Processing Therapy; CPT-C = Cognitive-Processing Therapy (cognitive only); CT = Cognitive Therapy; DBT-PTSD = Dialectic Behavior Therapy for PTSD; DESTRESS-WV = Delivery of Self Training and Education for Stressful Situations – Women Veterans version; DET = Dialogical Exposure Therapy; DRC = Democratic Republic of the Congo; EFST = Emotion Focused Supportive Therapy; EMDR = Eye Movement Desensitization and Reprocessing; f2f = face to face; FSTTP = From Survivor to Thriver Program; gCPT = Group Cognitive-Processing Therapy; gPCT = Group Present-Centered Therapy; GSI = Global Symptom Inventory; HE = Health Education; HOPE = Helping to Overcome PTSD through Empowerment; HYP = Holistic Yoga Program; iCBT = Internet-based Cognitive Behavioral Therapy; IE + placebo = Imaginal Exposure plus pill placebo; IES = Impact of Event Scale; IES-R = Impact of Event Scale - Revised; iPSY-EDU = Psycho-educational self-help website; IPT = Inter-Personal Therapy; IPV = Intimate Partner Violence; IR = Imagery Rescripting; ITT = Intent-To-Treat analysis; LKM = Loving-Kindness Meditation; MA = Minimal Attention; MCPT = Modified Cognitive Processing Therapy; MCT = Meta-Cognitive Therapy; min. = minutes; MM = Mantram Meditation; massed PE = trial involved a massed and a spaced version of PE delivery; n.a. = not assessed or not applicable; NET = Narrative Exposure Therapy; NL = the Netherlands; n.r. = not reported; NTCC = Non-specific Treatment Component Control; PCL-5 = PTSD Checklist for DSM-5; PCL-M = PTSD Check-List - Military Version; PCT = Present-Centered Therapy; PDS = Posttraumatic Diagnostic Scale; PE = Prolonged Exposure; PHQ-9 = Patient Health Questionnaire – 9 item version; PSS-I = PTSD Symptom Scale – Interview; PSY-EDU = Psychoeducation; r.b.i. = reported but irrelevant (i.e., no meaningful group comparison possible at follow-up); RT = Relaxation Therapy/Training; RTM = Reconsolidation of Traumatic Memories; SC = Supportive Counselling; SGT = Supportive Group Therapy; SMDT = Symptom-Monitoring Delayed Treatment group; SPT = Supportive Psychotherapy; STAIR = Skills Training in Affective and Interpersonal Regulation; TARGET = Trauma Affect Regulation Guide for Education and Therapy; TAU = Treatment-As-Usual; TF-CBT = Trauma-Focused Cognitive Behavioral Therapy; TMed = Transcendental Meditation; t-MBSR = telehealth Mindfulness-Based Stress Reduction; t-PSY-EDU = telehealth psychoeducation; UK = United Kingdom; USA = United States of America; VC = Veteran.Calm; WL = Wait-List control group; YI = Yoga Intervention.

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**56** Zoellner LA, Telch M, Foa EB, Farach FJ, McLean CP, Gallop R et al. Enhancing Extinction Learning in Posttraumatic Stress Disorder With Brief Daily Imaginal Exposure and Methylene Blue: A Randomized Controlled Trial. *J Clin Psychiatry* 2017; **78** (7): e782-e789.

**Supplement 6: Incidence and relative risk of pre-to-posttreatment deterioration (top) and pre-to-follow-up deterioration (bottom) – extended Table version.**

| **Comparison** | **k** | **Proportiona** | **τ2** | **95% CI** | **I2** | **NNT** | **kb** | **RR** | **95% CI** | **I2** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| ***PRE-TO-POSTTREATMENT*** |
| **Psychological interventionsvs. PCC – f2f data onlyc** | 8 | 0.83% | 0.00 | 0.00% - 3.32% | 0.00 | 9.76 | 6 | 0.21 | **0.15 – 0.28** | 0.00 |
| 8 | 11.08% | 0.04 | 2.82% - 22.88% | 82.20\*\*\* |
| **Psychological interventions vs. PCC – conservative data only** | 5 | 0.14% | 0.00 | 0.00% - 2.62% | 0.00 | 12.74 | 4 | 0.18 | **0.10 – 0.31** | 0.00 |
| 5 | 7.99% | 0.02 | 1.03% - 19.02% | 72.40\*\* |
| **TF-CBTdvs. PCC** | 8 | 0.85% | 0.00 | 0.00% - 3.33% | 0.00 | 9.78 | 6 | 0.21 | **0.15 – 0.28** | 0.00 |
| 8 | 11.08% | 0.04 | 2.82% - 22.88% | 82.20\*\*\* |
| **TF-CBTvs. PCC – conservative data only** | 5 | 0.16% | 0.00 | 0.00% - 2.66% | 0.00 | 12.77 | 4 | 0.18 | **0.11 – 0.29** | 0.00 |
| 5 | 7.99% | 0.02 | 1.03% - 19.02% | 72.40\*\* |
| **Psychological interventionsvs. ACC** | 9 | 0.38% | 0.00 | 0.00% - 2.21% | 0.00 | 25.06 | 8 | 0.36 | **0.14 – 0.92** | 0.00 |
| 9 | 4.37% | 0.01 | 1.10% - 9.07% | 46.20 |
| **Psychological interventions vs. ACC - conservative data only** | 8 | 0.46% | 0.00 | 0.00% - 2.42% | 0.00 | 26.04 | 7 | 0.36 | 0.12 – 1.09 | 0.00 |
| 8 | 4.30% | 0.01 | 0.89% - 9.36% | 51.80\* |
| **Psychological interventions vs. ACC – f2f data only** | 5 | 0.13% | 0.00 | 0.00% - 2.36% | 0.00 | 14.79 | 5 | 0.26 | **0.16 – 0.42** | 0.00 |
| 5 | 6.89% | 0.00 | 2.81% - 12.20% | 0.00 |
| **TF-CBTvs. ACC** | 7 | 0.58% | 0.00 | 0.00% - 2.74% | 0.00 | 26.95 | 7 | 0.41 | 0.14 – 1.17 | 0.00 |
| 7 | 4.29% | 0.00 | 1.11% - 8.86%  | 28.70 |
| **TF-CBTvs. ACC – conservative data only** | 6 | 0.74% | 0.00 | 0.00% - 3.07% | 0.00 | 28.74 | 6 | 0.42 | 0.11 – 1.53 | 0.00 |
| 6 | 4.22% | 0.01 | 0.92% - 9.12% | 38.10 |
| **TF-CBTvs. ACC – f2f data only** | 6 | 0.09% | 0.00 | 0.00% - 1.99% | 0.00 | 16.31 | 6 | 0.28 | **0.19 – 0.41** | 0.00 |
| 6 | 6.22% | 0.00 | 2.64% - 10.84% | 0.00 |
| **TF-CBTvs. other interventions** | 11 | 4.27% | 0.01 | 1.10% - 8.81% | 60.20 | 294.12 | 8 | 1.05 | 0.59 – 1.86 | 0.00 |
| 11 | 4.61% | 0.01 | 1.68% - 8.51% | 40.60 |
| **TF-CBTvs. other interventions – conservative data only** | 10 | 4.76% | 0.01 | 1.30% - 9.68% | 62.70\*\* | 303.03 | 8 | 1.05 | 0.59 – 1.86 | 0.00 |
| 10 | 5.09% | 0.01 | 1.94% - 9.26% | 42.80 |
| **TF-CBTvs. other interventions –individual data only/ outlier-adjustede** | 10 | 2.87% | 0.00 | 0.69% - 5.99% | 26.50 | 105.26 | 7 | 0.77 | 0.41 – 1.45 | 0.00 |
| 10 | 3.82% | 0.01 | 1.05% - 7.72% | 36.40% |
| ***PRE-TO-FOLLOW-UP*** |
| **Psychological interventionsvs. ACC** | 8 | 2.77% | 0.01 | 0.00% - 8.50% | 59.40\* | 19.69 | 6 | 0.61 | 0.14 – 2.69 | 31.30 |
| 8 | 7.85% | 0.02 | 1.91% -16.43% | 68.70\*\* |
| **Psychological interventions vs. ACC – conservative data only** | 6 | 4.33% | 0.02 | 0.09% - 12.20% | 62.60\* | 47.17 | 4 | 0.89 | 0.10 – 7.84 | 34.70 |
| 6 | 6.45% | 0.03 | 0.34% - 17.08% | 74.30\*\* |
| **Psychological interventions vs. ACC – f2f data only** | 6 | 2.42% | 0.02 | 0.00% - 9.96%  | 65.20\* | 10.28 | 5 | 0.55 | 0.17 – 1.81 | 7.70 |
| 6 | 12.15% | 0.01 | 4.53% - 22.18% | 54.00 |
| **TF-CBT vs. ACC** | 5 | 1.09% | 0.01 | 0.00% - 5.80% | 25.20 | 14.95 | 4 | 0.39 | 0.02 – 8.66 | 55.90 |
| 5 | 7.78% | 0.02 | 1.02% - 18.46% | 66.70\* |
| **TF-CBTvs. ACC – f2f data only** | 4 | 0.00% | 0.00 | 0.00% - 2.49% | 0.00 | 9.45 | 4 | 0.13 | **0.02 – 0.81** | 0.00 |
| 4 | 10.58% | 0.02 | 1.94% - 23.49% | 55.40 |
| **TF-CBTvs. other interventions** | 5 | 0.74% | 0.00 | 0.00% - 3.75% | 0.00 | 30.12 | 4 | 0.39 | 0.13 – 1.21 | 0.00 |
| 5 | 4.06% | 0.01 | 0.15% - 11.07% | 47.20 |
| **TF-CBTvs. other interventions – conservative data only** | 4 | 0.98% | 0.00 | 0.00% - 4.35% | 0.00 | 34.13 | n.a. (*k* = 3) |
| 4 | 3.91% | 0.01 | 0.00% - 12.43% | 58.00 |
| **TF-CBTvs. other interventions – individual data only** | 4 | 0.38% | 0.00 | 0.00% - 4.05% | 0.00 | 19.80 | n.a. (*k* = 3) |
| 4 | 5.43% | 0.01 | 0.02% - 15.97% | 54.40 |

ACC = Active Control Conditions; CI =confidence interval; conservative data only = only includes trials assessing clinically significant deterioration (rather than any deterioration); f2f data only = only includes trials with face-to-face delivery of intervention (rather than mainly or fully internet/technology-based delivery); I2 = amount of unexplained variance (in %) including the magnitude of statistical significance of the corresponding Q statistic as indicated by the asterisks; individual data only = only includes trials with individual delivery format of intervention (rather than group or mixed format); *k* = number of trials included in the analysis for the given comparison; n.a. = not applicable; NNT = numbers-needed-to-treat (i.e., to avoid one case of deterioration when the given treatment is compared to the given control group/other intervention); other intervention = other interventions (i.e., non-TF-CBT interventions); PCC = Passive Control Conditions; RR = relative risk; TF-CBT = Trauma-Focused Cognitive Behavior Therapy. Data in **bold** **font** indicates that 95% CI of RR excludes the null (i.e., differential risk).
anote that proportion refers to the proportion of participants per group who deteriorated (i.e., worsening of PTSD symptomatology) bnote that trials with zero cases (i.e., deterioraters) for both comparison groups did not contribute to the RR calculation (i.e., absolute risk = 0.00) and are therefore not part of *k*cnote that all trials comparing with a passive control condition and reporting on pre-to-posttreatment deterioration delivered the psychological intervention in individual delivery format dnote that the number of trials is the same to the overarching analysis (i.e., all psychological interventions) since one of the trials was a multi-arm trial that also included a TF-CBT arm enote that this analysis is identical to the outlier-adjusted analysis since the identified outlier (i.e., Resick et al.) was the only study applying a non-individual format (i.e., group treatment)\* *p* < .05, \*\* *p* < .01, \*\*\* *p* < .001

| **Supplement 7:** **Moderator results – incidences of pre-to-posttreatment deterioration.** |
| --- |
| **Comparison** | **Analyzed potential moderator** | **ka** | **b1** | **I2** |
| **TF-CBT**  | % with depressive comorbidity | n.a. (*k* = 5) |
| Trial quality/risk of bias | 11 | -0.04 | 58.18\* |
| Age | 11 | < 0.00 | 62.88\*\* |
| % females | 11 | < -0.00 | 62.76\*\* |
| % on concurrent psychotropic medication | n.a. (*k* = 6) |
| Total treatment length in minutes | 10 | < 0.00 | 61.45\*\* |
| **vs. other interventions** | % with depressive comorbidity | n.a. (*k* = 5) |
| Trial quality/risk of bias | 11 | 0.01 | 48.06 |
| Age | 11 | < 0.00 | 46.50 |
| % females | 11 | < 0.00 | 47.59 |
| % on concurrent psychotropic medication | n.a. (*k* = 6) |
| Total treatment length in minutes | 10 | < 0.00 | 25.55 |
| **TF-CBT**  | % with depressive comorbidity | n.a. (*k* = 5) |
| Trial quality/risk of bias | 10 | -0.05 | 59.06\* |
| Age | 10 | < 0.00 | 65.57\*\* |
| % females | 10 | < -0.00 | 65.71\*\* |
| % on concurrent psychotropic medication | n.a. (*k* = 5) |
| Total treatment length in minutes | n.a. (*k* = 9) |
| **vs. other interventions** **- conservative data only** | % with depressive comorbidity | n.a. (*k* = 5) |
| Trial quality/risk of bias | 10 | 0.01 | 50.58\* |
| Age | 10 | < 0.00 | 49.07 |
| % females | 10 | < 0.00 | 49.63 |
| % on concurrent psychotropic medication | n.a. (*k* = 5) |
| Total treatment length in minutes | n.a. (*k* = 9) |
| **TF-CBT**  | % with depressive comorbidity | n.a. (*k* = 5) |
| Trial quality/risk of bias | 10 | -0.01 | 33.18 |
| Age | 10 | < 0.00 | 32.21 |
| % females | 10 | < 0.00 | 24.11 |
| % on concurrent psychotropic medication | n.a. (*k* = 6) |
| Total treatment length in minutes | n.a. (*k* = 9) |
| **vs. other interventions** **- individual data only** | % with depressive comorbidity | n.a. (*k* = 5) |
| Trial quality/risk of bias | 10 | 0.03 | 42.94 |
| Age | 10 | < 0.00 | 39.84 |
| % females | 10 | < 0.00 | 37.91 |
| % on concurrent psychotropic medication | n.a. (*k* = 6) |
| Total treatment length in minutes | n.a. (*k* = 9) |

Conservative data only = only trials included with a definition targeting clinically significant deterioration (rather than any pre-to-post deterioration); I2 = remaining amount of unexplained variance including the magnitude of statistical significance of the corresponding Q statistic as indicated by the asterisks; individual data only = only trials included that delivered the psychological intervention in individual format (rather than group or mixed format); k = number of trials included in the analysis for the given comparison; n.a. = number of trials too small (k < 10) to conduct analysis; other interventions = non-TFCBT interventions (e.g., EMDR); TF-CBT = Trauma-Focused Cognitive Behavior Therapy.
anote that number of trials may differ depending on how many trials reported information on the respective moderator
\* *p* < .05, \*\* *p* < .01, \*\*\* *p* < .001

**Supplement 8: Publication bias and outlier checks.**

Note: In line with recommendations, publication bias checks were only performed when k ≥ 10. Heterogeneity and radial plots are only depicted when an outlier was identified.



Forest plot depicting the incidences of pre-to-posttreatment deterioration for Trauma-Focused Cognitive Behavior Therapy

Abbreviations. CT = Cognitive Therapy; CPT = Cognitive Processing Therapy; gCPT = group Cognitive Processing Therapy; NET = Narrative exposure therapy; PE = Prolonged exposure; TARGET = Trauma Affect Regulation: Guide for Education and Therapy.


Funnel plot - incidences of pre-to-posttreatment deterioration for Trauma-Focused Cognitive Behavior Therapy


Heterogeneity plot - incidences of pre-to-posttreatment deterioration for Trauma-Focused Cognitive Behavior Therapy



Radial plot - incidences of pre-to-posttreatment deterioration for Trauma-Focused Cognitive Behavior Therapy


Forest plot depicting incidences of pre-to-posttreatment deterioration for other psychological interventions

Abbreviations. AD = Adaptive Disclosure; EFST = Emotion-Focused Supportive Therapy; EMDR = Eye Movement Desensitization and Reprocessing; IR = Imagery Rescripting; LKM = Loving Kindness Meditation; MCT = Meta-Cognitive Therapy; PCT = Present Centered Therapy; SGT = Supportive Group Therapy


Funnel plot - incidences of pre-to-posttreatment deterioration for other psychological interventions


Heterogeneity plot - incidences of pre-to-posttreatment deterioration for other psychological interventions


Radial plot - incidences of pre-to-posttreatment deterioration for other psychological interventions



Forest plot depicting the incidences of pre-to-posttreatment adverse events for psychological interventions

Abbreviations. CT = Cognitive Therapy; IE = Imaginal Exposure; massed PE = massed Prolonged Exposure (i.e., intensely delivered PE); MCPT = Modified Cognitive Processing Therapy; RTM = Reconsolidation of Traumatic Memories; SE = Somatic Experiencing; TF-CBT = Trauma-Focused Cognitive Behavior Therapy; YI = Yoga Intervention.


Funnel plot - incidences of pre-to-posttreatment adverse events for psychological interventions


Heterogeneity plot - incidences of pre-to-posttreatment adverse events for psychological interventions


Radial plot - incidences of pre-to-posttreatment adverse events for psychological interventions


Forest plot depicting the incidences of pre-to-posttreatment adverse events for passive control conditions

Abbreviations. SMDT = Symptom Monitoring Delayed Treatment; WL = Wait-List controls.


Funnel plot - incidences of pre-to-posttreatment adverse events for passive control conditions


Heterogeneity plot - incidences of pre-to-posttreatment adverse events for passive control conditions


Radial plot - incidences of pre-to-posttreatment adverse events for passive control conditions

| **Supplement 9: Moderator results – incidences of pre-to-posttreatment adverse events.** |
| --- |
| **Comparison** | **Analyzed potential moderator** | **ka** | **b1** | **I2** |
| **Psychological interventions** | % with depressive comorbidity | n.a. (*k* = 5) |
| Trial quality/risk of bias | 10 | 0.00 | 74.04\*\*\* |
| Age | 10 | -0.02\* | 53.37\* |
| % females | 10 | -0.00 | 67.71\*\* |
| % on concurrent psychotropic medication | n.a. (*k* = 3) |
| Total treatment length in minutes | n.a. (*k* = 6) |
| **vs. PCC** | % with depressive comorbidity | n.a. (*k* = 5) |
| Trial quality/risk of bias | 10 | -0.01 | 69.25\*\*\* |
| Age | 10 | -0.02 | 55.50\* |
| % females | 10 | -0.00 | 64.97\*\* |
| % on concurrent psychotropic medication | n.a. (*k* = 4) |
| Total treatment length in minutes | n.a. (*k* = 7) |

I2 = remaining amount of unexplained variance including the magnitude of statistical significance of the corresponding Q statistic as indicated by the asterisks; k = number of trials included in the analysis for the given comparison; n.a. = number of trials too small (k < 10) to conduct analysis; PCC = Passive Control Conditions.
anote that number of trials may differ depending on how many trials reported information on the respective moderator
\* *p* < .05, \*\* *p* < .01, \*\*\* *p* < .001

| **Supplement 10: Moderator results – incidences of pre-to-posttreatment serious adverse events.** |
| --- |
| **Comparison** | **Analyzed potential moderator** | **ka** | **b1** | **I2** |
| **TF-CBT** | % with depressive comorbidity | n.a. (*k* = 3) |
| Trial quality/risk of bias | 12 | 0.04 | 0.00 |
| Age | 12 | 0.01 | 0.00 |
| % females | 12 | -0.00 | 25.25 |
| % on concurrent psychotropic medication | n.a. (*k* = 4) |
| Total treatment length in minutes | n.a. (*k* = 9) |
| **vs. other interventions** | % with depressive comorbidity | n.a. (*k* = 3) |
| Trial quality/risk of bias | 12 | 0.08 | 51.25\* |
| Age | 12 | 0.01 | 61.95\*\* |
| % females | 12 | -0.00 | 67.56\*\*\* |
| % on concurrent psychotropic medication | n.a. (*k* = 4) |
| Total treatment length in minutes | n.a. (*k* = 9) |
| **TF-CBT** | % with depressive comorbidity | n.a. (*k* = 3) |
| Trial quality/risk of bias | 11 | 0.04 | 0.00 |
| Age | 11 | 0.00 | 0.00 |
| % females | 11 | -0.00 | 0.00 |
| % on concurrent psychotropic medication | n.a. (*k* = 4) |
| Total treatment length in minutes | n.a. (*k* = 8) |
| **vs. other interventions** | % with depressive comorbidity | n.a. (*k* = 3) |
| Trial quality/risk of bias | 11 | 0.07 | 53.68\* |
| Age | 11 | 0.01 | 63.70\*\* |
| % females | 11 | -0.00 | 66.12\*\*\* |
| % on concurrent psychotropic medication | n.a. (*k* = 4) |
| Total treatment length in minutes | n.a. (*k* = 8) |

I2 = remaining amount of unexplained variance including the magnitude of statistical significance of the corresponding Q statistic as indicated by the asterisks; individual data only = only trials included that delivered the psychological intervention in individual format (rather than group or mixed format); k = number of trials included in the analysis for the given comparison; n.a. = number of trials too small (k < 10) to conduct analysis; other interventions = non-TF-CBT interventions (e.g., EMDR); TF-CBT = trauma-focused cognitive behavior therapy.
anote that number of trials may differ depending on how many trials reported information on the respective moderator
\* *p* < .05, \*\* *p* < .01, \*\*\* *p* < .001

|  |
| --- |
| **Supplement 11: Risk of bias assessment.** |
| **Trial** | **Q1 -100% PTSD rate** | **Q2 -manual-based** | **Q3 -therapist training** | **Q4 -integrity checks** | **Q5 -ITT analyses** | **Q6 – N > 50** | **Q7 -independent randomization** | **Q8 -blinded outcome assessment** | **Q sum score (out of 8)** |
| Andersen et al. (2021) | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 7 |
| Blanchard et al. (2003) | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 6 |
| Bohus et al. (2013) | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 7 |
| Bormann et al. (2013) | 1 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 6 |
| Brom et al. (2017) | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 7 |
| Bryant et al. (2011) | 1 | 0 | 1 | 0 | 1 | 0 | 1 | 1 | 5 |
| Bryant et al. (2019) | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 1 | 4 |
| Buhmann et al. (2016) | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 7 |
| Butollo et al. (2016) | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 7 |
| Chard (2005) | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 1 | 6 |
| Cloitre et al. (2002) | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 5 |
| Cloitre et al. (2010) | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 8 |
| Davis et al. (2020) | 1 | 1 | 0 | 1 | 0 | 1 | 1 | 1 | 6 |
| Duffy et al. (2007) | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 7 |
| Ehlers et al. (2014) | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 8 |
| Ertl et al. (2011) | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 1 | 6 |
| Foa et al. (2018) | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 8 |
| Forbes et al. (2012) | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 7 |
| Ford et al. (2011) | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 6 |
| Ford et al. (2013) | 0 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 6 |
| Galovski et al. (2012) | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 8 |
| Ghafoori et al. (2017) | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 6 |
| Gray et al. (2019) | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 7 |
| Gray et al. (2020) | 1 | 1 | 1 | 1 | 0 | 0 | 1 | 1 | 6 |
| Ivarsson et al. (2014) | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 8 |
| Johnson et al. (2011) | 0 | 1 | 1 | 1 | 0 | 1 | 1 | 0 | 5 |
| Johnson et al. (2016) posttreatment | 0 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 6 |
| Johnson et al. (2016) follow-up | 0 | 1 | 1 | 1 | 0 | 0 | 1 | 1 | 5 |
| Johnson et al. (2020) | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 1 | 6 |
| Kearney et al. (2021) | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 8 |
| Kelly et al. (2021) posttreatment | 1 | 1 | 1 | 0 | 0 | 1 | 1 | 0 | 5 |
| Kelly et al. (2021) follow-up | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 0 | 4 |
| Lang et al. (2019) | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 5 |
| Langkaas et al. (2017) | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 8 |
| Lehavot et al. (2021) | 1 | 0 | 1 | 1 | 1 | 1 | 0 | 1 | 7 |
| Lely et al. (2019) | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 7 |
| Lewis et al. (2017) | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 7 |
| Littleton et al. (2016) posttreatment | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 0 | 6 |
| Littleton et al. (2016) follow-up | 1 | 1 | 1 | 1 | 0 | 0 | 1 | 0 | 5 |
| Litz et al. (2021) | 1 | 1 | 0 | 1 | 0 | 1 | 1 | 1 | 6 |
| Markowitz et al. (2015) | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 7 |
| Mitchell et al. (2014) | 0 | 1 | 1 | 0 | 1 | 0 | 1 | 1 | 5 |
| Monson et al. (2006) | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 7 |
| Monson et al. (2012) | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 7 |
| NCT00607815 | 1 | 1 | 0 | 0 | 1 | 1 | 0 | 1 | 5 |
| Neuner et al. (2010) | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 7 |
| Nidich et al. (2018) | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 7 |
| Niles et al. (2012) | 1 | 1 | 1 | 1 | 0 | 0 | 1 | 0 | 5 |
| Reger et al. (2016) | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 8 |
| Resick et al. (2015) | 1 | 0 | 1 | 1 | 1 | 1 | 0 | 1 | 6 |
| Robjant et al. (2019) | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 7 |
| Schnurr et al. (2007) | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 7 |
| Suris et al. (2013) | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 7 |
| Taylor et al. (2003) | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 1 | 6 |
| ter Heide et al. (2016) | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 7 |
| van den Berg et al. (2015) | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 8 |
| van Gelderen et al. (2020) | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 7 |
| Wells et al. (2015) | 1 | 1 | 1 | 1 | 0 | 0 | 1 | 1 | 6 |
| Zoellner et al. (2017) | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 6 |