Supplementary Online Content

Merz J, Schwarzer G, Gerger H. Comparative efficacy and acceptability of pharmacological, psychotherapeutic, and combination treatments in adults with posttraumatic stress disorder: a network meta-analysis. *JAMA Psychiatry*. Published online June 12, 2019. doi:10.1001/jamapsychiatry.2019.0951

This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix 1. Search Terms

MEDLINE (Ovid)

Diagnosis	Exp Anxiety Disorders/
	((trauma* adj3 stress) or (stress adj3 disorder*) or PTSD).tw.
Design	randomized controlled trial.pt. OR controlled clinical trial.pt. OR randomized.ab. OR placebo.ab. OR clinical trials as topic.sh. OR randomly.ab. OR trial.ti,ab. OR groups.ab.
Intervention	psychotherapy/ or aromatherapy/ or art therapy/ or autogenic training/ or behavior therapy/ or aversive therapy/ or "biofeedback (psychology)"/ or cognitive therapy/ or desensitization, psychologic/ or implosive therapy/ or relaxation techniques/ or meditation/ or bibliotherapy/ or color therapy/ or crisis intervention/ or dance therapy/ or gestalt therapy/ or hypnosis/ or suggestion/ or autosuggestion/ or "imagery (psychotherapy)"/ or music therapy/ or nondirective therapy/ or psychoanalytic therapy/ or free association/ or transactional analysis/ or psychotherapeutic processes/ or abreaction/ or catharsis/ or association/ or "countertransference (psychology)"/ or psychotherapy, brief/ or psychotherapy, multiple/ or psychotherapy, rational-emotive/ or reality therapy/ or socioenvironmental therapy/ or milieu therapy/ or therapeutic community/ or psychodrama/ or role playing/
	(Psychotherap* or ((centered or based or focused or oriented or acceptance or attachment or behavio?r* or analytic* or brief or person or cognitive or dynamic or energetic or coherence or collaborative or contemplative or dasein* or drama* or emotion* or feminist or sensiti?ation or existen* or exposure or gestalt or holistic or humanistic or hypno* or integr* or short-term* or shortterm* or long-term* or longterm* or interpersonal* or inter-personal* or logo* or mindfulness* or multimodal or multi-modal or narrative or positive or provocative or psychol* or rational* or reality or solution* or system* or transactional* or transpersonal or eclectic* or experiential* or expressive* or individual or insight* or persuasion or relationship or supportive* or implosive or inhibition or aversion or relaxation or talk or confront* or schema*) adj5 (treatment* or therapy or therapies)) or intervention*).tw.
Humans	Humans/

EMBASE (Ovid)

Diagnosis	posttraumatic stress disorder/
	(see Medline term list of text words referring to posttraumatic stress disorder)
Design	exp controlled clinical trial/ or comparative study/ or treatment outcome/ or random*.tw. or clinical trial*.tw.
Intervention	counter transference/ or crisis intervention/ or hypnosis/ or psychoanalysis/ or suggestion/ or transference/ or psychotherapy/ or art therapy/ or assertive training/ or autogenic training/ or aversion therapy/ or behavior contracting/ or behavior modification/ or behavior therapy/ or cognitive behavioral stress management/ or cognitive rehabilitation/ or cognitive therapy/ or gestalt therapy/ or guided imagery/ or milieu therapy/ or music therapy/ or pet therapy/ or psychodrama/ or relaxation training/ or role playing/ or sex therapy/ or sociotherapy/ or therapeutic community/ or validation therapy/
	(see Medline term list of text words referring to psychological interventions)
Humans	"Human" [Subjects]

PsycINFO (Ovid)

Diagnosis	posttraumatic stress disorder/ OR emotional trauma/ OR stress reactions/ OR traumatic neurosis/
	(see Medline term list of text words referring to posttraumatic stress disorder)
Design	(random* or placebo* or assign* or allocat*).mp. or (control* or compar* or ((clin* or evaluat* or prospectiv*) adj3 (trial* or studi* or study))).tw. or exp treatment effectiveness evaluation/ or exp experimental design/ or versus.id. or vs.id.

Intervention	psychotherapy/ or adlerian psychotherapy/ or adolescent psychotherapy/ or analytical psychotherapy/ or autogenic training/ or brief psychotherapy/ or client centered therapy/ or cognitive behavior therapy/ or eclectic psychotherapy/ or emotion focused therapy/ or existential therapy/ or experiential psychotherapy/ or expressive psychotherapy/ or eye movement desensitization therapy/ or feminist therapy/ or geriatric psychotherapy/ or gestalt therapy/ or guided imagery/ or individual psychotherapy/ or insight therapy/ or integrative psychotherapy/ or interpersonal psychotherapy/ or logotherapy/ or narrative therapy/ or persuasion therapy/ or primal therapy/ or psychodrama/ or psychodynamic psychotherapy/ or rational emotive behavior therapy/ or reality therapy/ or relationship therapy/ or solution focused therapy/ or supportive psychotherapy/ or transactional analysis/ or exp behavior therapy/ or exp exposure therapy/ or exp aversion therapy/ or exp humanistic psychotherapy/ or exp hypnotherapy/ or exp psychoanalysis/ or psychotherapeutic counseling/ or behavior modification/ or biofeedback training/ or exp contingency management/ or "fading (conditioning)"/ or exp self management/ or bibliotherapy/ or computer assisted therapy/ or movement therapy/ or multimodal treatment approach/ or online therapy/ or partial hospitalization/ or personal therapy/ or sex therapy/ or exp cognitive techniques/ or exp creative arts therapy/ or exp cross cultural treatment/ or outpatient treatment/ or animal assisted therapy/ or mirroring/ or morita therapy/ or motivational interviewing/ or mutual storytelling technique/ or paradoxical techniques/ or exp relaxation therapy/
	(see Medline term list of text words referring to psychological interventions)

CENTRAL

Diagnosis	Stress, Psychological (Explode Tree 1) OR Anxiety Disorders (Explode all trees)
	(trauma* NEAR3 stress) OR (stress NEAR3 disorder*) OR PTSD
Design	-
Intervention	Psychotherapy (explode all trees)
	Psychotherap* or intervention* or (Centered NEAR5 treatment*) or (Centered NEAR5 therapy) or (Centered NEAR5 therapies) or (based NEAR5 treatment*) or (based NEAR5 therapy) or (based NEAR5 therapies) or (acceptance NEAR5 treatment*) or (acceptance NEAR5 therapy) or (acceptance NEAR5 therapies) or (attachment NEAR5 treatment*) or (attachment NEAR5 therapy) or (attachment NEAR5 therapies) or (behavio?r* NEAR5 treatment*) or (behavio?r* NEAR5 therapy) or (behavio?r* NEAR5 therapies) or (analytic* NEAR5 treatment*) or (analytic* NEAR5 therapy) or (analytic* NEAR5 therapies) or (brief NEAR5 treatment*) or (brief NEAR5 therapy) or (brief NEAR5 therapies) or (person NEAR5 treatment*) or (person NEAR5 therapy) or (person NEAR5 therapies) or (cognitive NEAR5 treatment*) or (cognitive NEAR5 therapy) or (cognitive NEAR5 therapies) or (dynamic NEAR5 treatment*) or (dynamic NEAR5 therapy) or (dynamic NEAR5 therapies) or (energetic NEAR5 treatment*) or (energetic NEAR5 therapy) or (energetic NEAR5 therapies) or (coherence NEAR5 treatment*) or (coherence NEAR5 therapy) or (coherence NEAR5 therapies) or (collaborative NEAR5 treatment*) or (collaborative NEAR5 therapy) or (collaborative NEAR5 therapies) or (contemplative NEAR5 treatment*) or (contemplative NEAR5 therapy) or (contemplative NEAR5 therapies) or (dasein* NEAR5 treatment*) or (dasein* NEAR5 therapy) or (dasein* NEAR5 therapies) or (drama* NEAR5 treatment*) or (drama* NEAR5 therapy) or (drama* NEAR5 therapies) or (emotion* NEAR5 treatment*) or (emotion* NEAR5 therapy) or (emotion* NEAR5 therapies) or (feminist NEAR5 treatment*) or (feminist NEAR5 therapy) or (feminist NEAR5 therapies) or (sensiti?ation NEAR5 treatment*) or (sensiti?ation NEAR5 therapy) or (sensiti?ation NEAR5 therapies) or (existen* NEAR5 treatment*) or (existen* NEAR5 therapy) or (existen* NEAR5 therapies) or (exposure NEAR5 treatment*) or (exposure NEAR5 therapy) or (exposure NEAR5 therapies) or (gestalt NEAR5 treatment*) or (gestalt NEAR5 therapy) or (gestalt NEAR5 therapies) or (holistic NEAR5 treatment*) or (holistic NEAR5 therapy) or (holistic NEAR5 therapies) or (humanistic NEAR5 treatment*) or (humanistic NEAR5 therapy) or (humanistic NEAR5 therapies) or (hypno* NEAR5 treatment*) or (hypno* NEAR5 therapy) or (hypno* NEAR5 therapies) or (integr* NEAR5 treatment*) or (integr* NEAR5 therapy) or (integr* NEAR5 therapies) or (short-term* NEAR5 treatment*) or (short-term* NEAR5 therapy) or (short-term* NEAR5 therapies) or (interpersonal* NEAR5 treatment*) or (interpersonal* NEAR5 therapy) or (interpersonal* NEAR5 therapies) or (logo* NEAR5 treatment*) or (logo* NEAR5 therapy) or (logo* NEAR5 therapies) or (mindfulness* NEAR5 treatment*) or (mindfulness* NEAR5 therapy) or (mindfulness* NEAR5 therapies) or (multimodal NEAR5 treatment*) or (multimodal NEAR5 therapy) or (multimodal NEAR5 therapies) or (narrative NEAR5 treatment*) or (narrative NEAR5 therapy) or (narrative NEAR5 therapies) or (positive NEAR5 treatment*) or (positive NEAR5 therapy) or (positive NEAR5 therapies) or (provocative NEAR5 treatment*) or (provocative NEAR5 therapy) or (provocative NEAR5 therapies) or (short-term NEAR5 treatment*) or (short-term NEAR5 therapy) or (short-term NEAR5 therapies) or (psychol* NEAR5 treatment*) or (psychol* NEAR5 therapy) or (psychol* NEAR5 therapies) or (oriented NEAR5 treatment*) or (oriented NEAR5 therapy) or (oriented NEAR5 therapies) or (rational* NEAR5 treatment*) or (rational* NEAR5 therapy) or (rational* NEAR5 therapies) or (reality NEAR5 treatment*) or (reality NEAR5 therapy) or (reality NEAR5 therapies) or (solution* NEAR5 treatment*) or (solution* NEAR5 therapy) or (solution* NEAR5 therapies) or (system* NEAR5

	treatment*) or (system* NEAR5 therapy) or (system* NEAR5 therapies) or (transactional* NEAR5 treatment*) or (transactional* NEAR5 therapy) or (transactional* NEAR5 therapies) or (transpersonal NEAR5 treatment*) or (transpersonal NEAR5 therapy) or (transpersonal NEAR5 therapies) or (eclectic* NEAR5 treatment*) or (eclectic* NEAR5 therapy) or (eclectic* NEAR5 therapies) or (experiential* NEAR5 treatment*) or (experiential* NEAR5 therapy) or (experiential* NEAR5 therapies) or (expressive* NEAR5 treatment*) or (expressive* NEAR5 therapy) or (expressive* NEAR5 therapies) or (individual NEAR5 treatment*) or (individual NEAR5 therapy) or (individual NEAR5 therapies) or (insight* NEAR5 treatment*) or (insight* NEAR5 therapy) or (insight* NEAR5 therapies) or (persuasion NEAR5 treatment*) or (persuasion NEAR5 therapy) or (persuasion NEAR5 therapies) or (relationship NEAR5 treatment*) or (relationship NEAR5 therapy) or (relationship NEAR5 therapies) or (supportive* NEAR5 treatment*) or (supportive* NEAR5 therapy) or (supportive* NEAR5 therapies) or (implosive NEAR5 treatment*) or (implosive NEAR5 therapy) or (implosive NEAR5 therapies) or (inhibition NEAR5 treatment*) or (inhibition NEAR5 therapy) or (inhibition NEAR5 therapies) or (aversion NEAR5 treatment*) or (aversion NEAR5 therapy) or (aversion NEAR5 therapies) or (focused NEAR5 treatment*) or (focused NEAR5 therapy) or (focused NEAR5 therapies) or (shortterm* NEAR5 treatment*) or (shortterm* NEAR5 therapy) or (shortterm* NEAR5 therapies) or (long-term* NEAR5 treatment*) or (long-term* NEAR5 therapy) or (long-term* NEAR5 therapies) or (longterm* NEAR5 treatment*) or (longterm* NEAR5 therapy) or (longterm* NEAR5 therapies) or (inter-personal* NEAR5 treatment*) or (inter-personal* NEAR5 therapy) or (inter-personal* NEAR5 therapies) or (multi-modal NEAR5 treatment*) or (multi-modal NEAR5 therapy) or (multi-modal NEAR5 therapies) or (relaxation NEAR5 treatment*) or (relaxation NEAR5 therapy) or (relaxation NEAR5 therapies) or (talk NEAR5 treatment*) or (talk NEAR5 therapy) or (talk NEAR5 therapies) or (confront* NEAR5 treatment*) or (confront* NEAR5 therapy) or (confront* NEAR5 therapies) or (schema* NEAR5 treatment*) or (schema* NEAR5 therapy) or (schema* NEAR5 therapies)

Psyndex (Ovid)

Diagnosis	posttraumatic stress disorder/ OR emotional trauma/ OR stress reactions/ OR traumatic neurosis/
	((trauma* adj3 stress) or (trauma* adj3 belastung*) or (stress adj3 stoerung*) or (Belastung* adj3 stoerung*) or belastungsstoerung* or PTSD or PTB or PTBS).tw.
Design	(random* or zufa?l* or placebo* or zuweis*).mp. or (kontrol* or kompar* or relativ* or vergleich* or ((klin* or evaluat* or prospektiv*) adj3 (trial* or studi* or untersuch*))).tw. or exp treatment effectiveness evaluation/ or exp experimental design/ or versus.id. or vs.id.
Intervention	psychotherapy/ or adlerian psychotherapy/ or adolescent psychotherapy/ or analytical psychotherapy/ or autogenic training/ or brief psychotherapy/ or client centered therapy/ or cognitive behavior therapy/ or eclectic psychotherapy/ or emotion focused therapy/ or existential therapy/ or experiential psychotherapy/ or expressive psychotherapy/ or eye movement desensitization therapy/ or feminist therapy/ or geriatric psychotherapy/ or gestalt therapy/ or guided imagery/ or individual psychotherapy/ or insight therapy/ or integrative psychotherapy/ or interpersonal psychotherapy/ or logotherapy/ or narrative therapy/ or persuasion therapy/ or primal therapy/ or psychodrama/ or psychodynamic psychotherapy/ or rational emotive behavior therapy/ or reality therapy/ or relationship therapy/ or solution focused therapy/ or supportive psychotherapy/ or transactional analysis/ or exp behavior therapy/ or implosive therapy/ or reciprocal inhibition therapy/ or "response cost"/ or systematic desensitization therapy/ or exp aversion therapy/ or covert sensitization/ or exp exposure therapy/ or implosive therapy/ or systematic desensitization therapy/ or exp humanistic psychotherapy/ or existential therapy/ or gestalt therapy/ or humanism/ or exp humanistic psychology/ or transpersonal psychology/ or exp hypnotherapy/ or "age regression (hypnotic)"/ or exp psychoanalysis/ or dream analysis/ or self analysis/ or exp psychotherapeutic counseling/
	(Psychotherap* or Intervention* or (Zentriert* or Basiert* or Fundiert* or Fokussiert* or Akzeptanz or Bindung* or Verhalten* or Behavio?r* or Analytisch* or Kurz* or Person* or Kognitiv* or Dynamisch* or Energetisch* or Kohaerenz or Kollaborativ* or Kontemplativ* or dasein* or drama* or emotion* or Feministisch* or Sensibilisierung* or existen* or Exposition* or Gestalt* or Holistisch* or Ganzheitlich* or Humanistisch* or hypno* or Integr* or Kurzzeit* or Langzeit* or interpersonal* or logo* or Achtsamkeit* or mindfulness* or Multimodal* or Narrativ* or Positiv* or Provokativ* or Orientiert* or psychol* or rational* or Realitaet* or Loesung* or system* or Transaktion* or Transpersonal* or eklektisch* or Empirisch* or Expressiv* or Individu?l* or einzel* or Einsicht* or Ueberzeugung* or Beziehung* or Supportiv* or Unterstuetz* or Implosiv* or Inhibition* or Hemm* or Aversion* or Abneig* or Konfront* or Schema* or Relaxation* or Entspannung* or Gespraech*) adj5 (Behandlung* or Therapie or Therapien)).tw

eAppendix 2. Addition to Methods

Selection criteria: Definition of psychotherapeutic treatments

Psychotherapeutic PTSD treatments had to be implemented at the level of individual patients, rather than in group, family, or couple therapy; they had to include face-to-face contact between the patient and the therapist, as opposed to telephone or internet-based interactions between patient and therapist; they had to be standardized (similar dose of treatment for all patients and treatment based on the same rational for all patients in one study); they had to consist primarily of verbal communication; and they had to directly address the trauma or subsequent PTSD symptoms. Pharmacological treatments needed to contain any pharmacological agent that was assumed to lead to a reduction in PTSD symptom severity.

Risk of Bias in the Included Studies

To evaluate the quality of studies and potential risk of bias (RoB), we related to the predefined criteria in the "Cochrane Handbook for Systematic Reviews of Interventions".[1] For the application of the RoB criteria in the context of psychotherapy research, we adhered to the recommendations by Munder & Barth.[2] For the combination of the individual RoB categories to one overall RoB rating we used the recommendations by Guyatt et al. .[3]

For each included study the risk for five potential bias categories was assessed: 1st *selection bias* (*sequence generation* and *allocation sequence concealment*), 2nd *performance bias*, 3rd *detection bias*, 4th *attrition bias* and 5th *reporting bias*.

1st we rated "low" risk of *selection bias*, if both relevant categories (*sequence generation* and *concealment of allocation* were considered as "low". Risk for *selection bias* was considered "unclear" if at least one of the two categories were considered "unclear", and risk for *selection bias* was considered "high", if both categories were considered "high". *Sequence generation* was considered adequate, if participants were randomly assigned to treatment conditions stating a randomization procedure that ensured that similarity of groups at baseline was warranted (e.g., computerized random sequence generation). *Concealment of allocation* was considered adequate if the procedures described ensured that the investigators responsible for patient selection did not suspect which treatment was next before allocation (e.g., if allocation to treatments was conducted by an external third party).

2nd risk of performance bias was rated "high", if participants as well as assessors were not blinded and knew which therapy the participant received and if the treatments differed with respect to their credibility. Risk of Iperformance bias was considered "low" if two equally credible treatments were compared, even if participants and treatment providers were not blinded.

3rd risk of detection bias was rated "high" if outcome assessors knew which therapy a participant was assigned to. Risk of *detection bias* was considered "low" if only self-rated outcome measures were used.[2]

4th risk of *attrition bias* was considered "high" if missing outcome data varied largely across conditions and analyses were not conducted according to the intention to treat (ITT) principle. Risk of *attrition bias* was considered "low" if all participants were analysed as randomized.

5th risk of *reporting bias* was considered "hig", if outcome reporting did not include all predefined outcomes or data for effect size generation was insufficient. If relevant information on any quality criterion were not reported, or if the reported information was insufficient for a clear "high" or "low" rating we coded the respective criterion as "unclear".
We rated a study as "high" regarding overall RoB, if three or more of the five criteria were rated with "high" RoB. We rated a study as "low" regarding overall RoB, if at least four criteria were rated "low", and maximum one criterion was rated "unclear". In any other case, we rated the study as having a "moderate" RoB.

Indirectness

We rated the indirectness of the available evidence as recommended by Guyatt et al. .[4] We assessed whether 1st a study differed from the studies of interest with respect to 1st the relevant study population, 2nd the applied intervention, 3rd the evaluated outcomes, and 4th whether a study provided direct evidence for at least one of the comparisons of interest.
Overall indirectness was considered "low," if at least 3 items were rated as "low" and maximum one item was rated "unclear". Overall indirectness was considered "high" if at least two items were rated as "high". All other combinations were rated "moderate".

Confidence in Network Meta-analysis (CINEMA)

We assessed the quality of the entire network using the CINEMA framework.[5] This includes evaluations of within study bias, across study bias, indirectness, imprecision, heterogeneity and incoherence. The RoB rating was used for evaluating within study bias. For across study bias we assumed that the likelihood of unpublished data was small because oft eh rather complex study designs with a high effort in implementing at least two active treatments. For the evaluation of indirectness, we used the rating as described above. For the evaluation of imprecision, heterogeneity and incoherence we defined the clinically important effect size as 0.6.[6]

1. Higgins JPT, Green S. Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1.0 ed: The Cochrane Collaboration; updated March 2011: http://www.cochrane-handbook.org.
2. Munder T, Barth J. Cochrane's risk of bias tool in the context of psychotherapy outcome research. *Psychotherapy Research.* 2018;28(3):347-355.
3. Guyatt GH, Oxman AD, Vist G, et al. GRADE guidelines: 4. Rating the quality of evidence—study limitations (risk of bias). *J Clin Epidemiol.* 2011;64(4):407-415.
4. Guyatt GH, Oxman AD, Kunz R, et al. GRADE guidelines: 8. Rating the quality of evidence—indirectness. *J Clin Epidemiol.* 2011;64(12):1303-1310.
5. Salanti G, Del Giovane C, Chaimani A, Caldwell DM, Higgins JP. Evaluating the quality of evidence from a network meta-analysis. *PLoS One.* 2014;9(7):e99682.
6. Stefanovics EA, Rosenheck RA, Jones KM, Huang G, Krystal JH. Minimal clinically important differences (MCID) in assessing outcomes of post-traumatic stress disorder. *Psychiatr Q.* 2018;89(1):141-155.

eAppendix 3. Additional Results (Main Analyses)

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################################################################################
> ## ----------------------------------------------------POST--------------
> postlong <- read_excel("postlong.xlsx")
> #View(postlong)
> #str(postlong)
>
> p1 <- pairwise(treat = t, n = posn, mean = posm, sd = possd, data=postlong, studlab=id, sm="SMD")
> #View(p1)
>
> ## -----------------------------
> # Conduct network meta-analysis
>
> net1 <- netmeta(p1, sm = "SMD", comb.fixed = FALSE, comb.random = TRUE)
> net1
Original data (with adjusted standard errors for multi-arm studies):

       treat1 treat2      TE   seTE seTE.adj narms multiarm
MA2     PTMed  PTPla  0.1986 0.4285   0.4285     2
ps2889    Med  PTMed -0.1397 0.4479   0.4479     2
ps3283    Med     PT  0.0902 0.5003   0.5003     2
ps3643    Med  PTMed  0.3768 0.2507   0.2507     2
ps3804    Med    Pla -0.0388 0.2604   0.3152     3        *
ps3804    Med     PT  0.4458 0.2639   0.3233     3        *
ps3804    Pla     PT  0.4844 0.2667   0.3306     3        *
TR1110  PTMed  PTPla -1.6776 0.5440   0.5440     2
TR1127  PTMed  PTPla -0.8525 0.6481   0.6481     2
TR1207  PTMed  PTPla -0.5206 0.4000   0.4000     2
TR1246  PTMed  PTPla -0.1925 0.2865   0.2865     2
TR1296    Med     PT  0.0127 0.2060   0.2324     3        *
TR1296    Med  PTMed  0.2180 0.2436   0.3947     3        *
TR1296     PT  PTMed  0.2066 0.1868   0.2045     3        *
TR1355    Med     PT -0.1571 0.1883   0.2600     4        *
TR1355    Med  PTMed  0.0000 0.1852   0.2521     4        *
TR1355    Med     WL  0.0000 0.1923   0.2698     4        *
TR1355     PT  PTMed  0.1570 0.1937   0.2761     4        *
TR1355     PT     WL  0.1569 0.2005   0.2957     4        *
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```
TR1355  PTMed     WL  0.0000 0.1975   0.2865     4        *
trials    Med  PTMed -0.0610 0.1691   0.2047     3        *
trials    Med  PTPla -0.3736 0.1718   0.2112     3        *
trials  PTMed  PTPla -0.3126 0.1726   0.2131     3        *

Number of treatment arms (by study):
       narms
MA2        2
ps2889     2
ps3283     2
ps3643     2
ps3804     3
TR1110     2
TR1127     2
TR1207     2
TR1246     2
TR1296     3
TR1355     4
trials     3

Results (random effects model):

       treat1 treat2     SMD             95%-CI
MA2     PTMed  PTPla -0.4146 [-0.6874; -0.1418]
ps2889    Med  PTMed  0.1169 [-0.1058;  0.3397]
ps3283    Med     PT  0.0272 [-0.2289;  0.2833]
ps3643    Med  PTMed  0.1169 [-0.1058;  0.3397]
ps3804    Med    Pla -0.2401 [-0.7559;  0.2757]
ps3804    Med     PT  0.0272 [-0.2289;  0.2833]
ps3804    Pla     PT  0.2673 [-0.2509;  0.7855]
TR1110  PTMed  PTPla -0.4146 [-0.6874; -0.1418]
TR1127  PTMed  PTPla -0.4146 [-0.6874; -0.1418]
TR1207  PTMed  PTPla -0.4146 [-0.6874; -0.1418]
TR1246  PTMed  PTPla -0.4146 [-0.6874; -0.1418]
TR1296    Med     PT  0.0272 [-0.2289;  0.2833]
TR1296    Med  PTMed  0.1169 [-0.1058;  0.3397]
TR1296     PT  PTMed  0.0897 [-0.1853;  0.3647]
TR1355    Med     PT  0.0272 [-0.2289;  0.2833]
TR1355    Med  PTMed  0.1169 [-0.1058;  0.3397]
TR1355    Med     WL  0.0965 [-0.3086;  0.5016]
```

```
TR1355     PT  PTMed  0.0897 [-0.1853;  0.3647]
TR1355     PT     WL  0.0693 [-0.3495;  0.4880]
TR1355  PTMed     WL -0.0204 [-0.4311;  0.3902]
trials    Med  PTMed  0.1169 [-0.1058;  0.3397]
trials    Med  PTPla -0.2977 [-0.6111;  0.0158]
trials  PTMed  PTPla -0.4146 [-0.6874; -0.1418]

Number of studies: k = 12
Number of treatments: n = 6
Number of pairwise comparisons: m = 23
Number of designs: d = 7

Random effects model

Treatment estimate (sm = 'SMD'):
          Med     Pla      PT  PTMed   PTPla      WL
Med         . -0.2401  0.0272 0.1169 -0.2977  0.0965
Pla    0.2401       .  0.2673 0.3570 -0.0576  0.3366
PT    -0.0272 -0.2673       . 0.0897 -0.3249  0.0693
PTMed -0.1169 -0.3570 -0.0897      . -0.4146 -0.0204
PTPla  0.2977  0.0576  0.3249 0.4146       .  0.3942
WL    -0.0965 -0.3366 -0.0693 0.0204 -0.3942       .

Lower 95%-confidence limit:
          Med     Pla      PT   PTMed   PTPla      WL
Med         . -0.7559 -0.2289 -0.1058 -0.6111 -0.3086
Pla   -0.2757       . -0.2509 -0.1876 -0.6494 -0.2991
PT    -0.2833 -0.7855       . -0.1853 -0.6917 -0.3495
PTMed -0.3397 -0.9017 -0.3647       . -0.6874 -0.4311
PTPla -0.0158 -0.5342 -0.0419  0.1418       . -0.0843
WL    -0.5016 -0.9722 -0.4880 -0.3902 -0.8727       .

Upper 95%-confidence limit:
         Med    Pla     PT  PTMed   PTPla     WL
Med        . 0.2757 0.2833 0.3397  0.0158 0.5016
Pla   0.7559      . 0.7855 0.9017  0.5342 0.9722
PT    0.2289 0.2509      . 0.3647  0.0419 0.4880
PTMed 0.1058 0.1876 0.1853      . -0.1418 0.3902
PTPla 0.6111 0.6494 0.6917 0.6874       . 0.8727
WL    0.3086 0.2991 0.3495 0.4311  0.0843      .
```

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Quantifying heterogeneity / inconsistency:
tau^2 = 0.0177; I^2 = 19.8%

Tests of heterogeneity (within designs) and inconsistency (between designs):
                    Q d.f. p-value
Total           14.96   12  0.2437
Within designs   9.58    5  0.0881
Between designs  5.37    7  0.6145
> #forest(net1, ref = "Med")
>
>
> # Inconsistency
> net1$d
[1] 7
>
> designs1 = as.character(decomp.design(net1)$Q.het.design$design)
> designs1
[1] "Med:PT"          "Med:PTMed"       "PTMed:PTPla"     "Med:Pla:PT"      "Med:PT:PTMed"    "Med:PT:PTMed:WL"
"Med:PTMed:PTPla"
>
> split1 = netsplit(net1)
> print(split1, showall = FALSE, digits = 2)
Random effects model:

  comparison k prop   nma direct indir.  Diff     z p-value
     Med:Pla 1 0.81 -0.24  -0.04  -1.10  1.06  1.58  0.1143
      Med:PT 4 0.86  0.03   0.05  -0.14  0.19  0.50  0.6143
   Med:PTMed 5 0.91  0.12   0.08   0.53 -0.45 -1.11  0.2663
   Med:PTPla 1 0.54 -0.30  -0.37  -0.21 -0.17 -0.52  0.6055
      Med:WL 1 0.78  0.10   0.00   0.44 -0.44 -0.88  0.3767
      Pla:PT 1 0.79  0.27   0.48  -0.54  1.02  1.58  0.1143
    PT:PTMed 2 0.73  0.09   0.18  -0.16  0.34  1.09  0.2758
       PT:WL 1 0.79  0.07   0.16  -0.26  0.42  0.79  0.4279
 PTMed:PTPla 6 0.91 -0.41  -0.38  -0.82  0.44  0.89  0.3725
    PTMed:WL 1 0.77 -0.02   0.00  -0.09  0.09  0.18  0.8566

Legend:
 comparison - Treatment comparison
 k          - Number of studies providing direct evidence
```

```
 prop       - Direct evidence proportion
 nma        - Estimated treatment effect (SMD) in network meta-analysis
 direct     - Estimated treatment effect (SMD) derived from direct evidence
 indir.     - Estimated treatment effect (SMD) derived from indirect evidence
 Diff       - Difference between direct and indirect treatment estimates
 z          - z-value of test for disagreement (direct versus indirect)
 p-value    - p-value of test for disagreement (direct versus indirect)
>
> decomp.design(net1)
Q statistics to assess homogeneity / consistency

                    Q df p-value
Total           14.95 12  0.2441
Within designs   9.58  5  0.0881
Between designs  5.37  7  0.6145

Design-specific decomposition of within-designs Q statistic

      Design    Q df p-value
   Med:PTMed 1.01  1  0.3143
 PTMed:PTPla 8.57  4  0.0729

Between-designs Q statistic after detaching of single designs

 Detached design    Q df p-value
          Med:PT 5.34  6  0.5006
       Med:PTMed 4.78  6  0.5726
     PTMed:PTPla 5.37  6  0.4976
      Med:Pla:PT 2.02  6  0.9176
    Med:PT:PTMed 4.81  5  0.4398
 Med:PT:PTMed:WL 4.22  5  0.5175
 Med:PTMed:PTPla 4.01  5  0.5478

Q statistic to assess consistency under the assumption of
a full design-by-treatment interaction random effects model

                   Q df p-value tau.within tau2.within
Between designs 1.26  7  0.9895     0.3951      0.1561
```

```
> ############################################################################
> ## ------------------------------------------------------FU-------------
> fulong <- read_excel("fulong.xlsx")
> #View(fulong)
> #str(fulong)
>
> p3 <- pairwise(treat = t, n = fun, mean = fum, sd = fusd, data=fulong, studlab=id, sm="SMD")
> #View(p3)
>
> ## ------------------------------
> # Conduct network meta-analysis
>
> net3 <- netmeta(p3, sm = "SMD", comb.fixed = FALSE, comb.random = TRUE)
> net3
Original data (with adjusted standard errors for multi-arm studies):

       treat1 treat2      TE   seTE seTE.adj narms multiarm
ps2889    Med  PTMed  1.9910 0.5687   0.5687     2
ps3283    Med     PT  1.2915 0.6458   0.6458     2
ps3804    Med     PT  0.8540 0.2967   0.2967     2
TR1110  PTMed  PTPla -1.2729 0.5087   0.5087     2
TR1246  PTMed  PTPla -0.3037 0.3070   0.3070     2
TR1296    Med     PT  0.2646 0.2066   0.2336     3        *
TR1296    Med  PTMed  0.2045 0.2435   0.3931     3        *
TR1296     PT  PTMed -0.0589 0.1864   0.2041     3        *

Number of treatment arms (by study):
       narms
ps2889     2
ps3283     2
ps3804     2
TR1110     2
TR1246     2
TR1296     3

Results (random effects model):

       treat1 treat2     SMD            95%-CI
ps2889    Med  PTMed  0.9552 [ 0.0408; 1.8696]
```

```
ps3283    Med     PT  0.8300 [ 0.0748; 1.5851]
ps3804    Med     PT  0.8300 [ 0.0748; 1.5851]
TR1110  PTMed  PTPla -0.7094 [-1.6814; 0.2625]
TR1246  PTMed  PTPla -0.7094 [-1.6814; 0.2625]
TR1296    Med     PT  0.8300 [ 0.0748; 1.5851]
TR1296    Med  PTMed  0.9552 [ 0.0408; 1.8696]
TR1296     PT  PTMed  0.1252 [-0.8658; 1.1163]

Number of studies: k = 6
Number of treatments: n = 4
Number of pairwise comparisons: m = 8
Number of designs: d = 4

Random effects model

Treatment estimate (sm = 'SMD'):
          Med      PT  PTMed   PTPla
Med         .  0.8300 0.9552  0.2458
PT    -0.8300       . 0.1252 -0.5842
PTMed -0.9552 -0.1252      . -0.7094
PTPla -0.2458  0.5842 0.7094       .

Lower 95%-confidence limit:
          Med      PT   PTMed   PTPla
Med         .  0.0748  0.0408 -1.0887
PT    -1.5851       . -0.8658 -1.9723
PTMed -1.8696 -1.1163       . -1.6814
PTPla -1.5802 -0.8039 -0.2625       .

Upper 95%-confidence limit:
          Med     PT  PTMed  PTPla
Med         . 1.5851 1.8696 1.5802
PT    -0.0748      . 1.1163 0.8039
PTMed -0.0408 0.8658      . 0.2625
PTPla  1.0887 1.9723 1.6814      .

Quantifying heterogeneity / inconsistency:
tau^2 = 0.3287; I^2 = 70.8%

Tests of heterogeneity (within designs) and inconsistency (between designs):
```

```
                   Q d.f. p-value
Total          13.68    4  0.0084
Within designs  3.04    2  0.2188
Between designs 10.64    2  0.0049
> #forest(net3, ref = "Med")
>

> # Inconsistency
> net3$d
[1] 4
>
> designs3 = as.character(decomp.design(net3)$Q.het.design$design)
> designs3
[1] "Med:PT"       "Med:PTMed"    "PTMed:PTPla"  "Med:PT:PTMed"
>
> split3 = netsplit(net3)
> print(split3, showall = FALSE, digits = 2)
Random effects model:

 comparison k prop  nma direct indir.  Diff     z p-value
     Med:PT 3 0.95 0.83   0.70   3.61 -2.91 -1.57  0.1165
  Med:PTMed 2 0.89 0.96   0.87   1.67 -0.80 -0.53  0.5988
   PT:PTMed 1 0.70 0.13  -0.06   0.56 -0.62 -0.56  0.5749

Legend:
 comparison - Treatment comparison
 k          - Number of studies providing direct evidence
 prop       - Direct evidence proportion
 nma        - Estimated treatment effect (SMD) in network meta-analysis
 direct     - Estimated treatment effect (SMD) derived from direct evidence
 indir.     - Estimated treatment effect (SMD) derived from indirect evidence
 Diff       - Difference between direct and indirect treatment estimates
 z          - z-value of test for disagreement (direct versus indirect)
 p-value    - p-value of test for disagreement (direct versus indirect)
>
> decomp.design(net3)
Q statistics to assess homogeneity / consistency

                   Q df p-value
Total          13.68  4  0.0084
```

```
Within designs   3.04  2  0.2188
Between designs 10.64  2  0.0049

Design-specific decomposition of within-designs Q statistic

      Design    Q df p-value
      Med:PT 0.38  1  0.5381
 PTMed:PTPla 2.66  1  0.1029

Between-designs Q statistic after detaching of single designs

 Detached design    Q df p-value
          Med:PT 8.34  1  0.0039
       Med:PTMed 3.84  1  0.0501
    Med:PT:PTMed 0.00  0      --

Q statistic to assess consistency under the assumption of
a full design-by-treatment interaction random effects model

                  Q df p-value tau.within tau2.within
Between designs 6.04  2  0.0487     0.3286      0.1080
>
```

```
##############################################################################
> ## ----------------------------------------Drop-outs-------------
> droplong <- read_excel("droplong.xlsx")
> #str(droplong)
>
> p5 <- pairwise(treat = t, event = d, n = nr,
+                data = droplong, studlab = id, allincr = TRUE, allstudies = TRUE, sm = "OR")
> #View(p5)
>

> net5 <- netmeta(p5, sm = "OR", comb.fixed = FALSE, comb.random = TRUE)
> summary(net5, digits = 2)
Number of studies: k = 12
Number of treatments: n = 6
Number of pairwise comparisons: m = 23
Number of designs: d = 7

Random effects model

Treatment estimate (sm = 'OR'):
         Med     PT  PTMed  PTPla    Pla     WL
Med        . 1.3452 0.5525 0.4637 1.7356 0.4086
PT    0.7434      . 0.4107 0.3447 1.2903 0.3038
PTMed 1.8099 2.4347      . 0.8392 3.1414 0.7396
PTPla 2.1567 2.9011 1.1916      . 3.7432 0.8813
Pla   0.5762 0.7750 0.3183 0.2672      . 0.2354
WL    2.4472 3.2920 1.3521 1.1347 4.2475      .

Lower 95%-confidence limit:
         Med     PT  PTMed  PTPla    Pla     WL
Med        . 0.6017 0.2649 0.1749 0.3051 0.1139
PT    0.3325      . 0.1685 0.1114 0.2286 0.0825
PTMed 0.8678 0.9988      . 0.3845 0.5028 0.2031
PTPla 0.8135 0.9373 0.5460      . 0.5322 0.2018
Pla   0.1013 0.1373 0.0510 0.0380      . 0.0292
WL    0.6821 0.8945 0.3712 0.2598 0.5276      .

Upper 95%-confidence limit:
         Med      PT  PTMed  PTPla     Pla     WL
Med        .  3.0073 1.1523 1.2293  9.8721 1.4660
PT    1.6619       . 1.0012 1.0669  7.2809 1.1179
PTMed 3.7749  5.9353      . 1.8316 19.6267 2.6938
PTPla 5.7175  8.9800 2.6006      . 26.3267 3.8491
```

```
Pla   3.2771  4.3735 1.9888 1.8789       . 1.8955
WL    8.7801 12.1153 4.9248 4.9562 34.1985      .

Quantifying heterogeneity / inconsistency:
tau^2 = 0.3962; I^2 = 52%

Tests of heterogeneity (within designs) and inconsistency (between designs):
                   Q d.f. p-value
Total          25.02   12  0.0147
Within designs  3.12    5  0.6815
Between designs 21.90    7  0.0026
>
>

> # Inconsistency
> net5$d
[1] 7
>
> designs5 = as.character(decomp.design(net5)$Q.het.design$design)
> designs5
[1] "Med:PT"          "Med:PTMed"       "PTMed:PTPla"     "Med:PT:PTMed"    "Med:PT:PTMed:WL" "Med:PT:Pla"      "Med:PTMed:PTPla"
>
> split5 = netsplit(net5)
> print(split5, showall = FALSE, digits = 2)
Random effects model:

  comparison k prop  nma direct indir.   RoR     z p-value
      Med:PT 4 0.91 1.35   1.59   0.24  6.73  1.32  0.1856
   Med:PTMed 5 0.90 0.55   0.61   0.22  2.73  0.80  0.4265
   Med:PTPla 1 0.45 0.46   0.27   0.73  0.37 -1.01  0.3141
     Med:Pla 1 0.80 1.74   1.29   5.90  0.22 -0.68  0.4946
      Med:WL 1 0.70 0.41   0.37   0.53  0.69 -0.26  0.7913
    PT:PTMed 2 0.74 0.41   0.49   0.25  1.93  0.64  0.5249
      PT:Pla 1 0.83 1.29   1.70   0.34  4.93  0.68  0.4946
       PT:WL 1 0.77 0.30   0.53   0.05 11.05  1.52  0.1284
 PTMed:PTPla 6 0.94 0.84   0.93   0.18  5.27  1.02  0.3075
    PTMed:WL 1 0.75 0.74   0.47   2.91  0.16 -1.21  0.2278

Legend:
 comparison - Treatment comparison
 k          - Number of studies providing direct evidence
 prop       - Direct evidence proportion
 nma        - Estimated treatment effect (OR) in network meta-analysis
 direct     - Estimated treatment effect (OR) derived from direct evidence
```

```
 indir.     - Estimated treatment effect (OR) derived from indirect evidence
 RoR        - Ratio of Ratios (direct versus indirect)
 z          - z-value of test for disagreement (direct versus indirect)
 p-value    - p-value of test for disagreement (direct versus indirect)
>
> decomp.design(net5)
Q statistics to assess homogeneity / consistency

                    Q df p-value
Total           25.02 12  0.0147
Within designs   3.12  5  0.6815
Between designs 21.90  7  0.0026

Design-specific decomposition of within-designs Q statistic

      Design    Q df p-value
   Med:PTMed 0.76  1  0.3827
 PTMed:PTPla 2.36  4  0.6702

Between-designs Q statistic after detaching of single designs

 Detached design     Q df p-value
          Med:PT 21.84  6  0.0013
       Med:PTMed 21.31  6  0.0016
     PTMed:PTPla 21.19  6  0.0017
    Med:PT:PTMed  3.35  5  0.6468
 Med:PT:PTMed:WL 11.65  5  0.0399
      Med:PT:Pla 20.27  6  0.0025
 Med:PTMed:PTPla 17.45  5  0.0037

Q statistic to assess consistency under the assumption of
a full design-by-treatment interaction random effects model

                    Q df p-value tau.within tau2.within
Between designs 21.90  7  0.0026          0           0
```

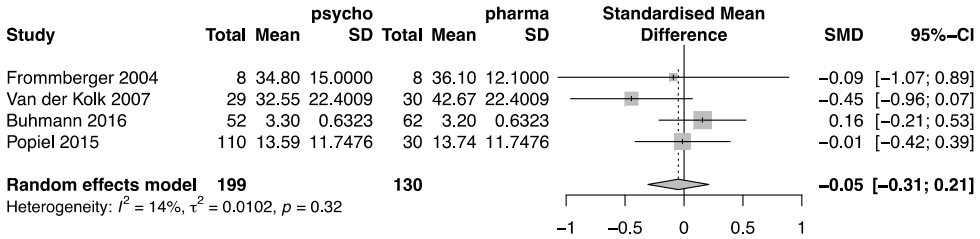
eAppendix 4. Sensitivity Analyses

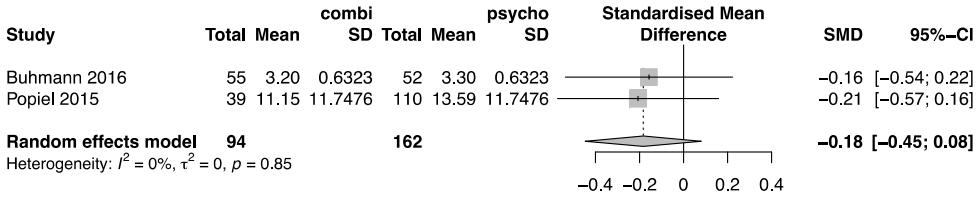
```
> ## ----------------------------------------POST Sensitivityanalysis-------------
> ## Simon excluded (SD imputed)
> ## Mithoefer, Simon, Hien & Oehen excluded (indirectness = high)
> ## Frommberger excluded (inadequate blinding: Reviewer Comment)
> ## Simon, Schnieder, Rauch, Oehen, Buhman, Rothbaum excluded (reported only short-term data: Reviewer Comment)
> ## Favoring self-rated outcomes

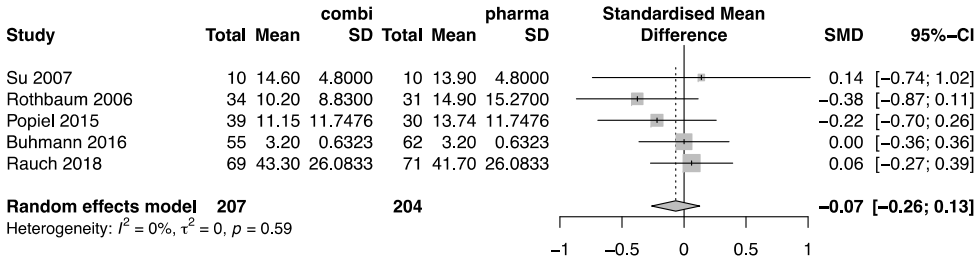
> ## ----------------------------------------FU Sensitivityanalysis-------------
> ## Frommberger excluded (SD imputed & inadequate blinding)
> ## Mitohefer excluded (indirectness = high)
> ## Favoring self-rated outcomes
```

eAppendix 5. Pairwise Meta-analyses

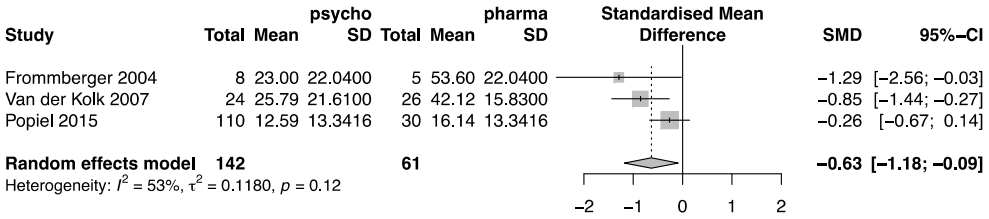
Comparative efficacy on PTSD symptom severity from pairwise meta-analyses at the end of treatment.

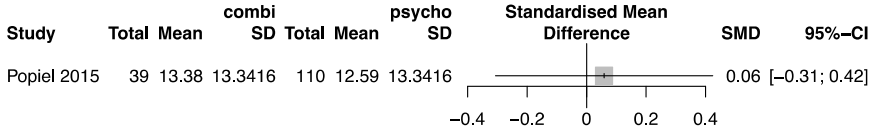


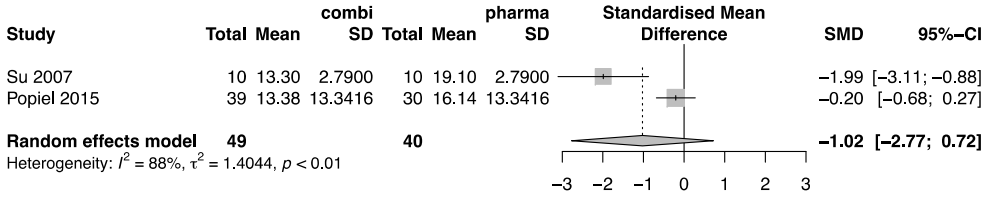




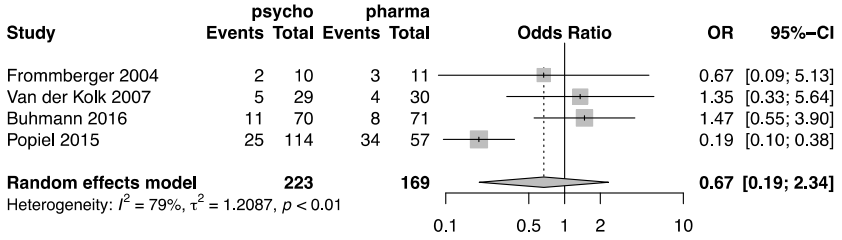
Comparative efficacy on PTSD symptom severity from pairwise meta-analyses at the last available follow-up.

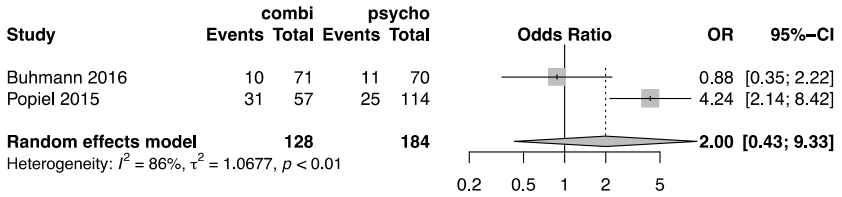


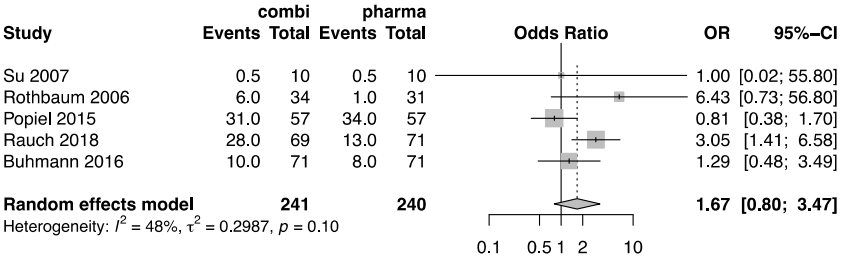




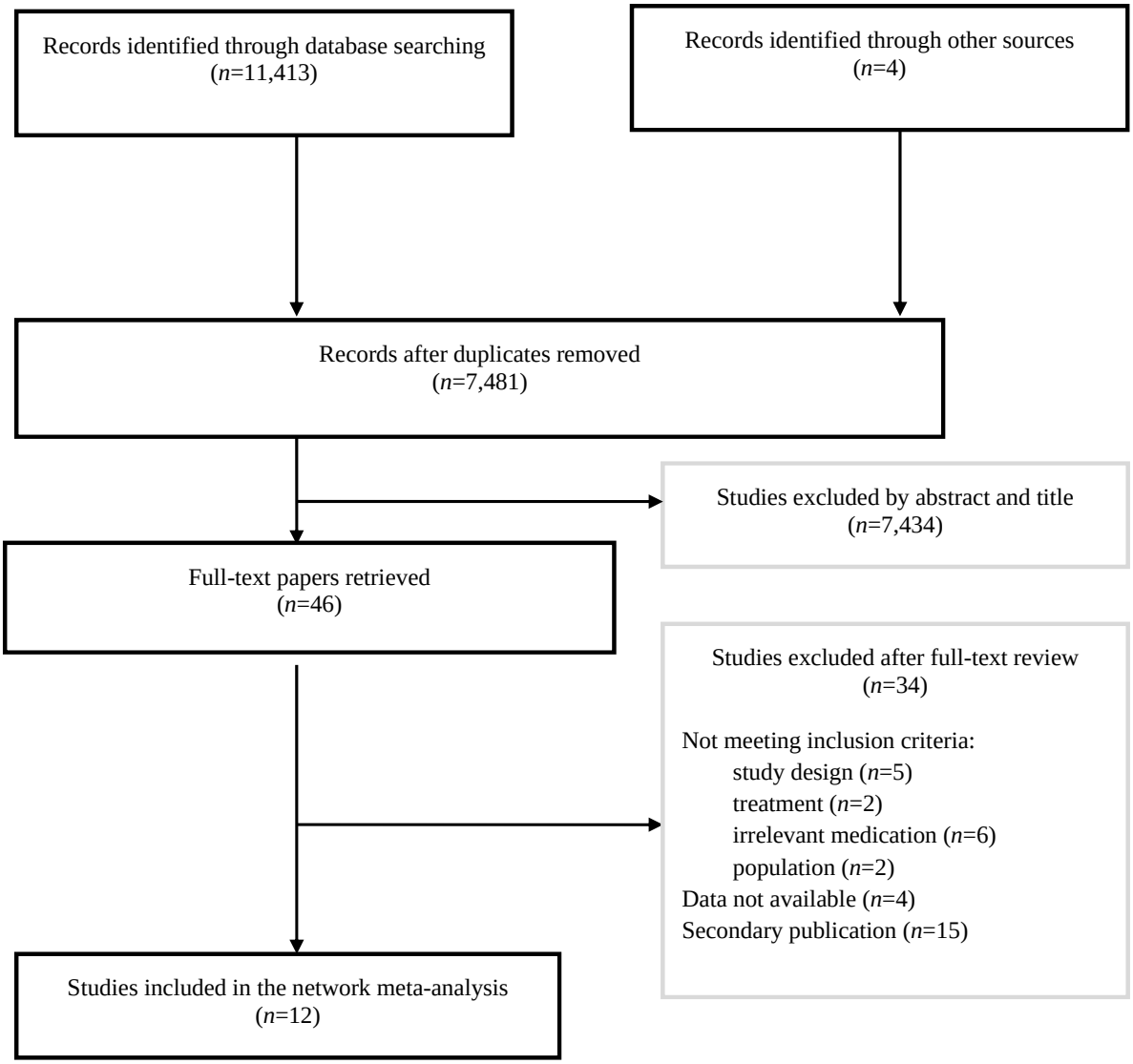
Comparative efficacy on treatment drop outs from pairwise meta-analyses at the end of treatment.





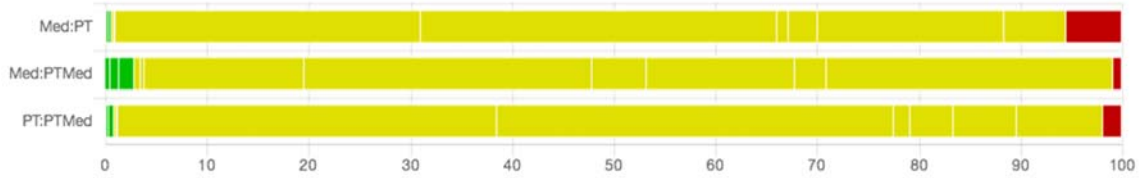


eFigure 1. Flow Chart

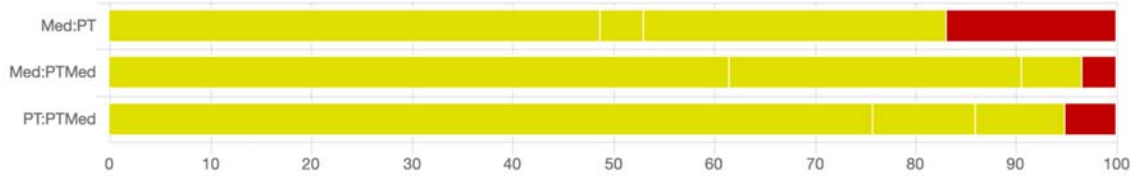


eFigure 2. Risk of Bias Contributions

A. End of treatment



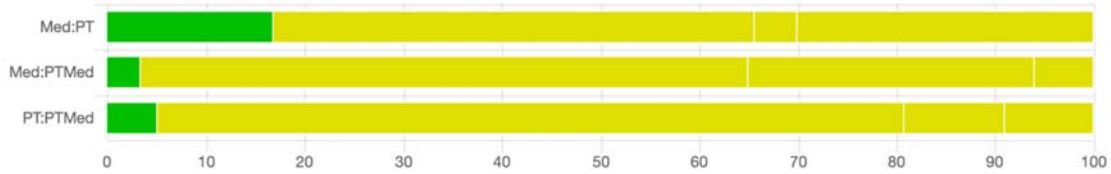
B. Follow-up



eFigure 3. Indirectness Contributions

A. End of treatment

B. Follow-up



eTable 1. Risk of Bias for Each Included Study

Author	Year	Selection bias	Performance bias	Detection bias	Attrition bias	Reporting bias	RoB
Trials with short-term data only							
Buhmann	2016	unclear	low	low	high	low	moderate
Oehen	2013	unclear	low	low	unclear	low	moderate
Rauch	2018	unclear	unclear	unclear	unclear	unclear	moderate
Rothbaum	2006	unclear	high	low	low	low	moderate
Schneier	2012	low	low	low	unclear	low	low
Simon	2007	unclear	unclear	low	low	low	moderate
Trials with short- and long-term data							
Frommberger	2004	unclear	low	high	high	high	high
Hien	2015	low	low	low	unclear	low	low
Mithoefer	2010	low	low	low	unclear	low	low
Popiel	2015	unclear	low	low	high	high	moderate
Su	2007	unclear	unclear	low	low	unclear	moderate
Van der Kolk	2007	unclear	low	low	unclear	low	moderate

eTable 2. Indirectness for Each Included Study

Author	Year	Population		Intervention		Outcomes		Comparisons	Indirectness total
Trials with short-term data only									
Buhmann	2016	low		low		low		low	low
Oehen	2013	high	female	high	MDMA	low		high	high
Rauch	2018	high	male	low		low		low	moderate
Rothbaum	2006	low		unclear	somewhat different implementation	low		low	low
Schneier	2012	low		low		low		high	moderate
Simon	2007	high	treatmen resistant	unclear	somewhat different implementation	low		high	high
Trials with short- and long-term data									
Frommberger	2004	low		low		low		low	low
Hien	2015	high	alcohol	unclear	+ alcohol treatment	low		high	high
Mithoefer	2010	high	female	high	MDMA	low		high	high
Popiel	2015	high	female and highly educated	low		low		low	moderate
Su	2007	unclear		low		unclear	subscale	low	moderate
Van der Kolk	2007	high	female	low		low		low	moderate

eTable 3: Confidence in Network Meta-analysis (CINEMA) Rating

A. End of treatment

Comparison	Number of studies	Within-study bias	Across-studies bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
Med:PT	4	Some concerns	Undetected	Some concerns	No concerns	No concerns	Some concerns	High
Med:PTMed	5	Some concerns	Undetected	Some concerns	No concerns	No concerns	Some concerns	High
PT:PTMed	2	Some concerns	Undetected	Some concerns	No concerns	No concerns	Some concerns	High

B. Follow-up

Comparison	Number of studies	Within-study bias	Across-studies bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
Med:PT	3	Some concerns	Undetected	Some concerns	Some concerns	Some concerns	No concerns	High
Med:PTMed	2	Some concerns	Undetected	Some concerns	Some concerns	Some concerns	Some concerns	Moderate
PT:PTMed	1	Some concerns	Undetected	Some concerns	Major concerns	No concerns	No concerns	Moderate

eTable 4. Comparisons of Results Across Different Network Models

Reason for study exclusion	No. of studies	PT-Pharma	Combi-PT	Combi-Pharma	Tau^2	I^2
Short-term						
None (all studies in)	12	-.03 (-.28 to .23)	-.09 (-.36 to .19)	-.12 (-.34 to .11)	.02	19.8%
SD imputed	11	-.03 (-.27 to .22)	-.09 (-.36 to .16)	-.12 (-.34 to .09)	.01	14.3%
High indirectness ratingw	8	-.01 (-.22 to .21)	-.10 (-.32 to .13)	-.10 (-.29 to .09)	0	0%
Inadequate outcome assessment	11	-.03 (-.31 to .25)	-.09 (-.39 to .20)	-.12 (-.35 to .12)	.02	26.3%
Only short-term data	6	-.15 (-.66 to .36)	-.02 (-.69 to .64)	-.17 (-.80 to .46)	.12	52.8%
Preference for self-rated outcome (all studies in)	12	-.10 (-.39 to .18)	-.04 (-.35 to .26)	-.14 (-.39 to .10)	.03	29%
Long-term						
None (all studies in)	**6**	**-.83 (-1.59 to -.07**)	-.13 (-1.13 to .87)	**-.96 (-1.88 to -.04)**	.33	70.8%
SD imputed / inadequate outcome assessment	5	-.72 (-1.60 to .16)	-.21 (-1.27 to .86)	-.93 (-1.89 to .04)	.36	75.9%
High indirectness rating	**4**	**-.83 (-1.59 to -.07)**	-.13 (1.13 to .87)	**-.96 (-1.88 to -.04)**	.34	72.8%
Preference for self-rated outcome (all studies in)	**6**	**-.84 (-1.57 to -.11)**	-.11 (-1.06 to .84)	**-.95 (-1.83 to -.07)**	.30	68.8%