REVIEW ARTICLE

Impact of comorbid personality disorders on psychotherapy for post-traumatic stress disorder: systematic review and meta-analysis

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ABSTRACT

Background: Although personality disorders are common in PTSD patients, it remains unclear to what extent this comorbidity affects PTSD treatment outcome.

Objective: This constitutes the first meta-analysis investigating whether patients with and without comorbid personality disorders can equally benefit from psychotherapy for PTSD.

Method: A systematic literature search was conducted in PubMed, EMBASE, PsychINFO and Cochrane databases from inception through 31 January 2020, to identify clinical trials examining psychotherapies for PTSD in PTSD patients with and without comorbid personality disorders (PROSPERO reference CRD42020156472).

Results: Of the 1830 studies identified, 12 studies reporting on 918 patients were included. Effect sizes were synthesized using a random-effects model. Patients with comorbid personality disorders did not have significantly higher baseline PTSD severity (Hedges' $g = 0.23$, 95%CI $-0.09–0.55$, $p = .140$), nor were at higher risk for dropout from PTSD treatment (RR = 1.19, 95% CI $0.83–1.72$, $p = .297$). Whilst pre- to post-treatment PTSD symptom improvements were large in patients with comorbid PDs (Hedges' $g = 1.31$, 95%CI $0.89–1.74$, $p < .001$) as well as in patients without comorbid PDs (Hedges' $g = 1.57$, 95%CI $1.08–2.07$, $p < .001$), personality disorders were associated with a significantly smaller symptom improvement at post-treatment (Hedges' $g = 0.22$, 95%CI $0.05–0.38$, $p = .010$).

Conclusion: Although the presence of personality disorders does not preclude a good treatment response, patients with comorbid personality disorders might benefit less from PTSD treatment than patients without comorbid personality disorders.

HIGHLIGHTS
• This meta-analysis suggests that although patients with comorbid PDs do not have more severe PTSD symptoms at baseline, nor are at higher risk for dropout from PTSD treatment, they might benefit less from PTSD treatment compared to patients without comorbid PDs.

Impacto de los Trastornos de Personalidad Comórbidos en la psicoterapia para el Trastorno de Estrés Postraumático: Revisión Sistemática y Meta-análisis

Antecedentes: Aunque los trastornos de la personalidad son comunes en los pacientes con TEPT, sigue sin estar claro en qué medida afecta esta comorbilidad al resultado del tratamiento del TEPT.

Objetivo: Este constituye el primer meta-análisis que investiga si los pacientes con ysin trastornos de la personalidad comórbidos pueden beneficiarse de la misma forma de la psicoterapia para el TEPT.

Método: Se realizó una búsqueda sistemática de literatura en las bases de datos PubMed, EMBASE, PsycINFO yCochrane desde su creación hasta el 31 de enero de 2020, para identificar estudios clínicos que examinaron psicoterapias para el TEPT en pacientes con TEPT, con ysin trastornos de la personalidad comórbidos. (referencia PROSPERO CRD42020156472).

Resultados: De los 1830 estudios identificados, se incluyeron 12 estudios, que reportaron 918 pacientes. Los tamaños de efecto fueron sintetizados usando un modelo de efectos aleatorios. Los pacientes con trastornos de la personalidad comórbidos no tuvieron una severidad del TEPT basal significativamente mayor ($g$de Hedges = 0.23, IC 95% $-0.09 – 0.55$, $p= .140$), ni tuvieron un mayor riesgo de abandono del tratamiento del TEPT (RR=1.19, IC 95% $0.83 – 1.72$, $p= .297$). Mientras que la mejoría de los síntomas de TEPT pre apost tratamiento fue grande en los pacientes con TP comórbidos (g de Hedges = 1.31, IC 95% $0.89 – 1.74$, $p< .001$) así como también en pacientes sin TP comórbidos (g de Hedges = 1.57, IC 95% $1.08 – 2.07$, $p< .001$), los trastornos de la personalidad se asociaron auna mejoría sintomática significativamentemás pequeña en el post-tratamiento (g de Hedges = 0.22, IC 95% $0.05 – 0.38$, $p= .010$).

Conclusión: Aunque la presencia de trastornos de la personalidad no impide una buena respuesta atratamiento, los pacientes con trastornos de la personalidad comórbidos podrían beneficiarse menos del tratamiento del TEPT que los pacientes sin trastornos de la personalidad comórbidos.

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并发性人格障碍对创伤后应激障碍心理治疗的影响: 系统评价和元分析

背景: 尽管人格障碍在 PTSD 患者中很常见, 尚不清楚该并发症在多大程度上影响 PTSD 治疗结果。

目的: 这是第一个研究有无并发性人格障碍的患者是否可以从心理治疗 PTSD 中同样受益的元分析。

方法: 从开始到2020年1月31日, 在 PubMed, EMBASE, PsychINFO 和 Cochrane 数据库中进行了系统文献检索, 以识别出考查在有无并发性人格障碍的 PTSD 患者中进行 PTSD 心理治疗的临床试验 (PROSPERO参考号CRD42020156472) 。

结果: 在识别出的1830项研究中, 纳入了报告了918例患者的12项研究。使用随机效应模型综合效应量大小。有并发性人格障碍患者的PTSD基线严重程度没有显著更高 (Hedges' g = 0.23, 95％CI −0.09–0.55, p = .140), 也没有更高的退出PTSD治疗风险 (RR = 1.19, 95) ％CI 0.83–1.72, p = 0.297) 。在有并发性PD患者 (Hedges' g = 1.31, 95％CI 0.89–1.74, p <.001) 以及无合并PD的患者 (Hedges' g = 1.57) 的治疗前后 PTSD 症状改善很大 (95％CI 1.08–2.07, p <.001), 人格障碍与治疗后症状改善更小显著相关 (Hedges' g = 0.22, 95％CI 0.05-0.38, p = .010) 。

结论: 尽管人格障碍的存在不会阻止良好的治疗反应, 但并发性人格障碍患者从PTSD治疗中获得的收益可能少于无并发性人格障碍的患者。

1. Introduction

After exposure to a traumatic event, the average risk for developing a posttraumatic stress disorder (PTSD) is 5 to 10% (Kessler et al., 2017), but can go up to 49% depending on the nature of the traumatic event (e.g. rape, held captive, tortured or kidnapped) (Breslau et al., 1998). PTSD has an estimated lifetime prevalence of 8.3% (Kilpatrick et al., 2013) and is characterized by symptoms of re-experiencing, avoidance of trauma-related stimuli, trauma-related negative alterations in cognitions or mood and symptoms of hyperarousal, following direct or indirect exposure to a traumatic event (American Psychiatric Association, 2013).

Hundreds of clinical trials have investigated a wide range of treatment methods for PTSD, aimed at alleviating its distressing symptoms (Institute of Medicine of the National Academies, 2013). The American Psychological Association (APA) strongly recommends the use of Prolonged Exposure (PE), Cognitive Behavioural Therapy (CBT), Cognitive Processing Therapy (CPT) or Cognitive Therapy (CT), and conditionally recommends the use of Eye Movement Desensitization and Reprocessing (EMDR), Narrative Exposure Therapy (NET) or Brief Eclectic Psychotherapy (BEP) for treating PTSD (American Psychological Association, 2017). The Dutch clinical practice guideline for PTSD, on the other hand, strongly recommends the use of PE, CBT, CPT, CT and EMDR for treating PTSD and, while less researched, also recommends the use of NET and BEP (see: *https://www.ggzstandaarden.nl/zorgstandaarden/psychotrauma-en-stressorgerelateerde-stoornissen*). Despite the evidence pointing to the efficacy of these treatments, 36% (Imel, Laska, Jakupcak, & Simpson, 2013) to 54% (Schottenbauer, Glass, Arnkoff, Tendick, & Gray, 2008) of patients drop out from treatment and response rates vary around 56–67% (Bradley, Greene, Russ, Dutra, & Westen, 2005). The latter might be an overestimation since roughly 30% of patients were excluded from PTSD treatment due to broad and often insufficiently specified exclusion criteria.

One promising possibility for optimizing treatment efficacy, substantiated by the large heterogeneity of PTSD by nature, lies within an increased understanding of the patient characteristics that determine the diverse response to PTSD treatment. The identification of such predictor variables could specify for whom and under which conditions a specific treatment might or might not be effective, thereby maximizing treatment efficacy while minimizing dropout. The presence of personality disorders (PDs) might be of particular importance in predicting PTSD treatment outcome, since patients with a PTSD exhibit high rates of PDs (22–26%) (Friborg, Martinussen, Kaiser, Øvergård, & Rosenvinge, 2013; Pagura et al., 2010) and there is some evidence that an additional PD diagnosis aggravates PTSD symptomology and increases psychosocial impairment (Frías & Palma, 2015; Pagura et al., 2010), although other studies suggest the opposite (Hefferman & Cloitre, 2000; Walter, Bolte, Owens, & Chard, 2012). PDs refer to enduring and inflexible maladaptive patterns of behaviour, cognition and inner experience that have their onset in adolescence and are more or less stable over time, leading to significant distress or impairment (American Psychiatric Association, 2013). PDs are often viewed as a contra-indication for PTSD treatment due to certain personality characteristics that might interfere with treatment, such as emotion dysregulation and self-injurious behaviour (Van Minnen, Harned, Zoellner, & Mills, 2012). In addition, a large subgroup of patients with comorbid PDs is excluded from PTSD treatment due to the common confluence of exclusion criteria for suicidality or self-destructive behaviour (American Psychological Association, 2017; National Collaborating Centre for Mental Health National Collaborating Centre for Mental Health,

2005). Ambiguity in the existing literature with regard to the impact of PDs on PTSD treatment outcome further complicates this issue: while some studies found an association between comorbid PDs and an enhanced risk for dropout (McDonagh et al., 2005) as well as a poorer response to treatment (Cloitre & Koenen, 2001; Forbes et al., 2002; Hembree, Cahill, & Foa, 2004; Stalker, Palmer, Wright, & Gebotys, 2005), other studies failed to find a relationship between PDs and PTSD treatment outcome (Clarke, Rizvi, & Resick, 2008; Feeny, Zoellner, & Foa, 2002; Markowitz et al., 2015; Tarrier, Sommerfield, Pilgrim, & Faragher, 2000; Van Minnen, Arntz, & Keijsers, 2002; Walter et al., 2012) and a recent meta-analysis concluded that PTSD interventions can be safe and effectively applied in patients with comorbid borderline PD (Slotema, Wilhelmus, Arends, & Franken, 2020). Given these inconsistencies, it remains unclear if and to what extent comorbid PDs affect the severity of PTSD symptoms and whether psychotherapies for PTSD can be just as effectively applied in patients with comorbid PDs as in patients without comorbid PDs.

The present meta-analysis aims to clarify this ongoing debate by investigating whether patients with and without comorbid PDs can equally benefit from PTSD treatment. To answer this question, patients with and without comorbid PDs are compared on (1) baseline PTSD severity, (2) dropout from PTSD treatment and (3) response to PTSD treatment.

2. Method

2.1. Identification of studies

The aims and methods of this meta-analysis were registered at the International Prospective Register of Systematic Reviews (PROSPERO; registration number CRD42020156472). A systematic review was performed in PubMed, EMBASE, PsycINFO and Cochrane databases from inception through 31 January 2020. A wide range of keywords was used to capture the variety in diagnostic and treatment terminology over time, including MeSH search terms and free text terms of ('Stress Disorders, Post-traumatic [Mesh]' AND ('Treatment' [Mesh]) NOT ('Animals' [Mesh]) (see Appendix for full search).

2.2. Inclusion of studies

Inclusion criteria were defined according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) group, describing the Population (P), Intervention (I), Comparison (C), Outcome (O) and Study design (S):

(P) At least ten patients meeting diagnostic criteria for PTSD, with comorbid PD(s), according to the Diagnostic and Statistical Manual of Mental Disorders (DSM)-III, DSM-III-R, DSM-IV or DSM-5 (American Psychiatric Association, 1987, 2000, 2013; resp.);

(I) In order to comply with both the American and the Dutch PTSD treatment guidelines for PTSD, we included PE, CBT, CPT, CT, EMDR, BEP and NET, either stand-alone or integrated within a larger treatment protocol (American Psychological Association, 2017, for the Dutch guideline see: *https://www.ggzstandaarden.nl/zorgstandaarden/psychotrauma-en-stressorgerelateerde-stoornissen*);

(C) At least ten patients meeting diagnostic criteria for PTSD, without comorbid PD(s), according to the Diagnostic and Statistical Manual of Mental Disorders (DSM)-III, DSM-III-R, DSM-IV or DSM-5 (American Psychiatric Association, 1987, 2000, 2013; resp.);

(O) Assessment of pre- and post-treatment PTSD severity by means of a validated structured clinical interview such as the Clinician Administered PTSD Scale (CAPS) (American Psychiatric Association, 2000) or the PTSD Symptom Scale Interview (PSS-I) (Blake et al., 1995; Foa, Riggs, Dancu, & Rothbaum, 1993). Assessment of baseline PDs by means of a structured clinical interview or a validated self-report measure;

(S) Clinical trials, including randomized controlled trials (RCTs), controlled clinical trials (CCT) and clinical trials without a control group (CT).

In addition, selective case reports, letters, literature reviews, doctoral dissertations, non-human studies and non-adult studies were excluded from the current meta-analysis. After removing all duplicates, two reviewers (J.N. and A.S.) independently screened the remaining abstracts. Full-text publications were then assessed for eligibility. Disagreement between raters was settled by consensus discussion with a third reviewer (K.T.) and re-evaluation of the information in question.

2.3. Data extraction

Raw data were requested from all authors through email. Data were extracted by two independent raters (A.S. and K.T.). From the publications meeting inclusion criteria, the following data was extracted: number of patients with and without comorbid PDs who were assigned to PTSD treatment and subsequently dropped out or completed treatment, baseline and post-treatment PTSD severity, trauma type, PD diagnostic status at baseline, type and duration of the PTSD treatment. If PD symptoms were assessed by a clinical interview method as well as a self-report questionnaire, data from the clinical interview method were extracted. When multiple assessments were completed at post-treatment, the first clinician-administered measurement of PTSD severity upon treatment completion was used. Primary outcomes included the difference in dropout rates and the difference in post-treatment

PTSD symptom improvement between patients with and without comorbid PDs, to represent treatment feasibility and efficacy respectively. In addition, the difference in the number of treatment responders between patients with and without comorbid PDs was assessed as a second indicator of treatment efficacy.

2.4. Study quality

Two independent reviewers (A.S. and J.N.) critically appraised the methodological quality of each included study according to six domains from the Cochrane Risk of Bias Assessment tool: (1) random sequence generation (selection bias), (2) allocation concealment (selection bias), (3) blinding of the outcome assessor-(s) (detection bias) and (4) assessment of incomplete outcome data (attrition bias) (Higgins & Wells, 2019). The risk of bias for each domain was categorized as low, moderate or high. For each domain categorized as low risk of bias, the study in question was awarded one point, with a higher total number of points indicating lower risk of bias.

2.5. Statistical analyses

Hedges' g and its 95% confidence interval (CI) of the difference in post-treatment PTSD scores between patients with and without comorbid PDs was computed using a random effects model was computed in Comprehensive Meta-Analysis, Version 3 (Borenstein, Hedges, Higgins, & Rothstein, 2013). All other analyses were performed through a random effects model using the *meta* and *metafor* packages in R (Schwarzer, 2007). Hedges' g corrects for biases associated with small sample sizes (Cuijpers, 2016) and can be interpreted with Cohen's convention of small (0.2), medium (0.5) and large (0.8) effects (Cohen, 1988).

2.5.1. Pre-treatment PTSD severity
To determine whether PTSD severity differed between patients with and without comorbid PDs, individual study data (mean, SD and sample size) were pooled to obtain the overall Hedges' g of the difference in pre-treatment PTSD severity between the two groups.

2.5.2. Dropout from PTSD treatment
To determine whether risk for dropout from PTSD treatment differed between patients with and without comorbid PDs, differences in dropout rates were pooled to obtain the relative risks (RR) of treatment dropout between the two groups.

2.5.3. Response to PTSD treatment
2.5.3.1. Difference in post-treatment PTSD symptom improvement. First, Hedges g' of the pre- to post-treatment improvement in PTSD scores was calculated for patients with and without comorbid PDs

separately. Then, to determine whether patients with and without comorbid PDs equally benefit from PTSD treatment, the difference in post-treatment PTSD mean scores between patients with and without comorbid PDs was calculated. The correlation between pre- and post-treatment scores was estimated at 0.7, while controlling for pre-treatment mean scores (Cuijpers, Weitz, Cristea, & Twisk, 2017). Effect sizes were pooled across studies to obtain the overall Hedges' g of the difference in post-treatment PTSD symptom improvement between patients with and without comorbid PDs.

2.5.3.2. Difference in treatment response status. To determine whether patients with and without comorbid PDs benefit equally benefit from PTSD treatment, treatment response status was also defined binary by estimating the number of responders (i.e. ≥ 50% reduction of pre-treatment PTSD scores) vs. the number of non-responders (i.e. ≤ 50% reduction of pre-treatment PTSD scores), using a validated method by Furukawa et al (Cuijpers et al., 2017). In order to follow the intention-to-treat principle, randomized patients who were not included in the primary studies' final responder analyses were considered as non-responders and thereby included in the current meta-analysis (Furukawa, Cipriani, Barbui, Brambilla, & Watanabe, 2005). Binary data were then pooled across studies to obtain the RR of treatment response status between patients with and without comorbid PDs.

2.5.4. Heterogeneity
Higgins' I^2 and its 95% CI was calculated as an indicator of the total variation in pooled effects size estimates that are due to heterogeneity between studies. Higher percentages indicate higher heterogeneity, with values of 25%, 50% and 75% indicating low, moderate and high heterogeneity respectively (Higgins & Thompson, 2002).

2.5.5. Publication bias
The tendency for publication bias was assessed through visual inspection of the funnel plot and through Egger's test of the intercept. When Egger's test was significant, Duval and Tweedie's trim-and-fill procedure was used to estimate the true effect size (Harrer, Cuijpers, Furukawa, & Ebert, 2019).

2.5.6. Meta-regression and sensitivity analyses
To examine the impact of between-study differences in risk of bias on the meta-analysis results, a meta-regression analysis was conducted according to the quality assessments of each study ranging from 0 (high risk of bias) to 4 (low risk of bias). Lastly, sensitivity analyses with only low risk of bias studies (4 points) were performed to assess the impact of low-quality studies on the meta-analysis results.

3. Results

3.1. Study characteristics

Figure 1 depicts the study selection process. The electronic search resulted in 1830 hits including 1341 duplicates. After screening titles and abstracts of the remaining 468 publications, 438 publications were excluded mostly due to the lack of a strongly or conditionally recommended therapy for PTSD, PTSD and/or PD diagnostics. Accordingly, full texts of 30 studies were assessed for eligibility. This led to the exclusion of 19 studies, due to the lack of a strongly or conditionally recommended therapy for PTSD (6 studies), the lack of PTSD/PD diagnostics (7 studies), the lack of PTSD-only patients (1 study), a too small sample (2 studies), lack of response from the corresponding authors (2 studies) or because the authors indicated that the requested raw data were no longer available (1 study). In addition, four ongoing studies were excluded. Cross-referencing (i.e. screening the reference of an identified study in order to identify other relevant studies) led to the inclusion of five additional studies. Accordingly, 12 publications reporting on a total of 918 patients were included in this meta-analysis.

Characteristics of each included study are summarized in Table 1. Table 2 displays the extracted data from the included studies. Raw data were provided by authors from all studies, except for four studies (Feeny et al., 2002; McDonagh et al., 2005; Walter et al., 2012; Zayfert et al., 2005). For these studies, data were extracted directly from the publication. Ten out of twelve included studies provided adequate data on pre- and post-treatment PTSD severity, and dropout data was also provided by ten out of twelve studies. The median sample size of the data extracted for this meta-analysis was 57 (range 29–157) and approximately 84% of the patients were female. Whereas eight study designs concerned an RCT, there were four clinical trials (pre- vs. post-design) without a control group (Walter et al., 2012;
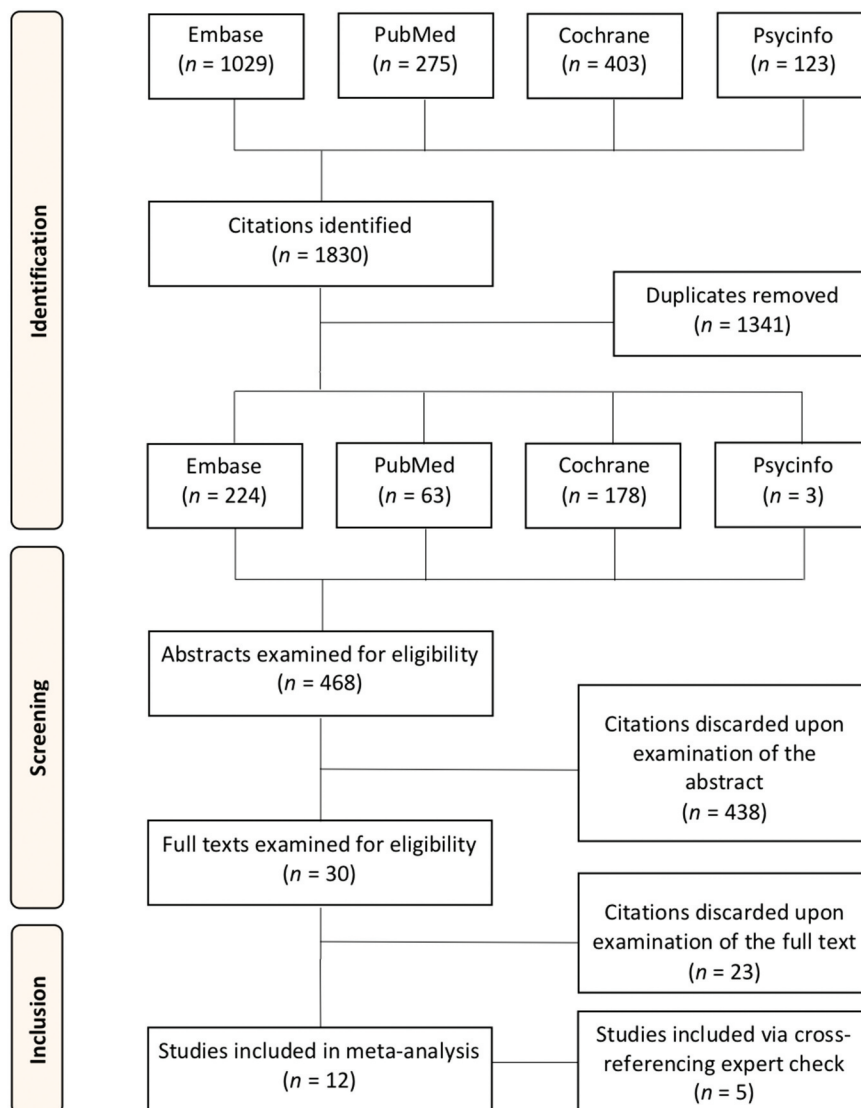

Figure 1. Flowchart of the search and selection process up to 31 January 2020.

Table 1. Characteristics of included studies

NR	Study	Total N in study (No. of females)	N included in meta-analysis[a] (No. Of PTSD + PD patients, No. of PTSD-only patients)	Baseline PD diagnostic status in PTSD + PD group	Type of traumatic event	PTSD and PD measures	Intervention(s)
EXPOSURE-BASED INTERVENTIONS							
1	Feeny et al., 2002	72 (All F)	58 (9, 49)	Approx. 58% full BPD (I.e. ≥ 5 symptoms and 42% partial BPD (I.e. 3 or 4 symptoms) Excluded: current suicidal ideation or recent history of parasuicidal behaviour	Sexual (72%) or physical (28%) assault	(DSM-III-R) PSS-I SCID-II	9 twice-weekly 90–120-minute sessions of individual of PE, SIT or PE+SIT ($n = 58$) vs. WL ($n = 14$)
2	Minnen et al., 2002 (study 1)	59 (35 F)	47 (24, 23)	PD, not further specified	Car or other accident (24%), witnessing an accident or violence (10%), sexual abuse (25%), work-related trauma (15%), severe violence (8%), finding a dead person after suicide or homicide (8%), severe ill-treatment at home/work (8%)	(DSM-III-R/-IV) PSS-I PDQ (>28)	9 weekly 90-minute sessions of individual PE ($n = 59$)
3	Van Minnen et al., 2002 (study 2)	63 (39 F)	54 (15, 39)	PD, not further specified	Car or other accident (27%), witnessing an accident or violence (5%), sexual abuse (22%), work-related trauma (5%), severe violence (21%), finding a dead person after suicide or homicide (2%), severe ill-treatment at home/work (20%)	(DSM-III-R/-IV) PSS-I SCID-II	9 weekly 90-minute sessions of individual of PE ($n = 63$)
4	Zayfert et al., 2005	115 (94 F)	115 (39, 76)	BPD	Childhood sexual (50%) or physical (10%) abuse, adulthood sexual (10%) or physical (10%) abuse, accident (10%), other (11%)	(DSM-IV) CAPS ADIS-IV-R incl. BPD criteria	Individual CBT for PTSD (incl. imaginal and in vivo exposure and cognitive restructuring – number of sessions adapted to participants' needs) ($n = 115$)
5	McDonagh et al., 2005	74 (all F)	29 (15, 14)	BPD ($n = 4$) and avoidant PD ($n = 11$)	Childhood sexual abuse	(DSM-IV) CAPS SCID-I/SCID-II	14 sessions of individual CBT (incl. PE, in vivo exposure and cognitive restructuring) ($n = 29$) vs. PCT ($n = 22$) vs. WL ($n = 23$)
6	Clarke et al 2008	131 (all F)	131 (39, 92)	BPD	Sexual assault	(DSM-IV) CAPS SNAP (>15)	12 bi-weekly sessions of individual PE or CPT ($n = 131$) vs. WL (all waitlist patients received PE or CPT afterwards)
7	Markowitz et al., 2015[2]	110 (78 F)	78 (35, 43)	28% paranoid, 27% obsessive-compulsive, 23% avoidant, 15% narcissistic, 3% dependent PD. Excluded: borderline PD.	Physical (63%) or sexual (36%) abuse	(DSM-IV) CAPS SCID-II	10 90-minute sessions of individual PE ($n = 38$) vs. 14 50-minute sessions of individual IP ($n = 40$) vs. 9 90-minute and one 30-minute session of individual relaxation therapy ($n = 32$)
EXPOSURE-BASED INTERVENTIONS FOR PTSD IN COMBINATION WITH SKILLS TRAINING FOR COMORBID DISORDERS							
8	Mills et al 2012	103 (64 F)	55 (38, 17)	BPD. Excluded: current suicidal ideation (plan and intent) self-harm past 6 months.	Physical assault (95%), sexual abuse (76%), threatened or held captive (91%), witnessed injury or death (84%), accident (73%), torture (27%), combat (2%), other (71%)	(DSM-IV) CAPS IPDE	13 90-minute sessions of individual COPE (i.e. psychoeducation, imaginal exposure, in vivo exposure, cognitive therapy for PTSD and CBT for substance use disorders) + TAU ($n = 55$) vs. TAU ($n = 48$)
9	Bohus et al., 2013[3]	74 (all F)	36 (17, 19)	BPD	Childhood sexual abuse	(DSM-IV) CAPS IPDE	12-week inpatient DBT-PTSD (exposure-based techniques in combination with DBT skills training) ($n = 36$) vs. TAU/WL ($n = 38$)

(Continued)

Table 1. (Continued).

NR	Study	Total N in study (No. of females)	N included in meta-analysis^a (No. Of PTSD + PD patients, No. of PTSD-only patients)	Baseline PD diagnostic status in PTSD + PD group	Type of traumatic event	PTSD and PD measures	Intervention(s)
COGNITIVE INTERVENTIONS FOR PTSD IN COMBINATION WITH SKILLS TRAINING FOR COMORBID DISORDERS							
10	Walter et al., 2012	179 (Approx. 25%F)	157 (104, 53)	45% paranoid, 30% avoidant, 15% borderline, 11% obsessive–compulsive, 5%, 4% passive–aggressive, dependent, 3% antisocial, 2% narcissistic and 1% schizotypal PD	Combat (54%), sexual assault (24%), 22% other (e.g. physical assault, childhood sexual abuse, transportation accident	(DSM-IV) CAPS SCID-II	12 twice-weekly 90-minute sessions of group CPT + 13 twice-weekly 50–60-minute sessions of individual CPT + 15 60–90-minute sessions of group skills training (n = 179)
11	Kredlow et al., 2017 (study 1)[48]	108 (No. F unknown)	54 (15, 39)	BPD	Child sexual (89%) and/or physical (82%) abuse, adult sexual (85%) and/or physical (96%) abuse, death (93%), witness (89%), threat (82%), accident (78%).	(DSM-IV) CAPS SCID-II	12–16 weekly 50-minute sessions of individual CBT (psycho-education, skills training and cognitive restructuring) (n = 54) vs. TAU (n = 54)
12	Kredlow et al., 2017 (study 2)[48]	201 (No. F unknown)	104 (29, 75)	BPD	Child sexual (91%) and/or physical (93%) abuse, adult sexual (82%) and/or physical (93%) abuse, witness (86%), death (86%), threat (76%), accident (60%), combat (6%).	(DSM-IV) CAPS SCID-II	12–16 weekly 50-minute sessions of individual CBT (psycho-education, skills training, and cognitive restructuring) (n = 104) vs. Brief treatment (n = 97)

^1In order to compute treatment effect sizes for the current meta-analysis, only those patients that received PTSD treatment *and* of whom pre- and post-treatment data on PTSD and PD diagnostics were available were included in the current meta-analysis. Since not all patients were randomized to the active PTSD treatment condition and/or not all patients meeting PTSD and PD criteria and/or missing data, the number of patients included in this meta-analysis does not always correspond to the total sample size of the included study.

^2Authors of the study indicated that SCID-II data was available for 78 patients. Therefore, data from these 78 patients were used for the current meta-analysis.

^3DBT-PTSD consisted of group sessions focusing on identifying cognitive, emotional and behavioural escape strategies (week 1–4) and individual trauma-focused cognitive and exposure-based sessions + acceptance of trauma-related facts (week 5–12) ADIS = Anxiety Disorders Interview Schedule for DSM-IV – Revised; BDI = Beck Depression Inventory; BPD = Borderline Personality Disorder; CAPS = Clinician Administered PTSD Scale; CBT = Cognitive behaviour therapy; COPE = Concurrent Treatment of PTSD and substance use disorders using Prolonged Exposure; CPT = Cognitive Processing Therapy; CR = Cognitive Restructuring; CT = Clinical Trial; DBT = Dialectical Behaviour Therapy; DBT-PTSD = group sessions of Dialectical Behaviour Therapy and individual sessions of trauma-focused interventions; DSM = Diagnostic and Statistical Manual of Mental Disorders; DTS-I = Davidson Trauma Scale – Interview; F = Female; IPDE = International Personality Disorder Examination; PCT = Present-Centered Therapy; PD = Personality Disorder; PDQ = Personality Diagnostic Questionnaire; PE = Prolonged Exposure; PSS-I = PTSD Symptom Scale Interview; PTSD = Post-Traumatic Stress Disorder; RCT = Randomized Controlled Trial; SCID = Structured Clinical Interview for DSM; SIT = Stress Inoculation Training; SNAP = Schedule for Adaptive and Non-adaptive Personality; TAU = Treatment As Usual; WL = Wait List.

Table 2. Data extracted from included studies

Nr	Study	Group 1: PTSD + PD			Group 2: PTSD only		
		Pre-treatment (N[a], mean, SD)	Post-treatment (N[b], mean, SD)	Dropout (%) (i.e. number of dropouts/number of patients that were intended to start treatment)	Pre-treatment (N[a], mean, SD)	Post-treatment (N[b], mean, SD)	Dropout (%) (i.e. number of dropouts/number of patients that were intended to start treatment)
EXPOSURE-BASED INTERVENTIONS							
1	Feeny et al., 2002	N = 9 PSS-I = 29.11 (7.55)	N = 9 PSS-I = 18.66 (10.71)	NR	N = 49 PSS-I = 29.78 (8.53)	N = 48 PSS-I = 11.18 (7.10)	NR
2	Van Minnen et al., 2002 (study 1)	N = 24 PSS-I = 29.88 (8.59)	N = 24 PSS-I = 21.17 (12.53)	7 (29%)	N = 23 PSS-I = 22.78 (6.74)	N = 23 PSS-I = 11.87 (9.81)	5 (22%)
3	Van Minnen et al., 2002 (study 2)	N = 15 PSS-I = 32.33 (8.67)	N = 15 PSS-I = 23.40 (12.81)	6 (40%)	N = 39 PSS-I = 25.49 (11.29)	N = 39 PSS-I = 18.64 (13.93)	16 (41%)
4	Zayfert et al., 2005	NR N = 39	NR	33 (85%)	NR N = 76	NR	50 (66%)
5	McDonagh et al., 2005	NR N = 15	NR	11 (73%)	NR N = 14	NR	1 (7%)
6	Clarke et al., 2008[3]	N = 39 PSS-I = 82.23 (19.87)	N = 39 PSS-I = 28.46 (19.33)	15 (38%)	N = 92 PSS-I = 73.83 (17.60)	N = 92 PSS-I = 24.40 (20.37)	30 (33%)
7	Markowitz et al., 2015	N = 35 CAPS = 66.60 (15.60)	N = 35 CAPS = 41.80 (28.40)	4 (11%)	N = 43 CAPS = 71.20 (16.00)	N = 43 CAPS = 38.30 (28.50)	2 (5%)
EXPOSURE-BASED INTERVENTIONS FOR PTSD IN COMBINATION WITH SKILLS TRAINING FOR COMORBID DISORDERS							
8	Mills et al 2012	N = 38 CAPS = 91.50 (15.97)	N = 38 CAPS = 51.80 (31.19)	30 (79%)	N = 17 CAPS = 90.40 (14.94)	N = 17 CAPS = 47.00 (23.19)	15 (88%)
9	Bohus et al., 2013[4]	N = 14 CAPS = 85.06 (15.61)	N = 14 CAPS = 61.44 (25.92)	1 (6%)	N = 15 CAPS = 90.53 (12.62)	N = 15 CAPS = 53.29 (25.21)	1 (5%)
COGNITIVE INTERVENTIONS FOR PTSD IN COMBINATION WITH SKILLS TRAINING FOR COMORBID DISORDERS							
10	Walter et al., 2012[5]	N = 104 CAPS = 75.60 (13.38)	N = 104 CAPS = 43.20 (22.78)	NR	N = 53 CAPS = 78.49 (16.48)	N = 53 CAPS = 42.79 (22.29)	NR
11	Kredlow et al., 2017 (study 1)	N = 15 CAPS = 81.73 (18.21)	N = 8 CAPS = 53.50 (31.71)	3 (20%)	N = 39 CAPS = 71.67 (16.70)	N = 24 CAPS = 56.21 (27.26)	7 (18%)
12	Kredlow et al., 2017 (study 2)	N = 29 CAPS = 91.52 (14.49)	N = 26 CAPS = 73.19 (25.67)	9 (31%)	N = 75 CAPS = 83.95 (12.52)	N = 61 CAPS = 59.75 (26.84)	29 (39%)

[1] Since this number refers to the number of patients of whom pre-treatment data were available to compute treatment effect sizes for the current meta-analysis, it does not always correspond to the total number of patients that were randomized to PTSD treatment.

[2] Since this number refers to the number of patients of whom post-treatment data were available to compute treatment effect sizes for the current meta-analysis it does not always corresponds to the total number of treatment completers.

[3] Since there is an inconsistency of 2 points between the dropout data reported in the publication and the raw dropout data provided by the authors of the study, we contacted the authors to clarify this inconsistency. The authors of the included study confirmed that the raw dropout data and thus the data that was used for this meta-analysis, is correct.

[4] Authors of the included study indicated that data were missing for 3 of the 17 patients with a comorbid PD and for 4 of the 19 patients without a comorbid PD. For the current study, treatment effect sizes were therefore calculated with a pre-treatment N of 14 and 15 respectively for patients with and without comorbid PDs.

[5] Although 110 patients met criteria for at least one PD and 57 patients did not meet PD criteria, the publication only reported on pre-and post-treatment CAPS data for 104 PD+ and 53 PD- patients.

NR = Not reported; PD = Personality Disorder; PTSD = Post-Traumatic Stress Disorder; SD = Standard deviation.

Van Minnen et al., 2002, study 1 and 2; Zayfert et al., 2005). Patients developed PTSD in association with different traumatic events, with childhood physical or sexual abuse being reported as the most common form of traumatic experience. All included studies investigated a strongly recommended treatment method for PTSD according to the APA (American Psychological Association, 2017), ranging from PE (Feeny et al., 2002; Van Minnen et al., 2002, study 1 and 2; Markowitz et al., 2015), PE or CPT (Clarke et al., 2008), CBT for PTSD including PE and cognitive restructuring (McDonagh et al., 2005; Zayfert et al., 2005), CBT for PTSD including CPT and skills training (Kredlow et al., 2017, study 1 and 2), a combination of PE and cognitive therapy for PTSD (Mills et al., 2012), a combination of exposure-based techniques and skills training (Bohus et al., 2013) and a combination of CPT and skills training (Walter et al., 2012). All patients in the comorbid PD group met full PD criteria except for one study in which approximately half of the patients met full PD criteria while the other half met partial PD criteria (Feeny et al., 2002). PTSD and PD symptoms were assessed by a clinical interview method, except for two studies that used a self-report measure to assess PDs (Van Minnen et al., 2002, study 1; Clarke et al., 2008).

3.2. Study quality

The estimated risk of bias for each study is presented in Table 3. Figure 2 provides a graphical summary of study quality. Of the 12 included studies, the majority used a randomly generated sequence for allocation concealment ($n = 8$, 67%). Fewer studies concealed the allocation to treatment ($n = 4$, 33%). Most studies blinded the outcome assessor(s) ($n = 9$, 75%) and adequately addressed incomplete outcome data ($n = 11$, 92%). In total, three studies were assessed as low risk of bias in all four domains (Bohus et al., 2013; Markowitz et al., 2015; Mills et al., 2012).

3.3. Pre-treatment PTSD severity

We did not find a statistically significant difference in pre-treatment PTSD severity between patients with and without comorbid PDs (Hedges' $g = 0.23$, 95%CI −0.09–0.55, $p = .140$). Heterogeneity was moderate ($I^2 = 66\%$, 95%CI 34–83, $p = .002$). Visual inspection of the funnel plot suggested no indications for publication bias, which was confirmed by a nonsignificant Egger's test ($t = 0.571$, $p = .583$). As can be observed from Figure 3, there were no outlier studies.

3.4. Dropout from PTSD treatment

We did not find a statistically significant difference in dropout rates between patients with and without comorbid PDs (RR = 1.19, 95%CI 0.83–1.72, $p = .297$). A heterogeneity analysis indicated low heterogeneity between studies ($I^2 = 28\%$, 95%CI 0–66, $p = .186$). Based on visual inspection of the funnel plot and Egger's test ($t = 0.910$, $p = .389$) there were no indications for publication bias. The forest plot shown in Figure 4 gave no indication for outlier studies.

3.5. Response to PTSD treatment

3.5.1. Difference in post-treatment PTSD symptom improvement between patients with and without PDs

A statistically significant large effect size of pre- to post-treatment improvement in PTSD scores was found in patients with comorbid PDs (Hedges' $g = 1.31$, 95%CI 0.89–1.74, $p < .001$) as well as in patients without comorbid PDs (Hedges' $g = 1.57$, 95%CI 1.08–2.07, $p < .001$) (Figure 5). When comparing post-treatment PTSD scores, a significantly higher post-treatment PTSD mean score was found in patients with comorbid PDs compared to patients without comorbid PDs (Hedges' $g = 0.22$, 95%CI 0.05–0.38, $p = .010$). Visual inspection of the funnel plot and Egger's test ($t = 0.336$, $p = .745$) suggested that publication bias was unlikely. No outlier studies were detected (Figure 6).

Table 3. Risk of bias assessment for included studies.

| Nr	Study	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of outcome assessors (detection bias)	Incomplete outcome data assessed (attrition bias)	Overall risk of bias judgment
1	Feeny et al., 2002	Low	Low	Low	High	3
2	Van Minnen et al., 2002 (study 1)	High	High	Low	Low	2
3	Van Minnen et al., 2002 (study 2)	High	High	Low	Low	2
4	Zayfert et al., 2005	High	High	Unclear	Low	1
5	McDonagh et al., 2005	Low	Unclear	Low	Low	3
6	Clarke et al., 2008	Low	Unclear	Unclear	Low	2
7	Mills et al., 2012	Low	Low	Low	Low	4
8	Markowitz et al., 2015	Low	Low	Low	Low	4
9	Bohus et al., 2013	Low	Low	Low	Low	4
10	Walter et al., 2012	High	High	Unclear	Low	1
11	Kredlow et al., 2017 (study 1)	Low	Unclear	Low	Low	3
12	Kredlow et al., 2017 (study 2)	Low	Unclear	Low	Low	3
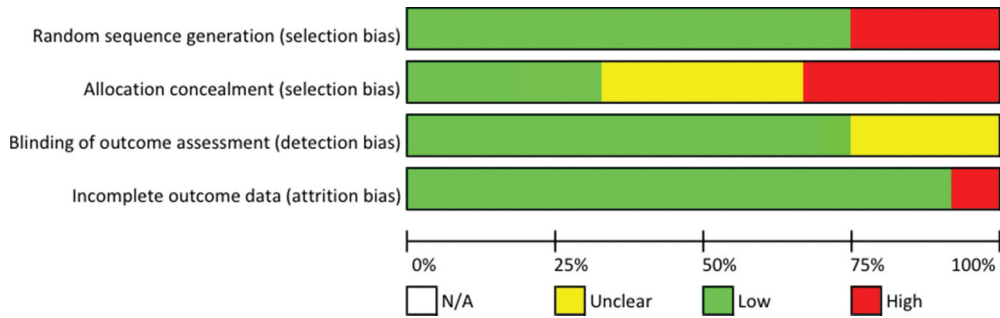
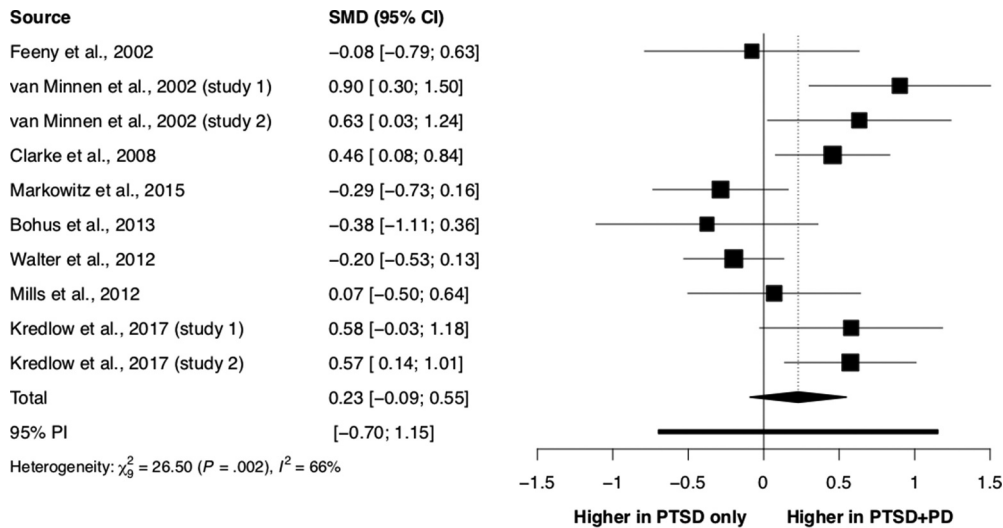**Figure 2.** Graphical representation of study quality.

Figure 3. Forest plot illustrating the standardized mean difference (SMD) of pre-treatment PTSD severity, comparing patients with and without comorbid PDs.

PTSD mean scores, comparing patients with and without comorbid PDs.

3.5.2. Difference in treatment response status between patients with and without PDs

When comparing the number of treatment responders at post-treatment, no statistically significant difference was found between patients with and without comorbid PDs (RR = 1.18, 95%CI 0.97–1.42, p = .082). Heterogeneity was low (I^2 = 0%, 95%CI 0–41, p = .762). There were no indications for publication bias (Egger's test; t = 2.304, p = .050). No outlier studies were detected (Figure 7).

3.6. Exploratory analyses: borderline PD

Since 7 of the 12 included studies reported on borderline PD patients, exploratory analyses comparing PTSD patients with and without comorbid borderline PD were conducted. No statistically significant difference was found between patients with and without comorbid borderline PD in pre-treatment PTSD severity (Hedges' g = 0.27, 95%CI −0.12–0.66, p = .141), dropout from PTSD treatment (Hedges' g = 1.07, 95%CI 0.87–1.32, p = .452), pre- to post-treatment improvement in PTSD symptoms (Hedges'

g = 0.26, 95%CI −0.06–0.58, p = .120) or the number of treatment responders (Hedges' g = 1.18, 95%CI 0.79–1.75, p = .337). A statistically significant large effect size of the pre- to post-treatment improvement in PTSD scores was found in patients with comorbid borderline PD (Hedges' g = 1.45, 95%CI 0.71–2.18, p = .004).

3.7. Meta-regression and sensitivity analyses

Meta-regression analyses indicated that between-study differences in risk of bias ratings did not significantly explain the variability in effect sizes with regard to pre-treatment PTSD severity (p = .365), dropout from PTSD treatment (p = .905), pre- to post-treatment PTSD symptom improvement in patients with comorbid PDs (p = .435) and in patients without comorbid PDs (p = .880), treatment response when defined as post-treatment PTSD mean score (p = .527) or treatment response when defined as a symptom reduction of at least 50% (p = .314).

Sensitivity analysis with the three low risk of bias studies yielded results similar to the primary meta-analysis findings of pre-treatment PTSD severity (Hedges' g = −0.19, 95%CI −0.74–0.36, p = .275)

Source	RR (95% CI)
van Minnen et al., 2002 (study 1)	1.34 [0.50; 3.63]
van Minnen et al., 2002 (study 2)	0.98 [0.47; 2.01]
Zayfert et al., 2005	1.29 [1.04; 1.59]
McDonagh et al., 2005	10.27 [1.52; 69.55]
Clarke et al., 2008	1.18 [0.72; 1.93]
Markowitz et al., 2015	2.46 [0.48; 12.64]
Bohus et al., 2013	1.12 [0.08; 16.52]
Mills et al., 2012	0.89 [0.70; 1.14]
Kredlow et al., 2017 (study 1)	1.11 [0.33; 3.75]
Kredlow et al., 2017 (study 2)	0.80 [0.43; 1.48]
Total	1.19 [0.83; 1.72]
95% PI	[0.37; 3.83]

Heterogeneity: $\chi^2_9 = 12.50$ ($P = .19$), $I^2 = 28\%$

Higher in PTSD only   Higher in PTSD+PD
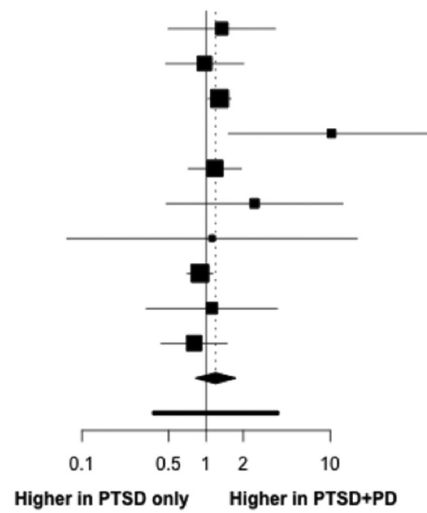
Figure 4. Forest plot illustrating the relative risk (RR) of dropout from PTSD treatment, comparing patients with and without comorbid PDs.

a

Source	SMD (95% CI)
Feeny et al., 2002	1.07 [0.08; 2.07]
van Minnen et al., 2002 (study 1)	0.80 [0.21; 1.39]
van Minnen et al., 2002 (study 2)	0.79 [0.05; 1.54]
Clarke et al., 2008	2.72 [2.10; 3.33]
Markowitz et al., 2015	1.07 [0.57; 1.57]
Bohus et al., 2013	1.07 [0.28; 1.87]
Walter et al., 2012	1.73 [1.41; 2.05]
Mills et al., 2012	1.59 [1.07; 2.10]
Kredlow et al., 2017 (study 1)	1.15 [0.23; 2.08]
Kredlow et al., 2017 (study 2)	0.88 [0.32; 1.43]
Total	1.31 [0.89; 1.74]
95% PI	[0.05; 2.58]

Heterogeneity: $\chi^2_9 = 34.87$ ($P < .001$), $I^2 = 74\%$

SMD
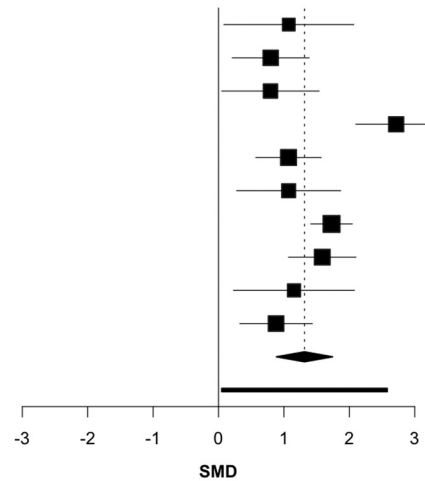
b

Source	SMD (95% CI)
Feeny et al., 2002	2.35 [1.83; 2.87]
van Minnen et al., 2002 (study 1)	1.27 [0.64; 1.91]
van Minnen et al., 2002 (study 2)	0.53 [0.08; 0.99]
Clarke et al., 2008	2.59 [2.19; 2.98]
Markowitz et al., 2015	1.41 [0.94; 1.88]
Bohus et al., 2013	1.82 [0.96; 2.68]
Walter et al., 2012	1.81 [1.36; 2.26]
Mills et al., 2012	2.17 [1.32; 3.03]
Kredlow et al., 2017 (study 1)	0.72 [0.19; 1.24]
Kredlow et al., 2017 (study 2)	1.19 [0.82; 1.56]
Total	1.57 [1.08; 2.07]
95% PI	[0.03; 3.11]

Heterogeneity: $\chi^2_9 = 73.41$ ($P < .001$), $I^2 = 88\%$
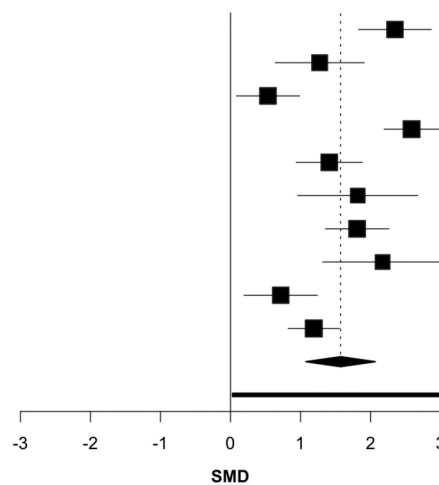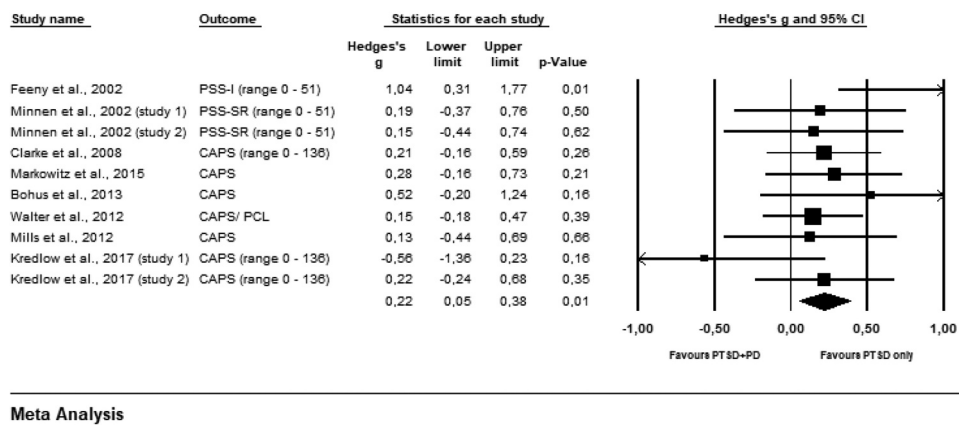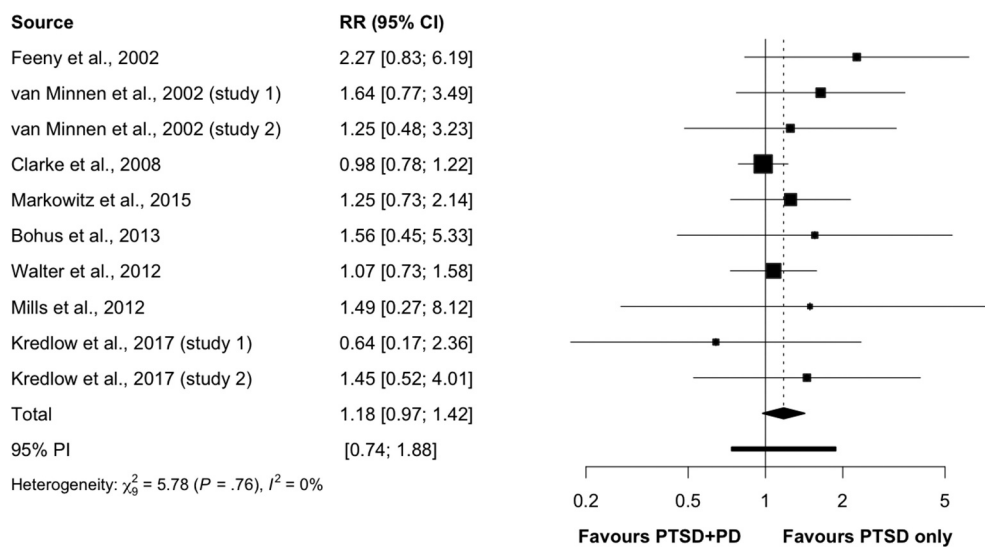
SMD

Figure 5. Forest plots illustrating the standardized mean difference (SMD) of the pre- to post-treatment improvement in PTSD symptoms, in patients with comorbid PDs (top) and without comorbid PDs (bottom).

Meta Analysis

Figure 6. Forest plot illustrating the Hedges' *g* effect size of the difference in post-treatment.

Figure 7. Forest plot illustrating the relative risk (RR) of treatment response status (i.e. at least 50% reduction in pre- to post-treatment PTSD scores), comparing patients with and without comorbid PDs.

and dropout from PTSD treatment (RR = 1.01, 95% CI 0.39–2.65, $p = .967$), while the treatment effect size became lower in patients with comorbid PDs (Hedges' $g = 1.27$, 95%CI 0.51–2.04, $p = .019$) but higher in patients without comorbid PDs (Hedges' $g = 1.70$, 95%CI 0.73–2.67, $p = .017$). With regard to the difference in treatment response between patients with and without comorbid PDs, sensitivity analyses did alter the findings such that the initial significant difference in post-treatment PTSD mean scores between patients with and without comorbid PDs became nonsignificant (Hedges' $g = 0.28$, 95%CI −0.04–0.60, $p = .080$), while the primary nonsignificant difference in the number of treatment responders became significantly higher in favour of patients without comorbid PDs (RR = 0.76, 95%CI 0.59–0.99, $p = .046$). Lastly, when comparing the mean PTSD scores at post-treatment, sensitivity analyses with correlations of 0.25, 0.5 and 0.99 yielded identical results.

Additional sensitivity analyses were performed excluding two studies that assessed PD with a self-report measure (Van Minnen et al., 2002 – study 1; Clarke et al., 2008), since this possibly resulted in a group with less severe PD pathology. A third study was excluded (Feeny et al., 2002) as not all patients in its PD group met full PD criteria (Feeny et al., 2002). Sensitivity analyses with the remaining studies yielded results similar to the primary meta-analysis findings of pre-treatment PTSD severity (Hedges' $g = 0.14$, 95%CI −0.27–0.54, $p = .445$) and dropout from PTSD-treatment (RR = 1.22, 95%CI 0.72–2.06, $p = .407$). The treatment response effect size remained significant in both the comorbid PD group (Hedges' $g = 1.26$, 95%CI 0.90–1.61, $p < .001$) and PTSD-only group (Hedges' $g = 1.33$, 95%CI 0.80–1.87, $p = .001$). The difference in post-treatment PTSD scores became nonsignificant (Hedges' $g = 0.17$, 95%CI −0.02–0.35, $p = .080$) and the same was true for the difference in the number of treatment responders (RR = 1.17, 95%CI 0.97–1.40, $p = .084$).

4. Discussion

This constitutes the first meta-analysis investigating whether psychotherapy can be as effectively applied in patients with comorbid PDs as in patients without comorbid PDs. Findings suggest that patients with comorbid PDs do not have significantly more severe PTSD symptoms at baseline, nor are at higher risk for dropout from PTSD treatment compared to patients without comorbid PDs. Although pre- to post-treatment improvements in PTSD symptoms were large in both groups, PDs were associated with a significantly smaller symptom improvement at post-treatment.

Current findings contradict the commonly held view that an additional PD diagnosis aggravates PTSD pathology or increases the chance on dropout from PTSD treatment. With regard to previous research, only a small number of studies explicitly addressed the impact of PDs on baseline PTSD symptomatology (Frías & Palma, 2015; Hefferman & Cloitre, 2000; Pagura et al., 2010; Walter et al., 2012), while the few studies that examined the association between PDs and dropout from PTSD treatment yielded inconsistent results (Clarke et al., 2008; Feeny et al., 2002; Hembree et al., 2004; McDonagh et al., 2005; Van Emmerik, Kamphuis, Noordhof, & Emmelkamp, 2011; Van Minnen et al., 2002). Current findings of treatment response are more nuanced. Although pre- to post-treatment PTSD symptom improvements were large in both groups and no significant difference in the number of treatment responders was found, patients with comorbid PDs had a significantly smaller improvement in PTSD symptoms at post-treatment compared to patients without comorbid PDs. These results suggest that, although the presence of comorbid PDs does not preclude a good response to PTSD treatment, patients with comorbid PDs benefit less from PTSD treatment than patients without comorbid PDs. The magnitude of our pre- to post-treatment effect size in patients without comorbid PDs ($g = 1.46$) was similar to those found in previous PTSD effect studies ($d = 1.43$) (Bradley et al., 2005) and our pre- to post-treatment effect size in patients with comorbid PDs ($g = 1.16$) was comparable to the effect size of a recent meta-analysis on psychotherapy for PTSD in patients with comorbid borderline PD ($g = 1.04$) (Slotema et al., 2020). It should, however, be noted that visual inspection of the data presented Table 2 shows that the average PTSD symptom severity at post-treatment remained significant in most included studies. Findings from previous studies regarding the impact of comorbid PDs on PTSD treatment response are divergent. While some studies found a poorer response in patients with comorbid PDs (Cloitre & Koenen, 2001; Forbes et al., 2002; Hembree et al.,

2004; Stalker et al., 2005; Tarrier et al., 2000) others concluded that both groups of patients can equally benefit from PTSD treatment (Clarke et al., 2008; Feeny et al., 2002; Markowitz et al., 2015; Van Minnen et al., 2002; Walter et al., 2012). These inconsistent findings could be explained by varying definitions of treatment response. Studies that did find a negative relationship between PDs and the response to PTSD treatment generally relied on continuous change scores (e.g. pre- to post-treatment improvement in CAPS-5 scores) (Cloitre & Koenen, 2001; Forbes et al., 2002; Stalker et al., 2005; Tarrier et al., 2000), while studies that did not find such a relationship based their conclusions on binary definitions of treatment response, such as the absence of a PTSD diagnosis at the end of treatment or a symptom reduction of at least 30% (Feeny et al., 2002; Markowitz et al., 2015; Walter et al., 2012). In line with this, Hembree et al. (2004) did find a significant difference in good-end-state functioning (i.e. PSS-I score ≤ 15 plus BDI and BAI scores ≤ 10) in favour of patients without comorbid PDs, while no differences were found in the prevalence of a PTSD diagnosis at the end of treatment (Hembree et al., 2004). Since our findings also depend on whether treatment response was defined continuously or binary, future studies should be aware of the impact that different clinical definitions can have on the significance of findings.

There are several issues within the examined literature that warrant further discussion. The fairly small number of included studies ($N = 12$) may have limited the power to detect effects. Systematic and well-powered research is therefore needed to further establish the role of comorbid PDs in the treatment of PTSD. The lack of power also impeded subgroup analyses with regard to potential moderating pathways. Due to the low number of studies available we could not address the type of PDs, but instead merged the data from all included studies. This approach dismisses the great variety in PD pathology and thereby masks potential relationships between certain PD types and PTSD treatment outcome. Although exploratory analyses yielded similar results for borderline PD patients, future studies should further address this important issue. A second likely moderator concerns the severity of PD symptoms. The restrictive eligibility criteria that some of the included studies used (e.g. exclusion of patients with suicidal ideations, self-injurious behaviour and/or borderline PD), along with the fact that not all patients in the comorbid PD group of Feeny et al. (2002) met full borderline PD criteria and two studies used self-report measures as an indicator of PD diagnosis (Van Minnen et al., 2002 – study 1; Clarke et al., 2008), likely resulted in a group of patients with less severe PD pathology. It is conceivable that PTSD treatment outcome will be worse in patients with more

severe PD symptoms, which may result in differential dropout rates and even larger differences in PTSD treatment response between patients with and without comorbid PDs. While this finding was not confirmed by our sensitivity analyses, future studies with more power should further investigate this. A third moderator constitutes the type of PTSD treatment. After all, the impact of comorbid PDs might depend on the technique used to treat PTSD. Also, while some studies examined stand-alone PTSD treatments, others added management- or skills trainings to their PTSD treatment arsenal. It can be argued that the addition of such therapeutic components as to address both PTSD and PDs holds the potential to enhance treatment effects. Future studies should thus investigate the impact of these potential moderators, for example through an individual patient data meta-analysis in order to distinguish between clinical patient profiles and to assess moderators at the individual patient level. Next to these power considerations, any conclusions drawn from the current meta-analysis must be cognizant with the quality of the reviewed literature. Studies were heterogeneous regarding age, trauma history, treatment type and duration, while the majority of patients (approx. 72%) were female. Differences in study quality further hampered comparison. In order to statistically account for this anticipated heterogeneity, a random effects model was applied. Reassuringly, meta-regression analyses indicated that none of our findings was affected by differences in the quality between studies. Sensitivity analyses with low risk of bias studies yielded similar results with regard to pre-treatment PTSD severity and dropout from PTSD treatment, while they did alter our findings with regard to treatment response. It should however be noted that only three studies were deemed as low risk of bias, while not all potential sources of bias were assessed. For instance, blinding of participants and personnel was not assessed, as these can generally not be blinded in psychological intervention studies. Selective outcome reporting was not assessed either, since we believe that a careful assessment of this criterion requires a prospectively registered study protocol. Unfortunately, the vast majority of included studies was not prospectively registered, which is typically the case for psychotherapy trials (Harriman & Patel, 2016; Miguel et al., in press). Other potential sources of bias (e.g. baseline imbalances, deviations from treatment protocol) were not assessed in this meta-analysis either. Taken together, the true risk of bias of included studies might be higher than currently estimated. In order to increase reliability of the data and between-study consensus, we encourage future studies to prospectively register their study protocol, include intention-to-treat analyses, masked outcome assessments, a clear description of trauma history, well-defined and empirically supported exclusion criteria, systematic data on comorbid conditions, both a continuous (e.g. pre- to post-treatment symptom improvement) and binary definition (e.g. 50% reduction in PTSD symptoms, no longer meeting PTSD criteria) of treatment response and follow-up measurements.

Despite these limitations, current meta-analysis findings suggest that trauma-focused interventions can be safely and effectively applied in patients with comorbid PDs. There seems to be no reason, at least not on an empirical level, to exclude patients with PDs from PTSD treatment. This does not mean, however, that all patients with comorbid personality pathology will equally benefit from PTSD treatment, let alone that treating these patients can be extra challenging to the therapist in question. Various theories have been proposed to account for the negative relationship between PDs and PTSD treatment outcome. For instance, high rates of dissociation, emotion dysregulation and substance abuse in patients with borderline personality pathology could interfere with emotional engagement and corrective information processing, thereby suppressing the efficacy of exposure therapy for PTSD (Gratz, Rosenthal, Tull, Lejuez, & Gunderson, 2006; Hagenaars, Van Minnen, & Hoogduin, 2010; Van Minnen et al., 2002). In addition, the generally extensive trauma histories in combination with the often-fragmented nature of traumatic memories in borderline PD patients, can further complicate PTSD treatment (Harned, 2013). We therefore want to underline the importance of an elaborate case conceptualization prior to treatment. Clinicians treating patients with a PTSD should inquire about the presence and severity of PDs more routinely, in order to estimate if and to what extent comorbid PDs might affect the severity and the presentation of PTSD symptoms, as well as the subsequent treatment of these symptoms. Especially in patients with more severe comorbid PDs, currently available PTSD treatments might then profit from certain modifications in order to optimally address individual patients' needs. Various methods have been proposed to improve treatment adherence and efficacy in patients with a PTSD and comorbid PDs, ranging from increasing the number of exposure in vivo tasks (Foa, Hembree, & Rothbaum, 2007) to adding skills training (Dorrepaal et al., 2010) or dialectical behavioural therapy (DBT) for borderline PD to prolonged exposure (PE) for PTSD (DBT + DBT PE) (Harned, Korslund, Foa, & Linehan, 2012). Next to further establishing the feasibility and clinical efficacy of already established PTSD treatments, the same should thus be done for more integrated, multi-component treatments.

In conclusion, the current meta-analysis suggests that patients with a PTSD and comorbid PDs do not have significantly more severe PTSD symptoms prior to

treatment, nor are at higher risk for dropout from PTSD treatment compared to patients without comorbid PDs. Findings also suggest that although the presence of comorbid PDs does not preclude a good response to PTSD treatment, patients with comorbid PDs might benefit less from PTSD treatment. Assessment of PD symptoms prior to treatment may support case conceptualization, while the integration of therapeutic elements that address both PTSD and PDs could enhance treatment effects. These findings emphasize the need for further research exploring the manner in which PTSD and PD symptoms interact prior to and during treatment, leading to a more accurate treatment allocation and higher clinical efficacy in patients with a PTSD and comorbid PDs.

Authors' contributions

All authors contributed to the design of the study. Statistical analyses were performed by A.S and M.C. The manuscript was drafted by A.S., J.N. and K.T. All authors contributed to the revisions of the manuscript and approved the final version of the manuscript for publication.

Availability of data and material

All data analyzed during this study are included in Tables 1 and 2 in the published article.

Consent for publication

Not applicable.

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References

American Psychiatric Association. (1987). *Diagnostic and statistical manual of mental disorders* (3rd ed., revised). Washington, DC: Author.

American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders* (4th ed.). Washington, DC: Author.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Arlington, VA: Author.

American Psychological Association. (2017). *Clinical practice guideline for the treatment of posttraumatic stress disorder (PTSD) in adults*. Washington, DC: American Psychological Association.

Blake, D. D., Weathers, F. W., Nagy, L. M., Kaloupek, D. G., Gusman, F. D., Charney, D. S., & Keane, T. M. (1995). The development of a clinician-administered PTSD scale. *Journal of Traumatic Stress*, 8(1), 75–90. doi:10.1002/jts.2490080106

Bohus, M., Dyer, A., Priebe, K. K., Kleindienst, N., Schmahl, C., Niedtfeld, I., . . . Steil, R. (2013). Dialectical behaviour therapy for post-traumatic stress disorder after childhood sexual abuse in patients with and without borderline personality disorder: A randomised controlled trial. *Psychotherapy and Psychosomatics*, 82(4), 221–233. doi:10.1159/000348451

Borenstein, M., Hedges, L. V., Higgins, J., & Rothstein, H. (2013). *Comprehensive meta-analysis version 3*. Englewood, NJ: Biostat.

Bradley, R., Greene, J., Russ, E., Dutra, L., & Westen, D. (2005). A multidimensional meta-analysis of psychotherapy for PTSD. *American Journal of Psychiatry*, 162(2), 214–227. doi:10.1176/appi.ajp.162.2.214

Breslau, N., Kessler, R. C., Chilcoat, H. D., Schultz, L. R., Davis, G. C., & Andreski, P. (1998). Trauma and posttraumatic stress disorder in the community: The 1996 Detroit area survey of trauma. *Archives of General Psychiatry*, 55(7), 626–632. doi:10.1001/archpsyc.55.7.626

Clarke, S., Rizvi, S., & Resick, P. (2008). Borderline personality characteristics and treatment outcome in cognitive-behavioral treatments for PTSD in female rape victims. *Behavior Therapy*, 39(1), 72–78. doi:10.1016/j.beth.2007.05.002

Cloitre, M., & Koenen, K. (2001). The impact of borderline personality disorder on process group outcome among women with posttraumatic stress disorder related to childhood abuse. *International Journal of Group Psychotherapy*, 51(3), 379–398. doi:10.1521/ijgp.51.3.379.49886

Cohen, J. (1988). *Statistical power analysis for the behavioral sciences* (2nd Ed.). Hillsdale, NJ: Lawrence Erlbaum Associates, Publishers.

Cuijpers, P. (2016). *Meta-analyses in mental health research. A practical guide*. Amsterdam: VU University Amsterdam.

Cuijpers, P., Weitz, E., Cristea, I. A., & Twisk, J. (2017). Pre-post effect sizes should be avoided in meta-analyses. *Epidemiology and Psychiatric Sciences*, *26*(4), 364–368. doi:10.1017/S2045796016000809

Dorrepaal, E., Thomaes, K., Smit, J. H., van Balkom, A. J., van Dyck, R., Veltman, D. J., & Draijer, N. (2010). Stabilizing group treatment for complex posttraumatic stress disorder related to childhood abuse based on psycho-education and cognitive behavioral therapy: A pilot study. *Child Abuse & Neglect*, *34*(4), 284–288. doi:10.1016/j.chiabu.2009.07.003

Feeny, N. C., Zoellner, L. A., & Foa, E. B. (2002). Treatment outcome for chronic PTSD among female assault victims with borderline personality characteristics: A preliminary examination. *Journal of Personality Disorders*, *16*(1), 30–40. doi:10.1521/pedi.16.1.30.22555

Foa, E., Hembree, E., & Rothbaum, B. O. (2007). *Prolonged exposure therapy for PTSD: Emotional processing of traumatic experiences therapist guide*. Oxford University Press.

Foa, E. B., Riggs, D. S., Dancu, C. V., & Rothbaum, B. O. (1993). Reliability and validity of a brief instrument for assessing post-traumatic stress disorder. *Journal of Traumatic Stress*, *6*(4), 459–473. doi:10.1002/jts.2490060405

Forbes, D., Creamer, M., Allen, N., Elliott, P., McHugh, T., Debenham, P., & Hopwood, M. (2002). The MMPI-2 as a predictor of symptom change following treatment for posttraumatic stress disorder. *Journal Of Personality Assessment*, *79*(2), 321–336. doi:10.1207/S15327752JPA7902_13

Frías, Á., & Palma, C. (2015). Comorbidity between post-traumatic stress disorder and borderline personality disorder: A review. *Psychopathology*, *48*(1), 1–10. doi:10.1159/000363145

Friborg, O., Martinussen, M., Kaiser, S., Øvergård, K. T., & Rosenvinge, J. H. (2013). Comorbidity of personality disorders in anxiety disorders: A meta-analysis of 30 years of research. *Journal of Affective Disorders*, *145*(2), 143–155. doi:10.1016/j.jad.2012.07.004

Furukawa, T. A., Cipriani, A., Barbui, C., Brambilla, P., & Watanabe, N. (2005). Imputing response rates from means and standard deviations in meta-analyses. *International Clinical Psychopharmacology*, *20*(1), 49–52. doi:10.1097/00004850-200501000-00010

Gratz, K. L., Rosenthal, M. Z., Tull, M. T., Lejuez, C. W., & Gunderson, J. G. (2006). An experimental investigation of emotion dysregulation in borderline personality disorder. *Journal of Abnormal Psychology*, *115*(4), 850. doi:10.1037/0021-843X.115.4.850

Hagenaars, M. A., Van Minnen, A., & Hoogduin, K. A. (2010). The impact of dissociation and depression on the efficacy of prolonged exposure treatment for PTSD. *Behaviour Research and Therapy*, *48*(1), 19–27. doi:10.1016/j.brat.2009.09.001

Harned, M. S. (2013). Treatment of posttraumatic stress disorder and comorbid borderline personality disorder. In E. A. Storch & D. McKay (Eds.), *Handbook of treating variants and complications in anxiety disorders* (pp. 203–221). New York, NY: Springer.

Harned, M. S., Korslund, K. E., Foa, E. B., & Linehan, M. M. (2012). Treating PTSD in suicidal and self-injuring women with borderline personality disorder: Development and preliminary evaluation of a dialectical behavior therapy prolonged exposure protocol. *Behaviour Research and Therapy*, *50*(6), 381–386. doi:10.1016/j.brat.2012.02.011

Harrer, M., Cuijpers, P., Furukawa, T. A., & Ebert, D. D. (2019). *Doing meta-analysis in R: A hands-on guide*. doi:10.5281/zenodo.2551803

Harriman, S. L., & Patel, J. (2016). When are clinical trials registered? An analysis of prospective versus retrospective registration. *Trials*, *17*(1), 1–8. doi:10.1186/s13063-016-1310-8

Heffernan, K., & Cloitre, M. (2000). A comparison of posttraumatic stress disorder with and without borderline personality disorder among women with a history of childhood sexual abuse: Etiological and clinical characteristics. *The Journal of Nervous and Mental Disease*, *188*(9), 589–595. doi:10.1097/00005053-200009000-00005

Hembree, E. A., Cahill, S. P., & Foa, E. B. (2004). Impact of personality disorders on treatment outcome for female assault survivors with chronic posttraumatic stress disorder. *Journal of Personality Disorders*, *18*(1), 117–127. doi:10.1521/pedi.18.1.117.32767

Higgins, J. P., & Thompson, S. G. (2002). Quantifying heterogeneity in a meta-analysis. *Statistics in Medicine*, *21*(11), 1539–1558. doi:10.1002/sim.1186

Higgins, J. P., Thomas, J., Chandler, J., Cumpston, M., Li, T., Page, M. J., & Welch, V. A. (Eds.). (2019). *Cochrane handbook for systematic reviews of interventions*. John Wiley & Sons.

Imel, Z. E., Laska, K., Jakupcak, M., & Simpson, T. L. (2013). Meta-analysis of dropout in treatments for posttraumatic stress disorder. *Journal of Consulting and Clinical Psychology*, *81*(3), 394. doi:10.1037/a0031474

Institute of Medicine of the National Academies. (2013). *Treatment for posttraumatic stress disorder in military and veteran populations: Final assessment*. Washington DC: National Academies Press.

Kessler, R. C., Aguilar-Gaxiola, S., Alonso, J., Benjet, C., Bromet, E. J., Cardoso, G., ... Florescu, S. (2017). Trauma and PTSD in the WHO world mental health surveys. *European Journal of Psychotraumatology*, *8*(sup5), 1353383. doi:10.1080/20008198.2017.1353383

Kilpatrick, D. G., Resnick, H. S., Milanak, M. E., Miller, M. W., Keyes, K. M., & Friedman, M. J. (2013). National estimates of exposure to traumatic events and PTSD prevalence using DSM-IV and DSM-5 criteria. *Journal of Traumatic Stress*, *26*(5), 537–547. doi:10.1002/jts.21848

Kredlow, M. A., Szuhany, K. L., Lo, S., Xie, H., Gottlieb, J. D., Rosenberg, S. D., & Mueser, K. T. (2017). Cognitive behavioral therapy for posttraumatic stress disorder in individuals with severe mental illness and borderline personality disorder. *Psychiatry Research*, *249*, 86–93. doi:10.1016/j.psychres.2016.12.045

Markowitz, J., Petkova, E., Biyanova, T., Ding, K., Suh, E., & Neria, Y. (2015). Exploring personality diagnosis stability following acute psychotherapy for chronic posttraumatic stress disorder. *Depression and Anxiety*, *32*(12), 919–926. doi:10.1002/da.22436

McDonagh, A., Friedman, M., McHugo, G., Ford, J., Sengupta, A., Mueser, K., ... Descamps, M. (2005). Randomized trial of cognitive–behavioral therapy for chronic posttraumatic stress disorder in adult female survivors of childhood sexual abuse. *Journal of Consulting and Clinical Psychology*, *73*(3), 515–524. doi:10.1037/0022-006X.73.3.515

Miguel, C., Karyotaki, E., Cuijpers, P., & Cristea, I. A. (in press). Selective outcome reporting and the effectiveness of psychotherapies for depression. *World Psychiatry*.

Mills, K. L., Teesson, M., Back, S. E., Brady, K. T., Baker, A. L., Hopwood, S., Sannibale, C., Barrett, E. L., Merz, S., Rosenfeld, J. & Ewer, P. L. (2012). Integrated exposure-based therapy for co-occurring posttraumatic stress disorder and substance dependence. *Journal of the American Medical Association*, *7*(308), 690–699. doi:10.1001/jama.2012.9071

National Collaborating Centre for Mental Health National Collaborating Centre for Mental Health. (2005). *Posttraumatic stress disorder. the management of PTSD in adults and children in primary and secondary PTSD in adults and children in primary and secondary care*. Leicester: British Psychological Society; Leicester: British Psychological Society & Gaskell.

Pagura, J., Stein, M. B., Bolton, J. M., Cox, B. J., Grant, B., & Sareen, J. (2010). Comorbidity of borderline personality disorder and posttraumatic stress disorder in the US population. *Journal of Psychiatric Research*, *44*(16), 1190–1198. doi:10.1016/j.jpsychires.2010.04.016

Schottenbauer, M. A., Glass, C. R., Arnkoff, D. B., Tendick, V., & Gray, S. H. (2008). Nonresponse and dropout rates in outcome studies on PTSD: Review and methodological considerations. *Psychiatry: Interpersonal and Biological Processes*, *71*(2), 134–168. doi:10.1521/psyc.2008.71.2.134

Schwarzer, G. (2007). meta: An R package for meta-analysis. *R News*, *7*(3), 40–45. doi:10.1007/978-3-319-21416-0

Slotema, C. W., Wilhelmus, B., Arends, L. R., & Franken, I. H. (2020). Psychotherapy for posttraumatic stress disorder in patients with borderline personality disorder: A systematic review and meta-analysis of its efficacy and safety. *European Journal of Psychotraumatology*, *11*(1), 1796188. doi:10.1080/20008198.2020.1796188

Stalker, C., Palmer, S., Wright, D., & Gebotys, R. (2005). Specialized inpatient trauma treatment for adults abused as children: A follow-up study. *The American Journal of Psychiatry*, *162*(3), 552–559. doi:10.1176/appi.ajp.162.3.552

Tarrier, N., Sommerfield, C., Pilgrim, H., & Faragher, B. (2000). Factors associated with outcome of cognitive–behavioural treatment of chronic post-traumatic stress disorder. *Behaviour Research and Therapy*, *38*(2), 191–202. doi:10.1016/S0005-7967(99)00030-3

Van Emmerik, A. A., Kamphuis, J. H., Noordhof, A., & Emmelkamp, P. M. (2011). Catch me if you can: Do the five-factor model personality traits moderate dropout and acute treatment response in post-traumatic stress disorder patients? *Psychotherapy and Psychosomatics*, *80*(6), 386. doi:10.1159/000329111

Van Minnen, A., Arntz, A., & Keijsers, G. (2002). Prolonged exposure in patients with chronic PTSD: Predictors of treatment outcome and dropout. *Behaviour Research and Therapy*, *40*(4), 439–457. doi:10.1016/S0005-7967(01)00024-9

Van Minnen, A., Harned, M., Zoellner, L., & Mills, K. (2012). Examining potential contraindications for prolonged exposure therapy for PTSD. *European Journal of Psychotraumatology*, *3*(1), 1–14. doi:10.3402/ejpt.v3i0.18805

Walter, K., Bolte, T., Owens, G., & Chard, K. (2012). The impact of personality disorders on treatment outcome for veterans in a posttraumatic stress disorder residential treatment program. *Cognitive Therapy and Research*, *36*(5), 567–584. doi:10.1007/s10608-011-9393-8

Zayfert, C., DeViva, J. C., Becker, C. B., Pike, J. L., Gillock, K. L., & Hayes, S. A. (2005). Exposure utilization and completion of cognitive behavioral therapy for PTSD in a "real world" clinical practice. *Journal of Traumatic Stress: Official Publication of the International Society for of the International Society for Traumatic Stress Studies*, *18*(6), 637–645. WAS 19. doi:10.1002/jts.20072