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Review article

Functional impairment in Posttraumatic Stress Disorder: A systematic review and meta-analysis

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ABSTRACT

Posttraumatic Stress Disorder (PTSD) is a serious and debilitating condition often associated with significant impairments in daily functioning. To date, research on the complexity of functional impairment in individuals with PTSD is scarce and only limited. Yet, a quantitative synthesis and comprehensive review of existing evidence is needed to better characterize the magnitude of functional impairment in PTSD in distinct domains.

We conducted a systematic literature search including observational studies comparing functioning of individuals with and without PTSD. Random effects meta-analyses were performed for the different functional domains according to the WHO International Classification of Functioning, Disability and Health (ICF). The protocol followed the MOOSE guidelines for systematic reviews.

A total of thirty-four studies comprising 14 206 participants were included in the study. Compared to healthy individuals, subjects with PTSD showed significant ($ps < 0.001$) impairments with large to very large effect sizes ($ds > 1$) in all domains. Subjects with, compared to without, PTSD showed significant ($ps < 0.001$) impairments with medium to large effect sizes ($ds > 0.5$) in the domains *General Tasks and Demands*, *Mobility*, *Self Care*, *Domestic Life*, *Interpersonal Interactions and Relationships*, *Major Life Areas* and *Community, Social and Civic Life*. Significant impairments with small to medium effect sizes in the same domains were observed comparing PTSD to other mental disorders.

In conclusion, PTSD has a significant impact on most areas of daily functioning as conceptualized in the International Classification of Functioning, Disability and Health (ICF) of the WHO. Early detection and targeted treatment of functional deficits is warranted in this patient population.

1. Introduction

Posttraumatic stress disorder (PTSD) is a serious and debilitating mental disorder, which develops in about 10% of survivors in the aftermath of a traumatic event (Kessler et al., 1995). The current classification system DSM-5 defines PTSD based on symptoms of persistent re-experiencing of traumatic memories, avoidance of stimuli reminiscent of the traumatic event, negative alterations in cognition and mood, and alterations in arousal persisting for at least one month (American Psychiatric Association, 2013). The diagnosis of PTSD requires symptoms to cause significant distress or impairment in social, occupational, or other important areas of functioning. Consequently, impairment may accompany a PTSD diagnosis, however, it need not necessarily be present (if significant distress is observed). Prior reviews and meta-analyses have provided sound evidence on impaired neurocognitive functioning associated with PTSD (Golier et al., 2006; Lambert and McLaughlin, 2019; Qureshi et al., 2011; Schuitevoerder et al., 2013; Scott et al., 2015). A large study on almost 37 000 individuals of the Canadian general population, 1% of whom stated being diagnosed with PTSD, reported a significant association of PTSD with disability (assessed as a self-reported reduced amount or kind of activity a) "at home," b) "at school," c) "at work," or d) "in other activities, for example transportation or leisure") (Sareen et al., 2007). However, a different study, albeit with a comparatively small sample size and a sample of

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predominantly male armed services personnel, concluded that the clinical importance of PTSD may be questionable as they found no association of PTSD with disability, conceptualized as functional impairments in the domains of work, family life/home responsibilities and social/leisure activities (Neal et al., 2004).

Only one brief review of empirical literature addressed the association of PTSD and various aspects of functional impairments in areas of daily life, including intimate relationships, friendships and socializing, parenting, work and academic performance, financial problems, and homelessness (Rodriguez et al., 2012). Further, a small set of meta-analyses have specifically explored intimate relationship functioning in PTSD (Birkley et al., 2016; Taft et al., 2011) and the impact of PTSD on the relationship quality of intimate partners (Lambert et al., 2012).

However, to our knowledge, no comprehensive review and meta-analysis has investigated the extent to which functional impairment actually manifests itself in the framework of PTSD and which particular areas may be affected. A well-grounded evaluation regarding the complex symptomatology and the extent of impairment associated with PTSD is of paramount interest in forensic evaluation in insurance medicine, guidance of therapy planning, and conceptualizing targeted therapeutic interventions in this vulnerable population.

Our aim was therefore to conduct a timely and comprehensive review and meta-analysis on daily functioning and/or disability to summarize the emerging evidence on social and occupational functioning and impairments in patients suffering from PTSD. For this, we included observational studies in trauma-exposed populations or general population. To ensure better comparability, we assigned outcome measures of functioning to the domains of the WHO International Classification of Functioning, Disability and Health (ICF), which provides an international standard language and framework for the description of health-related functioning and disability (World Health Organization, 2002). The ICF has two parts, each with two components. Part 1 refers to Functioning and Disability and includes 1) Body Functions and Structures and 2) Activities and Participation. Part 2 refers to Contextual Factors and includes 1) Environmental Factors and 2) Personal Factors. In this meta-analysis, we used the domains of the Activities and Participation component as outcome measure for functional impairment. The domains for the Activities and Participation component are given in a single list that covers the full range of life activity domains, from basic skill learning or watching television to composite domains such as interpersonal interactions or employment. Activity is defined as the execution of a task or action by an individual. Participation is defined as involvement in a life situation.

This meta-analysis intends to weigh available evidence and support clarification on PTSD and disability. Herein, we strive to provide a profound insight into the complexity of impaired functioning that can ultimately guide clinicians in their evaluation and treatment of patients with PTSD.

2. Method

2.1. Search strategy and eligibility criteria

Based on a priori set inclusion and exclusion criteria, an electronic systematic literature search in Scopus, PubMed, PsyINFO, Embase, Medline, Ovid and ClinicalTrials.gov databases was performed by two independent reviewers (N.V. and J.M.). “PTSD” or “Posttraumatic Stress Disorder” and “Functioning” or “Disability” were used as keywords to establish database adapted search algorithms and to identify all eligible articles until November 2019. Reference lists of relevant articles were checked to locate additional potentially eligible studies (backward reference searching). Three of 16 authors contacted for further data provided us with additional results of their studies which could, hence, be included in the meta-analysis. Two reviewers (C.M., L.J.) were consulted in case of inconsistencies about inclusion of a study.

We included published, peer-reviewed, English or German articles that reported data of observational studies (cross-sectional, prospective and retrospective cohort, or case-control studies) comparing social and/or occupational functioning in adults (18+ years) with, compared to a control group without PTSD, drawn from the general population or a trauma-exposed population (e.g., combat veterans, accident victims). Both, comparison groups of individuals without psychiatric disorders and comparison groups of individuals with psychiatric disorders other than PTSD, as rated by a systematic diagnostic assessment were eligible as control groups. We excluded studies conducted in populations recruited primarily for specific somatic disorders as well as studies that reported merely on subthreshold PTSD symptoms. The presence or absence of a current (past-month) PTSD diagnosis according to DSM–III–R, DSM-IV, DSM-5, or ICD-10 had to be ascertained by a systematic diagnostic assessment using a validated interview-based measure. Current levels of functioning needed to be evaluated using a validated measure for functioning and/or disability; moreover, the identified areas of functioning had to be suitable to be assigned to specific domains (Table 1) within the component *Activities and Participation* of the International Classification of Functioning, Disability and Health (ICF) of the World Health Organization (WHO) (World Health Organization, 2002).

2.2. Data extraction

Two reviewers (N.V., J.M.) screened titles, abstracts and full texts for eligible studies and independently extracted data using a predetermined spreadsheet form comprising: First author, year, study type, diagnostic group, sample (number, gender, age), type of trauma, categorized disorder (current PTSD, current mental disorder other than PTSD, no current mental disorder), diagnostic classification of PTSD, diagnostic measure, measure of functioning with name of (sub)scale, corresponding ICF domain. Measures of central tendencies and variation (e.g. means and standard deviations) to adequately calculate the individual studies’ effect sizes were recorded. Any disagreements were resolved by discussion or a third reviewer (C.M.)

2.3. Quality assessment

Our meta-analysis was performed according to the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) reporting checklist (Stroup et al., 2000). Its protocol was registered a priori in the prospective register of systematic reviews (PROSPERO, ID: CRD42016032549).

Two independent reviewers (J.M., N.V) assessed the study quality using the Study Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies and the Quality Assessment Tool of Case-Control Studies (National Heart, Lung and Blood Institute (NIH), 2020). The sample was sorted alphabetically and divided into two halves, each reviewer evaluating 17 of the 34 studies. Four of each half were randomly selected and reviewed by a senior reviewer (L.J.). Inconsistencies and disagreements were resolved by discussing and reaching consensus.

Table 1
ICF domains of the component *Activity and Participation*.

Domain	Name
d1	*Learning and Applying Knowledge*
d2	*General Tasks and Demands*
d3	*Communication*
d4	*Mobility*
d5	*Self-care*
d6	*Domestic Life*
d7	*Interpersonal Interactions and Relationships*
d8	*Major Life Areas*
d9	*Community, Social and Civic Life*

2.4. Data analysis

Individual studies' effect sizes and their corresponding 95% confidence intervals were calculated and expressed as standardized mean differences (Cohen's d). In case that a study compared more than one group with the control group, the sample size was divided by the number of comparison groups to correct for an erroneously overestimation of certainty in the analysis. Random effects meta-analyses were conducted using the inversed-variance method from Laird and DerSimonian (Veroniki et al., 2016) for the different functional areas according to the ICF. Heterogeneity between the individual studies' effect sizes was tested using a Chi-squared test and its corresponding degrees of freedom and p-value. Higgins's I^2 statistic was used to quantify the degree of between studies' heterogeneity. I^2 values around 25%, 50% and 75% were interpreted as low, moderate, and high heterogeneity respectively. Control over heterogeneity was accomplished by the allocation of study outcomes to the different *d* domains of the ICF, as well as by pooling studies according to their control group into three distinct comparison groups. In a first group we pooled studies which compared subjects with PTSD to subjects without any current mental disorder (PTSD vs. healthy), a second group comprised studies which compared subjects with PTSD to a control group in which PTSD was excluded (PTSD vs. Non-PTSD) and a third group consisted of studies which compared subjects with PTSD to subjects with specific other mental disorders (PTSD vs. other mental disorders). Sensitivity analyses were conducted to assess the robustness of the overall weighted effect size against studies with extremely strong effect size or against studies with rated low quality.

The CMA-2 software (Comprehensive Meta-Analysis, Version 2, Biostat Inc., Englewood, NJ, 2013, USA) was used to calculate the meta-

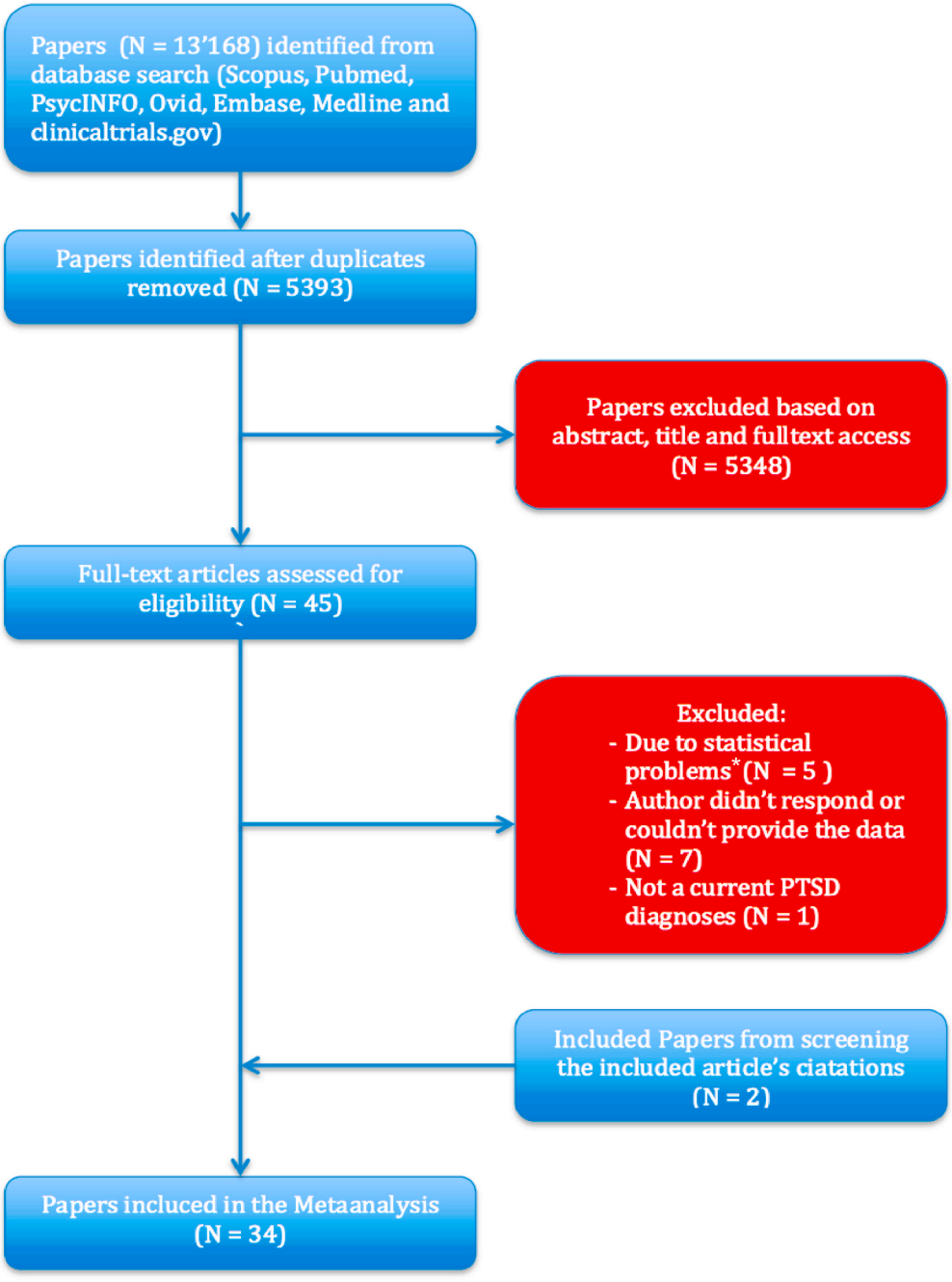


Fig. 1. Flowchart of eligibility screening. *e.g., no conversion of beta-coefficient to pearson r was possible.

analyses and to produce the different forest plots. Statistical significance was set at 5%.

3. Results

The database search identified 13′168 citations, 5′393 remained after duplicate removal.

A total of 5′348 studies were excluded after first screening, leaving 45 eligible for full text assessment. Of those, 13 studies had to be excluded: 7 due to incomplete data, e.g., Holbrook et al., 2001 (Holbrook et al., 2001) as only a total score of functioning was reported, which did not allow the allocation to a specific domain within the component *Activities and Participation*), 5 were excluded due to statistical reasons, e.g., no conversion of beta-coefficient to pearson r was possible, e.g., Erbes et al., (2011) (Erbes et al., 2011) and one study was excluded for not meeting all inclusion criteria. Two studies were additionally included after screening the reference lists of relevant articles, resulting in a total set of 34 studies (Fig. 1).

3.1. Description of included studies

34 studies were included in the meta-analysis. The assessment of study quality yielded 10 ‘fair to good’, 20 ‘fair’, one ‘poor to fair’ and four ‘poor’ rated studies (see supplemental A for detailed study quality assessment); one study that reported the results from samples collected using distinct study designs (cohort, cross sectional) was rated separately for each design (Kuhn et al., 2003). The meta-analysis comprised studies of 9 different countries from four different continents: USA (Barton et al., 1996a; Beard et al., 2010; Blanchard et al., 1995; Bovin et al., 2019; Bromet et al., 2016; Evans et al., 2009; Fang et al., 2015; Gros et al., 2011; Johnson et al., 2003; Kroenke et al., 2007; Kuhn et al., 2003; Moitra et al., 2014; Mostoufi et al., 2014; Pérez Benítez et al., 2014; Sautter et al., 1999; Shea et al., 2010; Stein et al., 2005; Zayfert et al., 2002, 2005; Zlotnick et al., 2002), Germany (Bornefeld-Ettmann et al., 2018; Haase et al., 2009; Löwe et al., 2011; Muschalla et al., 2018), The Netherlands (Geuze et al., 2009), Norway (Kristensen et al., 2015), Croatia (Antičević and Britvić, 2008; Arbanas, 2010), Israel (Caspi et al., 2008; Kotler et al., 2000; Kupchik et al., 2007), Taiwan (Lai et al., 2004), Japan (Narita-Ohtaki et al., 2018), Australia (McFarlane, 1994). Most of the studies had a cross-sectional (k = 29), three a cohort, and two a case-control design. In most studies (k = 27), a PTSD diagnosis was ascertained according to DSM-IV criteria; four studies followed DSM III-R and one DSM-5 criteria. One study reported on diverse samples based on DSM-IV and DSM-5, respectively (Bovin et al., 2019). In one study, the applied DSM version remained unclear (Muschalla et al., 2018). Most studies comprised mixed samples of females and males, only few studies examined only males (k = 4) or females (k = 3).

The studies were pooled by comparison group (PTSD vs. healthy, PTSD vs. mental disorders other than PTSD, PTSD vs. Non-PTSD) and according to the type of functional impairment assessed corresponding to the domains within the ICF component *Activity and Participation.* In part, a direct assignment to an ICF domain was feasible, e.g., in Caspi et al. (2008), where we assigned the subcategory *Self-care* of the SF-36 questionnaire to the corresponding domain *Self-care* of the ICF. In some cases, the allocation was less straightforward, e.g. in Evans et al. (2009), whose subcategory *Family Life* of the Sheehan Disability Scale (Sheehan, 2000) was assigned to both the domain *Domestic Life* and the domain *Interpersonal Interactions and Relationships* of the ICF. Subgroup analyses were performed within each control group and domain. Except for domain *Learning and Applying Knowledge*, all domains within the ICF component *Activities and Participation* were covered by the included studies: *General Task and Demands (k = 9), Communication (k = 2), Mobility (k = 12), Self-care (k = 13), Domestic life k = 20), Interpersonal Interactions and Relationships (k = 31), Major Life Areas k = 22), Community, Social and Civic Life (k = 21).* Table 2 depicts an overview of study characteristics of the included studies.

Table 2
Characteristics of included studies. Groups: 1 = vs. healthy; 2 = vs. Non-PTSD, 3 = vs. other mental disorders; ICF-domains: d2 *General Tasks and Demands*, d3 *Communication*, d4 *Mobility*, d5 *Self-care*, d6 *Domestic Life,* d7 *Interpersonal Interactions and Relationships*, d8 *Major Life Areas*, d9 *Community, Social and Civic Life*.

Study name	Year	Study design	Type of trauma	Group	ICF Domains
Antičević et al.	2008	cross sectional	combat trauma/ veterans	1	d7
Arbanas et al.	2010	cross sectional	combat trauma/ veterans	1	d7
Barton et al.	1996	case-control	accident	2, 3	d6, d8
Beard et al.	2010	cohort	various	3	d2, d4-9
Blanchard et al.	1995	case-control	accident	2	d6-9
Bornefeld-Ettmann et al.	2018	cross sectional	child abuse	1	d7
Bovin et al.	2019	cross sectional	combat trauma/ veterans	2	d4-9
Bromet et al.	2015	cross sectional	terror	2	d7
Caspi et al.	2008	cross sectional	combat trauma/ veterans	2	d5-9
Evans et al.	2009	cross sectional	terror	2	d6-9
Fang et al.	2015	cross sectional	combat trauma/ veterans	2	d2, d4-9
Geuze et al.	2009	cross sectional	combat trauma/ veterans	1	d2, d6-9
Gros et al.	2011	cross sectional	combat trauma/ veterans	2, 3	d2, d4-9
Haase et al.	2009	cross sectional	various	3	d7
Johnson et al.	2003	cross sectional	various	2	d7-9
Kotler et al.	2000	cross sectional	various	1	d7
Kristensen et al.	2015	cross sectional	natural disaster	1, 3	d6-9
Kroenke et al.	2007	cross sectional	various	2, 3	d2, d4-9
Kuhn et al.	2003	cohort/cross sectional	accident	2	d6-9
Kupchik et al.	2007	cross sectional	accident	2	d7
Lai et al.	2004	cross sectional	natural disaster	2	d6-9
Löwe et al.	2011	cross sectional	various	2	d2, d4-9
McFarlane et al.	1994	cohort	accident	2	d3-9
Moitra et al.	2014	cross sectional	various	3	d2, d4-9
Mostoufi et al.	2014	cross sectional	various	1, 3	d2, d4-9
Muschalla et al.	2018	cross sectional	combat trauma/ veterans	3	d2-5, d7
Narita-Othaki et al.	2018	cross sectional	various	1	d6-9
Pérez-Benitez et al.	2013	cross sectional	various	2	d4, d5
Sautter et al.	1999	cross sectional	combat trauma/ veterans	3	d7, d8
Shea et al.	2010	cross sectional	combat trauma/ veterans	2	d7
Stein et al.	2000		various	1	d6-9

(*continued on next page*)

Table 2 (*continued*)

Study name	Year	Study design	Type of trauma	Group	ICF Domains
		cross sectional			
Zayfert et al.	2002	cross sectional	various	3	d2, d4-9
Zayfert et al.	2005	cross sectional	various	3	d7, d9
Zlotnick et al.	**2002**	**cross sectional**	**various**	**2**	**d7-9**

3.2. Functional impairment in subjects with PTSD compared to healthy subjects

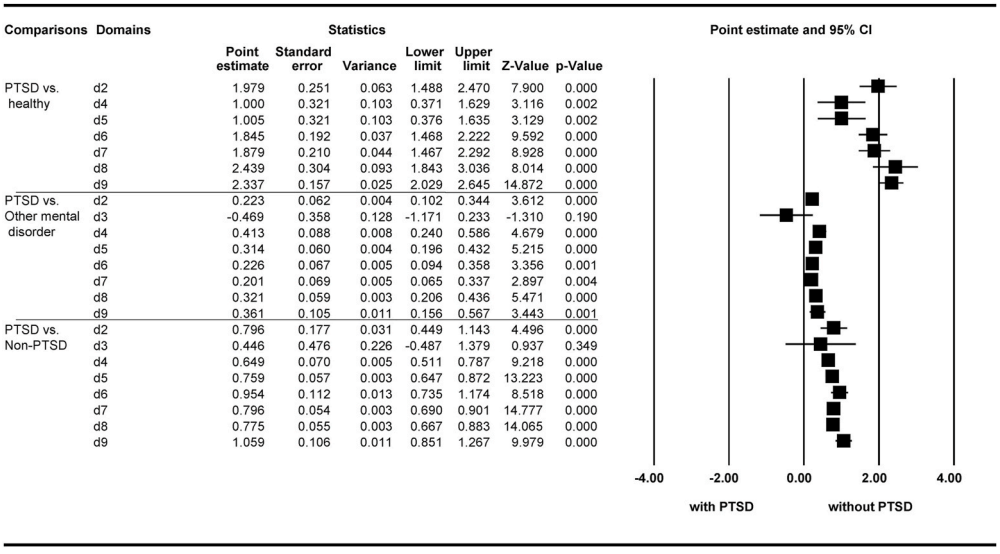
Nine studies reported on data comparing functional impairment between subjects with PTSD and subjects without any current mental disorder (Antičević and Britvić, 2008; Arbanas, 2010; Bornefeld-Ettmann et al., 2018; Geuze et al., 2009; Kotler et al., 2000; Kristensen et al., 2015; Mostoufi et al., 2014; Narita-Ohtaki et al., 2018; Stein et al., 2005). The studies investigated the following index traumas: combat trauma/veterans (k = 3) (Antičević and Britvić, 2008; Arbanas, 2010; Geuze et al., 2009); childhood abuse (k = 1) (Bornefeld-Ettmann et al., 2018); natural disaster (k = 1) (Kristensen et al., 2015); various trauma (k = 4) (Kotler et al., 2000; Mostoufi et al., 2014; Narita-Ohtaki et al., 2018; Stein et al., 2005).

In these studies, random effects meta-analyses showed significant (*ps* < 0.001) impairments of subjects with PTSD with large to very large effect sizes (*ds* > *1*) as compared to healthy subjects in all domains (Fig. 2). The majority of studies (k = 8) investigated *Interpersonal Interactions and Relationships* (Antičević and Britvić, 2008; Bornefeld-Ettmann et al., 2018; Geuze et al., 2009; Kotler et al., 2000; Kristensen et al., 2015; Mostoufi et al., 2014; Narita-Ohtaki et al., 2018; Stein et al., 2005). Except for Arbanas et al. (Arbanas, 2010) (where there was only a trend for statistical significance) all reported significant impairment in PTSD. Except Kristensen et al. (2015) (where there was only a trend for statistical significance), all studies on *Domestic Life* (Geuze et al., 2009; Mostoufi et al., 2014; Narita-Ohtaki et al., 2018; Stein et al., 2005) observed statistically significant functional disability in PTSD subjects. In *Major Life Areas* (Geuze et al., 2009; Kristensen et al., 2015; Mostoufi et al., 2014; Narita-Ohtaki et al., 2018; Stein et al., 2005), *Community, Social and Civic Life* (Geuze et al., 2009; Kristensen et al., 2015; Mostoufi et al., 2014; Narita-Ohtaki et al., 2018; Stein et al., 2005), *General Tasks and Demands* (Geuze et al., 2009; Muschalla et al., 2018), *Mobility* (Mostoufi et al., 2014) and *Self-care* (Mostoufi et al., 2014) PTSD was associated with significantly impaired functioning in all studies. See supplemental B for detailed data of individual studies.

3.3. Functional impairment in subjects with PTSD compared to subjects without PTSD

Half of the studies (k = 18) compared functional impairment between subjects with and without PTSD (Barton et al., 1996b; Blanchard et al., 1995; Bovin et al., 2019; Bromet et al., 2016; Caspi et al., 2008; Evans et al., 2009; Fang et al., 2015; Gros et al., 2011; Johnson et al., 2003; Kroenke et al., 2007; Kuhn et al., 2003; Kupchik et al., 2007; Lai et al., 2004; Löwe et al., 2011; McFarlane, 1994; Pérez Benítez et al., 2014; Shea et al., 2010; Zlotnick et al., 2002). These studies excluded PTSD in the control group. Only few individual studies corrected for comorbid psychiatric disorders in their evaluation of impairment (Bromet et al., 2016; Evans et al., 2009; Shea et al., 2010; Zlotnick et al., 2002). Most, however, did not account for other potential and comorbid mental disorders in their analysis, partly not even ascertaining them, e.g., Mc Farlane et al., (1994) (McFarlane, 1994). The studies comprised investigations on the following index traumas: accident (k = 5) (Barton et al., 1996b; Blanchard et al., 1995; Kuhn et al., 2003; Kupchik et al., 2007; McFarlane, 1994); combat trauma/veterans (k = 5) (Bovin et al., 2019; Caspi et al., 2008; Fang et al., 2015; Gros et al., 2011; Shea et al., 2010); terror (k = 2) (Bromet et al., 2016; Evans et al., 2009); natural disaster (k = 1) (Lai et al., 2004); various (k = 1) (Johnson et al., 2003; Kroenke et al., 2007; Löwe et al., 2011; Pérez Benítez et al., 2014; Zlotnick et al., 2002).

In these studies, random effects meta-analyses showed significant (*ps* < 0.001) impairment of subjects with PTSD with medium to large effect sizes (*ds* > 0.5) compared to the control group in all ICF domains except for *Communication* (*p* = 0.35; *d* = 0.47) (Fig. 2). All studies showed significant impairments in the domains *General Tasks and Demands* (k = 4) and *Domestic Life* (k = 11) in subjects with, compared to without, PTSD. In the domains *Mobility* (k = 7), *Self-care* (k = 8) and *Community, Social, and Civic Life* (k = 12), McFarlane et al. (McFarlane, 1994) did not observe differences between groups while in domain *Major Life Areas* (k = 14) both McFarlane et al. and Barton et al. reported no group differences (Barton et al., 1996b; McFarlane, 1994). In the domain *Interpersonal Interactions and Relationships* (k = 15), Kupchik



Comparisons	Domains	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
PTSD vs. healthy	d2	1.979	0.251	0.063	1.488	2.470	7.900	0.000
	d4	1.000	0.321	0.103	0.371	1.629	3.116	0.002
	d5	1.005	0.321	0.103	0.376	1.635	3.129	0.002
	d6	1.845	0.192	0.037	1.468	2.222	9.592	0.000
	d7	1.879	0.210	0.044	1.467	2.292	8.928	0.000
	d8	2.439	0.304	0.093	1.843	3.036	8.014	0.000
	d9	2.337	0.157	0.025	2.029	2.645	14.872	0.000
PTSD vs. Other mental disorder	d2	0.223	0.062	0.004	0.102	0.344	3.612	0.000
	d3	-0.469	0.358	0.128	-1.171	0.233	-1.310	0.190
	d4	0.413	0.088	0.008	0.240	0.586	4.679	0.000
	d5	0.314	0.060	0.004	0.196	0.432	5.215	0.000
	d6	0.226	0.067	0.005	0.094	0.358	3.356	0.001
	d7	0.201	0.069	0.005	0.065	0.337	2.897	0.004
	d8	0.321	0.059	0.003	0.206	0.436	5.471	0.000
	d9	0.361	0.105	0.011	0.156	0.567	3.443	0.001
PTSD vs. Non-PTSD	d2	0.796	0.177	0.031	0.449	1.143	4.496	0.000
	d3	0.446	0.476	0.226	-0.487	1.379	0.937	0.349
	d4	0.649	0.070	0.005	0.511	0.787	9.218	0.000
	d5	0.759	0.057	0.003	0.647	0.872	13.223	0.000
	d6	0.954	0.112	0.013	0.735	1.174	8.518	0.000
	d7	0.796	0.054	0.003	0.690	0.901	14.777	0.000
	d8	0.775	0.055	0.003	0.667	0.883	14.065	0.000
	d9	1.059	0.106	0.011	0.851	1.267	9.979	0.000

Fig. 2. Overview of group comparisons. ICF domains: d2 *General Tasks and Demands*, d3 *Communication*, d4 *Mobility*, d5 *Self-care*, d6 *Domestic Life,* d7 *Interpersonal Interactions and Relationships*, d8 *Major Life Areas*, d9 *Community, Social and Civic Life*.

et al. (2007) did not observe significant group differences. See supplemental B for detailed data of individual studies.

3.4. Functional impairment in subjects with PTSD compared to subjects with other mental disorders than PTSD

Twelve studies compared functioning in PTSD to specific other mental disorders, including anxiety disorders (k = 10) (Beard et al., 2010; Gros et al., 2011; Haase et al., 2009; Kristensen et al., 2015; Kroenke et al., 2007; Moitra et al., 2014; Mostoufi et al., 2014; Zayfert et al., 2002, 2005), depressive disorders (k = 4) (Haase et al., 2009; Kristensen et al., 2015; Zayfert et al., 2002, 2005), psychotic disorder (k = 1) (Sautter et al., 1999), acute distress disorder (k = 1) (Barton et al., 1996b), somatoform disorder (k = 1) (Kristensen et al., 2015), alcohol abuse (k = 1) (Kristensen et al., 2015), and unspecified 'other common mental disorders' (k = 1) (Muschalla et al., 2018). Mental disorders other than PTSD were assessed using validated diagnostic measures. The index traumas of the studies were: accident (k = 1) (Barton et al., 1996b); natural disaster (k = 1) (Kristensen et al., 2015); combat trauma/veterans (k = 3) (Gros et al., 2011; Muschalla et al., 2018; Sautter et al., 1999); various traumatic events (k = 8) (Beard et al., 2010; Haase et al., 2009; Kroenke et al., 2007; Moitra et al., 2014; Mostoufi et al., 2014; Zayfert et al., 2002, 2005).

In these studies, random effects meta-analyses showed significant ($ps \leq 0.001$) impairments in subjects with PTSD with small to medium effect sizes in all ICF domains except for *Communication* ($p = 0.19$; $d = -0.47$) (Fig. 2). The domain *Communication* was investigated by one study (Muschalla et al. (2018)) that did not find significant differences in subjects with PTSD, compared to an unspecified control group of 'other common mental disorders'. Individual studies investigated distinct diagnostic comparison groups. Since the different comparison groups were pooled for analysis, no direct conclusions can be drawn regarding the comparison to individual diagnostic classes. See supplemental B for detailed data of individual studies.

3.5. Sensitivity analysis of study quality and large study effect size

The study quality rating yielded four studies with a 'poor' overall rating (Antičević and Britvić, 2008; McFarlane, 1994; Sautter et al., 1999; Stein et al., 2005) due to methodological problems comprising poor statistical analysis without controlling for potential confounders, not validated questionnaire, insufficient description of study population and recruitment from different populations (see supplemental A for the detailed rating of study quality). A sensitivity analysis excluding the 'poor' rated studies consistently showed significant results in all comparison groups with an impact on heterogeneity to varying degrees. In the comparison group with healthy subjects, after exclusion of the studies by Antičević et al. (Antičević and Britvić, 2008) and Stein et al. (2005), a decrease in heterogeneity was observed in all (*d*7-*d*9) but one domain (*d*6). Effect sizes remained similar in *Domestic Life* (from $d = 1.85$ to $d = 1.84$) and increased in *Interpersonal Interactions and Relationships* (from $d = 1.88$ to $d = 1.98$), *Major Life Areas* (from $d = 2.44$ to $d = 2.60$) and *Community, Social and Civic Life* (from $d = 2.34$ to $d = 2.52$). In the comparison group including subjects with other mental disorders, after exclusion of the study by Sautter et al. (1999), heterogeneity decreased in one domain (*d*8) and remained unaltered in another (*d*7). Effect sizes remained similar in *Interpersonal Interactions and Relationships* ($d = 0.2$) and increased slightly in *Major Life Areas* (from $d = 0.32$ to $d = 0.34$). In the comparison group with subjects without PTSD, heterogeneity remained unchanged or increased after exclusion of the study by McFarlane et al. (McFarlane, 1994). Effect size slightly increases in *Mobility* (from $d = 0.65$ to $d = 0.68$), *Self-care* (from $d = 0.76$ to $d = 0.77$) and *Community, Social and Civic Life* (from $d = 1.06$ to $d = 1.07$), a slight reduction in *Domestic Life* (from $d = 0.95$ to $d = 0.94$) and no alteration in *Interpersonal Interactions and Relationships* ($d = 0.8$) and *Major Life Areas* ($d = 0.78$) (See supplemental C for detailed data).

In the forest-plots, we identified the study by Evans et al. (2009) as an outlier with highly significant results possibly overestimating the pooled estimates. It was one of two studies on PTSD in the context of the September 11, 2001 World Trade Center (WTC) attacks (Bromet et al., 2016; Evans et al., 2009). While Bromet et al. (2016) focused on follow-up of PTSD symptoms 11–13 years after the attacks of people with diverse WTC experience, Evans et al. examined workers from directly at the WTC site about two years after the attacks. Methodology comprised validated assessments of outcome and exposure measures, adequate statistical control of potential confounders and the study quality was in a fair range. The severity of the index trauma being directly threatened by life during and after the attack and witnessing many most serious human fates, thus, might have explained the very high effect size and statistically highly significant results in this study. After removal of this study the pooled estimates remained significant ($p < 0.001$); the effect size was slightly reduced (*Domestic Life*: from $d = 0.95$ to $d = 0.87$, *Interpersonal Interactions and Relationships* from $d = 0.79$ to $d = 0.75$, *Major Life Areas* from $d = 0.78$ to $d = 0.75$, *Community, Social and Civic Life* from $d = 1.06$ to $d = 0.9$) and heterogeneity (I^2) decreased in the *d* domains in question (See supplemental D for detailed data).

4. Discussion

This is the first systematic review and meta-analysis to summarize available evidence of observational studies on social and occupational functional impairments associated with PTSD. Despite considerable heterogeneity of design and samples across the included studies, the meta-analysis revealed substantial and reliable impairments of functioning across multiple domains of the ICF in individuals with PTSD. Compared to healthy individuals, we found impaired functioning in individuals suffering from PTSD with high effect sizes in all ICF *d* domains and throughout all individual studies except for *Communication*. Compared to individuals with other mental disorders, functioning in all ICF domains except *Communication* was impaired in PTSD; however, effect sizes were smaller. When comparing individuals with PTSD to individuals without PTSD, significant impairment in all domains except *Communication* was found in PTSD. However, potentially comorbid mental disorders were partly not even ascertained and, in most studies, not accounted for in the analysis, which reduces validity of this group comparison. Particularly within the PTSD group, other mental disorders may have contributed to the extent of impairments and hampers conclusions of this group comparison as impairments caused by pure PTSD are beyond reach. Moreover, the types of trauma reported in the PTSD group (particularly accident and combat trauma) could indicate concomitant physical disability, e.g., caused by the index trauma itself, which could aggravate functional impairment. While some studies did capture physical functioning, e.g., Caspi et al., (2008) (Caspi et al., 2008) and somatic symptom burden, e.g., Löwe et al., (2011) (Löwe et al., 2011), no study explicitly corrected for these aspects in their group comparison between PTSD and Non-PTSD subjects. Effects sizes were medium to large; however, heterogeneity was most pronounced in these studies, probably due to the unspecified comparison group. While most of the individual studies in this group reported significant results, three studies did not (Barton et al., 1996b; Kupchik et al., 2007; McFarlane, 1994), which was probably due to small sample size and consistency not being ensured. Also, one of the studies drew a comparison between PTSD and acute stress disorder, which possibly correlated too strongly in functional impairment. The highly significant and outlying results of Evans et al. (2009) were accounted for by a sensitivity analysis which reduced effect sizes slightly and, as expected, decreased heterogeneity, but did not affect overall significance of the pooled estimates. The sensitivity analysis excluding the poor rated studies yielded a decrease in heterogeneity primarily in the comparison group of healthy subjects.

4.1. Comparison with other research

A recent meta-analytical review of Birkley et al. on relationship functioning and PTSD symptom clusters found associations for emotional numbing with marital and parent problems, parent, child and family functioning and intimacy problems (Birkley et al., 2016). The latter two were also associated with avoidance symptoms. However, the symptom clusters were almost exclusively given as self-reports, which limits the reliability of diagnostic measure. Also, the sample (n = 9935) comprised almost exclusively military personnel. Still, these results support our own findings on impaired interpersonal interactions and relationships in subjects with PTSD.

Also in line with our results, prior meta-analytic evidence of empirical studies reported on an association between PTSD and intimate relationship discord, as well as intimate relationship physical aggression perpetration and intimate relationship psychological aggression perpetration (Taft et al., 2011). The systemic impact of PTSD on relationship quality from the perspective of the intimate partners has been emphasized previously (Lambert et al., 2012), which indirectly points to and underpins the interpersonal and relationship difficulties associated with PTSD.

In agreement with our results on compromised interpersonal interactions and relationships in subjects with PTSD, a previous review pertaining to quality of life in such patients gathered evidence on difficulties in social and interpersonal functioning, marital, parental and family functioning (Schnurr et al., 2009). Moreover, corresponding to our results on affected major life areas (including carrying out tasks and actions required to engage in work and employment), this study reported impaired occupational functioning in patients suffering from PTSD (Schnurr et al., 2009). This is in accordance with the results of an earlier meta-analytical review on quality of life in anxiety disorders that reported impaired quality of life of PTSD subjects in the domains home and family, social and work compared to controls (Olatunji et al., 2007). Noteworthy, compared to other anxiety disorders, impairments were particularly prominent among patients with PTSD. Our results further support these findings given that other anxiety disorders were by far the most frequent diagnostic group within the comparison group of other mental disorders in our data.

Several studies had to be excluded from our meta-analysis due to statistical reasons, e.g., quality of effect sizes. Qualitative comparison still revealed some agreement of these studies with our results. For instance, Erbes et al. reported lower levels of work role functioning in subjects with PTSD compared to healthy controls (Erbes et al., 2011). Our results of PTSD associated disabilities in interpersonal interactions and relationships, as well as impaired community, social and civic life and self-care are also in line with Lippa et al., who described impairments in the corresponding World Health Organization Disability Assessment Schedule 2.0 (WHODAS) categories Getting Around, Self-Care, Getting Along with People, Life Activities, and Participation in Society (Lippa et al., 2015). Corresponding to our results, Magruder et al. and Schonfeld et al. both described worse functioning of subjects with PTSD in every subscale of the SF-36 compared to subjects without PTSD (Magruder et al., 2005; Schonfeld et al., 1997).

4.2. Strengths and limitations

This review highlights the profound functional implications associated with PTSD. The broad inclusion criteria allowed us to meta-analyze a set of 34 studies totaling 14 206 participants (from n = 24 (McFarlane, 1994) to n = 3504 (Bromet et al., 2016)), which supports the clinical relevance of the results. Despite considerable heterogeneity regarding samples, index trauma, geographical regions and measures, the included studies very consistently demonstrated impairments caused by PTSD. The heterogeneity of study outcomes was controlled by preliminarily grouping the results within the ICF domains and performing analyses relating functional outcome measures to ICF domain. Though the individual studies employed diverse functional measures, by assigning them to an ICF domain we were able to bundle the outcomes of different functional measures. We were further able to include additional unpublished data by contacting authors, which thus strengthens our results.

Some limitations of this meta-analysis must be considered. Since we included observational studies only, of which the majority were cross-sectional and of fair quality, conclusions regarding causality of impairment and PTSD cannot be drawn. The mostly cross-sectional design also could not adequately account for important covariates such as time since onset of PTSD or the index trauma, which, however, may have a relevant impact on type and magnitude of impairments. Since we only included original work published in English or German language, articles in other languages were not considered. However, the sample of studies from 9 countries and 4 continents provided a broad diversification and thus allows sociocultural generalization. Only Asian studies were underrepresented. The low number of included studies on childhood trauma was remarkable, covered by only one study, which warrants precautions regarding generalizing our results to this population of trauma survivors. In contrast, studies on veterans and accidents were overrepresented in our sample. Most studies comprised subjects of both genders, so that the results do not represent gender specificity. In the comparison group with other mental disorders, the results of the individual studies were more heterogeneous despite significant overall estimates. Our evaluation did not allow for allocation and direct comparison to specific diagnosis groups. However, the significance of the results would have been limited owing to the small size of some groups. The possibility of a publication bias that overestimates the effects cannot be precluded. Due to insufficient data among the studies, we could not perform an additional moderator analysis regarding potentially influencing variables such as gender, type of trauma and comorbid mental disorder.

4.3. Implications

This meta-analysis underscores the major importance of functional impairment in individuals with PTSD. While the psychological impact of PTSD has been widely recognized, little has been reported on a comprehensive understanding of functional impairment, whose diagnostic classification itself is vague (American Psychiatric Association, 2013). The advent of increasingly specialized psychotherapeutic interventions in recent years has kept the focus mainly on targeted psychological interventions of the specific symptomatology of the illness (Watkins et al., 2018; Wilson et al., 2018). Functional impairments themselves, yet, have not been the subject of close attention. However, as these functional impairments may severely impact on everyday life, they can considerably reduce the quality of life of those affected.

The results of this meta-analysis emphasize the importance of functioning assessment as a central component of therapeutic treatment planning in these patients extending beyond the specific symptomatology of PTSD. Special consideration should therefore focus on therapeutic functioning-oriented interventions to mitigate these, such as group interventions like social competence training or social support skill-training. The latter, comprising communication skills and emotional management skills, has proven to be beneficial in PTSD by increasing the perceived social support (Sirati-Nir et al., 2018). Our findings that PTSD is associated with functional impairments in interpersonal interactions and relationships underscore that such functional training might be a valuable adjunct to symptom-focused therapies.

Future studies, thus, should place more emphasis on this aspect of symptom-related burden by incorporating an expanded assessment of functional impairments. Given the complexity of impairments (including, e.g., social and partnership-related difficulties), we suggest a multifaceted approach including clinical interviews and self-report, complemented with an evaluation of significant others. Moreover, clear characterization of type, onset, and duration of the index trauma

may elucidate potential differences in PTSD-associated functional impairment. Comorbid psychiatric disorders or physical comorbidities, e.g., originating from the trauma itself, likely confound "true" PTSD-related impairments and need to be thoroughly taken into account. Prospective longitudinal studies following trauma could provide further insights regarding causality between PTSD and functional impairment.

In the field of insurance medicine, our results enable a more thorough validation of the functional impairments reported by claimants in expert investigations. In the process of vocational reintegration, the awareness of functional impairments associated with PTSD can help to counteract them with specific training or to neutralize them by adjusting the workplace accordingly.

Credit

Lena Jellestad: Draft preparation, senior reviewer of study quality, supervisor of study eligibility, interpretation of data. *Nicolà A. Vital*: Literature search, data extraction, study quality assessment. *Jolanda Malamud*: Literature search, data extraction, study quality assessment. *Jan Taeymans*: Data analysis and interpretation of data. *Christoph Mueller-Pfeiffer*: Conceptualization, supervisor of study eligibility, writing- reviewing and editing.

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Appendix A. Supplementary data

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