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Post-traumatic Stress Disorder Assessment of current diagnostic definitions

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Abstract

Bondjers, K. 2020. Post-traumatic Stress Disorder – Assessment of current diagnostic definitions. *Digital Comprehensive Summaries of Uppsala Dissertations from the Faculty of Medicine* 1634. 54 pp. Uppsala: Acta Universitatis Upsaliensis. ISBN 978-91-513-0861-6.

Post-traumatic stress disorder (PTSD) is a debilitating condition that may arise after exposure to shocking, frightening, or dangerous events. Hallmark symptoms are re-experiencing, avoidance, and hyperarousal. Other common symptoms are more ancillary and overlap with other psychiatric disorders (e.g., anhedonia, interpersonal problems, and affective dysregulation). The variety of symptoms associated with PTSD allows for large differences in symptom presentation between individuals. Studies of the latent structure of PTSD (e.g., latent class analysis, confirmatory factor analysis) have been highly influential in the conceptualisation of the disorder. The fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) and the eleventh edition of the International Classification of Diseases (ICD-11) have taken vastly different approaches to handling the symptom variety, with DSM-5 encompassing a broad definition, and the ICD-11 instead proposing a narrow PTSD construct and introducing the new diagnosis complex PTSD (CPTSD), comprising PTSD in conjunction with ancillary symptoms.

The principal aims of the present thesis were to examine how different symptom presentations of PTSD were associated with well-known predictors of PTSD and prospective outcome, to evaluate the dimensional structure of PTSD as it is proposed in current diagnostic nomenclature, to provide methods for assessing PTSD in the Swedish language, and to evaluate the diagnostic agreement between DSM-5 and ICD-11.

Using latent class analysis, subgroups with differences in PTSD symptom presentation were examined and assessed regarding their predictive validity. In a sample of natural disaster survivors, subgroups differed mainly in symptom severity. In a mixed trauma sample, subgroups differed in their likelihood of fulfilling hallmark versus ancillary symptoms, and in self-reported concurrent and prospective psychological distress.

As for the dimensional structure of DSM-5 symptomology, support was not found for the four-factor DSM-5 model, but rather for a six-factor and a seven-factor model. For ICD-11 symptomatology, the ICD-11 model was supported, both with and without a higher-order separation of PTSD and CPTSD. Two instruments for assessing PTSD were evaluated: the PTSD checklist for DSM-5 (PCL-5) and the International Trauma Interview for ICD-11 (ITI). Results indicated support for both instruments as valid and reliable tools. The diagnostic agreement between DSM-5 and ICD-11 was moderate.

Summarised, the studies suggest that variables such as secondary stressors and event-specific exposure influence symptom expression, and that the combination of hallmark and ancillary symptoms of PTSD is associated with the long-term maintenance of psychological distress. Results support the use of the PCL-5 and the ITI as assessment tools for DSM-5 and ICD-11 PTSD. The insufficient agreement between DSM-5 and ICD-11 PTSD and CPTSD poses a challenge for future researchers and clinicians.

Keywords: PTSD, Complex PTSD, Post-traumatic Stress, Psychological assessment, DSM-5, ICD-11, Confirmatory factor analysis, Latent class analysis, Structural equation modelling, psychometric, psychiatric diagnoses

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"The classifications made by philosophers and psychologists are as if one were to classify clouds by their shape."
Wittgenstein, Philosophical Remarks

List of Papers

This thesis is based on the following papers, which are referred to in the text by their Roman numerals.

I Bondjers, K., Willebrand, M., & Arnberg, F K. (2018) Similarity in symptom patterns of posttraumatic stress among disaster-survivors: A three-step latent profile analysis. *European Journal of Psychotraumatology,* 9:1, 1546083.

II Bondjers, K., Hyland, P., Roberts, N P., Bisson, J I., Willebrand, M., & Arnberg F K. (2019) Validation of a clinician-administered diagnostic measure of ICD-11 PTSD and Complex PTSD: The International Trauma Interview in a Swedish sample. *European Journal of Psychotraumatology,* 10:1, DOI: 10.1080/20008198.2019.1665617

III Bondjers, K., Willebrand, M., & Arnberg, F K. (2019) Psychometric properties of the Swedish version of the PTSD checklist for DSM-5 (PCL-5): Sensitivity, specificity, diagnostic accuracy and structural validity in a mixed trauma sample. *Manuscript under review in Psychological Assessment*.

IV Bondjers, K., Willebrand, M., & Arnberg, F K. Symptom patterns of DSM-5 PTSD and ICD-11 DSO criteria, and their associations with functional disability, quality of life and long-term outcome. Manuscript in preparation

Contents

Abbreviations

PTE	Potentially traumatic event
PTSD	Post-traumatic stress disorder
CPTSD	Complex post-traumatic stress disorder
DSM	Diagnostic and Statistical Manual of Mental Disorders
ICD	International Classification of Diseases
DSO	Disturbances in self-organisation
PCL-5	The PTSD checklist for DSM-5
ITI	International Trauma Interview
IES-R	Impact of Event Scale-Revised
CFA	Confirmatory factor analysis
LCA	Latent class analysis
LPA	Latent profile analysis
MIIC	Mean inter-item correlation
CAPS-5	Clinician-administered PTSD scale for DSM-5
TRACES	Trauma and Stress in a Longitudinal Survey

Introduction

Post-traumatic stress disorder (PTSD) refers to a long-lasting psychiatric illness after exposure to a potentially traumatic event (PTE), such as a disaster, serious accident, unexpected death, war, terror, rape, or violence (1, 2). Estimated lifetime prevalence of PTSD in Sweden is 5.6% (3), and worldwide prevalence around 4% (4). Probability of remission varies considerably, with rates between 6% and 92% (5).

There is broad agreement regarding a set of hallmark symptoms of PTSD such as re-experiencing (e.g., flashbacks, nightmares), avoidance of stimuli related to the event or triggering re-experiencing, and hyperarousal, manifested as a heightened sense of threat (e.g., hypervigilance, startle reactions) (2, 6, 7).

However, survivors from potentially traumatic events also report ancillary reactions not specifically related to the events, such as persistent negative thoughts and emotions, anhedonia, sleep disturbances, difficulties concentrating, problems with affect regulation (e.g., irritability, dissociation, self-destructiveness), negative self-image, and disturbances in interpersonal functioning (8-10). Several of these ancillary symptoms overlap with symptoms of other psychiatric disorders, and there is a lack of consensus regarding their inclusion into the nomenclature of PTSD (2, 6, 8, 11). In the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (1), such reactions are included in the definition of PTSD, whereas the eleventh edition of the International Classification of Diseases (ICD-11) (2) has proposed the diagnosis of complex PTSD (CPTSD), comprising hallmark PTSD symptoms in conjunction with ancillary reactions.

The heterogeneity in symptoms associated with PTEs has led to the suggestion that PTSD may not be best understood as one homogeneous disorder, but as several subtypes of post-traumatic symptomatology (12, 13).

PTSD in the diagnostic nomenclature

Humans have been exposed to threatening events throughout history, and records of reactions to such events are present in myths, poetry, novels, and clinical reports. Up until 1980, labels included in the diagnostic nomenclature were often focused on the traumatic event itself (e.g., shell shock, combat ex-

haustion, rape trauma, abused child syndrome, or concentration camp syndrome). Symptom descriptions often include a pattern of autonomic arousal, fatigue, and trouble re-integrating the event into cognitive schemas. The term PTSD was introduced as an official psychiatric diagnosis when the DSM-III was published in February 1980. Diagnostic criteria were defined as re-experiencing, emotional numbing, and symptoms of either arousal, avoidance, or memory impairment, arising after exposure to a PTE (10).

In the DSM-IV-TR (1994), PTSD was described by three symptom criteria: re-experiencing, avoidance/emotional numbing of general responsiveness, and persistent symptoms of increased arousal (10, 11, 14).

The ICD-10 (1992) had already included a similar description of PTSD, comprising three symptom criteria: re-experiencing, avoidance, and either an inability to recall important aspects of the stressful event or persistent symptoms of increased arousal, arising after exposure to a PTE (15).

Thus, the DSM-IV-TR and ICD-10 definitions of PTSD were similar in terms of re-experiencing and arousal criteria. Both required that the disorder should be preceded by exposure to a PTE. A marked difference was the DSM-IV-TR's inclusion of numbing symptoms.

The concept of complex PTSD (CPTSD) was introduced in the early 1990s, with the argument that the DSM and ICD definitions did not accurately describe individuals whose most debilitating problems after a PTE were not the symptoms of PTSD, but rather externalising behaviours, affective dysregulation, dissociation, somatisation, and interpersonal problems (16). Neither the DSM nor the ICD included a diagnosis of CPTSD, but the ICD-10 included the provisional category *Enduring Personality Change After Catastrophic Experiences*. This manifested as a hostile or distrustful attitude, estrangement, social withdrawal, and chronic feelings of being on edge. These symptoms should affect interpersonal functioning (15, 17). For DSM-IV-TR, a *Disorder of Extreme Stress Not Otherwise Specified* was suggested but not included, due to a lack of specificity and boundaries towards PTSD (8).

As for the current diagnostic nomenclature, both the DSM and the ICD have been revised in the past five years. Despite suggestions that this created opportunities to increase agreement, the definitions are still strikingly different (18).

DSM-5

According to the DSM-5, a diagnosis of PTSD requires exposure to an identifiable PTE, and consists of twenty symptoms arranged in four clusters: re-experiencing (5 symptoms), avoidance (2 symptoms), negative alterations in cognition and mood (7 symptoms), and alterations in arousal and reactivity (6 symptoms). Clusters with < 5 symptoms require one symptom and clusters with > 5 symptoms require two symptoms for criteria to be fulfilled. Duration

must be at least one month and the disturbance must create distress or functional impairment and not be due to medication, substance use, or other illness (1). Table 1 lists the symptoms in their respective clusters. The DSM-5 also contains a subtype of PTSD, presenting with dissociative symptoms (i.e., derealisation and depersonalisation). The definition has been criticised for the multitude of symptom combinations it can entail and the symptom overlap with other psychiatric disorders (19).

Table 1. *PTSD symptoms according to DSM-5.*

Re-experiencing	Avoidance	Negative alterations in cognition and mood	Alterations in arousal and reactivity
Intrusive thoughts	Internal stimuli	Negative cognitions	Hypervigilance
Nightmares	External stimuli	Exaggerated blame	Startle reactions
Flashbacks		Negative emotions	Irritability or aggression
Emotional reactivity		Anhedonia	Risky or destructive behaviour
Physical reactivity		Feeling isolated	Concentration difficulties
		Decreased interest	Sleep disturbances
		Dissociative amnesia	

ICD-11

The ICD-11 has proposed two parallel diagnoses, PTSD and CPTSD (Table 2). Both require exposure to an identifiable PTE. PTSD is described as 6 symptoms arranged in three clusters; re-experiencing (2 symptoms), avoidance (2 symptoms), and a heightened sense of threat (2 symptoms). CPTSD is defined as fulfilling the criteria for PTSD in addition to disturbances in self-organisation (DSO), manifested through three symptom criteria: persistent disturbance in affective dysregulation (2 symptoms), persistent negative self-concept (2 symptoms), and disturbances in relationships (2 symptoms). Each cluster require one symptom for criteria to be fulfilled. For both PTSD and CPTSD, symptoms must persist for at least several weeks and cause functional impairment in work or social life. The inclusion of CPTSD garnered criticism regarding symptom overlap with other psychiatric disorders and lack of distinction from PTSD (20).

Table 2. *Symptoms of PTSD and CPTSD according to ICD-11.*

PTSD			DSO criteria for CPTSD		
Re-experiencing	Avoidance	Sense of threat	Affective dysregulation	Negative self-concept	Disturbances in relationships
Flashbacks	Internal stimuli	Hypervigilance	Hyperactivation	Feeling worthless	Feeling distant
Nightmares	External stimuli	Startle reactions	Hypoactivation	Feeling like a failure	Hard to stay emotionally close

Similarities and differences between DSM-5 and ICD-11

Hallmark symptoms (e.g., flashbacks, nightmares, avoidance of internal or external reminders, hypervigilance, and startle reactions) are included in both DSM-5 and ICD-11. So are some ancillary reactions, although these are sorted and worded differently in the two nomenclatures.

There are also non-shared features. Dissociative amnesia (included in DSM-5 negative alterations in cognition and mood) is not directly addressed in ICD-11, although the definition states that individuals who have limited memories of the event can experience strong emotional reactions rather than flashbacks or nightmares. The ICD-11 does not address symptoms of concentration disturbances or sleep problems. As of today, there is no definitive answer on which diagnostic definition to favour. In general, prevalence rates of PTSD according to DSM-5 are higher than rates for ICD-11, and results indicate that the definitions identify partially different cases (21-24).

Dimensional models of PTSD

Examining the validity of psychiatric disorders comes with specific challenges, since we, as of today, are not able to directly test them, but instead infer their presence from observable psychological phenomena, often assessed via self-report questionnaires or clinician-administered interviews.

Both the DSM and the ICD provide specific, observed symptoms as a guide in assessing psychiatric disorders, but it is generally assumed that these symptoms are manifestations of unmeasured (i.e., latent) dimensions (e.g., re-experiencing, avoidance, hyperarousal). Structural models focused on such dimensions (i.e., factor analysis) allow examination of how variables are related and separated from one another and if the variability in observed symptoms is explained by latent variables (25-27).

Factor analytical studies of the DSM-IV-TR (14) symptoms have suggested that internal and external avoidance are best described as a single dimension, not including symptoms of emotional numbing. As for emotional numbing, findings have suggested that such symptoms could be part of a broader dysphoria factor combining numbing symptoms with irritability, sleep disturbances, and concentration difficulties. However, support was also found for

models that included irritability, sleep disturbances, and concentration difficulties alongside the hallmark symptoms hypervigilance and startle reactions (28).

DSM-5

Factor analytical investigations of the four-factor DSM-5 model suggest that it is superior to the three-factor DSM-IV-TR model, but it has generally been outperformed by more constrained models. Most support has been shown for a six-factor Anhedonia model (29), a six-factor Externalising Behaviour model (30) and a seven-factor Hybrid model (31). Current evidence suggests that these models are superior to the DSM-5 model, with the Hybrid model outperforming or proving equivalent to the six-factor models (32-37). Table 3 presents an overview of these models, as well as of the DSM-5 and ICD-11 definitions.

Studies of the dimensional structure of PTSD were highly influential in the DSM revisions. However, diagnostic rates are rarely reported in relation to other dimensional models suggested for DSM-5 and ICD-11 symptomatology. Following the DSM-5 convention, where clusters with < 5 symptoms require one symptom and clusters with > 5 symptoms require two symptoms for criteria to be fulfilled, recent studies suggest that using the Anhedonia, the Externalising behaviour, or the Hybrid model as the basis for a diagnostic algorithm greatly decreases the prevalence rate of PTSD (26, 38).

Table 3. *Item mapping of DSM-5 and ICD-11 symptoms of PTSD with alternative latent structure models.*

Symptom	DSM-5	ICD-11 PTSD	ICD-11 CPTSD	EB	AN	HY
Memories	RE			RE	RE	RE
Nightmares	RE	RE	RE	RE	RE	RE
Flashbacks	RE	RE	RE	RE	RE	RE
Cued distress	RE			RE	RE	RE
Cued physical reactions	RE			RE	RE	RE
Internal avoidance	AV	AV	AV	AV	AV	AV
External avoidance	AV	AV	AV	AV	AV	AV
Dissociative amnesia	NACM			NACM	NACM	NA
Negative beliefs	NACM			NACM	NACM	NA
Distorted guilt	NACM			NACM	NACM	NA
Negative feelings	NACM			NACM	NACM	NA
Loss of interest	NACM			NACM	AN	AN
Detachment estrangement	NACM			NACM	AN	AN
Numbing	NACM			NACM	AN	AN
Irritability				EB	DA	EB
Reckless behaviour				EB	DA	EB
Hypervigilance	AR	TH	TH	AA	AA	AA
Startle reactions	AR	TH	TH	AR	AA	AA
Concentration difficulties	AR			DA	DA	DA
Sleep disturbances	AR			DA	DA	DA
Affective dysregulation			AD			
Negative self-concept			NS			
Disturbances in relationships			DR			

Note: RE = re-experiencing, AV = avoidance, NACM = negative alterations in cognition and mood, AR= alterations in arousal and reactivity, TH = heightened sense of threat, EB = externalising behaviour, AA = anxious arousal, DA = dysphoric arousal, AN = anhedonia, NA = negative affect, AD = affective dysregulation, NS = negative self-concept, DR = disturbances in relationships, HY = hybrid.

ICD-11

The ICD-11 proposal of PTSD and CPTSD comprises two higher-order factors (PTSD and DSO) that subsume six first-order factors. Apart from this model, six other models have been proposed for the ICD-11 symptoms (Figure 1). These models were developed with the aim of testing if the higher-order PTSD and DSO factors were distinct dimensions, and if there was a hierarchical structure that explained the association between the first-order factors (i.e., the diagnostic criteria) (39, 40).

Using self-report questionnaires, support has been found for the ICD-11 construct, separating PTSD and DSO symptoms (Model 4), and for a six-factor correlated model without the PTSD and DSO separation (Model 2) (22, 40-45).

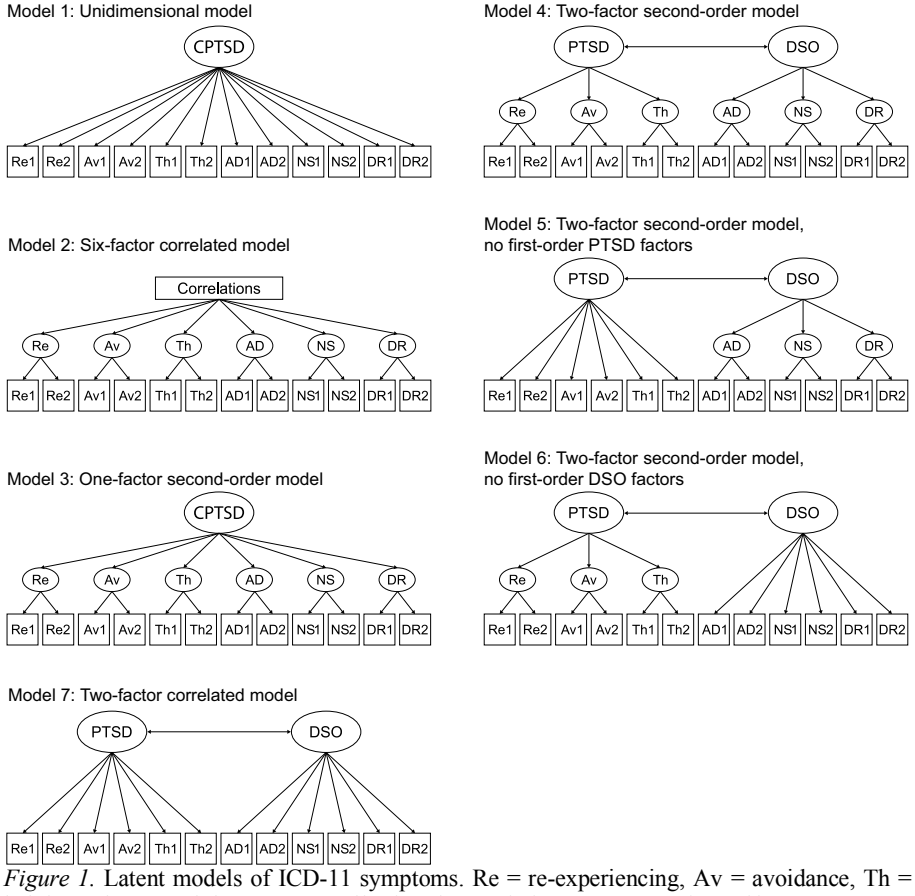

Figure 1. Latent models of ICD-11 symptoms. Re = re-experiencing, Av = avoidance, Th = heightened sense of threat, AD = affective dysregulation, NS = negative self-concept, DR = disturbances in relationships, PTSD = post-traumatic stress disorder, DSO = disturbances in self-organisation, CPTSD = complex PTSD.

Subtypes of PTSD

Due to the heterogeneity in presentation of PTSD and the high level of comorbidity, it has been suggested that current definitions may include subgroups that differ from each other with regard to comorbidity, personality, underlying processes, or internal relations between symptoms (i.e., symptom presentation) (12, 13, 19). Subgroups are reflected in both the DSM-5 (dissociative subtype of PTSD) and the ICD-11 (complex PTSD) (1, 2).

It has been suggested that for such subgroups to be clinically useful, and warrant inclusion as distinct entities in a diagnostic manual, three conditions should be fulfilled. First, criteria for the subgroups should be clearly defined and measurable. Second, individuals within a subgroup should differ from individuals in other groups, either by symptom presentation or by underlying mechanisms of the disorder. Third, the distinction between subgroups should

be clinically meaningful (e.g., individuals should show differing courses, risk factors, or responses to treatment) (13).

There is support for a dissociative subgroup of PTSD (46). There is also some support for a depressive and psychotic subgroup, temperament-based subgroups (e.g., externalising or internalising), and personality-based subgroups (distinguished by levels of emotional stability) (47-52). However, the research on subgroups based on symptoms included in the diagnostic definitions of PTSD is more contradictory. Studies using DSM-IV-TR and DSM-5 symptoms have identified three to six subgroups. Some studies have indicated that these subgroups differ mainly in symptom severity, whereas others have found types distinguished by distinct symptom profiles, such as high levels of emotional numbing, arousal, or dysphoric (ancillary) symptoms (53-57).

As for ICD-11 symptoms, studies have extracted two to five groups, and often found distinct groups with PTSD (hallmark) symptoms and CPTSD (DSO/ancillary) symptoms. No studies, as of today, have examined subgroups using both DSM-5 and ICD-11 symptoms. Moreover, there is a lack of studies examining associations between subtypes and prospective outcomes.

Assessment of PTSD

Despite the disagreement in how to define PTSD, the diagnostic categories carry weight in day-to-day clinical work. Thus, it is important to evaluate the reliability, validity, and clinical utility of the current definitions. To do so, it is necessary to have measurements that assess the current constructs.

Reliability refers to a construct's or measurement's consistency, across items (internal reliability), time (test-retest reliability), and raters (interrater reliability) (58, 59). Validity refers to the accuracy of a construct, if it assesses what it is intended to represent. Aspects of validity include construct validity, often separated into convergent validity (associations with similar constructs) and divergent validity (association with unrelated constructs, aiming for a low correlation) (60). Clinical utility can be defined as the extent to which a diagnosis assists clinical decision-makers in fulfilling the diverse functions of psychiatric classification, such as communicating information, providing a diagnosis in clinical practice, selecting treatment, and predicting future needs (61).

The changes in current diagnostic criteria have led to the development of new screening and assessment instruments for PTSD. Among these are the PTSD checklist for DSM-5 (PCL-5) (62), a self-report scale corresponding to DSM-5 symptomatology, and the International Trauma Interview (ITI) (22, 63), a clinician-administered interview for ICD-11 PTSD and CPTSD.

None of these instruments has yet been validated in a Swedish setting. A validation of such instruments facilitates clinical detection of PTSD cases and is necessary in order to examine the structure and potential subtypes of PTSD.

Aims

Overall aims

The overall aims of the present thesis were to examine how different symptom presentations of PTSD were associated with well-known predictors of PTSD and prospective outcome, to evaluate the dimensional structure of PTSD symptomatology according to current diagnostic nomenclature, to examine how different models of PTSD affect prevalence rates, and to provide methods for assessing PTSD – as the disorder is proposed in the DSM-5 and the ICD-11 – in Swedish.

Specific research questions were:

1. Are there subgroups of post-traumatic stress symptoms? (Papers I and IV)
1. Do specific symptoms or possible subsets predict comorbidity, recovery, and functional impairment? (Papers I and IV)
2. What are the psychometric properties of novel measures of PTSD? (Papers II and III)
3. What are the dimensional structures of diagnostic conceptualisations of PTSD? (Papers II and III)
4. What is the diagnostic agreement between DSM-5 and ICD-11 PTSD? (Paper IV)

Specific aims and hypotheses

Paper I

The aims in Paper I were to examine the presence of subgroups with different symptom presentations of PTSD in a cohort affected by a natural disaster and how such subgroups were associated with long-term PTSD symptoms.

The hypothesis was that three or more classes or subgroups would be extracted. The limited amount of research on latent classes in this type of sample precluded further hypotheses about the characteristics of the classes or the relationship between them.

Paper II

Paper II aimed to evaluate the interrater agreement, latent structure, internal reliability, and construct validity of a structured clinical interview for ICD-11 PTSD and CPTSD (ITI).

Based on data from self-report measures of ICD-11 PTSD and CPTSD, it was hypothesised that the ITI would possess satisfactory interrater and internal reliability, that the ICD-11 model of CPTSD would provide a satisfactory representation of the data, and that PTSD symptoms would be most strongly related to measures of fear and anxiety and DSO symptoms to measures of depression and general dysphoria.

Paper III

Paper III aimed to evaluate the reliability, construct validity, latent dimensions, and diagnostic utility of the PTSD checklist for DSM-5 (the PCL-5) in Swedish. A secondary aim was to compare diagnostic rates between the DSM-5 model and other models suggested in the literature.

Based on the constructs and previous studies, strong associations were expected between the PCL-5 and other measures of post-traumatic stress, moderate associations with measures of depression, agoraphobia, and dissociation, and weak associations with measures of social phobia, mistrust, insomnia, and alcohol use. It was also hypothesised that more constrained confirmatory factor analysis (CFA) models would provide better fit to data as compared with the DSM-5 model.

Paper IV

Paper IV aimed to evaluate the interrater agreement between DSM-5 and ICD-11 PTSD, and to examine subgroups of DSM-5 PTSD and ICD-11 DSO symptom criteria and how such subgroups were related to self-reported long-term outcome.

Methods

Participants and procedures

The current thesis uses data from two samples, the Swedish Tsunami cohort (Paper I) and the Trauma and Stress in a Longitudinal Survey (TRACES) study (Papers II–IV).

Paper I

The 2004 Southeast Asia tsunami devastated coastal regions in the area and more than 227,000 people perished (64). Approximately 20,000 Swedish citizens were in Southeast Asia at the time, of whom 7,000 were in areas hit by the waves (65). The Swedish tsunami survivors returned to a society not affected by the disaster, and the cohort is characterised by high socioeconomic status and experienced few stressors afterwards (66). Individuals ≥ 16 years of age from ten Swedish counties were invited to participate in a survey 14 months after the event (the one-year survey), and those who participated were later invited to participate in a second survey three years after the disaster. The study was approved by the regional ethics committee in Uppsala (DNR 2005/157).

Data from 1,638 highly exposed individuals (defined as being pulled or almost pulled into the waves) were used in Paper I. In addition to being highly exposed, participants also needed a valid response to a question about subjective life threat and a question about loss of a relative or friend, and had to have reported at least one symptom of PTS at the one-year survey. Mean age of the participants was 43 years (SD = 14, range 17–90). The sample included 55% females. Out of the 1,638 participants included in the analysis, 409 participants had missing data on one or more variables from the three-year assessment. These participants were excluded from analyses regarding long-term outcome.

Papers II–IV

Papers II–IV included data from the TRACES study, an ongoing prospective study following individuals ≥ 18 years of age who had experienced a potentially traumatic event in the past five years. Participants were recruited via

flyers in care facilities and via advertisements in local and social media. Participants signed up for the study via an online form or via contact with health care staff, who provided the research group with contact information. A phone interview was conducted to screen for inclusion and exclusion criteria. Included participants were sent further information and a consent form. After written consent was received, data were collected as shown in Figure 2.

Exclusion criteria were (1) currently living in high-risk/stressful circumstances (e.g., refugees or persons currently living in abusive relationships), (2) suffering from severe psychiatric disorders (e.g., persons with schizophrenia), or (3) not being fluent in the Swedish language. The current thesis reports on data from the first, second, and third time points.

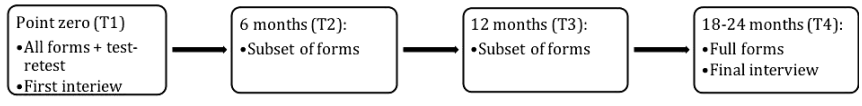

Figure 2. Flowchart of participation in the TRACES study.

At the first and last time points, participants were assessed with structural clinical interviews regarding PTSD, other psychiatric disorders, and functional disability. A test-retest form was given at the end of the first interview and participants were instructed to complete the forms on the following day at the earliest. To prevent interviewer drift, interrater assessments were performed every two months. The study was approved by the regional ethics committee in Uppsala (DNR 2014/283).

Papers II–IV were based on three different data extractions, described in detail in the attached papers. Paper II reports on data from 184 participants, Paper III on data from 258 participants, and Paper IV on data from 266 participants. The samples were similar in their demographic characteristics (reported in the attached papers). Nearly half were working full- or part-time, and the rest were students, unemployed, on parental leave or sick leave, retired, or in rehab/work training. The majority of participants had a university degree or ongoing university education. Participants reported a wide range of PTEs. A third of the sample indicated traumatic loss of a loved one as their worst event, a third indicated interpersonal violence (e.g., assault, sexual violence), and a third indicated a non-interpersonal event (e.g., accident, natural disaster, somatic injury/illness).

Measures

Post-traumatic stress

Clinical interviews

The Clinician-Administered PTSD scale for DSM-5 (CAPS-5) (67) is a structured clinical interview that was used as the reference standard for assessing PTSD in accordance with DSM-5 in Papers III and IV.

The International Trauma Interview (ITI) is a two-part semi-structured clinical interview that assesses symptoms of PTSD and complex PTSD in accordance with ICD-11 (22, 63) The first part assesses ICD-11 PTSD, using questions from the CAPS-5, and the second part assesses DSO symptoms. Data in the TRACES study have been collected using two versions of the ITI: versions 1.1 and 3.1 (63). Alterations from version 1.1 to 3.1 include changes in the prompts, but the symptoms and the rating structure are identical. The ITI was used to assess PTSD and CPTSD in accordance to ICD-11 in Paper II and IV.

For ancillary symptoms, both CAPS-5 and ITI requires assessment of symptoms trauma-relatedness. Trauma-relatedness is assessed as "definite", "probable, or "unlikely". A professed symptom with a rating of "unlikely" does not count towards a potential diagnosis, and is excluded from the severity scoring.

Both the CAPS-5 and the ITI rate symptoms on a scale from *Not present* (0) to *Extreme* (4), and a symptom score of ≥ 2 indicates a clinically significant problem that counts towards a diagnosis. The interrater agreement for the instruments in this sample was fair (Krippendorff alpha for CAPS-5 $\alpha = .79$, and ITI $\alpha = .76$).

Self-report

PTSD checklist for DSM-5 (PCL-5)

The PTSD checklist for DSM-5 (PCL-5) is a widely used instrument designed to assess the twenty DSM-5 PTSD symptoms. Each item is scored 0 to 4, indicating the extent to which the respondent has been bothered by the symptom during the past month (32).

The PCL-5 allows for several forms of scoring: (1) a total severity score (0–80), (2) cluster severity scores, where the clusters correspond to DSM-5 factors, and (3) PTSD caseness, where a symptom score of ≥ 2 is viewed as clinically significant, thus allowing individuals to obtain a tentative PTSD diagnosis.

Impact of Event Scale-Revised

The Impact of Event Scale Revised (IES-R; (68)) was used in Paper I to assess symptoms of PTSD in relation to the tsunami, in Papers II and III as a measure

of convergent validity, and in Paper IV for self-reported post-traumatic stress at all time points. Respondents indicate how bothersome each of the 22 items has been in the past seven days, from *Not at all* (0) to *Extremely* (4). The total score ranges from 0 to 88 (subscale scores: intrusion 0–32, avoidance 0–32, and hyperarousal 0–25). Factor analytical studies of the IES-R has indicated that the three-factor models in the DSM-IV describe its latent structure best, but the instrument is not specific to any manual. The Swedish version of the IES-R has previously proved to have excellent psychometric properties (69).

Other psychiatric disorders

To assess the prevalence of depression, anxiety (i.e., panic disorder, agoraphobia, social phobia, and general anxiety disorder) and suicidality, the Mini International Neuropsychiatric Interview (MINI) 6.0 and MINI 7.0 were used (70, 71). The Structured Clinical Interview for DSM-IV Axis II personality disorders (SCID-II) borderline module was used to assess borderline personality disorder (72). Diagnosis according to the MINI or the SCID was used to assess differences in comorbidity between subgroups in Paper IV.

Adverse life events

Trauma exposure in Papers II–IV was assessed with the Swedish version of the Life Event Checklist 5 (LEC-5), a self-report measure assessing exposure to sixteen traumatic events and one additional item for any other stressful events. The LEC-5 was given to participants during the interview, and was used to assess a worst experience that was used as the index event in the CAPS-5 and the ITI assessment (67).

Functional disability

The World Health Organization Disability Assessment Scale 2.0 (WHODAS 2.0; 73) is a tool developed by the World Health Organization for assessing functional disability in the past 30 days. Two versions of the WHODAS have been used in this thesis, the 12+24 interview schedule (WHODAS 12+24), and the 12-item self-rating schedule (WHODAS 12 SR).

The WHODAS 12+24 comprises an initial set of 12 items, and an additional set of 24 items that are given conditional on items in the first set. Items not given on account of no reported disability are scored 0. Total score ranges from 0 (*No disability*) to 100 (*Full disability*). The total score of the WHODAS 12+24 was used in Paper II to examine associations between latent factors and functional disability.

The WHODAS 12 SR asks respondents to rate how difficult they perceived different areas to be, ranging from *Not at all* (1) to *Extremely* (5). The WHODAS 12 SR was used for self-evaluation of functional disability at all

time points in the TRACES study. In this study, responses were coded 0–4, and total scores ranged from 0–48. The total score of the WHODAS 12 SR was used in Paper IV to examine differences in functional disability between subgroups.

Both versions of the WHODAS 2.0 have demonstrated excellent psychometric properties (73, 74).

Dissociation

The Dissociative Experience Scale-Taxon (DES-T; 75) includes eight items, extracted from the full-scale DES, that reflects pathological dimensions of dissociation. The total score ranges from 0–100 and a score ≥ 30 is generally found among patients with dissociative disorders. The DES-T has been proven to be reliable and highly correlated with the full-scale DES. The DES-T was used as a measure of divergent validity in Papers II and III and to assess class differences in Paper IV.

Insomnia

The Insomnia Severity Index (ISI) is a 7-item self-report measure for sleep-related problems. The score ranges from 0 to 28 and scores ≥ 10 are indicative of insomnia. The scale has previously demonstrated good psychometric properties (76, 77). The ISI was used as a measure of divergent validity in Papers II and III and to assess class differences in Paper IV.

General psychological distress

The Symptom Checklist 27 (SCL-27; 78) is a 27-item self-report measure assessing general psychological distress in the past two weeks. The total score ranges from 0 to 108 and subscale scores are as follows: depressive (score 0–16), dysthymic (0–16), somatisation (0–24), mistrust (0–16), social phobic (0–16), and agoraphobic (0–20) symptoms. The SCL-27 has shown adequate psychometric properties across different samples (78, 79). The SCL-27 was used in Papers II and III as a measure of convergent and divergent validity, and total score was used in Paper IV as a measure of general psychological distress at all time points.

Alcohol use

The Alcohol Use Disorder Identification Test (AUDIT; 80) is a 10-item screening tool that assesses problematic alcohol use. The form is standard screening procedure for alcohol use disorder within Swedish health care. For men a total score of ≥ 8 and for women a total score of ≥ 6 indicates harmful

use. The Swedish version of AUDIT has good psychometric properties (81). The AUDIT was used as a measure of divergent validity in Paper II.

Quality of life

The Brunnsviken Brief Quality of Life Scale (BBQ) consists of 12 items assessing quality of life. Respondents rate their satisfaction in six different life areas (leisure, view on life, creativity, learning, friends, and view on self), and the importance of each area for their quality of life. All items are scored from *Don't agree at all* (0) to *Agree completely* (4). A total score is computed by multiplying the satisfaction and importance rating for each area, and summing the six products for a total score that ranges from 0 to 96. A lower score indicates lower quality of life. The total score of the BBQ was used in Papers II and IV. The Swedish BBQ has shown satisfactory psychometric properties (82).

Demographic data and other measures

In Paper I, the surveys included questions about the participants' demographics, disaster exposure, and bereavement. The subjective experience of life threat was indicated by endorsement of the yes/no question *"Did you experience the situation as life-threatening regarding your own person when the wave struck?"* and loss of a relative or friend with the yes/no question *"Did you lose family members, other relatives or friends in the tsunami?"*. In Papers II–IV, demographics were examined via a questionnaire including questions about age, gender, employment, and education.

Statistical analyses

Detailed descriptions of the analytical procedure are included in the attached manuscripts.

Papers I and IV

Papers I and IV examined if there were subgroups with varying symptom presentations, using latent class analysis (LCA). The aim of LCA is to categorise individuals into groups where the individuals within a group are as similar as possible to one another, but different from individuals in other groups (83). It relies on the a priori assumption that the population is heterogeneous and made up of a finite number of homogeneous subgroups. In the context of psychiatric symptoms, this heterogeneity would be expressed as variability in symptom presentation. When conducting an LCA, standardised procedure is

to fit models with increasing numbers of classes, evaluated based on fit indices, parsimony, and interpretability (84, 85). A three-step LCA was applied to examine if there were subgroups of individuals with different symptom patterns in Papers I and IV, and the association between such subgroups and external variables. The three-step approach allows for examination of class membership and external variables, taking class uncertainty into consideration. The LCAs were conducted with Mplus 8 software (86).

In Paper I, participants were categorised into classes based on the IES-R item scores at the first measurement point. Loss of a relative or friend and subjective life threat have previously shown strong impact on symptom severity in this sample and were included in the model as predictors of class belonging (87). Associations between the predictors and class membership were evaluated with regression analysis. The long-term outcome was examined with differences in the IES-R full score three years after the event.

In Paper IV, participants were categorised into classes based on fulfilment of DSM-5 PTSD and ICD-11 DSO symptom criteria. The associations between classes and gender, age, and event type were evaluated with regression analysis. Differences in prevalence rates of psychiatric disorders and mean scores of self-reported symptoms, functional disability, and quality of life between classes were examined. Paper IV also examined the agreement between the DSM-5 and the ICD-11. This part of the analysis was conducted using R software and the package *irr* (88, 89).

Papers II and III

Confirmatory factor analysis (CFA) is a method for evaluating construct validity. It relies on the assumption that the variance between specific observed items is dependent on unmeasured latent factors. CFA is commonly used to test if the researchers' a priori understanding of latent dimensions of a construct provides an accurate description of data. It thus requires a pre-specified model that is evaluated based on the available data. Model fit is assessed using multiple fit indices (90).

In Paper II, data analysis was conducted in three steps. First, interrater agreement between various interviewers was evaluated using Krippendorff alpha. Next, a CFA model was used to evaluate the fit of seven alternative factor models suggested for the ITI (Figure 1). The internal consistency of the ITI was evaluated using composite reliability analysis. Then, the latent variables from the best fitting model were entered into a structural equation model to determine (a) how well-known predictors of PTSD (i.e., gender, age, and interpersonal/non-interpersonal event) influenced the ITI factors, and (b) how strongly the ITI factors predicted scores on self-report measures while controlling for the association between PTSD and DSO, as well as for the covariates gender, age, and type of traumatic event. Scores of post-traumatic stress,

depression, dysthymia, social phobia, agoraphobia, somatisation, mistrust, dissociation, insomnia, and alcohol use were assessed.

In Paper III, the internal consistency of the PCL-5 was evaluated using Cronbach's alpha and MIIC, and test-retest reliability using Spearman's rho correlation. The validity of the PCL-5 was evaluated by examining the correlation between PCL-5 scores and other measures of post-traumatic stress, depression, dysthymia, dissociation, and insomnia. The structural validity of the instrument was evaluated using CFA, examining the DSM-5 model, the six-factor Anhedonia model, the six-factor Externalising Behaviour model, and the seven-factor Hybrid model. Probable prevalence rates of PTSD were calculated for each model based on previously suggested diagnostic algorithms (26). The diagnostic utility of the PCL-5, using the DSM-5 algorithm and various threshold scores, was examined with signal-detection analyses, using clinician-assessed diagnosis as reference (CAPS-5).

Ethical considerations

The data collection procedures followed standards in trauma research. Nonetheless, when enquiring about potentially traumatic events and psychological symptoms, there is a risk of discomfort for participants. In general, participants in trauma research are positive towards research, which is true also for those who experience discomfort when reminded of a traumatic event. Participants describe that it feels important to contribute to increased knowledge (91-93). The studies in this thesis may contribute to the understanding of the different ways in which post-traumatic stress can manifest and have direct clinical implications for future patients.

For participants included in Papers II–IV, recruitment was non-intrusive, using flyers and adverts instead of face-to-face recruitment, to limit violation of integrity. Participants in Paper I were actively sought out, but informed of their right to not participate. In all studies, participants were allowed to withdraw at any time without further explanation. They were also informed of the possibility to contact the research group at any time. The research team included licensed clinical psychologists and psychotherapists, with experience working in psychiatric care settings, who were able to guide participants to proper care if needed. Lastly, for Papers II–IV, there was a risk that the participants might interpret participation in the studies as related to their regular care. They were therefore explicitly informed that participation was independent from any care they sought or received.

Results

Paper I

One to five classes were fitted and evaluated. A four-class model was chosen as the best model for representing the data in this sample, based on interpretation of several fit indices. Classes differed mainly in terms of symptom severity, but there was a tendency towards divergence in symptom levels of hyperarousal relative to symptom levels of avoidance/numbing between classes with moderate and severe symptoms as compared with classes with lower symptom levels. Figure 3 illustrates the profiles in terms of the class mean IES-R score for each item.

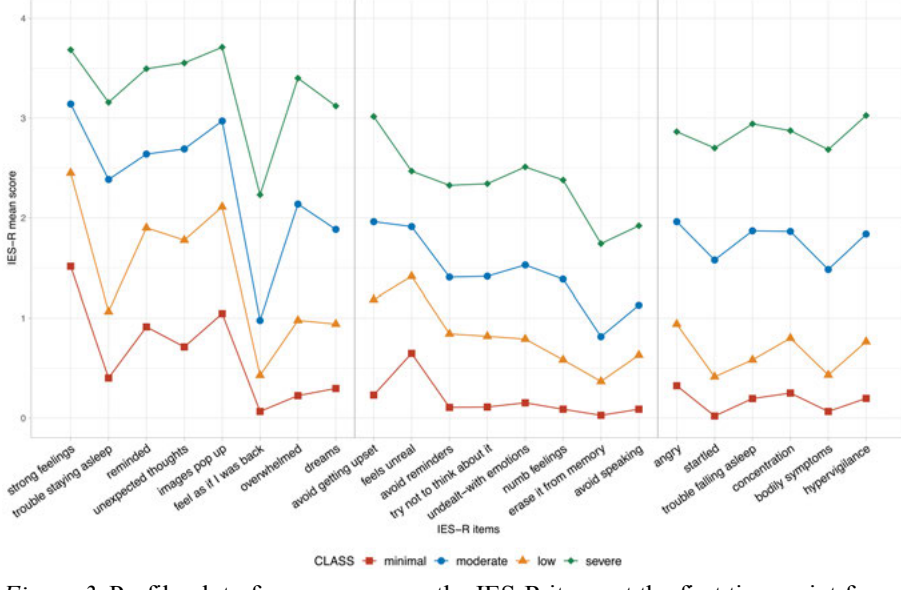

Figure 3. Profile plot of mean scores on the IES-R items at the first time point for each respective class, sorted by the IES-R clusters intrusion (left), avoidance/numbing (centre), and hyperarousal (right).

Subjective life threat and loss of a relative or a friend were associated with a higher likelihood of belonging to a class other than the minimal symptom class, and the likelihood increased monotonically with symptom load. Belonging to a more symptom-burdened class at baseline was associated with greater symptom load at follow-up.

Paper II

Interrater agreement of the ITI was fair (Krippendorff $\alpha = .76$). Most participants did not meet the ICD-11 criteria for PTSD or CPTSD (n = 144, 78%), although 29 (16%) fulfilled criteria for PTSD and 11 (6%) fulfilled criteria for CPTSD.

CFA analysis suggested that Model 4 (Figure 1) provided excellent fit to data, as did Model 2 and Model 5. Model 4 is consistent with the current ICD-11 nomenclature and was used for further analysis.

Internal consistency of the latent factors was acceptable, based on composite reliability analysis. Standardised factor loadings were high, except for items included in the affective dysregulation factor. The standardised factor correlation between PTSD and DSO was moderate.

Associations with convergent and divergent measures were as expected. PTSD, but not DSO, was strongly associated with self-reported post-traumatic stress. PTSD was moderately associated with fear- and stress-related measures, whereas DSO was moderately associated with depression and dissociation measures. PTSD and DSO were both associated with functional disability, with DSO scores being associated with greater functional disability and lower quality of life as compared with PTSD scores. Interpersonal trauma was associated with higher levels of PTSD and DSO.

Paper III

Internal consistency and test-retest reliability were acceptable for the full and subscales of the PCL-5, based on Cronbach's alpha, mean inter-item correlation (MIIC), and test-retest analysis (n = 196). The avoidance subscale demonstrated higher MIIC values than recommended (94). Associations with convergent and divergent measures were as expected, with the PCL-5 being highly related to other measures of post-traumatic stress and moderately related to measures of depression, dysthymia, and anxiety.

The CFA analysis indicated that the Anhedonia and Hybrid model provided excellent fit, whereas the DSM-5 and Externalising Behaviour models did not produce acceptable fit. Worth mentioning is item 8, dissociative amnesia, which provided low factor loadings in all models. Large differences in prevalence rates were found between models, with the DSM-5 algorithm yielding 38% PTSD cases, the Externalising Behaviour model 20%, the Anhedonia model 26%, and the Hybrid model 17%. The DSM-5 model had a prevalence 2.2 times higher than the Externalising Behaviour model.

Threshold scores of 31, 32, and 33 led to acceptable diagnostic accuracy (.83–.84), albeit with lower levels of sensitivity as compared with previous studies (33, 37). The highest level of overall accuracy was obtained with a

threshold score of 37, although this threshold had unacceptably low sensitivity. A threshold score of 29 yielded equal levels of sensitivity and specificity, while retaining acceptable quality of overall accuracy (Figure 4).

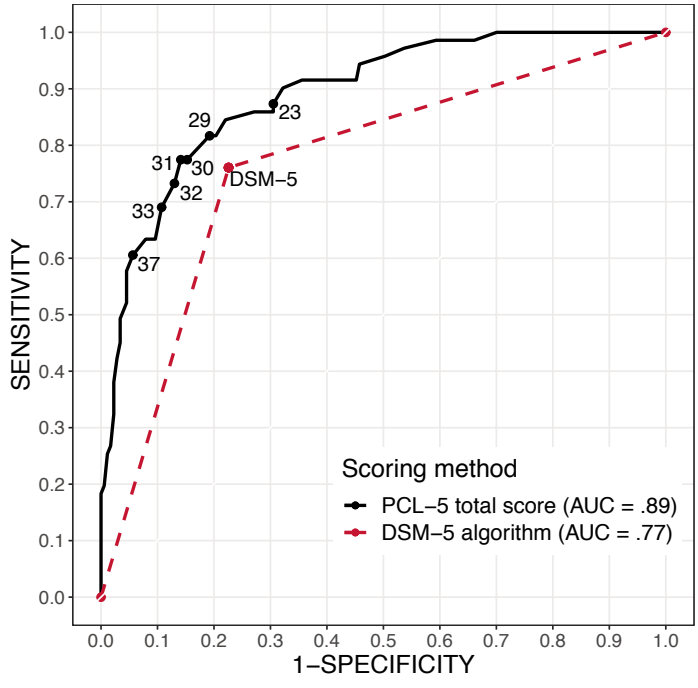

Figure 4. Receiver operating characteristics curves for PCL-5 total scores (black) and the DSM-5 algorithm applied to the PCL-5 (red) in relation to CAPS-5 PTSD diagnosis. AUC = Area under the curve.

Paper IV

Diagnostic rates of PTSD were: 29% for DSM-5, 12% for ICD-11 PTSD, and 7% for ICD-11 CPTSD. Agreement between diagnostic manuals was moderate (82% ($k = 0.52$, $p < .001$)). Only 46% of clinically assessed PTSD cases fulfilled criteria according to both manuals. All ICD-11 CPTSD cases also fulfilled criteria for DSM-5 PTSD.

A four-class model was chosen as the best model in this sample (Figure 5), with three classes being symptomatic (labelled *PTSD+DSO, PTSD,* and *DSO*) and one being non-symptomatic (*Low*). All clinically assessed PTSD cases belonged to the *PTSD+DSO* class or the *PTSD* class. Being female and having experienced interpersonal violence were both associated with increased odds of belonging to a class with DSO symptoms and younger age was associated with increased odds of belonging to a symptomatic class.

The *PTSD+DSO* class had higher rates of comorbidity, self-reported psychiatric symptoms, and functional disability compared with all other classes at all time points. The *DSO* class had higher rates of suicidality than the *PTSD* and *Low* class, and higher rates of depression and borderline personality disorder compared with the *Low* class. At the first time point, there were no differences between the *PTSD+DSO* class and the *PTSD* class in levels of post-traumatic stress, but while the *PTSD+DSO* symptom class remained at elevated levels of post-traumatic stress, the *PTSD* class levels decreased, rendering significant differences at the follow-up assessments.

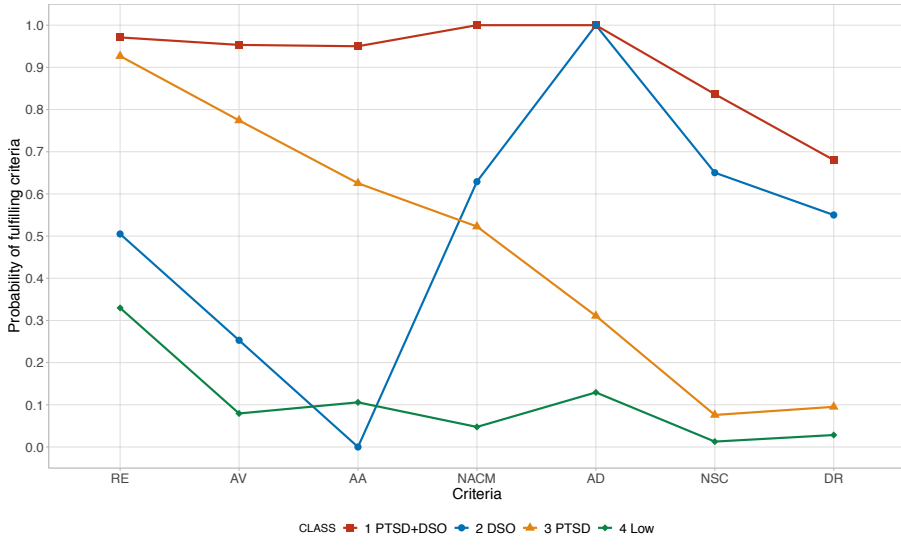

Figure 5. Probability of fulfilling PTSD and DSO criteria. RE, re-experiencing; AV, avoidance; AA, alterations in arousal and reactivity; NACM, negative alterations in cognition and mood; AD, affective dysregulation; NSC, negative self-concept; DR, disturbances in relationships.

Discussion

Main findings

Symptom presentations and prospective outcome

As described in the introduction to this thesis, it has been suggested that PTSD may not be best understood as one homogeneous disorder, but rather as a set of subtypes with different symptom presentation. It was also stated that clinically meaningful subtypes should differ with regard to symptom presentation or functional mechanisms in the development or maintenance of the disorder, and show differing courses, risk factors, or responses to treatment (13).

In Paper I, it was demonstrated that although there were homogeneous subgroups of individuals in the Swedish Tsunami cohort, these groups were distinguished mostly in terms of symptom severity rather than symptom presentation. Despite differences in long-term outcome, this should not be taken as an indication of clinically meaningful subtypes, but rather as a replication of the previous finding that higher initial symptom load is associated with higher symptom levels over time (87).

In Paper IV, four subgroups with different likelihoods of fulfilling DSM-5 PTSD and ICD-11 DSO criteria were extracted (Figure 5). These groups differed in symptom presentation and course, and could be understood as clinically meaningful subtypes. All symptomatic groups had moderate to high likelihood of fulfilling the DSM-5 negative alterations in cognition and mood (NACM) criteria. As noted in the introduction, the DSM-5 and ICD-11 definitions both include ancillary symptoms associated with PTSD, but arrange these differently. The results suggested a potential overlap between DSM-5 NACM and ICD-11 DSO symptoms, and that the clinical pictures of DSM-5 PTSD and ICD-11 CPTSD are not entirely different.

Individuals with hallmark PTSD symptoms remained at elevated levels of distress, whereas individuals with only ancillary symptoms had equivalent levels of post-traumatic stress and functional disability as non-symptomatic individuals over time. Individuals with both hallmark PTSD and ancillary symptoms experienced more distress than all other groups, at all time points. Thus, the patterns indicated that hallmark symptoms are better predictors of long-term psychopathology than only ancillary symptoms, and that the combination of hallmark PTSD and ancillary symptom may contribute to long-term maintenance of psychopathology.

Dimensional structure of PTSD

As described in the introduction, dimensional models of PTSD, examining the covariance of symptoms, have been highly influential in the diagnostic conceptualisation.

Results from Paper II supported the distinction between PTSD and DSO as two separate but related constructs. This study is the first examining this model using a disorder-specific clinician-administered instrument, and replicated previous studies using self-report (40, 42, 43, 45). These results support the validity of the ICD-11 model. However, as in most studies using self-report, a model without a hierarchal separation of PTSD and DSO (Model 4, including six first-order factors) also provided excellent fit (see Figure 1 in introduction). This could indicate that the separation of PTSD and DSO is not the only possible solution to explain the covariance of these specific symptoms, but that a first-order six factor model would work equally well.

There were some parameter problems, most notably within the affective dysregulation factor. Indicators in this factor could be viewed as two extremes of the affective dysregulation dimension: hyperactivation (a tendency of strong emotional response when confronted with minor stressors) and hypoactivation (a tendency of numb emotional response when confronted with minor stressors). It has been noted that it is unlikely that a person presents with both of these responses (95). The lower factor loadings of these items are therefore not surprising. However, it is also possible that they are not part of one dimension, but are reflective of different latent constructs.

As for DSM-5, results from Paper III did not find support for the DSM-5 model. Three other models (Externalising Behaviour, Anhedonia and Hybrid) suggested in previous literature were examined. The Externalising Behaviour model was not supported, but the Anhedonia and Hybrid model provided excellent fit, in accordance with earlier research (32, 33, 35-37).

The consistent findings in the literature that more constrained models outperform the DSM-5 model imply a need for a revision of this diagnostic conceptualisation. However, results have been inconsistent as to which model best represents the latent structure of DSM-5 PTSD symptomatology and altering the underlying model for diagnostic criteria would have large effects on prevalence rates, as suggested by both this and previous studies (26, 38).

Paper III replicated the consistent finding that the symptom dissociative amnesia produces lower factor loadings across all models (e.g. 96, 97). Dissociative amnesia tends to be experienced more often by individuals fulfilling criteria for the dissociative subtype of PTSD (98). Thus, although suboptimal from a psychometric perspective, the item may still serve as an important clinical marker.

Assessment of PTSD

Two instruments for assessing PTSD according to current diagnostic definitions were evaluated in this thesis, the International Trauma Interview for ICD-11 (ITI) (Paper II) and the PTSD checklist for DSM-5 (PCL-5) (Paper III).

The International Trauma Interview (ITI)

Overall, the results were consistent with the study hypotheses and supported the interrater agreement, internal reliability, and the convergent and divergent validity of the Swedish ITI. Interrater agreement was higher using the ITI, as compared with results from previous studies using unstructured interviews (99).

Rates of CPTSD were lower than rates of PTSD in the current study. This is incongruent with most studies using self-report measures, which have typically found lower rates of probable PTSD than of probable CPTSD (40, 44, 45). There are several possible explanations for this dissimilarity. A large proportion of participants in this sample did not fulfil criteria for either PTSD or CPTSD, and the rates may differ in purely clinical samples. Another possibility is that the ITI provides conservative estimates of PTSD and CPTSD rates. It is possible that DSO items, required for a CPTSD diagnosis, are difficult to assess as being trauma-related or not. Compared with self-reports, clinical interviews are likely to be more conservative in attributing DSO items to trauma and may be needed to more accurately assess whether problems consistent with DSO should count towards a CPTSD diagnosis.

Associations with measures of convergent and divergent validity indicated that PTSD symptoms were robustly associated with fear and anxiety and DSO symptoms with depression, general distress, and dissociations, and that DSO was associated with greater functional disability and lower quality of life, as compared with PTSD. This is congruent with research based on self-report measures (40, 41, 44, 45) The findings support the theory behind the ICD-11 distinction between PTSD and DSO; that hallmark PTSD symptoms reflect a fear-based response, whereas DSO symptoms reflect pervasive distress and disturbances.

The PTSD checklist for DSM-5 (PCL-5)

The results indicate strong support for the reliability of the PCL-5 in Swedish. However, the MIIC of the avoidance subscale was above the recommended level, a result that has been found also with the German version of the PCL-5 (97). Considering that the clinical relevance of the avoidance items is high, it would be disadvantageous to omit one of them solely for psychometric purposes, and thus risk excluding individuals who only acknowledge one aspect of avoidance.

Strong associations were found with other measures of post-traumatic stress, supporting the convergent validity of the PCL-5. Measures of other psychological problems, such as depression, dysthymia, dissociation, and insomnia, followed an expected pattern, taking symptom overlap into account. However, some precautions should be noted for the associations with other phenomena. A person could score moderately high on the PCL-5 without acknowledging any symptoms that are in themselves trauma-related, such as re-experiencing and avoidance. Thus, the total severity score of the PCL-5 might not adequately reflect PTSD, but could also reflect other psychiatric problems that may arise after a potentially traumatic event. This does not necessarily mean that the PCL-5 lacks discriminative ability, but could also indicate that the DSM-5 PTSD construct is inherently non-discriminative against other disorders.

As there are no official guidelines, the decision of which threshold score to use should depend on the effects of false positive versus false negative cases (100). For the PCL-5 in Swedish, Paper III suggests that a threshold score of 29 is appropriate if sensitivity and specificity are given equal importance, for example when used as a screening tool in clinical practice and followed up with a clinical assessment. A higher threshold of 37 could be more appropriate for detecting probable PTSD cases in non-clinical settings, such as survey research, when a follow-up assessment is not possible. Nonetheless, all thresholds reported in this study fall short of providing perfect agreement with careful clinical assessment.

Agreement and diagnostic rates

Examination of diagnostic rates of dimensional models for DSM-5 corroborated previous research findings, in that more constrained dimensional models yielded lower diagnostic rates compared with DSM-5, indicating that model selection has a large impact on diagnostic rates (26, 38).

Diagnostic rates of DSM-5 PTSD were higher than ICD-11 PTSD and CPTSD. The agreement between diagnostic manuals was moderate, and both DSM-5 and ICD-11 identified partly different cases, with only 46% of clinically assessed PTSD cases fulfilling criteria according to both manuals. Results are in line with other studies on the agreement between DSM-5 and ICD-11 PTSD, and suggest that the use of only one model may lead to missed cases (23, 101, 102). All ICD-11 CPTSD cases also fulfilled criteria for DSM-5 PTSD, and the results suggest that the disagreement is due to the criteria for PTSD, rather than the criteria for DSO.

Methodological considerations

The Tsunami cohort

Members of the Tsunami cohort (Paper I) were repatriated to an unaffected area and had similar types of exposure. This enabled the examination of classes in a sample relatively free from unknown confounders. However, exposure was defined as closeness to the wave and the retrospective reporting of life threat, and there are several aspects of exposure that were not measured. These include, for example, cognitive interpretations of what happened and acute psychological symptoms, such as strong emotions or dissociation. As for secondary stressors, loss was included as a predictor, but there could have been other secondary stressors, such as somatic injuries, which were not included in the analysis. Finally, the generalisability of the results in relation to disaster-stricken communities where survivors continue to reside in affected areas may be limited.

The TRACES study

The TRACES sample (Papers II–IV) consisted of a self-recruited mixed trauma sample in the Uppsala region of Sweden. In contrast to the Tsunami cohort, this sample was highly heterogeneous and participants varied greatly in exposure, both in type of traumatic event and potentially in secondary stressors. Unknown confounding variables may thus very well have affected the formation of the subgroups found in Paper IV. In clinical practice, patients present with a large variety of risk factors and experiences, and it is seldom possible to assess them all. Rather, clinical assessment is focused on the present symptomatology, and the subgroups found in paper IV likely has high ecological validity in a Swedish clinical setting.

The TRACES sample is of a relatively small size, has a skewed gender proportion, and moderate prevalence of diagnosis. It is unclear how the results would generalise to samples with a higher overall symptom burden and to predominantly male samples, for example in regard to prevalence rates and threshold scores. It is also possible that the self-selection recruitment process eliminated specific groups, such as individuals with high levels of avoidance.

Response rate

In the Tsunami cohort, response rates in both the first and second survey were modest. This is not uncommon in studies of disaster survivors. Non-response patterns in a similar sample have been thoroughly investigated and suggest that individuals less exposed are less likely to respond (103). As classes differed mainly in symptom severity, and only individuals indicating at least one symptom of PTS were included, the impact of non-response is likely low.

Similarly, in Paper IV, based on data from the TRACES study, a large proportion of participants were lost to follow-up. The impact of this may have been reduced by imputing missing data for these cases; however, imputation requires the assumption that data are missing at random, which is often not the case. At the second assessment point, attrition rates were higher in more symptom-burdened groups, and discomfort or a specific symptom could be one possible explanation for attrition. At the third assessment point, attrition rates were comparable across groups. Nonetheless, attrition poses a threat to the ecological validity of results regarding differences in prospective outcome between individuals with varying symptom presentation.

Data collection

A strength of both the Tsunami study and the TRACES study was the use of longitudinal data collection. Data were collected prospectively (with the exception of exposure variables, which may have been subject to recall bias), enabling examination of how symptomatology influenced trajectory. In the TRACES study, the use of standardised clinical assessment to evaluate symptomatology minimised common biases with self-report, such as extreme responding or a lack of understanding of concepts. In Paper III, the use of a gold standard structured clinical assessment enabled valid examination of threshold scores.

Interrater reliability

In the TRACES study, all interviewers had ample training in the instruments, were well-versed in both DSM-5 and ICD-11 criteria, and underwent continuous supervision. This increases the internal validity of the data collected. However, it is unclear if the results regarding interrater reliability hold when used in settings where interviewers are less familiar with the diagnostic conceptualisations, or when supervision is lacking. Furthermore, for the ITI, only a small subsample was used for analysing interrater reliability, and the results need to be replicated in larger samples.

Validity

There was a lack of measures of externalising symptomatology, negative self-concept, and relational disturbance, other than items in the PTSD measures. This limits the conclusions that can be drawn with regard to the convergent validity of these items. Analyses of concurrent and divergent validity of the assessment tools were partly based on data collected using different methods (i.e., clinician-administered vs. self-report). It might have been preferable to base these analyses on data collected using one and the same method. The

associations are, however, unlikely to be heavily influenced by common-method bias.

Symptom presentations

In Paper I, symptoms of grief were not included in the analysis, despite loss being used as a predictor. Studies of latent classes and/or profiles of PTSD and grief have indicated the presence of subgroups of PTSD distinguished by levels of grief (104), and it is possible that including grief would have led to more diverse profiles. However, this might have transformed the model into one examining subtypes of comorbidity, and the aim of the study was to examine subtypes of post-traumatic stress.

In Paper IV, DSM-5 criteria were used as indicators. As has been noted above, the DSM-5 model has limited support in previous studies, and it is possible that results would have differed if using one of the other models suggested in the literature. However, adherence to current diagnostic criteria was necessary in relation to the study aims.

A recent paper suggested that using binary vs. ordinal indicators renders different patterns between classes when conducting LCA (105). In Paper I, ordinal indicators (i.e., symptom severity scores) were used to assess subgroups, while binary indicators (fulfilment of diagnostic criteria) were used in Paper IV. Thus, caution should be applied when comparing classes from Paper I and Paper IV, not only on the basis of the different samples, but also from a methodological viewpoint.

Strengths of the examination of symptom presentations include the use of the three-step latent class methodology that allows for examining associations while accounting for class uncertainty, and the use of a prospective design that allows for further validation of the models.

Conclusions

The aims of this thesis, described in its introduction, were to examine how different symptom presentations of PTSD were associated with predictors and prospective outcomes, to evaluate the dimensional structure of PTSD, to examine how different models of PTSD affect prevalence rates, and to provide methods for assessing PTSD – as the disorder is proposed in the DSM-5 and ICD-11 – in Swedish.

- Subgroups with different symptom presentations were not found in a highly homogeneous sample. This suggests that features, such as event-specific exposure or additional stressors, may influence symptom presentation (Paper I).
- The ICD-11 model, separating PTSD and DSO, was supported for the first time, using a disorder-specific clinician-administered instrument (Paper II).
- The International Trauma Interview appeared to be a reliable and valid tool for assessing ICD-11 PTSD and CPTSD (Paper II).
- The DSM-5 four-factor model of PTSD was not supported. Rather, DSM-5 PTSD was better described as consisting of six or seven latent factors. This may suggest the need for a revision of the DSM-5 model; however, this would have large effect on prevalence rates (Paper III).
- The PTSD checklist for DSM-5 possessed reliability and validity as a self-report instrument for DSM-5 PTSD, but should not be used as a stand-in for a thorough clinical assessment (Paper III).
- Four subgroups with different symptom presentations were found in a mixed trauma sample. Individuals with both hallmark PTSD and ancillary symptoms had higher symptom load over time. This symptom combination likely indicates a greater need for clinical intervention (Paper IV).
- There is insufficient agreement between DSM-5 and ICD-11 PTSD and CPTSD. This poses a challenge for future researchers and clinicians (Paper IV).

Implications and directions for future research

In February 2020, the diagnosis of PTSD celebrates the 40th anniversary of its inclusion in the diagnostic nomenclature. Despite it having reached middle age, it is clear that the diagnostic formulation still suffers from growing pains. Categorical psychiatric definitions are models that assist in identification of individuals experiencing psychological distress, facilitate research, and communicate knowledge. Notwithstanding their limitations, they serve an important function, both clinically and scientifically. They should thus be evaluated continuously and subject to change.

The current definitions of PTSD not only identify different numbers of cases, but also identify partly different cases. Thus, research based on one definition will not necessarily translate into cases fulfilling criteria for the other definition, and it is still unclear how patients endorsing criteria according to one or both definitions differ clinically (21, 102). In settings like Sweden, where clinicians often work with the DSM-5 but record diagnoses according to ICD-11, care must be taken as to which definition is used.

Notably, all cases fulfilling criteria for ICD-11 CPTSD also fulfilled criteria for DSM-5 PTSD. This suggests that DSM-5 and ICD-11 agree on a clinical presentation of PTSD that includes both hallmark and ancillary symptoms. Rather, we lack consensus in how to define PTSD among those who only have hallmark symptoms. The discourse has largely focused on the separation between hallmark and ancillary symptoms, reflected in separation of PTSD and disturbances in self-organisation. As noted in this thesis, this separation has been supported using both self-report and clinician-assessed data. However, most studies have examined such a separation using only ICD-11 symptom indicators. The potential overlap between DSM-5 negative alterations in cognition and mood and ICD-11 disturbances in self-organisation, a possible route forward would be to design a hierarchical latent model of DSM-5 symptomatology. As the DSM-5 four-factor model lacks support, this would preferably be done using six- or seven-factor models at the first-order level. If the separation between hallmark and ancillary symptoms is supported there as well, this would significantly increase the construct validity of the ICD-11 model.

This thesis highlights some similarities and differences between current diagnostic definitions of PTSD. The papers and discussions have largely focused on the psychometric aspects of each formulation, and it is clear that several latent models may provide accurate descriptions of the observed data.

This thesis also provides clinicians with validated assessment tools for the current diagnostic definitions, thus hopefully facilitating clinical work and improving the assessment of patients suffering from trauma-related illness.

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Svensk sammanfattning

Posttraumatiskt stressyndrom (PTSD) är ett psykiatriskt sjukdomstillstånd som kan uppkomma efter exponering för allvarliga händelser såsom naturkatastrofer, våld, krig, olyckor och plötslig död. Tillståndet utmärks av kärnsymptom såsom återupplevande (t.ex. flashbacks och mardrömmar), undvikande av inre och yttre påminnelser, och ökad reaktivitet inför potentiella hot (t.ex. hypervigilans och lättskrämdhet). Personer med PTSD har dock ofta även andra, indirekta, symptom såsom nedstämdhet, negativa tankar, skuldkänslor, ilska, dissociation, problem med känsloreglering och med relationer. Det stora antalet olika symptom som karakteriserar PTSD tillåter betydande skillnader i symptompresentation mellan individer.

De senaste utgåvorna av de två diagnosmanualerna som oftast används i svensk hälso- och sjukvård, DSM-5 och ICD-11, har olika sätt att hantera den mängd symptom som är associerade med PTSD. I DSM-5 definieras PTSD brett och inkluderar såväl kärnsymptom som indirekta symptom. I ICD-11 är beskrivningen av PTSD smal och innefattar enbart kärnsymptom. ICD-11 inkluderar istället de indirekta symptomen under diagnosen Komplex PTSD (CPTSD), som innebär att uppfylla kriterier för PTSD samt störningar i självorganisation (eng: disturbances in self-organization; DSO), definierat som besvär med känsloreglering, ihållande negativ självbild och problem i interpersonella relationer. Metoder för att undersöka samvariation mellan symptom genom att mäta bakomliggande faktorer (dvs. konfirmatorisk faktoranalys) har haft stort inflytande på utformningen av diagnosen.

Syfte

Syftet med denna avhandling var att undersöka hur olika symptompresentationer av PTSD är associerade med långtidsutfall, att med konfirmatorisk faktoranalys utvärdera den latenta strukturen hos PTSD såsom det är föreslaget i DSM-5 och ICD-11, att bidra med svenskspråkiga metoder för att bedöma PTSD enligt DSM-5 och ICD-11, samt att undersöka den diagnostiska samstämmigheten mellan DSM-5 och ICD-11.

Metod

Avhandlingen baserar sig på fyra studier, varav en använder sig av tidigare insamlade data från svenska tsunamiöverlevare (tsunamikohorten, studie I) och tre använder nyinsamlade data från individer i Mälardalsregionen som exponerats för en stor variation av händelser (TRACES-studien, studie II-IV). Studie I och IV undersökte symptompresentationer av PTSD genom Latent Class Analysis (LCA). LCA är en datadriven metod som syftar till att undersöka om individer i en grupp kan delas in i homogena subgrupper. Studie II och III utvärderade de psykometriska egenskaperna och den latenta strukturen hos två instrument för att bedöma PTSD enligt DSM-5 och ICD-11.

Resultat

I studie I undersöktes subgrupper baserade på svar på en självskattningsskala för PTSD. Individerna skiljde sig åt främst avseende symptomsvårighet, och inte i symptompresentation. En viss tendens till divergens mellan grupper fanns i nivåer av hyperarousal relativt nivåer av undvikande/känslomässig bedövning, där tyngre symptombelastade grupper hade högre nivåer av hyperarousal jämfört nivåer av undvikande/känslomässig bedövning.

I studie IV undersöktes subgrupper av individer utifrån uppfyllande av symptomkriterier för PTSD i DSM-5 och DSO i ICD-11. Fyra subgrupper hittades, som skiljde sig åt i sannolikhet att uppfylla kärnsymptom jämfört med indirekta symptom på PTSD. Personer med både kärnsymptom och indirekta symptom hade svårare psykiska besvär sex och tolv månader efter första mätningen, jämfört med de övriga grupperna. Studie IV visade också att samstämmigheten mellan DSM-5 och ICD-11 vad gäller uppfyllande av diagnosen PTSD var måttlig.

I studie II undersökes de psykometriska egenskaperna hos en strukturerad klinisk intervju för ICD-11 PTSD och CPTSD, the International Trauma Interview (ITI). ITI uppvisade acceptabel intern reliabilitet och validitet. Konfirmatorisk faktoranalys hittade stöd för ICD-11 modellen för PTSD och CPTSD.

I studie III undersöktes de psykometriska egenskaperna hos en självskattningsskala för DSM-5, the PTSD Checklist for DSM-5 (PCL-5). Resultaten indikerade god reliabilitet och validitet. Inget gränsvärde uppvisade en perfekt samstämmighet med klinisk bedömning, men 29 poäng gav en acceptabel sensitivitet och specificitet. Konfirmatorisk faktoranalys hittade inte stöd för DSM-5s fyrfaktormodell för PTSD, men däremot stöd för mer restriktiva modeller som delade in symptomen i sex och sju latenta faktorer. Vilken modell som användes hade stor relevans för prevalensen av PTSD.

Slutsatser

Sammantaget indikerar resultaten att personer som drabbats av traumatiska händelser huvudsakligen verkar skilja sig åt i hur svåra kärnsymptom de har, men att långtidsutfallet också påverkas negativt av indirekta symptom. De framtagna svenska mätmetoderna för PTSD är reliabla och valida enligt sin egen modell, men även andra modeller kan förklara symptomvariation. Den diagnostiska träffsäkerheten hos PCL-5 var inte stark nog att användas för diagnostik i sig självt, utan PCL-5 bör användas som ett screeninginstrument tillsammans med klinisk bedömning. Val av diagnostisk modell påverkar prevalensen av sjukdomen, och modellerna identifierar bara delvis överlappande fall. Detta innebär en utmaning för både forskare och kliniker, och en osäkerhet för de drabbade, då valet av modell avgör huruvida en person får en PTSD diagnos eller inte.

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