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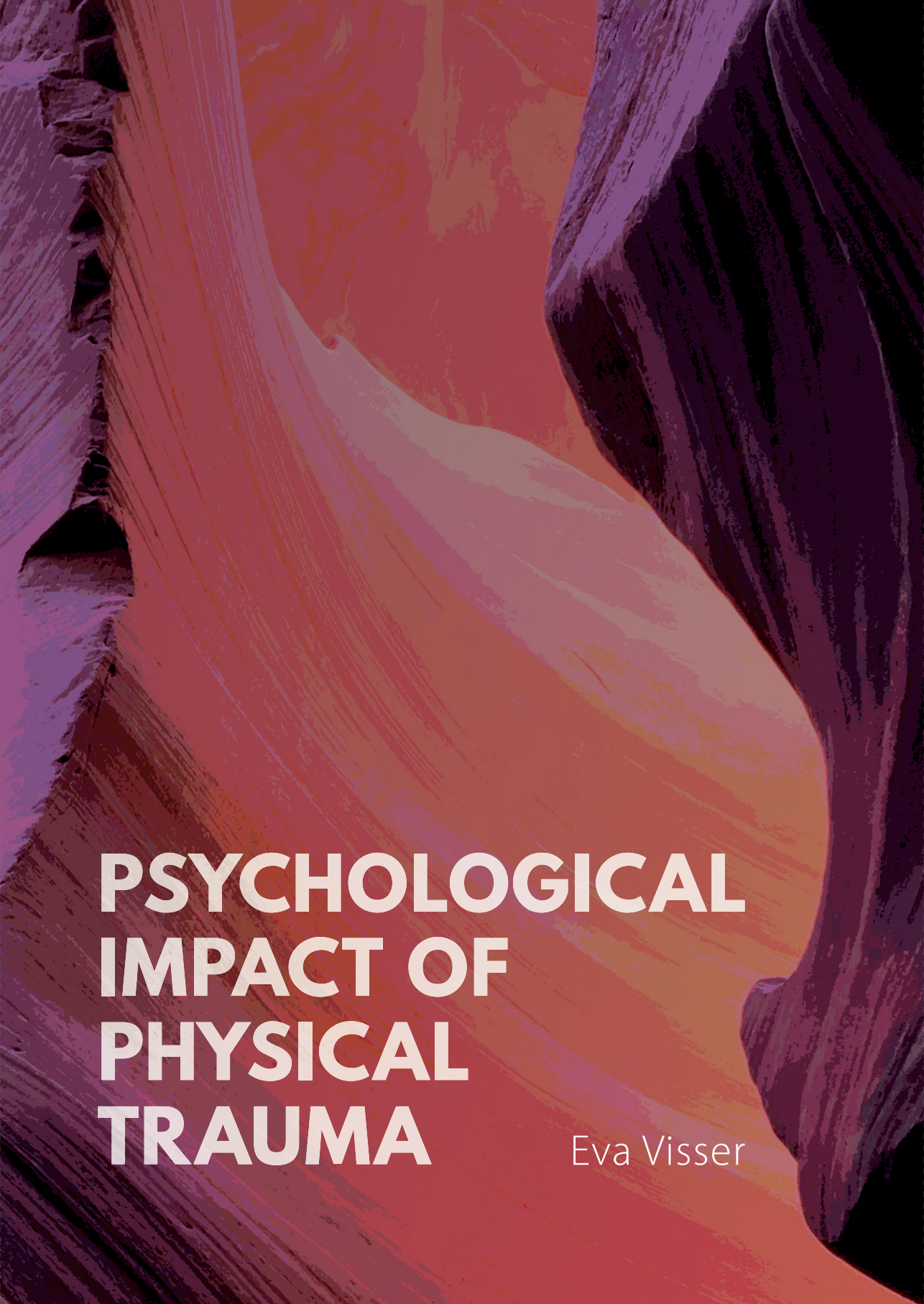
PSYCHOLOGICAL IMPACT OF PHYSICAL TRAUMA
Eva Visser

"It is more important to know what sort of person has a disease than to know what sort of disease a person has"

- Hippocrates -

UITNODIGING

Voor het bijwonen
van de openbare verdediging
van het proefschrift

PSYCHOLOGICAL IMPACT OF PHYSICAL TRAUMA

Op vrijdag 1 oktober 2021
om 13.30u
in de Aula van Tilburg University,
Warandelaan 2 te Tilburg.

Aansluitende bent u van harte welkom
op de receptie bij Grand Café Esplanade.

De verdediging is ook online
te volgen via een livestream.

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PSYCHOLOGICAL IMPACT OF PHYSICAL TRAUMA

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Over de omslag | *About the cover*

Op de omslag staat een foto van de Lower Antelope Canyon, Arizona, Verenigde Staten. Het symboliseert de gedachte dat, ondanks dat het leven soms moeilijk kan zijn, er altijd weer een nieuw en beter perspectief is.

The cover is a photo from the Lower Antelope Canyon, Arizona, United States of America. It represents the idea that, even when life can be difficult, there is a new or better perspective.

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Eva Visser

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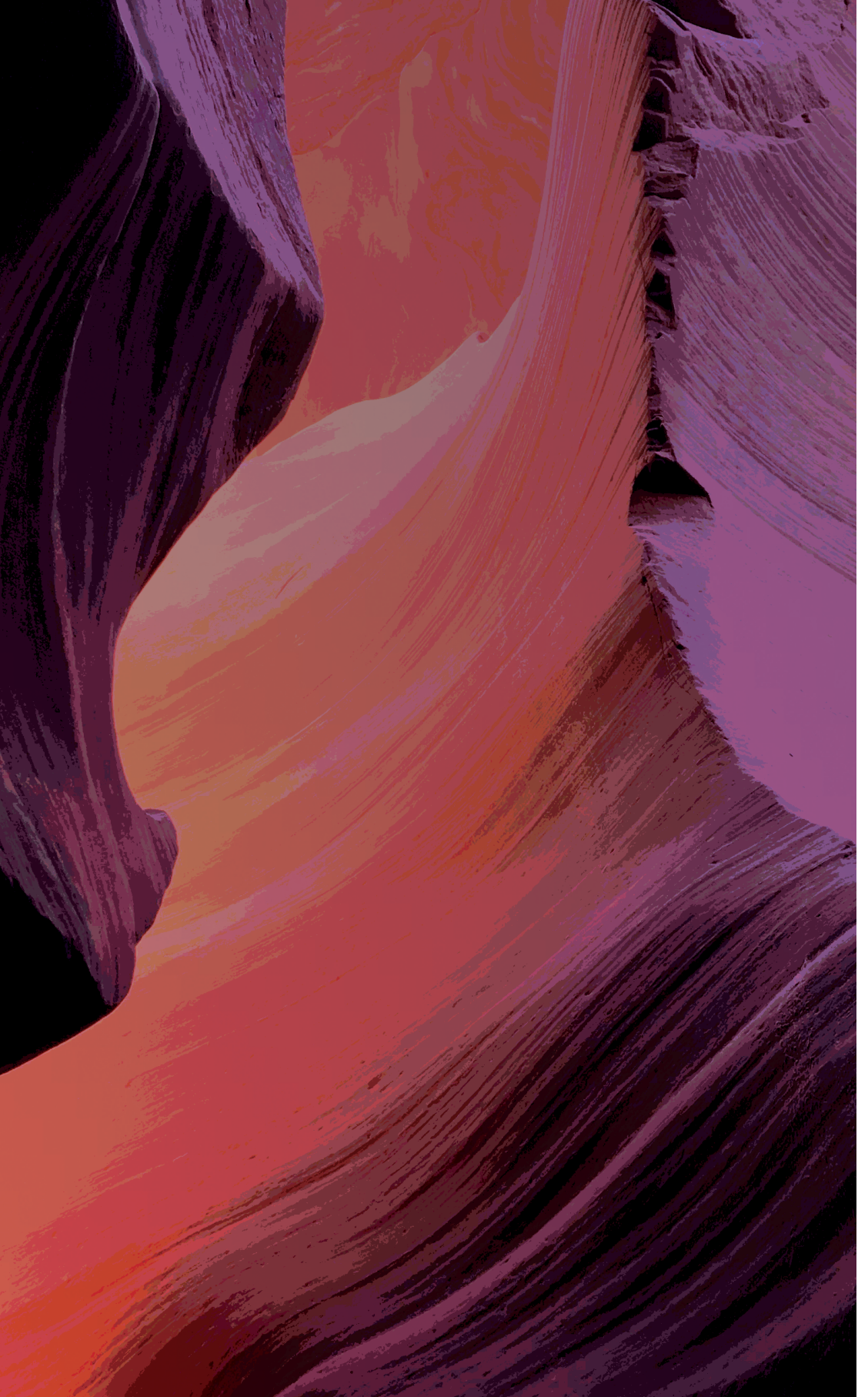
Voor Roos en Esmee



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Chapter 1

GENERAL INTRODUCTION AND OUTLINE OF THIS THESIS

THE TRAUMA POPULATION

The definition of trauma

The word trauma, which literally means wound, is used inconsistently referring to an event as well as to a psychological injury arising from an event[1]. Trauma is used routinely in medical jargon to describe an injury. In psychology, it refers to an injury to the 'psyche', which is damage to a person's emotional or psychological health and wellbeing[2].

Terr (1991) explains that there are two distinct types of trauma: Type-I and Type-II trauma[3]. Type-I trauma refers to the experience of a sudden and unexpected single traumatic event that is brief in duration[4] and is characterized by full, detailed memories, omens, and misperceptions[3]. Examples are a traffic accident, fall, work related accident, or hospitalization. A Type-II trauma refers to prolonged and repeated traumatization and is characterized by denial and numbing, self-hypnosis and dissociation, and rage[3]. Sexual abuse and domestic violence are examples of Type-II trauma[4,5]. This study focusses on patients who have experienced a Type-I trauma.

The epidemiology of physical trauma

According to the World Health Organization, about 55% of the 5.8 million deaths from injuries are related to Type-I trauma[6]. In the Netherlands, the number of deaths from trauma increased in the last decade, probably due to an increase in fatal road traffic accidents[7], including cyclists[8,9]. The rates of motor vehicle accidents were the highest in persons younger than 35 years of age, while the mortality rates of cyclists were the highest in elderly (> 75 years)[8].

In the Netherlands, the number of patients who were treated at an emergency department (ED) after injury has increased in the last years from about 68,000 in 2010 to about 78,000 in 2018[9]. The Dutch Trauma Registry provided several reasons for this development[9]. First, about 25% of trauma patients were aged 80 and older. Second, approximately 94% of patients had a mild or moderate injury (Injury Severity Score (ISS) < 16) and 25% of these patients were admitted to the hospital with a hip fracture. Third, especially with regard to cyclists, more road traffic accidents were reported. In line with this, more severely injured (ISS ≥ 16) needed specialized trauma care in a level-I trauma center. These patients had significantly more physical injuries (Abbreviated Injury Score ≥ 3) compared to patients, with comparable severe injuries, from previous registries. Subsequently, the total costs of trauma care increased as well[10,11] from €1.15 billion in 2006[11] to €3.5 billion in 2016[12].

Trauma treatment in the shock room

After experiencing a physical trauma, patients go through a process of medical treatment and rehabilitation: from the ambulance or trauma helicopter to the ED, possible hospital admission, and, finally, rehabilitation[13]. Especially severely injured (ISS ≥ 16) patients will be treated in the shock room in a level-I trauma center after a physical trauma.

In the Netherlands, there are 11 level-I trauma centers[9]. In this study, all trauma patients were treated in the shock room (see Figure 1) of the ETZ (Elisabeth-TweeSteden) Hospital, Tilburg, The Netherlands, which is the level-I trauma center of the province of Noord-Brabant. Presence of a surgical team in the ED, instant availability of ultrasonography, angiography, computed tomography scanner, a stand-by operating room, and intensive care beds are essential to become categorized as a level-I trauma center[13-15].

FIGURE 1. The shock room in the ETZ Hopital[16]

To deal with increasing numbers of trauma patients, multidisciplinary (i.e., trauma surgeon, neurologist, neurosurgeon, orthopedic surgeon, anesthesiologist, emergency doctor, intensivist, specialized nurse, and radiologist) specialized trauma care has been implemented and the quality of trauma care subsequently evolved[17]. The ETZ Hospital has shown that by optimizing the organization of trauma care with in-hospital coverage by senior clinicians

24 hours a day and seven days a week[18], survivorship after injury increased[19]. Moreover, as a result of multidisciplinary trauma care, the quality of medical treatment improved as well as patients' outcomes. For instance, patients had less complications and reported better recovery[20,21].

PSYCHOLOGICAL CONSEQUENCES AFTER TRAUMA

Adverse physical (e.g., problems on wound repair and pain)[22-24], psychological[25,26], and social (e.g., broken marriages and difficulties in resumption to work)[27,28] outcomes may occur after trauma. Patients can experience anxiety[29], depressive symptoms[29,30], acute stress disorder (ASD)[31], and posttraumatic stress disorder (PTSD)[25,29,32,33] after trauma. These physical, psychological, and social problems and disorders can arise directly or months after trauma and can remain present years afterwards[34]. In addition, treatment in the shock room and during hospital admission can be overwhelming and can have a major impact on patients' wellbeing, because patients who were less satisfied with their general health and recovery short after trauma needed more medical care, had a longer hospital stay, and visited the hospital more often[10]. Qualitative research is needed to evaluate how patients' experiences and perspectives on treatment and recovery are related to psychological outcomes. In addition, a quantitative observational cohort and intervention research could focus on psychological problems and disorders and how they are related to patients' recovery, because traumatic stress can have a negative impact on physiological functioning and physical well-being[35-37]. Concrete, PTSD can affect wound repair and is related to more pain and fatigue[22-24,27,38].

Acute and posttraumatic stress disorder

Although ASD and PTSD are different diagnoses, diagnostic criteria, namely intrusion (e.g., recurrent distressing dreams, memories, and reactions), negative mood, avoidance (e.g., avoid thoughts, feelings or external reminders associated with the trauma), and arousal (e.g., sleep disturbance, irritable and angry behavior, hypervigilance, and problems with concentration) for ASD and PTSD are similar. However, dissociative symptoms (e.g., depersonalization, derealization, and dissociative amnesia) are only emphasized in ASD and not in PTSD. Moreover, ASD can only be diagnosed within the first month after injury and lasts for less than a month. If these symptoms persist for more than one month, than PTSD will be diagnosed[39]. If dissociative symptoms are present for more than a month, then these symptoms will separately be used along with PTSD as peritraumatic dissociation[40,41]. PTSD symptoms may begin after either trauma or start months or years afterwards[34]. Patients can also experience subclinical ASD or subclinical PTSD. If patients do not experience one or two symptom criteria of the full disorder, patients cannot be diagnosed with a clinical disorder.

In that case, patients experience subclinical ASD or PTSD[42]. Nevertheless, a subclinical disorder is associated with impaired functioning and levels of distress similar to that of a clinical disorder[42].

The prevalence rates for ASD as well as PTSD are mostly wide-ranging. About 1% to 37% reported subclinical ASD during hospitalization[43], whereas about 6 to 28% of trauma patients experienced ASD during hospitalization[44,45]. Moreover, approximately 17.5% to 30% was diagnosed with PTSD one month after trauma[43,45] and 42% reported PTSD six months post-injury[45]. Even after six years, PTSD was observed in 6% or 8% of the patients[46]. In addition, there is increasing interest in evaluating trajectories of PTSD. However, these studies focused solely on PTSD and did not incorporate ASD[32,47,48]. Moreover, they evaluated trajectories in a subset of the trauma population[49,50]. Even though patients, diagnosed with ASD, have a higher risk of developing PTSD[51,52], it is still unknown who will develop PTSD.

PTSD could be associated with sociodemographic, clinical, and psychological factors. Several risk factors for PTSD were found in physical trauma patients, including female sex, younger age[47,53], admission to intensive care unit (ICU), anxiety, depressive symptoms[25,29,32], and ASD[51,52]. Personality traits have hardly been examined in physical trauma population. Only one study found that personality traits predicted QOL in orthopedic patients[54]. Studies with various types of trauma exposure and injuries are needed to understand which factors characterize these trajectories[47] and to reveal which patients are at risk for developing PTSD.

Psychological treatment for ASD and PTSD after injury

Over the past years, a broad range of interventions was developed to treat trauma patients who suffer from ASD and PTSD, for example components of trauma-focused cognitive behavioral therapy (CBT)[55,56], in vivo or imaginary exposure[57], and Eye Movement Desensitization and Reprocessing (EMDR)[58,59]. According to the Trimbos Institute and new guidelines of the International Society of Traumatic Stress Studies, CBT and EMDR are considered the treatment of choice for patients with ASD and PTSD[39,60-63].

CBT is based on cognitive and behavioural theories[64]. The most effective CBT techniques are repeated exposure to the trauma memory, especially imaginary exposure or writing a trauma narrative, in vivo exposure to avoided situations that are related to the trauma, and cognitive restructuring of the meaning of the trauma[65]. Patients learn to identify triggers of re-experiencing and practice their perception of the past versus the present day by using exposure[66]. Cognitive restructuring focuses on teaching patients to identify dysfunctional thoughts and thinking errors, stimulate rational alternative thoughts, and reconsider beliefs about themselves, the trauma and their environment[64,66]. In addition, EMDR is also a psychotherapy that arose from CBT. EMDR focuses on four components of traumatic

memories that are stored as an image, body sensation, traumatic associated cognition and/or emotion. Therapist directed lateral eye movements are the most commonly used external stimulus during treatment. Other stimuli include finger taps, doing sums or eye movements in combination with one of these two stimuli. EMDR treatment probably stimulates the intrinsic information processing system in order to restore the targeted memory as a contextual memory[67]. The EMDR therapist uses restricted questioning together with bilateral stimulation to unblock the intrinsic information processing system[63,68]. Even tough CBT exposure, cognitive restructuring and EMDR are effective in patients with ASD and PTSD[63], EMDR requires less therapy sessions than exposure or cognitive restructuring. Subsequently, the costs of treatment for EMDR are lower[69].

These psychological interventions are largely applied to patients with PTSD after Type-II trauma. Also guidelines and research are mainly focussed on PTSD after Type-II trauma. Yet, a pilot RCT study showed that a single EMDR session, provided on the ED in the first hours after a type-I trauma, is feasible and probably reduces PTSD symptoms three months after ED admission[70]. This implies further research to examine the effectiveness of EMDR as in-hospital treatment in patients who are admitted to the ED, ICU or surgical department after type-I trauma to prevent them from developing psychological disorders during recovery from injury.

Quality of life

Physical trauma patients have reported long-term impaired quality of life (QOL), health-related QOL (HRQOL) or health status (HS)[71-77]. QOL is used as an umbrella term, since QOL, health-related quality of life (HRQOL) and health status (HS) are related multidimensional constructs and they all measure patients' physical, psychological, and social domains. However, these constructs are not identical. The World Health Organization defines QOL as: "An individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. It is a broad ranging concept affected in a complex way by the person's physical health, psychological state, personal beliefs, social relationships and their relationship to salient features of their environment"[78]. HRQOL is a more limited concept of QOL, as it solely focuses on patients' subjective perceptions on health (i.e., physical and mental health). In addition, HS refers to the extent of physical, psychological, and social functioning, but without taken patients' satisfaction with functioning into account[79].

The biopsychosocial model incorporates sociodemographic, clinical, and psychological characteristics to explain QOL[80-82]. This approach systematically considers biological, psychological, social factors, and their interactions in understanding health, illness, and health care delivery[80]. Moreover, not only biological factors determine patients' HS or (HR)

QOL, but also psychological and social factors need to be studied. Previous studies have shown females, as well as higher ISS, low social support, and PTSD are related to impaired HRQOL or HS[71,74,83-86]. The presence of these consequences show a negative impact on patients' lives up to six years after trauma[28,37,71,74,87,88]. However, as these studies focused on HS and HRQOL, it is still unknown how factors from the biopsychosocial model are related to QOL after a physical trauma. Therefore, research could examine patients' characteristics in QOL domains using a biopsychosocial approach.

Although an injury may result in impaired HS or (HR)QOL[72-75], according to the Disability Paradox, patients with severe limitations may still report good QOL[89], as impairments do not necessarily lead to decreased perceived health[90]. Hence, focusing on patients' QOL and their characteristics after trauma is crucial to determine how their QOL will develop during recovery. Clinicians with this knowledge are able to identify these patients at risk, and refer them for psychological treatment.

AIMS AND OUTLINE OF THE THESIS

To summarize, an injury is a public health problem, because each year more patients are treated on the ED. Moreover, an injury may have major physical, social, and psychological consequences. These consequences are, together with impaired QOL, reported up to six years after trauma. A short and intensive psychological treatment with EMDR could be effective to prevent patients from psychological consequences.

In order to examine patients' perspectives on injury, treatment and recovery, and to gain knowledge about the gaps in the literature of PTSD, QOL, and feasibility and effectiveness of EMDR after a physical trauma, the TraP study was performed.

THE TRAP STUDY

The TraP study started in February 2016 (see Figure 2). This study entails a focus group study, an observational prospective cohort study, and a feasibility study.

First, **Chapter 2** aimed to describe, in a systematic review, the course, risk factors and psychological treatments for ASD and PTSD. **Chapter 3** provided the protocol of the mixed-method study, describing the design of a focus group study and the design of an observational prospective cohort study in physical trauma patients. Next, **Chapter 4**

explored in a focus group study, patients' perspectives on the injury, treatment in the shock room and hospital, and rehabilitation after trauma and how their perspectives are related to physical and psychological consequences during treatment and recovery.

Using an observational prospective cohort study, different longitudinal trajectories of PTSD and QOL were studied (**Chapter 5** and **6**). In addition, it was examined whether these trajectories were characterized by socio-demographic, clinical, and psychological variables. Finally, a risk profile was developed to determine patients at risk for PTSD or impaired QOL at 12 months after trauma.

To determine which risk factors characterize trajectories of PTSD (**Chapter 5**), a model with related factors for PTSD was developed (see Figure 3). This model was based on systematically reviewed risk factors (**Chapter 2**) and the biopsychosocial approach[80,81].

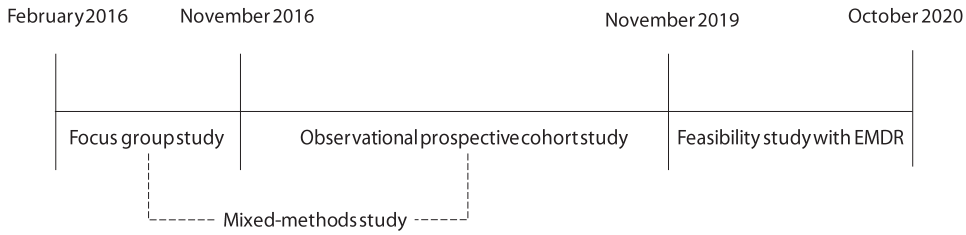

FIGURE 2. Timeline of TraP study
Abbreviations: EMDR: Eye Movement Desensitization and Reprocessing

Furthermore, the effect of ASD on PTSD was examined (**Chapter 5**) to evaluate who developed PTSD (see Figure 4). This made it possible to determine prevalence rates of patients with and without ASD, patients with or without PTSD, and patients with ASD and PTSD.

In addition to PTSD and in line with **Chapter 5**, a model with related risk factors for a low QOL was developed (see Figure 3), which was also based on the biopsychosocial approach[80,81]. The model with sociodemographic, clinical, and psychological characteristics for QOL is almost the same as the PTSD model. However, PTSD was also included as psychological predictor for QOL. This model was helpful in determining which risk factors characterized trajectories of QOL (**Chapter 6**).

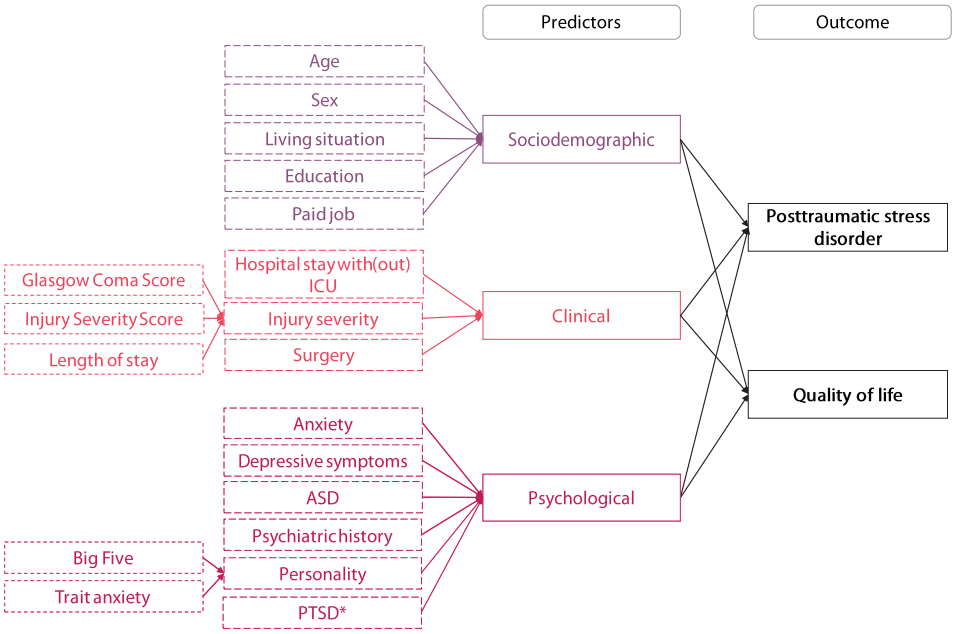

FIGURE 3. Model with sociodemographic, clinical, and psychological characteristics for Posttraumatic stress disorder and quality of life

Abbreviations: ICU: Intensive care unit, ASD: Acute stress disorder, PTSD: Posttraumatic stress disorder. Note: PTSD was included as psychological predictor for quality of life.

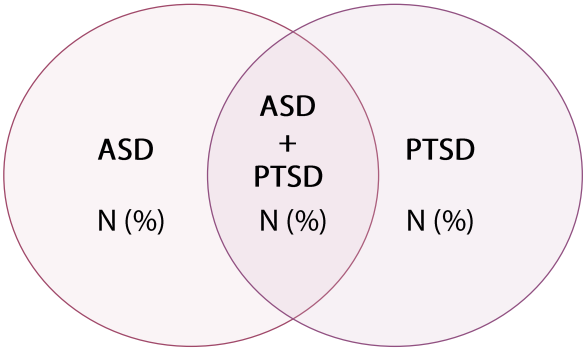

FIGURE 4. Cross-over, using Venn diagrams, of patients with acute stress disorder (at baseline) and posttraumatic stress disorder (at 3, 6, 9, and 12 months after trauma) amongst the study population

Abbreviations: ASD: Acute stress disorder, PTSD: posttraumatic stress disorder, N.: number of patients with corresponding percentages. Note: ASD is studied at baseline, whereas PTSD is examined at 3, 6, 9, and 12 months follow-up (FU). ASD+PTSD refers to patients with ASD at baseline and PTSD at 3, 6, 9, and 12 months FU. The number of patients without ASD and PTSD will also be provided.

Finally, **Chapter 7** described a short report about the feasibility of providing EMDR treatment in patients with symptoms of ASD who are hospitalized, as part of standard care. We concluded this thesis with a summary and general discussion of the dissertation, including implications for future research and clinical practice (**Chapter 8**).

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Chapter 2

THE COURSE, PREDICTION, AND TREATMENT OF ACUTE AND POSTTRAUMATIC STRESS IN TRAUMA PATIENTS: A SYSTEMATIC REVIEW

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ABSTRACT

Background: Trauma patients suffer from acute stress disorder (ASD) and posttraumatic stress disorder (PTSD). It is unknown how these disorders develop over time and when treatment is effective. Our aim was to systematically review (i) the course and predictors of ASD and PTSD after trauma and (ii) which and when psychological treatments are effective.
Methods: Embase, Medline, Web of Science, Scopus, PsycInfo, Cinahl, Cochrane, Pubmed, and Google Scholar were searched up to September 14, 2015. Quality was assessed with STROBE and CONSORT checklists.
Results: Overall, 45 (68%) observational studies and 21 (32%) intervention studies were included. Forty-seven studies (85%) were of lower (Level of Evidence (LoE) 3) or poor quality (LoE 4). ASD was present during hospitalization (range 1%-37%) and about 30% experienced PTSD one month after trauma (LoE 3). The onset of PTSD was within three months up to 12 months after trauma (LoE 3). Especially in patients with ASD, patients showed PTSD symptoms after six years (LoE 3). ASD and PTSD were associated with socio-demographic factors (e.g. being female, younger age, financial problems and low income), reduced cognitive functioning, physical (e.g. pain), social (e.g. low social support), and psychological problems (e.g. hyper-arousal) or disorders (e.g. ASD). Early treatment in the first weeks after trauma can be preventive for PTSD, but effective treatment for ASD is still unclear. Compared to other psychological treatments, the most common examined treatment for PTSD was Cognitive Behavioral Therapy (CBT), which seems to be effective (LoE 2).
Conclusions: A large number of poor qualitative studies present inconsistent findings on the course of ASD and PTSD. Predictors for ASD and PTSD were identified. Early treatment can prevent PTSD. CBT is effective, but mostly examined and it has limitations (e.g. engagement). Other intervention studies are necessary. Good qualitative observational and intervention studies are lacking and needed.

INTRODUCTION

Trauma (all types of injury) is a major public health problem, as it remains one of the leading causes of death and disability[1]. Due to specialized trauma care, survivorship has increased in severely injured patients[2-4]. As a result of injury, 43% to 84% of patients experience problems (e.g. opioid abuse) related to psychological disorders, such as acute stress disorder (ASD), posttraumatic stress disorder (PTSD), and/or depression[5-9]. These disorders are present long after trauma occurred. Subsequently, quality of life is diminished[10-13].

Six to 28% of the hospitalized trauma patients have ASD[14,15]. The prevalence rates for PTSD ranged from 17.5% up to 42% one to six months post injury[15]. However, these rates were based on narrative reviews that did not describe the prevalence rates of ASD and PTSD over time. Therefore, the course of PTSD over a longer period of time (e.g. up to 24 months after injury) is still unclear. To obtain an overview of the psychological trajectories and its predictors, it is important to systematically examine the current literature.

Treatment of ASD or PTSD after injury may prevent the development of other psychological problems (e.g. alcohol abuse) after trauma[16]. Persons with ASD or PTSD who were treated almost directly after trauma with trauma-focused cognitive behavioral therapy (CBT) had a reduction of PTSD symptoms[14]. However, the focus of this, not systematic, review was only on trauma-focused CBT. Patients with ASD or PTSD can experience different kind of symptoms (e.g. anxiety or cognitive impairment after Traumatic Brain Injury (TBI)). It is unclear if patients' treatment needs different approaches[17]. Moreover, information is lacking about which other psychological treatments are effective and when treatment after trauma is mostly effective to prevent PTSD.

Even though many trauma patients suffer from ASD and PTSD, no systematic review has been conducted that examines specifically the course, predictors, and the effect of treatment for ASD and PTSD. The first aim of this systematic review was to examine the course (using incidence rates) and predictors of ASD and PTSD in trauma. The second aim was to examine which and at what time psychological treatments are effective in trauma patients.

METHODS

Search strategy

A systematic computerized search was performed for the period September 11, 1993 to September 14, 2015. The following databases were searched: Embase, Medline, Web of Science, Scopus, PsycInfo, Cinahl, Cochrane, Pubmed and Google Scholar (see Table 1). The key words were combinations of (i) "Stress Disorders, Traumatic, Acute"[Mesh] OR ("acute stress"[tiab])) (ii) ("Emergency Medical Services"[Mesh] OR "Emergency Medicine"[Mesh] OR "Emergency Service, Hospital"[Mesh] OR (((emergen*[tiab] OR trauma*[tiab]) (iii) ward*[tiab] OR department*[tiab] OR patient*[tiab] OR service*[tiab] OR admiss*[tiab] OR admit*[tiab] OR hospital*[tiab] OR call*[tiab] OR center*[tiab] OR centre*[tiab]. Reference lists of the retrieved studies were checked for additional relevant articles.

Selection criteria

To be included, studies had to meet the following inclusion criteria: (i) studies examined the course and/or predictors of ASD or PTSD as a primary or secondary objective or determined the effectiveness of a psychological treatment (e.g. CBT, *Eye movement desensitization and reprocessing* (EMDR)) in (ii) patients with physical trauma who have been included at the emergency department. In addition, (iii) patients were aged 18 or older, (iv) studies were original full reports published in English or Dutch, (v) the article presented an original report with either a quantitative or a qualitative design and (vi) the studies were published in peer-reviewed journals. Studies focusing on veterans were excluded. Reviews, letters to the editor, comments and case reports were also excluded. Additional exclusion criteria were retrospective or cross-sectional design, animal studies, studies with patients with clinical comorbidity (e.g. severe TBI, psychiatric disorder or dementia), or studies that investigated or developed a screening instrument or questionnaire.

TABLE 1. Syntax search for databases

Database	Search syntax	Records identified through database searching	Records after duplicates removed
Embase.com	('acute stress disorder'/exp OR 'acute stress'/exp OR ('posttraumatic stress disorder'/exp AND ('early diagnosis'/exp OR prediction/exp OR Prognosis/de OR 'predictive value'/exp OR screening/de OR 'screening test'/exp OR 'disease course'/de OR 'disease exacerbation'/de OR deterioration/de OR 'recurrent disease'/de)) OR ('acute stress' OR ((early OR predict* OR screen* OR symptom* OR recogn* OR sever* OR course* OR exacerbat* OR deteriorat* OR recur* OR Progress*) NEAR/6 (trauma* OR posttrauma*) NEAR/3 stress*) OR ((early OR predict* OR screen* OR symptom* OR recogn* OR sever* OR course* OR exacerbat* OR deteriorat* OR recur* OR Progress*) NEAR/6 ptsd*)):ab,ti) AND ('emergency care'/exp OR 'emergency patient'/exp OR 'emergency ward'/exp OR 'emergency health service'/exp OR (((emergen* OR trauma*) NEAR/3 (ward* OR department* OR patient* OR service* OR admiss* OR admit* OR hospital* OR call* OR center* OR centre*))):ab,ti)	1243	1219
Medline ovid	("Stress Disorders, Traumatic, Acute"/ OR ("Stress Disorders, Traumatic"/ AND ("Early Diagnosis"/ OR prognosis/ OR "Disease Progression"/)) OR ("acute stress" OR ((early OR predict* OR screen* OR symptom* OR recogn* OR sever* OR course* OR exacerbat* OR deteriorat* OR recur* OR Progress*) ADJ6 (trauma* OR posttrauma*) ADJ3 stress*) OR ((early OR predict* OR screen* OR symptom* OR recogn* OR sever* OR course* OR exacerbat* OR deteriorat* OR recur* OR Progress*) ADJ6 ptsd*)).ab,ti.) AND ("Emergency Medical Services"/ OR "Emergency Medicine"/ OR exp "Emergency Service, Hospital"/ OR (((emergen* OR trauma*) ADJ3 (ward* OR department* OR patient* OR service* OR admiss* OR admit* OR hospital* OR call* OR center* OR centre*))).ab,ti.)	822	67
Web-of-science	TS=((("acute stress" OR ((early OR predict* OR screen* OR symptom* OR recogn* OR sever* OR course* OR exacerbat* OR deteriorat* OR recur* OR Progress*) NEAR/5 (trauma* OR posttrauma*) NEAR/2 stress*) OR ((early OR predict* OR screen* OR symptom* OR recogn* OR sever* OR course* OR exacerbat* OR deteriorat* OR recur* OR Progress*) NEAR/5 ptsd*))) AND ((((emergen* OR trauma*) NEAR/2 (ward* OR department* OR patient* OR service* OR admiss* OR admit* OR hospital* OR call* OR center* OR centre*)))))	902	239

TABLE 1. Continued

Database	Search syntax	Records identified through database searching	Records after duplicates removed
Scopus	TITLE-ABS-KEY((("acute stress" OR ((early OR predict* OR screen* OR symptom* OR recogn* OR sever* OR course* OR exacerbat* OR deteriorat* OR recur* OR Progress*) W/5 (trauma* OR posttrauma*) W/2 stress*) OR ((early OR predict* OR screen* OR symptom* OR recogn* OR sever* OR course* OR exacerbat* OR deteriorat* OR recur* OR Progress*) W/5 ptsd*))) AND ((((emergen* OR trauma*) W/2 (ward* OR department* OR patient* OR service* OR admiss* OR admit* OR hospital* OR call* OR center* OR centre*)))))	1129	145
Psycinfo ovid	("Acute Stress Disorder"/ OR ("Posttraumatic Stress Disorder"/ AND (prognosis/ OR "Disease course"/)) OR ("acute stress" OR ((early OR predict* OR screen* OR symptom* OR recogn* OR sever* OR course* OR exacerbat* OR deteriorat* OR recur* OR Progress*) ADJ6 (trauma* OR posttrauma*) ADJ3 stress*) OR ((early OR predict* OR screen* OR symptom* OR recogn* OR sever* OR course* OR exacerbat* OR deteriorat* OR recur* OR Progress*) ADJ6 ptsd*)).ab,ti.) AND ("Emergency Services"/ OR (((emergen* OR trauma*) ADJ3 (ward* OR department* OR patient* OR service* OR admiss* OR admit* OR hospital* OR call* OR center* OR centre*))).ab,ti.)	740	247
Cinahl ebsco	((MH "Stress Disorders, Post-Traumatic+" AND (MH "Early Diagnosis+" OR MH prognosis+ OR MH "Disease Progression+")) OR ("acute stress" OR ((early OR predict* OR screen* OR symptom* OR recogn* OR sever* OR course* OR exacerbat* OR deteriorat* OR recur* OR Progress*) N5 (trauma* OR posttrauma*) N2 stress*) OR ((early OR predict* OR screen* OR symptom* OR recogn* OR sever* OR course* OR exacerbat* OR deteriorat* OR recur* OR Progress*) N5 ptsd*))) AND (MH "Emergency Medical Services+" OR MH "Emergency Medicine+" OR MH "Emergency Service+" OR (((emergen* OR trauma*) N2 (ward* OR department* OR patient* OR service* OR admiss* OR admit* OR hospital* OR call* OR center* OR centre*))))	298	77
Cochrane	(('acute stress' OR ((early OR predict* OR screen* OR symptom* OR recogn* OR sever* OR course* OR exacerbat* OR deteriorat* OR recur* OR Progress*) NEAR/6 (trauma* OR posttrauma*) NEAR/3 stress*) OR ((early OR predict* OR screen* OR symptom* OR recogn* OR sever* OR course* OR exacerbat* OR deteriorat* OR recur* OR Progress*) NEAR/6 ptsd*)):ab,ti) AND ((((emergen* OR trauma*) NEAR/3 (ward* OR department* OR patient* OR service* OR admiss* OR admit* OR hospital* OR call* OR center* OR centre*))):ab,ti)	134	62

TABLE 1. Continued

Database	Search syntax	Records identified through database searching	Records after duplicates removed
Pubmed publisher	("Stress Disorders, Traumatic, Acute"[mh] OR ("acute stress"[tiab])) AND ("Emergency Medical Services"[mh] OR "Emergency Medicine"[mh] OR "Emergency Service, Hospital"[mh] OR (((emergen*[tiab] OR trauma*[tiab]) AND (ward*[tiab] OR department*[tiab] OR patient*[tiab] OR service*[tiab] OR admiss*[tiab] OR admit*[tiab] OR hospital*[tiab] OR call*[tiab] OR center*[tiab] OR centre*[tiab])))) AND publisher[sb]	14	12
Google scholar	early|prediction|predictors|screening|symptoms|recognize|severity|course|exacerbation|deterioration|recurence|Progression "acute|Posttraumatic|traumatic stress" "emergency|trauma ward|department|patient|services|admission|center|centre"	200	149

Data extraction and synthesis

The search results from the different databases were merged to identify all papers. Then, all duplicates were removed and inclusion criteria were applied by one author (EV). The same author screened the titles and abstracts for eligibility. Subsequently, the full texts of potential articles were screened to determine final eligibility for inclusion in this review. If an article fitted the inclusion criteria, hard copies of the manuscripts were obtained. If there was doubt about including an article, this article was discussed with another author (JDV/TG). Finally, the reference lists of included articles were checked for additional eligible studies (see Figure 1).

The included studies consisted of trauma populations with all types of injuries and different assessment methods were used. Due to this heterogeneity, it was not possible to perform a meta-analysis[18].

The methodological quality of the included studies were independently assessed by two reviewers (EV/JDV or EV/TG). The Strengthening the Reporting of Observational studies in Epidemiology (STROBE) checklist was used for observational studies[19]. The Consolidated Standards of Reporting Trials (CONSORT) checklist for intervention studies was used[20]. Each item was assigned using plus, minus or not applicable (NA). In case of disagreements, the reviewers discussed the differences and they selected the most appropriate one by consensus. It was a priori decided that in case of persistent disagreement, consultation of a third reviewer was required. This situation did not occur.

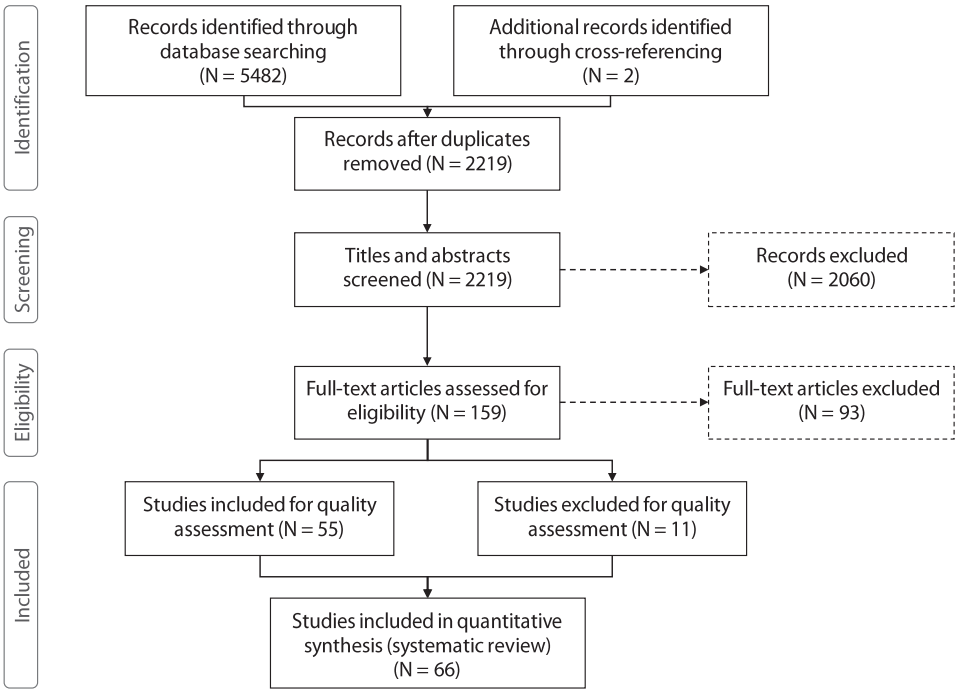

FIGURE 1. Flowchart of study selection process
Abbreviations: N: Number

Additionally, to judge the strength of the results and recommendations, level of evidence (LoE) was allocated using Oxford Centre for Evidence-based Medicine guidelines, taking good quality (observational studies LoE 2 and intervention studies LoE 1) and poor quality (observational studies LoE 4 and intervention studies LoE 3/4) studies into account[21].

During assessment, a number of studies resulted in several publications. To examine the aims of this review all articles were used, because different aims, outcomes and results were described. Only the studies with the most completely described design, methods, and results (highest score from STROBE/CONSORT) were used for quality assessment. Thus, studies with the lowest score were excluded for the methodological assessment in this late stage to prevent that the same study design was assessed twice.

RESULTS

Study selection process

The search resulted in 5482 hits. After removing 3265 duplicates, 2217 unique articles remained, of which 2060 were excluded based on title or abstract. Of 157 articles eligible for evaluation, 13 were conference papers or not available after contacting the corresponding author. The remaining 144 articles were examined using the inclusion and exclusion criteria. Eighty full-text papers were excluded based on inclusion criteria. Two papers were included using cross-referencing. In total, 66 papers were included in this review (see Figure 1). During the quality assessment, 9 observational studies[22-30] and two intervention studies[31,32] were excluded based on the same study design .

Study characteristics

Forty-three (65%) prospective cohort studies, two (3%) prospective case-control studies, and 21 (32%) intervention studies were included (see Supplementary tables 1 and 2). One study was labeled as a cross-sectional study design[33]. However, patients were assessed on multiple moments, therefore, this study was included in this review. Baseline measurements for observational studies ranged from 'in hospital' to 12 months after injury. The follow-up period ranged from one month until 72 months. Most studies (67%) examined patients with multiple injuries, but 13 (18%) only studied victims of motor vehicle injury. There was one study (1%) on patients with orofacial injury, three (4%) studies on patients with mild TBI and six (9%) studies without specification of the type of injury. Sample sizes varied greatly in observational studies (n = 42[34] to n = 2931[35]) as well as in the intervention articles (n = 8[36] to n = 1082[37]).

Different diagnostic questionnaires and interviews were used. The most frequently used questionnaire for ASD and/or PTSD was the Impact of Event Scale (IES) (n = 19[31,38-55]). The most frequently used structured interview was the Clinician Administered PTSD Scale (CAPS; n = 27[22-25,31,35,37,41-43,46,49-53,56-66]). All studies described their outcome measures and used psychometrically sound questionnaires, structured interviews, or a combination of both.

Methodological quality

The mean quality score of prospective cohort studies was 19 (SD=4.6) (min. 14 – max. 28). A description of the sample size calculation (item 10; 3%)[58] was often missing. Other methodological criteria that were rarely met are (i) a description of efforts to address potential bias (item 9; 66.6%), (ii) explanation how missing data were handled (item 12c; 77.8%), (iii) how loss to follow-up was addressed (item 12d; 86.1%), and (iv) a description of any sensitivity analyses (item 12e; 88.2%). Moreover, 27 articles did not describe a commonly

used term for their study design (item 1a; 75%). One of the two case-control studies did not give matching criteria (item 6b). In addition, 26 articles lacked reasons for non-participation at each stage (item 13b; 72.2%). A flow chart was not presented in 29 (item 13c; 80.6%) studies. Sixteen out of 19 (84.2%) studies calculating risk factors did not translated estimates of relative risk into absolute risk (item 16c). None of the observational studies were of good quality (LoE 2). Twenty-six studies had LoE 3 and 10 studies had LoE 4 (see Supplementary table 3).

The mean quality score for intervention studies was 18 SD=5.4 (min. 12 – max. 28;). The most common methodological shortcomings are (i) a description of study design (item 3a; 89.4%), (ii) an explanation how sample size was arrived at (item 7a; 73.7%), (iii) an explanation of allocation concealment mechanism (item 9; 68.4%), (iv) information about registration number (item 23; 78.9%) and protocol (item 24; 78.9%). Items 11b and 17b were mentioned only once each. Some criteria were not described at all: (i) changes to methods after trail commencement (item 3b), (ii) changes to trail outcome after commenced (item 6b), (iii) explanation of interim analyses and stopping guidelines (item 7b) and (iv) important harms of unintended effects (item 19). Eight studies had a LoE 2 and 11 studies had a LoE 3 or LoE 4. No LoE 1 studies were conducted (see Supplementary table 4).

The course of ASD and PTSD

Please note that across time different Diagnostic and Statistical Manuals of Mental Disorders (DSM) were used (DSM-III, DSM-IV and DSM-5), which affected the incidence/prevalence rates. ASD could not be examined by the use of DSM-III, because it was not included as a diagnosis in DSM-III. Recent research shows that, by using DSM-5, more persons were identified of who are likely to develop PTSD or another psychiatric disorder compared with to the DSM-IV (LoE 3)[58].

The prevalence rates during hospitalization ranged from 1%[23] - 37% (LoE 3)[33,67] (LoE 4)[63] on subsyndromal ASD. On the first post-trauma day, 66% of trauma patients persisted in re-experiencing their trauma (DSM-IV criteria B, e.g. flashbacks) and increased arousal (DSM-IV criteria D, e.g. difficulty concentrating). This rate increased to 95% in the third week after trauma. Persistent avoidance (DSM-IV criteria C, e.g. efforts to avoid thoughts, feelings or places associated with the trauma) began more slowly and increased up to 62% in the third week after the injury (LoE 3)[34]. In total, 36% presented symptoms of ASD one week after trauma (LoE 4)[61] and 22.4% patients showed PTSD symptoms (DSM-IV without duration criteria) after two weeks of injury (LoE 3)[56]. At one month post-injury, prevalence rates varied between 24% (LoE 3)[33,68] (LoE 4)[63] and 34.4% (LoE 4)[69]. A peak prevalence (25% - 29.9%) of

PTSD was reported at one month after injury (LoE 3)[70] (LoE 4)[43] and this decreased to 17.5% at four months after trauma[43]. Patients developed PTSD without showing ASD symptoms within one month after trauma (LoE 3)[24].

In the majority of cases, PTSD developed within three months after trauma (LoE 3)[71] and symptoms decreased throughout the year (LoE 3)[72], because of the observed natural remission of symptoms over time (LoE 3)[72] (LoE 4)[60]. However, patients can develop PTSD up to 12 months after injury (LoE3)[23,33,38,57,58,67]. A delayed onset of PTSD was reported in 49.3% of the cases. This percentage decreased to 20% at 24 months after injury (LoE 3)[39,57]. Even after two years, patients can report symptoms of PTSD as a result from the injury (LoE 3)[58]. Three years after trauma, 11% had PTSD and 5% of patients who did not have PTSD at 1 year reported PTSD at three years (LoE 3)[28]. After six years, 8% (DSM-IV) and 6% (DSM-5) had PTSD if they were diagnosed with ASD after injury (LoE 3)[58].

Different trajectories were found[57,73]: (i) resilience trajectory in which PTSD symptoms began low and remained low across time; (ii) recovery trajectory with severe PTSD symptoms with symptom reduction at follow-up; (iii) relapsing or remitting trajectory with moderate symptoms that varied slightly across time, but stayed relatively moderate, and (iv) chronic trajectory with high baseline symptom levels that persisted over time. About 28% of patients were in the resilience trajectory, 10% were in the recovery trajectory, 35% underwent the relapsing/remitting trajectory, and 27% had the chronic trajectory[74]. Subsequently, when patients were diagnosed with PTSD, different courses were found in the reduction of symptoms: (i) Rapid Remitting with a decrease in five months (56%), (ii) Slow Remitting with a decrease in 15 months (27%), and (iii) Non-Remitting with persistently elevated symptoms (17%)[37].

Predictors of ASD and PTSD

ASD and PTSD were associated with being female (LoE 3)[26,28,39,75-77] (LoE 4)[40] and younger age (LoE 3)[44,75] (LoE 4)[40]. Patients were more likely to develop PTSD if they had less than high school education (LoE 3)[38,78], financial problems (LoE 3)[26,28], or lower income (LoE 3)[40,44]. Higher income was inversely associated with lower risk of PTSD[78]. Patients were at risk for PTSD if they experienced low satisfaction with social support (LoE 3)[79] or lived alone (LoE 3)[38]. The odds of patients who lived alone were almost ten times as likely at 12 months than patients who did not live alone[38]. Patients with ASD were more confronted with dead than patients without ASD (LoE 4)[61].

Persistent health problems, following trauma, was the major predictor for PTSD (LoE 3)[26]. Two years after trauma, PTSD was associated with pre-existing disability at baseline (LoE 3)[78], comorbidity (LoE 3)[28,39,75], symptomatic distress and pain (LoE 3)[35], and injuries of the head

and extremities (LoE 3)[39]. Early predictors for PTSD at 24 months were poor mental health and reduced cognitive functioning (LoE 3)[75,80]. Moreover, poor cognitive functioning are associated with the continuation of emotional disorders following trauma[80], as PTSD was related with memory fragmentation (LoE 3)[29].

Most persons who met the ASD dissociative criteria developed PTSD at three months (76.8%) and 12 months (77.0%) (LoE 3)[22]. However, results are conflicting. First, diagnosis of ASD has limited benefit in predicting who will develop PTSD[22], because the predictive power of PTSD in the acute phase was higher than the positive predictive power of ASD (LoE 3)[25]. However, patients diagnosed with ASD were more likely to develop PTSD than patients without ASD (52% vs. 26%) (LoE 3)[79] (LoE 4)[40]. Also, a strong correlation was found between experiencing a psychiatric disorder (e.g. ASD) in the first six weeks after the accident and the presence of a psychiatric disorder (e.g. PTSD) six months later (LoE 4)[68]. Although ASD diagnosis was not used, high levels of PTSD predicted PTSD 12 months after trauma (LoE 3)[76]. Furthermore, 47% with PTSD at 12 months after injury reported PTSD at three years after trauma compared to 5% without PTSD at 12 months (LoE 3)[28].

Rumination was found to be one of the strongest predictors of PTSD[28,29]. In addition, avoidance-oriented coping strategies (LoE 3)[34,75] and psychological processes (e.g. negative interpretations and thought suppression) may underlie the development of PTSD (LoE 3)[28,71]. Moreover, re-experiencing the trauma and hyper-arousal predicted PTSD at 12 months (LoE 3), especially when patients experienced disability in addition to re-experiencing and hyper-arousal[26]. Furthermore, persistent dissociation seemed to be a stronger predictor for PTSD than experiencing dissociation during trauma[29]. Emotional predictors for PTSD were fright and anger (LoE 3)[28] (LoE 4)[61].

Treatment of ASD and PTSD

Treatment (e.g. CBT and supportive counseling (SC)) for ASD and PTSD was beneficial up to 15 months after treatment (LoE 2)[47,48,64,65] (LoE 3)[37,50] (LoE 4)[54] (see Supplementary table 2). However, treatment, almost directly after trauma or during the first two weeks, may prevent the development of PTSD, because symptoms reduced during the first six months after treatment (LoE 3)[50,53,81]. For example, patients with mild TBI who underwent CBT, in the first two weeks after injury, reported more improvement (76.4% versus 47.6%) (LoE 3)[49,50,53] and less PTSD symptoms (8% versus 58%)[53] after six months post-treatment, than patients who received SC. Moreover, patients seem to benefit from weekly CBT in the first three months, as PTSD symptoms reduced more in this period and declined after that time (LoE 2)[65]. Also being treated during 12 months, PTSD symptoms decreased throughout this year, but it was more rapid in the first six months after trauma[64].

A combination treatment of CBT and hypnosis may be more effective than SC, but not more effective than CBT only[50]. Also psycho-education in combination with psychotherapy[66], six extra psychotherapy sessions on top of the standard psychotherapy care (LoE 2)[48], and dyadic intervention were effective[51,52].

Twenty-four percent spontaneously recovered without intervention[49] and 12% recovered by self-monitoring (LoE 2)[65]. One study determined the beneficial effect of EMDR, as PTSD reduced over time (LoE 4)[54]. Self-help booklet (LoE 2)[65,82] (LoE 3)[32] and an internet CBT intervention (e.g. Trauma TIPS) (LoE 2)[46] were not effective .

DISCUSSION

The aims of this systematic review were (i) to examine the course and predictors of ASD and PTSD in trauma and (ii) to examine which psychological treatments are effective in trauma patients. This review included 49 observational and 22 intervention studies. According to the OCEBM guidelines[21], no study was of good quality (observational studies LoE 2 and intervention studies LoE 1). The majority of studies were of moderate (intervention studies LoE 2) to poor quality (observational studies LoE 3/LoE 4 and intervention studies LoE 3/4). In the future, the description of methods and results need to be described so that information about bias, confounding, and generalizability is transparent[19].

Results demonstrate that ASD and PTSD have different courses[37,57]. Almost directly after trauma and during hospitalization, symptoms of ASD (hyper-arousal, re-experiencing the trauma and dissociation) were found in 1% – 37%. One week after trauma, 36% had ASD and this decreased to 22.4% two weeks after trauma. At one month post-injury, prevalence rates varied between 24% and 34%. In most patients, the onset of PTSD would be within three months after trauma and decreased throughout the year, because of the natural reduction of symptoms[60,72,79]. Patients can develop PTSD without having ASD within one month after trauma[24]. However, PTSD at six months after trauma is more prevalent in patients who were diagnosed with ASD. Moreover, PTSD symptoms were found up to six years after trauma[58].

There are several reasons for the different courses of ASD and PTSD. First, studies used various versions of the DSM (DSM-III, DSM-IV and DSM-5). Before ASD was introduced in the DSM-IV, acute PTSD was used. Therefore, false negatives for ASD may occur. Moreover, the DSM-5 predict better who will develop ASD and PTSD compared to the DSM-IV[58]. Second, ASD and PTSD can be assessed by a structured interview (e.g. CAPS) or self-report questionnaires (e.g. IES-Revised). These different diagnostic measurements contributed to the heterogeneity of the study designs. Finally, 22 observational studies examined patients at two moments in time. Information between these time points is often lacking, which

hampers an interpretation and prediction of the course of (increase, decrease or fluctuation) ASD and PTSD. Therefore, the interpretation of the data for these studies must be done with caution.

The course of ASD and PTSD was influenced by several socio-demographic risk factors (e.g. being female and younger age). Lower income or financial problems also contributed to the development of ASD and PTSD. Higher income seems to have a protective role, as it was related to lower risk of PTSD[78]. However, this can depend on the degree of solidarity or social cohesion. Moreover, ASD and PTSD may be related to social risk factors (low satisfaction with social support and living alone) and medical risk factors (pre-existing disability[78], comorbidity[28,39,75], and pain[35]). Having ASD can have limited benefit in predicting who will develop PTSD[22] , because PTSD in the acute phase can be a better predictor than ASD[25]. However, considerably more studies confirm that patients diagnosed with ASD had a higher risk of developing PTSD[40,68,76,79].

PTSD may be prevented by early treatment, starting almost directly after trauma or in the first two weeks after trauma. Moreover, when patients are diagnosed with PTSD after trauma, treatment with CBT is mostly effective[31,37,47,49,50,64,65,82], though also mostly examined. Furthermore, another effective treatment for PTSD after trauma is EMDR[83]. However, only one study (LoE 4), examined the effect of EMDR[54]. In addition, CBT has some limitations. Engagement to treatment is the highest impending factor for trauma-focused CBT. Other factors are clinical (e.g. cognitive impairment or psychiatric disorders) and logistic (e.g. interpersonal violence) factors[84]. To obviate these barriers, a feasible stepped-care intervention or elements of CBT (e.g. psycho-education) could be implemented[85]. This review reveals differences regarding the moment of intervention, the type of intervention and different effects of the intervention. Therefore, findings concerning the intervention of ASD and PTSD must be carefully interpret. In addition, only three (13.6%) studies investigated the treatment of patients diagnosed with ASD. Unfortunately, two of these studies have the same study design, therefore information about treatment for ASD is still lacking.

The major strength of this review is that it provides information on the development of ASD and PTSD, by examining the course and which predictors may influence the development of ASD and PTSD. Subsequently, when and which type of interventions can be preventive and beneficial for ASD and PTSD in patient-centered care. Moreover, the search was carried out in nine databases with a result of 2217 screened articles. Therefore, the possibility of missing a paper that fits the inclusion criteria is relatively small. In addition, included full text papers were screened by two reviewers.

Some limitations must be taken into account. First, the included studies show a high heterogeneity as a result of the use of different types of study populations and study designs. Therefore, the results cannot be generalized to a single trauma population (e.g. patients with mild TBI). A general limitation is that selection and publication bias can occur, because studies with clinically favorable results are more likely to be published and to be selected by the researchers using the inclusion criteria[18]. Second, the majority of studied papers are of less, observational studies LoE 3 and intervention studies LoE 2, or poor, observational studies LoE 4 and intervention studies LoE 3/4, quality compared to good quality, observational studies LoE 2 and intervention studies LoE 1. However, this shows that there is room for improvement in describing the study design, results, and recommendations.

This systematic review obtains several implications for future research and clinical practice. To increase the quality of evidence concerning the course of ASD and PTSD and the long-term effects of treatment, good observational and RCT quality studies are needed with measurements at more than two moments in time. Moreover, to gain information about which factors may influence the course of ASD and PTSD or to predict which patients are at risk, latent class analysis needs to be conducted. Since it was introduced in the DSM-IV, ASD is a relatively new diagnosis. Therefore, more information about patients' symptoms almost directly after trauma is needed to investigate how ASD and PTSD can be prevented, e.g. by the use of EMDR. Further research is needed to examine the effect of CBT, or in combination with hypnosis, and EMDR in patients with ASD after injury. Furthermore, only one article described the population impact after treatment[62]. Therefore, interpretation of the treatment effects using population impact is difficult. Due to the limitations of CBT (e.g. engagement, cognitive impairment) and the range of symptoms in patients with ASD or PTSD different types of treatments and approaches are needed, so that stepped-care can be offered[17]. Moreover, medical staff must be aware that patients can suffer from ASD and PTSD and have knowledge about their symptoms and predictors (e.g. cognitive dysfunction or having ASD), so they are able to screen and identify patients who are at risk[86]. As a first intervention, trained nurses can provide psycho-education. Subsequently, if needed, the patient can be referred for further treatment.

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SUPPLEMENTAL TABLE 1. Overview of observational studies

First Author (year)	Type of trauma	N	Design	FU period	Baseline measurement	FU measurements	Independent variables	Dependent variables	Main conclusion
Creamer (2004)[22*]	MVA Other	307	Prospective cohort	3: prior to discharge, 3 and 12 months post-injury	CAPS	CAPS	ASD	PTSD	Only 1% had ASD about eight days after trauma. The incidence of PTSD was 9% at three months and 10% at 12 months. About 77% who had ASD dissociative symptoms developed PTSD. However, about 91% who had PTSD did not report dissociation in the acute stage.
Fuglsang (2004)[79]	Traffic accident	90	Prospective cohort	2: 1 month and 6-8 months post-injury	ISS ASDS CSS	PDS CSS	Socio-demographics ASD	ASD PTSD	About 28% had ASD between one or two weeks after trauma. Being female (β= 0.21, p<0.05), being afraid during the accident (β= 0.38, p<0.001) and low satisfaction with social support (β= -0.37, p<0.001) were predictors for ASD. Low satisfaction with social support (β= -0.20, p<0.05) and having ASD (β= 0.51, p<0.001) are predictors for PTSD.
Bryant (2015)[58]	MVA Assault Fall Industrial Other	314	Prospective cohort	5: in hospital, 3, 12, 24, 72 months	ASDI MINI	CAPS DSM-IV DSM-5 MINI	FU time	ASD	About 7% were diagnosed with ASD using DSM-IV and 14% had ASD using DSM-5. About 9% had PTSD (DSM-5) after three months, 10% at 12 months, 12% at 24 months and 8% at 72 months.
Bryant (2012)[24**]	Transport Assault Fall Work-related Other	1129	Prospective cohort	2: in hospital, 1 and 12 months post-injury	CAPS	CAPS MINI	ASD	PTSD	Ten percent had ASD after one month and 10% had PTSD after 12 months. Patients with ASD (36%) had PTSD after 12 months.
Bryant (2008)[25**]	MVA Assault Fall Industrial Other	507	Prospective cohort	2: in hospital and 3 months post-injury	ASDI	CAPS	ASD	PTSD	Six percent had ASD during hospitalization and 10% had PTSD after three months. Fifteen patients (45%) diagnosed with ASD and 34 patients (7%) not diagnosed with ASD had PTSD after three months.

SUPPLEMENTAL TABLE 1. Continued

First Author (year)	Type of trauma	N	Design	FU period	Baseline measurement	FU measurements	Independent variables	Dependent variables	Main conclusion
Soberg (2010)[75]	Severe multiple trauma	99	Prospective cohort	3: 6 weeks, 12 and 24 months post-injury.	Demographics SF-36 WHODAS II-cognitive subscale 4 structured questions	SF-36 WHODAS II-cognitive subscale 4 structured questions PTSS-10 BACQ	Age Gender Outcome variables from SF-36 WHODAS-II	PTSS-10 scores	About 20% had PTSD symptoms at 24 months. Being female (β= 0.21, p=0.002), younger age (β=-0.20, p=0.003) avoidance-oriented coping strategy (β= -0.34, p<0.001) and comorbidity (i.e. pain) (β= -0.23, p=0.004), poorer mental health (β= -0.22, p=0.01) and poorer cognitive functioning (β= 0.35, p<0.001) shortly after returning home were predictors for PTSD at two years after trauma and explained 70.2% of variance.
Ehring (2008)[80]	MVA	147	Prospective cohort	5: day of accident, 2 weeks, 1, 3 and 6 months post-injury	SCID PDS	SCID PDS	Predictors of PTSD model: Cognitive processing during MVA Memory disorganization Negative appraisals of trauma and sequel Safety behaviors Rumination about trauma and consequences Thought suppression Ongoing dissociation	PTSD	About 22% had PTSD without duration criterion at two weeks and 12% had PTSD six months after trauma. PTSD without duration 2 weeks after trauma predicted PTSD at 6 months (incidence rate ratio: 1.06, p<0.001). All predictors for PTSD model* were related with PTSD at 6 months. The strongest relation was found in rumination about the trauma and PTSD at six months FU (Spearman's Rho: 0.62, p<0.001).
Zatzick (2002)[76]	MVA Assault	101	Prospective cohort	4: in hospital, 1, 4, 12 months post-injury	PCL-C PDEQ 2 questions from ASI 2 questions from DSM-III	PCL-C PDEQ 2 questions from ASI 2 questions from DSM-III	Demographic History of psychiatric or substance disorder Time PTSD during hospitalization	PTSD	At one month, 41% had PTSD, 40% at four months, and 30% had PTSD 12 months after trauma. At all three assessment points, 13% had PTSD diagnosis. PTSD symptoms during hospitalization (β= 0.644, p<0.0001), greater prior trauma (β= 1.85, p=0.0005), stimulant intoxication (β= 9.65, p=0.01), and being female (β= -5.48, p<0.05) are predictors for PTSD after 12 months.

SUPPLEMENTAL TABLE 1. Continued

First Author (year)	Type of trauma	N	Design	FU period	Baseline measurement	FU measurements	Independent variables	Dependent variables	Main conclusion
Haagsma (2012)[39]	Injury of head, chest, abdomen, extremities or brain	94	Prospective cohort	2: 12 and 24 months post-injury	IES	IES	Time	PTSD	Two years after injury, 20% had PTSD symptoms. Comorbid disease (OR: 4.61, 95% CI 2.02-10.55, $p<0.01$) and being female (OR 2.36, 95% CI 1.06-5.25, $p<0.05$) were associated with PTSD at 12 months. Injuries of the head (OR 0.12, 95% CI 0.02-0.66, $p<0.05$) and extremities (OR 0.18, 95% CI 0.03-0.99, $p<0.05$) were associated with PTSD at two years. About 79% of the patients with PTSD at 12 months had also PTSD at 24 months.
Freedman (1999)[42]	MVA Other	236	Prospective cohort	4: 1 week, 1 and 4 and 12 months post-injury	CAPS IES MISS BDI PDEQ	CAPS IES MISS BDI PDEQ	IES-intrusion IES-avoidance MISS BDI PDEQ	PTSD at 12 months	About 40% with PTSD at four months, also had PTSD at 12 months. Five percent without PTSD at four months developed PTSD at 12 months. Experiencing depressive symptoms was the most consistent predictor of PTSD symptoms at 12 months (Adjusted $R^2 = 0.55$, $F(4,55) = 73.9$, $p<0.0001$).
Bryant (1999)[87]	TBI after MVA	134	Prospective cohort	2: within 1 month and 6 months post-injury	ASDI	CIDI - PTSD module	TBI length of hospitalization	ASD PTSD	No-TBI patients reported more often ASD and PTSD symptoms of fear than TBI patients (66% versus 33%) and helpless (75% versus 38%).
Holbrook (2001)[40]	MVA Pedestrian struck Assault Penetrating	824	Prospective cohort	4: at discharge, 6, 12 and 18 months post-injury	SARS	DSM-IV - PTSD	Injury event related factors	PTSD	PTSD was diagnosed in 32% six months after trauma. Early symptoms of ASD were higher in patients who developed PTSD (52% vs. 26%; OR 3.1, 95% CI 2.3-4.3, $p<0.001$). Perceived threat to life (OR 1.6, 95% CI 1.2-2.2, $p<0.01$), assaults (OR 1.5, 95% CI 1.0-2.2, $p<0.05$) and penetrating trauma (OR 2.3, 95% CI 1.4-3.8, $p<0.001$) were associated with PTSD at six months after trauma.

SUPPLEMENTAL TABLE 1. Continued

First Author (year)	Type of trauma	N	Design	FU period	Baseline measurement	FU measurements	Independent variables	Dependent variables	Main conclusion
Bryant (2013)[57]	Transport Assault Fall Work-related Other	705	Prospective cohort	4: in hospital, 3, 12 and 24 months post-injury	CAPS MINI - psychiatric disorder	CAPS RLEQ	Time	PTSD	Subsyndromal or full PTSD at baseline had various trajectories in 24 months. Of the 26 patients (3.7%) with PTSD at baseline 42.3% had PTSD after two years. Patients with PTSD at 3 (44.2%), 12 (45.4%), and 24 (50.0%) months had no PTSD at baseline. Delayed-onset of PTSD was reported by 49.3% at 12 months and by 18.8% at 24 months. The presence of mild TBI (explained variance= 3%, β= 4.15, p<0.001), the number of days spent in hospital (explained variance= 1%, β = 0.13, p=0.05), and the number of adverse life events after 3 months (explained variance= 9%, β = 1.55, p<0.001) predicted PTSD at 24 months.
Glynn (2007)[72]	Facial injury	336	Prospective cohort	5: at discharge, 10 days post discharge, 1, 6 and 12 months post-injury	MHI-5	SUAPS PDS	Pain SUAPS scores	PTSD	Although PTSD symptoms decreased throughout the year 20% had PTSD symptoms after 12 months (PDS score at one month: 31.14 (SD=11.97) versus PDS score at 12 months 27.15 (SD= 11.3)). Prior trauma exposure (t (49.86) = 2.64, p< 0.01) and sum of high rates of stressful life events (R (181) = 0.21, p< 0.01) were related with PTSD during 12 months.
Kühn (2006)[68]	Traffic Industrial Household	58	Prospective cohort	2: in hospital and 6 months post-injury	Semi-structured accident interview SCID-I	SCID-I	Time	ASD PTSD	About 7% had ASD and 12% had subsyndromal ASD in first six weeks after trauma. From the patients with ASD in the first six weeks, 25% developed PTSD and depression, 25% had subsyndromal PTSD and depression and 50% recovered completely. Being female was correlated with ASD (χ^2= 6.086, p<0.05)
Mayou (2001)[71]	MVA	1148	Prospective cohort	3: in hospital, 3 and 12 months post-injury	Demographics Previous tendency to worry Emotional problems	Physical recovery PTSS	Demographics Previous emotional problems Tendency to worry 4 reactions to the accident	PTSD	More patients were diagnosed with PTSD within three months (23%) after trauma compared with 12 months (17%). Being female was related with PTSD at three months (χ^2=14.46, p<0.001). In total, 11% had PTSD at three months and 5% developed PTSD after 12 months.

SUPPLEMENTAL TABLE 1. Continued

First Author (year)	Type of trauma	N	Design	FU period	Baseline measurement	FU measurements	Independent variables	Dependent variables	Main conclusion
Whitman (2013)[34]	MVA Gunshot Fall Burn Stabbing Assault	42	Prospective cohort	10: daily in first week post-injury, weekly thereafter until 1 month post-injury	DSM-IV	DSM-IV	ISS Time	group B (re-experiencing) group C (avoidance) group D (hyper-arousal) Full PTSD	In total, 63% were diagnosed with PTSD after one month if they reported symptoms of group B during the first four weeks after trauma, 96% if they had symptoms of group C and 63% were diagnosed with PTSD after one month if they had symptoms of group C.
Mason (2009)[55]	Unknown	210	Prospective cohort	4: in hospital, 6 weeks, 6 and 18 months post-injury	Demographics ISS	IES-R	Time ISS	PTSD	Ten percent reported severe PTSD symptoms after six months. No significant change was found in PTSD symptoms over time.
Shalev (1998)[43]	MVA Work-related Terrorist acts Combat event Assault	211	Prospective cohort	4: 1 week, 1, 4 and 12 months post-injury	IES PDEQ SCID CAPS	IES PDEQ SCID CAPS	Time Scores on questionnaires	PTSD	About 30% had PTSD at one month and 17.5% had PTSD at four months. About 62% with PTSD at four months had PTSD 12 months post-injury. Having PTSD one month after trauma was related to PTSD at four months (χ^2=15.53, p<0.0001).
Mayou (1993)[27]†	MVA Whiplash	188	Prospective cohort	3: almost direct after accident, 3 and 12 months post-injury	Demographics Nature of accident	PTSD from DSM-III-R	Demographics Type of injury	PTSD	During 12 months, 11% had PTSD, 42% had PTSD at three and 12 months 26% at three months and six (32%) at 12 months only.
Vaiva (2003)[61]	MVA	123	Prospective cohort	2: 1 week and 2 months post-injury	Trauma score DSM-IV Trauma exposure Fright reactions	CAPS	Peritraumatic responses	ASD PTSD	About 36% showed ASD after one week and they witnessed more death (e.g. seen someone else death) than patients without ASD (t(121)=3.1, p= 0.003). After two months, 51% had PTSD. Patients who experienced a feeling of fright had 17-times greater risk of developing PTSD (OR 16.75; 95% CI and *p-value* unknown).

SUPPLEMENTAL TABLE 1. Continued

First Author (year)	Type of trauma	N	Design	FU period	Baseline measurement	FU measurements	Independent variables	Dependent variables	Main conclusion
Forbes (2012)[56]	Interpersonal (e.g. assault) and non-interpersonal (e.g. accident) trauma	715	Prospective cohort	3: 3, 12 and 24 months post-injury	CAPS	CAPS	Time Group type (interpersonal versus non-interpersonal)	PTSD	Interpersonal trauma results in higher scores on 14 PTSD symptoms three months after injury and this decreased to six symptoms at 24 months ($p<0.01$), but at 24 months the groups did not differ anymore (three months: 24% versus 6%, 12 months 27% versus 8%, 24 months 13% versus 10%).
Warren (2013)[67]	Blunt Penetrating	118	Prospective cohort	2: in hospital and 6 months post-injury	Demographics PC-PTSD AUDIT-C	PC-PTSD PCL-C AUDIT-C	Demographics Alcohol use	PTSD	At baseline, 29% experienced PTSD and 41% experienced PTSD six months after injury. No differences in alcohol use were found in patients with PTSD and without PTSD at baseline ($p=0.976$) and at six months ($p=0.758$).
Shalev (2005)[41]	Terrorist attack MVA Other	426	Prospective cohort	2: 1 week and 4 months post-injury	IES PDEQ	CAPS	Type of injury Time	PTSD	At four months, more terror attack survivors (36.8%) were diagnosed with PTSD compared to MVA survivors (18.3%) ($\chi^2=7.34$, $p<0.01$).
Gil (2005)[62]	TBI	120	Prospective cohort	4: in hospital, 7-10 days, 4 weeks, 6 months post-injury	Memory questionnaire CAPS PSS	Memory questionnaire MTEQ CAPS PSS SCID ANAM	Memory	PTSD	At six months, 14% of patients with TBI were diagnosed with PTSD. PTSD was more prevalent in patients who remembered their injury (23%) than patients without memory of the injury (6%) (OR=4.6, 95% CI 1.1–9.9, $p<0.001$).
Shih (2010)[78]	Loss of consciousness from injury Assault	677	Prospective cohort	3: 9 days post injury, 6 and 12 months post-injury	Demographics Type of injury Duration of hospitalization	PCL	Baseline characteristics Time Type of injury	PTSD	At six months, 31% had PTSD and 28% had PTSD at 12 months after trauma. Patients who were disabled were 4 times more likely to develop PTSD (OR 4.05, 95% CI 1.46-11.20, $p\leq0.05$). Patients who had an assault (compared to MVA) were two times more likely to develop PTSD (OR 2.02, 95% CI 1.46-11.20, $p\leq0.05$).

SUPPLEMENTAL TABLE 1. Continued

First Author (year)	Type of trauma	N	Design	FU period	Baseline measurement	FU measurements	Independent variables	Dependent variables	Main conclusion
O'Donnell (2005)[23]*	Unkown	363	Prospective cohort	2: before discharge and 12 months post-injury	Injury characteristics CAPS BDI	CAPS SCID	ASD Injury characteristics	PTSD	After injury, 1% had ASD and 3% had acute PTSD (without time criteria). At 12 months, 10% had PTSD. When subsyndromal PTSD and minor depression were included, PTSD rates increased to 16%.
Haagsma (2015)[38]	Mild TBI Traffic Fall Sports Assault Other	1919	Prospective cohort	2: 6 and 12 months post-injury	IES	IES	Demographics	PTSD	At six months, 5% had PTSD and 6% had PTSD at 12 months.
Norman (2011)[77]	MVA Fall Motorcycle Pedestrian or automobile Burn All-terrain vehicle accident Occupational	163	Prospective cohort	4: in hospital, 1, 4 and 8 months post-injury	MPQ NISS PDEQ PCL-C CIDI	PCL-C CIDI	Time	PTSD	Being female (β=−.19, p=0.01), less severe injury (β=−.11, p=0.03), pain (β=0.20, p=0.001), PTSD symptoms within 48 hours of trauma (β=0.50, p<0.001) predicted PTSD symptoms one month after injury.
Norman (2008)[70]	MVA Burns Falls Occupational Recreational Stab and gunshot Assault	115	Prospective cohort	4: 1-2 days, 1, 4 and 8 months post-injury	MPQ-SF NISS	ASDI CIDI - PTSD	Pain	ASD PTSD	Patients with peritraumatic pain were almost six times (more likely to experience PTSD at four months OR=5.62, 95% CI 2.29–13.78, p<0.0001) and seven times more likely at eight months (OR=6.84, 95% CI 2.31–20.20, p<0.0001).

SUPPLEMENTAL TABLE 1. Continued

First Author (year)	Type of trauma	N	Design	FU period	Baseline measurement	FU measurements	Independent variables	Dependent variables	Main conclusion
Zatzick (2007)[35]	Unknown	2931	Prospective cohort	2:3 and 12 months post-injury	PCL CAPS SF-36 Socio-demographics Clinical variables	PCL CAPS SF-36	Socio-demographics Clinical variables	PTSD	In total, 22.9% showed symptoms of PTSD after 12 months. Lower mental health and pain (RR 0.97, 95% CI 0.96-0.98, $p<0.001$), use of benzodiazepine (RR 1.56, 95% CI 1.17-1.84, $p=0.001$) and depression (RR 1.33, 95% CI 1.15-1.54, $p<0.001$) were associated with increased risk of PTSD.
Bell (2014)[33]	Unknown	91	Cross-sectional	3: prior to discharge, 1 and 4 months post-injury	SASRQ PCL-S Socio-demographics	SASRQ PCL-S	ASD SASD	PTSD	During hospitalization, 24% had ASD and 37% had subsyndromal ASD. One month after injury, 25% had PTSD and 28% had PTSD after four months.
Zatzick (2007)[88]	Unintentional (MVA) and intentional (assaults)	120	Prospective cohort	5: in hospital, 1, 3, 6 and 12 months post-injury	Posttraumatic concerns PCL ISS	PCL	Posttraumatic concerns PCL ISS	PTSD	Most commonly concern was physical health (68%), work and financial (59%), social (44%), psychological (25%), medical (8%) and legal (5%) concerns. The number of concerns was a predictor for PTSD at 12 months (adjusted RR 1.68, 95% CI 1.11-2.54.
Lui (2009)[89]	Orofacial injury	287	Prospective cohort	4: 10 days, 1, 6 and 12 months post-injury	PDS Perceived social support	PDS Perceived social support	Socio-demographics Perceived social support	PTSD	There is a strong relationship between social support and PTSD (one month: $\beta = -.18$, $p<.01$); at 6 months $\beta = -.39$, $p<.01$); at 12 months $\beta = -.21$, $p<.01$).
Michaels (1999)[44]	Blunt Penetrating Burn	176	Prospective cohort	2: in hospital and 6 month post-injury	ISS MCEPS IES	MCEPS IES CMSP-R	ISS MCEPS IES	PTSD	Patients with PTSD were younger ($p= 0.023$) and earned less per year ($p= 0.001$). About 43.2% had PTSD six months after injury. They had poor baseline mental health ($p= 0.037$) and had previous life-threatening events ($p=0.002$). Baseline mental health was related with the development of PTSD*.
Nightingale (2000)[45]	Traffic accident	45	Prospective cohort	2: 1 and 6 weeks post-injury	IES AEE	IES AEE PDS	Attitudes to emotional expression	PTSD	About 30.8% had PTSD six weeks after trauma (PDS scores). After one week, 28% had PTSD symptoms and these decrease to 18% after six weeks (IES scores). Negative attitudes to emotional expression are related to more intrusive symptoms and predict the diagnosis of acute PTSD at six weeks post injury*.

SUPPLEMENTAL TABLE 1. Continued

First Author (year)	Type of trauma	N	Design	FU period	Baseline measurement	FU measurements	Independent variables	Dependent variables	Main conclusion
Ehlers (1998)[26]†	MVA	967	Prospective cohort	3: in hospital, 3, 12 months	Medical and financial Dissociation Negative interpretations of intrusive recollections Rumination and thought suppression	Medical and financial problems Negative interpretations of intrusive recollections Rumination and thought suppression	Medical and financial problems Dissociation Negative interpretations of intrusive recollections Rumination and thought suppression	PTSD	The criterion re-experiencing was related to PTSD at 12 months (11.6% vs. 3.3%, χ^2=14.5, p=0.0001). If they had disability in addition to re-experiencing and hyper arousal, the prevalence of having PTSD at 12 months increased to 15.9%.).
O'Donnell (2014)[59]	MVA Other	301	Prospective cohort	3: prior to discharge, 3, 12 months	CAPS SCID semi-structured interview for psychiatric conditions and treatment CIDI – PTSD module.	CAPS SCID semi-structured interview for psychiatric conditions and treatment CIDI – PTSD module.	Trauma and individual characteristics Cognitive vulnerabilities Acute stress responses	PTSD PTSD or depression	About 63% had PTSD at three months after injury and had depression, comorbid PTSD/ depression at 12 months. Patients (60%) with comorbid PTSD or depression at three months had also these diagnoses at 12 months after injury.
Murray (2002)[29]†	Traffic accidents	176	Prospective cohort	In-patients 6: in hospital, 1, 2 and 4 weeks, 3 and 6 months post-injury Out-patients 3: 1 and 4 weeks and 6 months post-injury	PDS SDQ TDQ RQ	PDS SDQ TDQ RQ	SDQ TDQ RQ	PDS ASD PTSD	Prevalence rates of ASD varied at baseline (in-patients 11% versus 25% out-patient) and during four weeks (in-patients 13% versus 10% out-patient) and PTSD varied at one month (in-patients 32% versus 28% out-patient) and 6 months after injury (in-patients 19% versus 24%out-patient). Dissociation at four weeks after injury was related with PTSD at six months (in-patients: Spearman's rho=0.51, p<0.05, out-patients: Spearman's rho=0.47, p<0.001). Rumination was one of the strongest predictors of PTSD (in-patients: Spearman's rho=0.56, p<0.05, out-patients: Spearman's rho=0.42, p<0.001.

SUPPLEMENTAL TABLE 1. Continued

First Author (year)	Type of trauma	N	Design	FU period	Baseline measurement	FU measurements	Independent variables	Dependent variables	Main conclusion
Bryant (2000)[90]	MVA	113	Prospective cohort	2: within 1 month and 6 months post-injury	Patient characteristics ASDI CIDI	ASDI CIDI	ASD ISS Length of hospitalization	Number of PTSD symptoms	In total, 14% were diagnosed with ASD and 14% had subsyndromal ASD one month after injury. Six months post-injury, 21% had PTSD. About 76% of the patients with ASD were diagnosed with PTSD six month after trauma. Having ASD is related with PTSD (χ^2=3.5, p<0.001).
Ursano (1999)[30‡]	MVA	122	Prospective cohort	2: 1 and 3 months post-injury	SCID - PTSD supplement PDEQ	SCID - PTSD supplement PDEQ	Peritraumatic dissociation	PTSD	About 34% had PTSD at one month and 25% at 3 months after injury. Patients who reported peritraumatic dissociation were 4.1 times more likely to develop acute PTSD (Wald χ^2=5.33, 95% CI=1.24–13.67, p=0.02). Patients with peritraumatic dissociation were 4.9 times more likely to develop chronic PTSD (Wald χ^2=3.86, 95% CI=1.00–23.50, p=0.05).
Mayou (2002)[28]†	MVA	546	Prospective cohort	3: 3 and 12 months and 3 years post-injury	PSS Dissociation Negative interpretations of intrusive recollections Rumination and thought suppression Anger	PSS Negative interpretations of intrusive recollections Rumination and thought suppression Anger	Dissociation Negative interpretations of intrusive recollections Rumination and thought suppression Anger	PTSD	At three years after injury, 11% had PTSD. About 47% who had PTSD at 12 had PTSD at three years. About 5% who did not meet PTSD at 12 months reported PTSD at three years. Negative interpretation of intrusive memories, rumination, thought suppression, and anger predict PTSD at three years (explained variance=38% F(4,454) =70.37, p<0.001) .
Ursano (1999)[69]	MVA	122	Case-control 2 groups: MVA and minor accident	2: 1 and 3 months post-injury	SCID - PTSD supplement	SCID - PTSD supplement	Group type Time	PTSD	MVA patients had higher rates of PTSD symptoms compared with the control group (34.4% versus 2.4%). At one month, women were almost five times more likely to develop PTSD (OR=4.64, 95% CI 2.06–10.46, p=0.003) and nonwhites were almost 4 times more likely to develop PTSD (OR=3.85, 95% CI 1.16–9.19, p=0.002).

SUPPLEMENTAL TABLE 1. Continued

First Author (year)	Type of trauma	N	Design	FU period	Baseline measurement	FU measurements	Independent variables	Dependent variables	Main conclusion
Mellman (2001)[63]	MVA Industrial accident Assault	50	Prospective cohort	2: in hospital and 6 weeks after baseline	PDS COPE	SCID CAPS	PDS COPE	CAPS	At baseline, 16% had ASD. After six weeks, 24% had PTSD and 22% had subsyndromal PTSD. There was no difference between patients with or without ASD. Early symptoms of hyper-arousal (β= 0.33, *p*=0.02) and coping with disengagement (β= 0.25, *p*=0.06) were predictors of PTSD severity at follow-up.
Blanchard (1997)[60]	MVA	145	Prospective cohort	2: 1-4 months and 6 months after injury	CAPS SCID	CAPS SCID	Baseline measures	PTSD at 6 months	At baseline, 55% with PTSD and 67% with subsyndromal PTSD had decreased symptoms of PTSD at six months, while 5% has worsened.

** same design as O'Donnell et al. (2014)59, ** same design as Bryant et al. (2015)58, † same design as Mayou et al. (2001)71, ‡ same design as Ursano et al. (1999)69, § Statistical rates, e.g. Beta, unknown*

Abbreviations: FU: follow-up, MVA: motor vehicle accidents, PTSD: posttraumatic stress disorder, CAPS: Clinician Administered PTSD Scale, ASD: acute stress disorder, ISS: injury severity score, ASDS: Acute Stress Disorder Scale, CSS: Crisis support scale, PDS: Posttraumatic Disorder Scale, ASDI: Acute Stress Disorder Interview, MINI: Mini International Neuropsychiatric Interview, DSM: Diagnostic and Statistical Manual of Mental Disorders, SF-36: Short-form-36, WHODAS: World Health Organization Disability Assessment Schedule, PTSS: Posttraumatic Stress Scale, BACQ: Brief Approach/Avoidance Coping Questionnaire, SCID: Structured Clinical Interview for DSM disorders, PCL-C: PTSD-checklist-Civilian Version, PDEQ: Peritraumatic Dissociation Experiences Questionnaire, ASI: Addiction Severity Index, IES: Impact of Event Scale, MISS: Mississippi Rating Scale for Combat Related PTSD, BDI: Beck Depression Inventory, TBI: traumatic brain injury, CIDI: Composite International Diagnostic Interview, SARS: Symptoms of Acute Stress Symptoms, RLEQ: Recent Life Events Questionnaire, MHI-5: Mental Health Inventory 5-item, SUAPS: Service Use and Adjustment Problem Screen, AUDIT: Alcohol Use Disorders Identification Test, ASS: Acute Stress Syndrome, PC-PTSD: Primary Care-Post-Traumatic Stress Disorder, MTEQ: Memory of Traumatic Event Questionnaire, ANAM: Automated Neuropsychological Assessment Metrics, MPQ: McGill Pain Questionnaire, NISS: New Injury Severity Score, SASRQ: Stanford Acute Stress Reaction Questionnaire, SASD: subsyndromal ASD, MCEPS: Michigan Critical Events Perception Scale, CMSP-R: Revised Civilian Mississippi Scale for PTSD, AEE: Attitudes to Emotional Expression Scale, SDQ: State Dissociation Questionnaire, TDQ: Trait Dissociation Questionnaire, RQ: Rumination Questionnaire, χ2: Chi square test, OR: Odds Ratio, RR: Relative Risk, β: Beta, SE: Standard Error

SUPPLEMENTAL TABLE 2. Overview of intervention studies

First Author (year)	Type of trauma	N	Design	Type of intervention	FU period	Baseline measurements	FU measurements	Independent variables	Dependent variables	Main conclusion
Price (2014)[81]	DSM-IV criterion A (i.e. traumatic event)	137	RCT	In vivo exposure Self-care tasks	3: in hospital, 4 and 12 weeks	STI CTQ ISRC HR Cortisol	PSS-I	History of trauma exposure Dissociation Physiological responses	PTSD	In the intervention (γ_{10}=-3.58, p=0.015) and control (γ_{10}=-4.89, p=0.015) group PTSD changed during four and 12 weeks. At 12 weeks, 26% of the intervention and 47% of the control group were diagnosed with PTSD.
Bryant (2003)[53]	Mild TBI	24	Un-known	CBT SC	3: pre-treatment, post-treatment and 6 months	ASDI IES CAPS	ASDI IES CAPS	Type of treatment	ASD PTSD	Compared with SC, patients who had CBT less often met criteria for PTSD at a post treatment evaluation (8% versus 58%), also at six months (17% versus 58%).
Scholes (2007)[32*]	Road traffic accident Occupational injury Assault	347	RCT	Self-help booklet	3: 1 month post injury, 3 months post-intervention and 6 months post intervention	Demographic Nature of injury PDS ASDS	PDS	Group Time	ASD PTSD	PTSD decreased in time ($F(2,174) = 44.23$, $p<0.001$). The use of self-help booklets was not an effective early intervention for ASD and PTSD (Wilks' Lambda=1.00, $F(1,178) <0.001$, p=1.00).
Galatzer-Levy (2013)[37]	MVA Terrorist attacks Work accidents Other	1082	RCT	CBT	3: 10 days post injury, 7 and 15 months	PSS K6 CAPS SCID	CAPS SCID Occurrence of new traumatic events	Demographics Group Time	PTSD Trajectories	Three trajectories were identified: Rapid Remitting (decrease in five months; 56%) Slow Remitting (decrease in 15 months; 27%) Non-Remitting (persistently elevated symptoms; 17%) CBT accelerated the recovery of the Slow Remitting but did not affect the other trajectories.
Bugg (2009)[91]	Road traffic accident Occupational injury Assault	67	RCT	Self-help booklet Writing intervention	3: 1 month post injury, 3 months post-intervention and 6 months post intervention	Demographics Nature of injury PDS	PDS	Group Time	Change in PTSD symptoms	Self-help booklet was not supported as early intervention, because the groups (self-help booklet group and writing group) did not differ ($F(1, 49) = 0.87$, p=0.36).

SUPPLEMENTAL TABLE 2. Continued

First Author (year)	Type of trauma	N	Design	Type of intervention	FU period	Baseline measurements	FU measurements	Independent variables	Dependent variables	Main conclusion
Bisson (2004)[47]	MVA Assault Other	152	RCT	CBT	3: baseline, 12 weeks and 13 months	Demographics Levels of functioning and perceptions of trauma and its' impact IES PDS	IES	Type of treatment Demographics Levels of functioning and perceptions of trauma and its' impact	PTSD	Thirty percent had PTSD of both the intervention and control groups at 3 months (RR 1.0, 95% CI 0.5–2.1). At 13 months, 16% of the intervention group and 27% of the control group had PTSD (RR 0.6, 95% CI 0.3–1.5).Reduction of PTSD symptoms was greater in the intervention group than the control group at 13 months after injury (adjusted mean difference=8.4, 95% CI 2.4-14.36, p=0.006). At 13 months, 45% of the intervention group had a 50% reduction in the baseline PTSD symptoms compared with 28% of the control group (RR 0.5, 95% CI 0.2–0.9).
Mouthaan (2013)[46]	Traffic Work-related Fall Interpersonal violence or physical abuse Other	300	RCT	Trauma TIPS: Psycho-education Stress management In vivo exposure	4: 1, 3, 6 and 12 months	CAPS MINI IES-R VAS scales for acute anxiety and arousal	CAPS MINI IES-R VAS scales for acute anxiety and arousal	Trauma TIPS	PTSD	An internet information-based prevention program was not effective in preventing PTSD symptoms (at 12 months: Internet intervention group: estimated means 13.0, 95% CI 11.2-14.8; control group: estimated means 13.0, 95% CI 11.4-14.6, p=.63).
Zatzick (2013)[64]	Unknown	207	RCT	Combination of care management, psycho-pharmacology and CBT	6: before RCT, 1, 3,6, 9 and 12 months	PCL-C CAPS	PCL-C CAPS	Group Time	PTSD	Patients who underwent the intervention had less PTSD symptoms at 12 months after injury (CAPS scores: $F(2,185) = 5.50$, $p<0.01$).

SUPPLEMENTAL TABLE 2. Continued

First Author (year)	Type of trauma	N	Design	Type of intervention	FU period	Baseline measurements	FU measurements	Independent variables	Dependent variables	Main conclusion
Osenbach (2014)[74]	MVA Assault Fall or jump Burn Sport injury Work-related Other	194	RCT	Care management (e.g. motivational interviewing, behavioral activation) and higher-intensity care (pharmacotherapy)	7: prior to randomization (1-3 weeks post-injury), 1, 3, 6, 9 and 12 months	PCL Prior traumatic life events Post-injury stressful traumatic life event	PCL	Group Risk factors	PTSD symptom trajectories	Four different PTSD trajectories were found: Resilience trajectory (PTSD symptoms began low and remained low across time points) Recovery trajectory (very high PTSD symptom severity initially with subsequent symptom reduction at FU) Relapsing/remitting trajectory (moderate symptoms that varied slightly across time, but stayed relatively moderate) Chronic trajectory (high baseline symptom levels that persisted over time). Patients (28%) were associated with the resilience trajectory, 10% with the recovery trajectory, 35% the relapsing/remitting trajectory and 27% the chronic trajectory.
Ehlers (2003)[65]	MVA	97	RCT	3 week self-monitoring phase, then RCT to CT, CBT or self-help booklet	3: before randomization, 3 and 9 months	PDS CAPS	PDS CAPS	Group Time	PTSD	In total, 12%) recovered after self-monitoring. The CBT group showed less PTSD symptoms than the self-help booklet group at post treatment (11% versus 61%, OR 12.9, 95% CI 3.1-53.1) and after nine months (11% versus 55%, OR 10.3, 95% CI 2.5-41.7).
Zatzick (2001)[66]	MVA Other	34	RCT	Collaborative intervention: psychotherapy and psycho-education	3: while hospitalized, 1 and 4 months	Demographics CIDI PCL-C CAPS PDEQ	Demographics CIDI PCL-C CAPS PDEQ	Group	PTSD	One month after injury, patients in the intervention group had a decrease in PTSD symptoms compared to the control group ($F(1,33)=6.8$, $p=.05$, effect size=0.99). After four months post-trauma, no differences were found (p-value unknown).

SUPPLEMENTAL TABLE 2. Continued

First Author (year)	Type of trauma	N	Design	Type of intervention	FU period	Baseline measurements	FU measurements	Independent variables	Dependent variables	Main conclusion
Tecic (2011)[48]	MVA Collapse Strike Other	113	RCT	Short-term: up to 8 inpatient psychotherapy sessions Long-term: short-term and in addition up to 6 out-patient psychotherapy over 6 months after discharge	5: inclusion, discharge, 6, 12 and 18 months	Demographics BDI STAI IES-R	BDI STAI IES-R	Group Time	Depression Anxiety PTSD	At baseline, 17.8% had PTSD. No differences were found between the short-term (p= 0.058) and the long-term group (p=0.059). However, 21% of the short-term group showed at least one mental health disorder (depression, anxiety or PTSD) compared with no patients in the long-term group one year after trauma (p=0.035).
Brunet (2013)[51]	MVA Leisure Physical assault Work	74	RCT	Dyadic intervention with psycho-education and motivational interviewing	3: 21 and 35 days post-trauma, 3 months post-treatment	PDEQ IES-R CAPS SCS MINI	PDEQ IES-R CAPS SCS MINI	Dyadic intervention	PTSD Social support	A time-by-group interaction (F(2,72)=4.17, p=0.019) was found, as treated patients had less PTSD symptoms over time than the controls. Social support was related with PTSD symptoms at post treatment (Spearman's rho= 0.45, p=0.001).
Des Groseilliers (2013)[52]	MVA Leisure Physical assault Work	46	RCT	Dyadic cognitive behavioral intervention	4: 3 and 5 weeks post-trauma, 2 and 24 months post-treatment	PDEQ IES-R CAPS MINI	PDEQ IES-R CAPS MINI	Dyadic intervention Outcome 24 months post treatment	PTSD	None of patients who were treated with CBT had PTSD at after 24 months compared with five (26%) patients with PTSD from the control group (Fisher's exact test, p=0.01). The intervention can be effective in reducing PTSD as it was offered as part of regular care in the hospital setting.
Turpin (2005)[92]	Assault Occupational Road traffic accident	142	RCT	Self-help booklet	3: 2 weeks, 10-12 weeks (post-intervention) and 24-26 weeks	PDS	PDS	Group	PTSD	PTSD decreased (p<0.05) with time. The efficacy of providing self-help information was not supported as an intervention for PTSD (Wilks' lambda $F(3,218) = 0.98$, p=0.19).

SUPPLEMENTAL TABLE 2. Continued

First Author (year)	Type of trauma	N	Design	Type of intervention	FU period	Baseline measurements	FU measurements	Independent variables	Dependent variables	Main conclusion
Sack (2009)[54]	MVA Assault Sudden death of relative Rape Work	16	Non-RCT	EMDR	3: before first treatment session, 1 week after treatment, 6 months FU	IES PDS	IES PDS	Treatment Time	PTSD	PTSD symptoms decreased one week (IES score: t=5.1, $p<0.001$; PDS score: t=5.5, $p<0.001$) and six months (IES score: t=5.3, $p<0.001$; PDS score: t=6.0, $p<0.001$) after treatment.
Bryant (1998)[31]†	Mild TBI	24	Unknown	CBT SC	3: pretreatment, post treatment and 6 months	ASDI IES CAPS	ASDI IES CAPS	Type of treatment	ASD PTSD	Less patients who had CBT met PTSD criteria at a post treatment evaluation compared with SC (8% versus 58%). There were also fewer patients with PTSD who had CBT (17%) than patients who had SC (67%) after six months.
Wagner (2007)[36]	Intentional and unintentional injuries	8	RCT	BA	2: 1 and 3 months post injury	PCL CIDI	PCL CIDI	Group	PTSD	The BA group reported more reduction of PTSD symptoms than the treatment as usual group (t=2.07; one-tailed $p<0.05$; unbiased Hedges's $g=1.27$).
Blanchard (2003)[49]	MVA	98	RCT	CBT Supportive psychotherapy	3: pre-treatment, post-treatment and 3 months FU	CAPS SCID IES PCL	CAPS IES PCL	Type of treatment Time	PTSD	About 76% reported an improvement of PTSD symptoms after treatment with CBT compared with about 48% who were treated with supportive psychotherapy and about 24% of the waiting list group reported an improvement of PTSD symptoms
Wu (2012)[82]	MVA	60	RCT	CBT Self-help program booklet	3: 1 month post-injury, 3 and 6 months post-treatment	IES-R	IES-R	Type of treatment Time	PTSD	To reduce PTSD symptoms CBT was more effective than self-help booklet after three and six months post-treatment (i.e. intrusion (Hedges' effect size= 1.17, 95% CI 0.57-1.77), avoidance (Hedges' effect size= 0.71, 95% CI 0.14-1.28) and hyper-arousal (Hedges' effect size= 1.27, 95% CI 0.66-1.87). After six months, intrusion (Hedges' effect size= 1.30, 95% CI 0.69-1.91) and hyper-arousal (Hedges' effect size= 1.35, 95% CI 0.74-1.97).

SUPPLEMENTAL TABLE 2. Continued

First Author (year)	Type of trauma	N	Design	Type of intervention	FU period	Baseline measurements	FU measurements	Independent variables	Dependent variables	Main conclusion
Bryant (2005)[50]	Nonsexual assault MVA	87	RCT	CBT CBT-hypnosis SC	3: pre-treatment, post-treatment, 6 months FU	SHCS: Adults ASDI IES Therapy confidence	IES CAPS	Type of treatment Time	PTSD	Post-treatment, more PTSD diagnoses were found in SC (46%) than CBT (13%) (χ^2=6.14, p<0.05) and CBT-hypnosis (9%) (χ^2=7.77, p<0.05). At six months FU, more PTSD diagnoses were found in SC (59%), than CBT (21%) (χ^2=7.05, p<0.01) and CBT-hypnosis (22%) (χ^2=6.54, p<0.01).

**Same design as Bugg et al. (2009)[91], † same design as Bryant (2003)[53]*

Abbreviations: FU: follow-up, RCT: randomized control trail, STI: Standardized Trauma Interview, CTQ: Childhood Trauma Questionnaire, ISRC: Immediate Stress Reaction Checklist, HR: heart rate, PTSD: posttraumatic stress disorder, PSS-I: PTSD Symptom Scale-Interview version, TBI: traumatic brain injury, CBT: cognitive behavioral therapy, SC: supportive counseling, ASDI: Acute Stress Disorder Interview, IES: Impact of Event Scale, BDI: Beck Depression Inventory, CAPS: Clinician Administered PTSD Scale, ASD: acute stress disorder, PDS: Posttraumatic Disorder Scale, ASDS: Acute Stress Disorder Scale, MVA: motor vehicle accidents, K6: Kessler-6, SCID: Structured Clinical Interview for DSM disorders, MINI: Mini International Neuropsychiatric Interview, VAS: Visual Analogue Scale, PCL: PTSD-checklist, CT: cognitive therapy, PCL-C: PTSD-Checklist-civilian version, PDEQ: Peritraumatic Dissociation Experiences Questionnaire, STAI: State-Trait Anxiety Inventory, IES-R: Impact of Event Scale-Revised, SCS: Social Constraints Scale, CIDI: Composite International Diagnostic Interview, BA: behavioral activation, SHCS Adults: Stanford Hypnotic Clinical Scale for Adults, χ^2: Chi square test, OR: Odds Ratio, RR: Relative Risk, β: Beta, SE: Standard Error

SUPPLEMENTAL TABLE 3. STROBE checklist and Oxford Level of Evidence

First Author (year)	1a	1b	2	3	4	5	6a	6b	7	8	9	10	11	12a	12b	12c	12d	12e	13a	13b	13c	14a	14b	14c	15	16a	16b	16c	17	18	19	20	21	22	LoE
Haagsma (2012)[39]	1	1	1	1	1	1	1	X	1	1	0	0	1	1	1	1	0	0	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	3
Zatzick (2007)[35]	0	1	1	1	1	1	1	X	1	1	1	0	1	1	1	1	1	0	1	1	1	1	1	1	1	1	0	0	1	1	1	1	0	1	3
Soberg (2010)[75]	1	1	1	1	1	1	1	X	1	1	1	0	1	1	1	0	0	0	1	1	1	1	1	1	1	1	X	0	1	1	1	1	0	1	3
Haagsma (2015)[38]	0	1	1	1	1	1	1	X	1	1	1	0	X	1	1	1	0	0	1	0	1	1	1	1	1	1	1	1	1	1	1	1	0	1	3
Bryant (2013)[57]	1	1	1	1	1	1	1	X	1	1	1	0	1	1	1	0	0	0	1	1	1	1	0	1	1	1	X	0	0	1	1	1	1	1	3
Mayou (2001)[71]	0	1	1	1	1	1	1	X	1	1	1	0	0	1	1	0	1	0	1	1	0	1	1	1	1	1	X	X	1	1	1	1	0	0	3
Glynn (2007)[72]	1	1	1	1	1	1	1	X	1	1	0	0	1	1	1	1	0	X	1	0	0	1	0	1	1	1	X	0	X	1	1	1	0	1	3
Zatzick (2002)[76]	0	1	1	1	0	0	1	X	1	1	1	0	1	1	1	1	0	0	1	1	0	1	1	1	1	1	X	0	0	1	1	1	1	1	3
Whitman (2013)[34]	0	0	1	1	0	1	1	X	1	1	1	0	0	1	1	1	1	1	1	1	0	1	1	1	1	0	X	X	0	1	1	0	1	1	3
Ehring (2008)[80]	1	0	1	1	1	1	1	X	1	1	1	0	0	1	1	0	0	0	1	0	1	1	0	1	1	0	X	0	1	1	1	1	1	1	3
Lui (2009)[89]	0	1	1	1	1	1	1	X	1	1	1	0	1	1	1	1	1	0	1	0	0	1	0	0	0	0	X	X	0	1	1	1	1	1	3
Norman (2008)[70]	0	1	1	1	0	1	1	X	1	1	0	0	0	1	1	0	0	1	1	0	0	1	0	1	1	1	X	0	1	1	1	1	1	1	3
Bryant (2015)[58]	0	1	1	0	1	1	1	X	1	1	1	1	0	0	0	0	0	1	1	0	0	1	1	1	1	0	X	X	0	1	1	1	1	1	3
Mason (2009)[55]	1	1	1	1	1	1	1	X	1	1	1	0	0	1	1	0	1	0	1	0	0	0	0	1	1	0	X	X	0	1	1	1	0	1	3
Warren (2013)[67]	1	1	1	1	0	1	1	X	1	1	0	0	0	1	0	0	0	0	1	1	1	1	1	1	1	0	X	X	0	1	1	1	0	1	3
Shih (2010)[78]	0	0	1	1	1	1	1	X	1	1	0	0	X	1	1	0	0	0	1	0	0	1	0	1	1	1	X	0	0	1	1	1	1	1	3
Norman (2011)[77]	0	1	1	1	1	1	1	X	1	1	0	0	0	1	1	0	0	0	1	0	0	1	1	1	1	0	X	X	0	1	1	1	0	1	3
O'Donnell (2014)[59]	0	1	1	1	0	0	1	X	1	1	0	0	1	1	1	0	0	0	1	0	0	1	1	1	1	1	0	0	1	0	1	1	1	1	3
Fuglsang (2004)[79]	0	1	1	1	1	1	0	X	1	1	0	0	1	1	0	0	0	X	0	0	0	1	1	1	1	0	X	X	X	1	1	1	1	1	3
Bell (2014)[33]	1	1	1	0	1	1	1	X	1	1	1	0	0	1	1	0	0	1	1	0	0	1	0	X	1	0	0	0	0	1	1	1	0	1	3
Michaels (1999)[44]	0	1	0	1	0	1	1	X	1	1	0	0	0	1	1	0	0	0	1	0	0	1	0	1	1	0	X	X	1	1	1	1	1	1	3
Forbes (2012)[56]	1	1	1	1	0	1	1	X	1	1	0	0	X	1	1	0	0	0	0	0	0	0	0	1	1	0	X	X	1	1	1	1	0	1	3
Bryant (2000)[90]	0	1	1	1	0	0	1	X	1	1	0	0	1	1	1	0	0	0	1	0	0	1	0	1	1	0	X	X	1	1	1	0	0	1	3
Freedman (1999)[42]	0	1	1	1	0	0	1	X	0	0	0	0	0	1	1	0	0	0	1	0	0	0	0	1	1	1	X	X	1	1	1	1	1	1	3

SUPPLEMENTAL TABLE 3. Continued

First Author (year)	1a	1b	2	3	4	5	6a	6b	7	8	9	10	11	12a	12b	12c	12d	12e	13a	13b	13c	14a	14b	14c	15	16a	16b	16c	17	18	19	20	21	22	LoE
Bryant (1999)[87]	0	1	1	1	0	1	1	X	0	1	0	0	1	1	1	0	0	0	1	1	0	1	0	1	1	0	X	X	0	1	0	0	0	1	3
Gil (2005)[62]	0	1	1	1	0	1	1	X	1	1	0	0	X	1	1	0	0	0	1	0	0	1	0	0	1	0	X	0	1	1	1	1	0	0	3
Kühn (2006)[68]	0	1	1	1	1	1	1	0	1	1	1	0	0	1	0	0	0	0	1	1	0	1	1	X	1	0	0	0	1	1	1	1	0	1	4
Zatzick (2007)[88]	0	0	1	1	1	1	1	X	1	1	0	0	1	1	0	0	0	0	1	0	0	0	0	X	0	0	1	X	0	1	1	1	0	1	4
Holbrook (2001)[40]	0	1	1	1	0	1	1	X	1	1	0	0	0	1	1	0	0	0	0	0	0	1	0	0	1	1	X	1	0	1	1	0	0	0	4
Vaiva (2003)[61]	0	1	1	1	0	1	1	X	1	1	0	0	0	1	1	0	0	0	1	0	0	1	0	1	1	0	X	0	0	1	0	1	0	0	4
Mellman (2001)[63]	0	0	1	0	0	1	1	X	1	1	0	0	1	1	0	0	0	0	0	0	0	1	1	0	1	0	X	X	0	0	1	1	1	1	4
Ursano (1999)[69]	0	1	1	0	0	0	1	0	1	1	0	0	X	1	0	1	0	0	0	0	0	1	1	1	1	1	0	0	X	1	0	0	0	1	4
Blanchard (1997)[60]	0	1	1	1	0	0	0	X	1	1	0	0	0	1	0	0	0	0	0	0	0	1	0	1	1	0	0	0	1	1	1	0	1	1	4
Shalev (1998)[43]	0	1	1	1	1	0	1	X	1	1	0	0	0	1	0	0	0	0	1	0	0	0	0	1	1	0	X	X	0	1	1	0	0	0	4
Nightingale (2000)[45]	0	1	1	0	0	0	1	X	1	1	0	0	0	0	0	0	0	0	1	0	0	1	0	0	1	0	X	X	X	1	1	1	1	0	4
Shalev (2005)[41]	0	0	1	1	0	1	0	X	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	0	X	0	0	1	0	1	0	1	4

Abbreviations: LoE: Level of Evidence, X: Not Applicable

SUPPLEMENTAL TABLE 4. CONSORT checklist and Oxford Level of Evidence

First Author (year)	1a	1b	2a	2b	3a	3b	4a	4b	5	6a	6b	7a	7b	8a	8b	9	10	11a	11b	12a	12b	13a	13b	14a	14b	15	16	17a	17b	18	19	20	21	22	23	24	25	LoE
Mouthaan (2013)[46]	1	1	1	1	1	X	1	1	0	0	X	1	X	1	1	1	1	1	X	0	X	1	1	1	1	1	0	1	X	0	0	1	1	1	1	1	1	2
Wu (2014)[82]	1	1	1	1	0	X	1	1	1	1	0	1	0	1	0	1	1	0	0	1	1	1	1	1	1	1	1	1	X	1	0	1	1	1	0	0	1	2
Zatzick (2013)[64]	1	1	1	1	0	0	1	1	0	1	0	1	0	1	1	1	0	1	0	1	1	1	1	1	0	1	0	1	0	1	0	1	1	1	1	1	1	2
Bisson (2004)[47]	1	1	1	1	0	0	1	1	1	1	0	1	0	1	1	1	0	0	0	1	1	1	0	1	0	1	1	1	1	0	0	1	1	1	0	0	1	2
Tecic (2011)[48]	1	0	1	1	0	0	1	1	1	1	0	0	0	1	0	1	1	1	0	1	1	1	1	1	0	1	1	0	0	1	0	1	1	1	0	0	1	2
Ehlers (2003)[65]	1	1	1	1	0	0	1	1	0	1	0	0	0	1	1	1	1	0	1	0	1	1	1	0	0	1	1	0	X	1	0	1	1	1	0	0	1	2
Brunet (2013)[51]	1	0	1	1	0	0	1	0	1	1	0	1	0	1	1	0	0	0	0	1	1	1	1	1	0	1	1	0	0	1	0	1	1	1	0	0	1	2
Turpin (2005)[92]	1	1	1	0	0	0	1	1	0	1	0	0	0	1	0	0	1	0	X	1	1	1	1	1	0	1	1	0	0	1	0	1	1	1	0	0	1	2
Zatzick (2001)[66]	1	0	1	1	0	0	1	1	0	1	0	0	0	0	1	0	1	1	X	1	0	1	1	0	0	1	0	0	0	1	0	1	1	1	0	0	1	3
Bugg (2009)[91]	1	0	1	1	0	0	1	1	0	1	0	0	0	0	0	0	0	0	0	1	0	1	1	1	0	1	1	1	0	0	0	1	1	1	0	0	1	3
Blanchard (2003)[49]	0	0	1	0	0	0	1	1	1	1	0	0	X	0	0	0	1	1	0	0	0	1	0	1	0	1	1	1	0	0	0	0	1	1	0	0	1	3
Price (2014)[81]	0	0	1	1	0	0	1	1	1	1	0	0	0	0	0	0	0	0	X	0	0	0	0	0	0	0	1	1	X	0	0	1	1	1	1	1	1	3
Bryant (2005)[50]	0	0	1	1	0	X	1	1	1	1	X	0	X	0	0	0	0	1	0	0	0	0	0	0	0	0	1	1	X	0	0	1	1	1	0	0	1	3
Osenbach (2014)[74]	0	1	1	1	1	0	0	0	1	1	0	0	0	0	0	0	0	0	X	1	1	1	0	0	0	1	1	1	0	0	0	1	0	1	0	0	0	3
Des Groseilliers (2013)[52]	0	0	1	1	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	1	0	1	0	0	0	1	1	1	0	1	0	1	1	1	0	0	1	3

SUPPLEMENTAL TABLE 4. Continued

First Author (year)	1a	1b	2a	2b	3a	3b	4a	4b	5	6a	6b	7a	7b	8a	8b	9	10	11a	11b	12a	12b	13a	13b	14a	14b	15	16	17a	17b	18	19	20	21	22	23	24	25	LoE
Bryant (2003)[53]	0	1	1	1	0	0	1	1	1	1	0	0	0	0	0	0	0	0	X	1	0	0	0	0	0	0	1	1	0	0	0	1	1	0	0	0	1	3
Wagner (2007)[36]	0	0	1	1	0	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	X	0	0	1	1	1	0	0	0	1	1	1	0	0	1	3
Galatzer-Levy (2013)[37]	0	1	1	1	0	0	1	1	0	1	0	0	0	0	0	0	0	0	0	1	0	1	0	1	0	0	0	0	0	0	0	0	0	0	1	1	1	3
Sack (2009)[54]	0	0	1	1	0	0	1	1	1	0	0	0	0	X	X	X	X	X	X	1	0	0	0	0	0	0	1	1	0	1	0	1	1	1	0	0	0	4

Abbreviations: LoE: Level of Evidence, X: Not Applicable

Chapter 3

PHYSICAL TRAUMA PATIENTS WITH SYMPTOMS OF AN ACUTE AND POSTTRAUMATIC STRESS DISORDER: PROTOCOL FOR AN OBSERVATIONAL PROSPECTIVE COHORT STUDY

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ABSTRACT

Background: Injury, medical treatment, and rehabilitation can have major impacts on patients' wellbeing. About 25-33% of the patients experience an acute stress disorder (ASD) or a posttraumatic stress disorder (PTSD) after injury. ASD is a relatively new diagnosis. Therefore, knowledge about patients' experiences, the course of ASD and PTSD, and who is at risk for developing ASD or PTSD is lacking.

Objectives: The aims of this multi-method study are to explore patients' experiences with injury (and their care) using a focus group study. Then, in the observational study, different courses of ASD, PTSD, and quality of life (QOL) will be examined. In addition, this study will examine if these courses could be characterized by socio-demographic, clinical, and psychological variables. Consequently, a risk profile will be developed to determine which patients are at risk for developing ASD or PTSD during the 12 months after injury.

Methods: Trauma patients treated in the shock room (in 2015) of the Elisabeth-TweeSteden Hospital will share their experiences with injury in the focus group study. Open, axial, and selective coding will be used to analyze the data. Concerning the observational study, patients treated in the shock room (during 2016 and 2017, Elisabeth-TweeSteden Hospital and Erasmus Medical Centre) will be asked to participate. The inclusion period is 12 months. Participants will complete the Impact of Event Scale-Revised, MINI-plus, the Hospital Anxiety and Depression Scale, and the World Health Organization Quality of Life-BREF after inclusion and at 3, 6, 9, and 12 months after injury. The NEO-Five Factor Inventory and the State-Trait Anxiety Inventory-Trait are completed after inclusion only. Repeated measures of latent class analysis and linear mixed models will be used to examine the research aims.

Results: This project was funded in August 2015 by ZonMw. The results of the focus group study are expected in the first trimester of 2018. With regard to the observational study, recruitment is currently underway. Data collection will be completed in November 2018. The first results will be expected in the first trimester of 2019.

Conclusions: This is the first multi-method study in trauma patients that examines patients' experiences (qualitative design) as well as psychological disorders (observational prospective). This study will contribute to necessary information on psychological consequences after injury. Moreover, it provides knowledge about which patients to include in future psychological intervention research. Finally, awareness in clinicians about the psychological consequences can be created, so they are able to act more effectively to provide patient-oriented care.

INTRODUCTION

Due to registration and implementation of specialized trauma care, the quality of medical treatment has been improved and survivorship has been increased[1-6]. Trauma is related to physical disabilities (e.g., pain, fatigue and impaired wound healing), acute stress disorder (ASD), posttraumatic stress disorder (PTSD), and psychological distress[7-12]. Moreover, trauma patients experience an impaired quality of life (QOL) compared to the general population[13-19].

About 25% of trauma patients have subsyndromal ASD during hospitalization and about 30% had PTSD one month after injury[8,20]. Six months after injury, 49% showed a delayed onset of PTSD. This percentage decreased to 20% at 24 months after injury. A recent systematic review showed that patients diagnosed with ASD had a higher risk of developing PTSD[8]. However, the prevalence rate of patients with ASD who develop PTSD is unknown. Diagnostic criteria for ASD and PTSD are similar, however, dissociative symptoms (e.g., depersonalization, derealization, and dissociative amnesia) are only emphasized in ASD and not in PTSD. Moreover, ASD can only be diagnosed within the first month after trauma and last for less than a month, while PTSD symptoms persist for at least one month after injury[21]. PTSD symptoms may begin either after trauma or months or years afterwards[22].

In addition to QOL, PTSD, anxiety, and depression are most frequently examined after injury[14-19]. However, information about ASD is scarce. The existing studies of ASD and PTSD are often cross-sectional. Moreover, in the case of an observational prospective design, examination of PTSD is limited to only several months after trauma. One or several measurements are needed to examine patients' psychological recovery shortly after injury. Important information about the courses of ASD and PTSD (i.e., main scores of onset and development, such as the stability of symptom severity over time) and patients' characteristics is lacking[8,23,24]. More specifically, it is unknown if and in what way patients' experiences with injury and treatment, for instance, in the shock room, contribute to psychological consequences. Moreover, factors related to communication between medical staff and patient, treatment of injury, and environment are not known. To gain information about the development of ASD and PTSD and their sustaining risk factors will increase the quality of care because patients at risk can be offered psychological treatment, thereby preventing the development psychological disorders, such as ASD and PTSD. Health care providers with the knowledge of medical and psychological consequences after trauma can better anticipate patients' needs so that patient-centered care can be provided.

This multi-method study consists of a focus group study and an observational prospective study. The ultimate goal of this multi-method study is to provide valuable insight into the severity of psychological consequences, including ASD and PTSD, and the need for a

psychological intervention study to prevent PTSD. First, focus groups are held to examine patients' experiences with injury (and their care). In this way, potential factors related to the development of psychological problems (e.g., depressive symptoms) and disorders (e.g., anxiety, ASD, and PTSD) can be obtained and taken into account for the observational study (aim 1). Subsequently, an aim of the observational study is to examine the courses of ASD and PTSD (aim 2). In addition, it will be examined which socio-demographic (i.e., sex, age, marital status, and education level), clinical (i.e., type of trauma, Injury Severity Score (ISS), Glasgow Coma Score, being hospitalized, being treated on the intensive care unit, complications during treatment, and treatment by a medical psychologist or psychiatrist), and psychological variables (e.g., anxiety, depressive symptoms, and personality) characterize the courses of ASD and PTSD. Subsequently, a risk profile will be developed to determine which patients are at risk for ASD and/or PTSD (aim 3). Finally, to study the effect(s) of the natural course of ASD symptoms on the development of PTSD, anxiety and depressive symptoms, and QOL across time will be analyzed (aim 4).

METHODS

Design

First, using a qualitative focus group study design, patients' perspectives on the injury, treatment in the shock room and hospital, and rehabilitation are explored. A focus group is a commonly used method of qualitative research as it is a valid and reliable technique. Moreover, focus groups facilitate the in-depth exploration of a person's perspective through group interaction. Participants can be triggered by a comment from another participant[25,26], and by the concept of sharing and comparing[27]. Then, as an extension of the focus group study, the observational prospective cohort study will examine ASD, PTSD, anxiety and depressive symptoms, and QOL. This will be assessed up to one year after treatment for physical trauma. A flow diagram of the observational study design and the main procedures that patients will undergo during the course of the observational study are shown in Figure 1.

Participants and Centers of Recruitment

Trauma patients treated in the shock room in 2015 of the Elisabeth-TweeSteden Hospital are asked to participate in the focus group study. A shock room is situated at the Emergency Department and is reserved for physical trauma patients (i.e., all types of injury) with a potentially life-threatening situation.

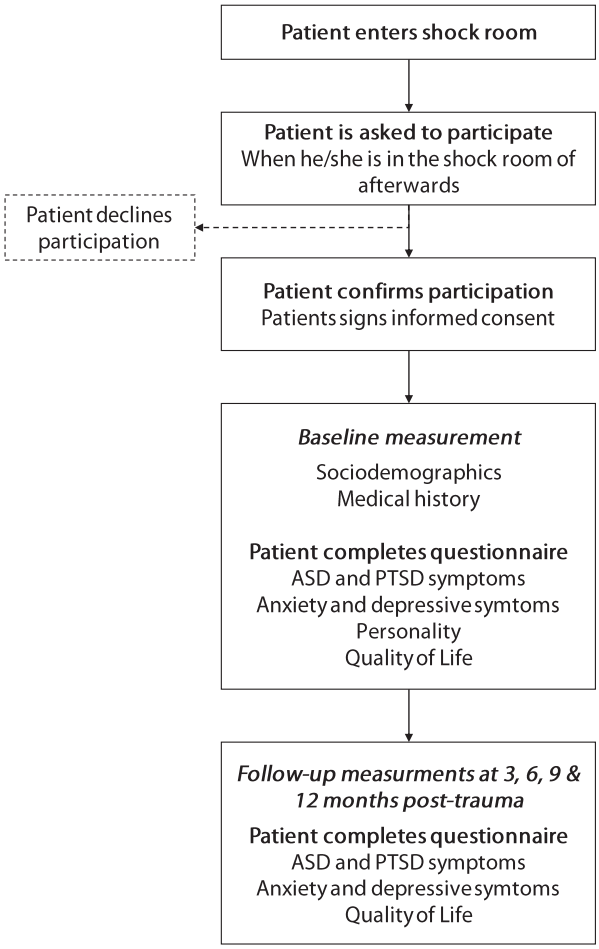

FIGURE 1. Flowchart of the study design
Abbreviations: ASD: acute stress disorder, PTSD: Posttraumatic stress disorder

Concerning the observational study, all adult patients who have been in the shock room at the Emergency Departments of the Elisabeth-TweeSteden Hospital (Tilburg) or the Erasmus Medical Centre (Rotterdam, The Netherlands) are asked to participate. The inclusion period is about 12 months after the start in November 2016.

Sample Size Calculation

This project is exploratory in nature. Moreover, the focus is on examining the stability of results. The sample size was calculated only for the observational study. According to the Dutch trauma registry, the shock room admission was about N=1440 in 2013 and N=986

in 2016 in the Elisabeth-TweeSteden Hospital. Using a mean of these admission numbers of (N=1213, α=0.05, β=0.80, and effect size=0.4), it was estimated that N=300 would be sufficient. This was also based on Monte Carlo simulations[28].

Inclusion and Exclusion Criteria

In order to be eligible to participate, patients (1) are treated in the shock room and (2) are aged 18 or older. Patients are excluded from participation in case of (1) severe traumatic brain injury (i.e., Glasgow Coma Score ≤ 8), (2) dementia, or (3) insufficient knowledge of the Dutch language (verbal and writing). These criteria are used in the focus group and the study observational study.

Study Procedures

Focus Groups

Trauma patients who were treated in the shock room of the Elisabeth-TweeSteden Hospital during 2015 were asked to participate in a qualitative focus group study. Patients were divided into 3 groups: (1) patients who went home after treatment in shock room (no hospitalization) or, in case of hospitalization, they had an ISS of less than 16; (2) ISS equal or higher than 16, and (3) mild or moderate traumatic brain injury (Glasgow Come Score > 8). Six to 10 patients were invited to participate in each group. To obtain a representative sample of the trauma population, the division into groups was based on type of injury, sex, and age. The purposive sampling method was used[25,26].

The focus group meetings took place in a conference room at the Elisabeth-TweeSteden Hospital. Each focus group was guided by a moderator and an assistant. The patients were asked to share their experiences by answering the main question, "What experience related to your injury impressed you the most?" Their experiences were clustered on a flipchart on the basis of the trauma procedure: (1) moment of injury, (2) treatment in the ambulance or the trauma helicopter, (3) treatment in the shock room, (4) hospital stay, (5) moment of discharge, and (6) period after discharge and/or rehabilitation. Finally, another main question, "In what way did you need and received psychological treatment?", was discussed. At the end of each focus group, participants were asked to complete questions about their socio-demographic status (i.e., age, sex, marital status, and education level). In addition, they completed the Impact of Event Scale revised (IES-R) for PTSD and the Hospital Anxiety and Depression Scale (HADS) for anxiety and depressive symptoms. All focus groups had the same structure and were audio-recorded. The duration of the meeting was about 90 minutes.

Observational Study

The emergency doctor or the resident will ask patients to participate in this study as soon as they can talk and are lucid. If the emergency doctor or the resident is not able to ask the patient to participate (e.g., due to transferring the patient to another department in the hospital), the researcher will ask the patient as soon as possible to participate in this study. The researcher will check medical records to see whether there are patients that have not yet been asked to participate in the study.

Patients will sign two informed consents. First, in the emergency department (after being treated in the shock room and being informed by the doctor). Then 1-5 days later, the patient will be asked to confirm participation again to make sure that they have sufficient time to consider participation in the study. In the case of a patient who is unconscious, the patient will be informed by the researcher and asked to participate as soon as the patient is lucid. If a patient declines participation by not signing the second informed consent, all obtained information will be destroyed.

After confirming participation, the patient will complete a questionnaire on socio-demographic questions, ASD and PTSD, anxiety and depressive symptoms, personality, and QOL at the first time-point (i.e., baseline). Clinical information will be retrieved from patients' medical records. The measurement points are at inclusion, 3, 6, 9, and 12 months after injury (see Figure 1).

Data Collection

Focus Groups

The topic of the interviews are focused on patients' experiences with the traumatic event (see Study Procedures). In addition, participants were asked to complete socio-demographic questions, the IES-R and the HADS. All focus groups have the same structure and are audio-recorded. The recorded focus groups are transcribed verbatim[25,26].

In case of observed severe symptoms of ASD or PTSD during focus group sessions, the treating physician was informed. The doctor could refer the patient for a consult with a psychologist in the department of Medical Psychology at the Elisabeth-TweeSteden Hospital who is specialized in psychological treatment after injury.

Observational Study

Data for the observational study will be collected using a structured interview (i) MINI-plus for ASD and PTSD as well as self-report questionnaires (i) the IES-R for ASD and PTSD, (ii) HADS, (iii) NEO Five-Factor Inventory (NEO-FFI) and the State Trait Anxiety Inventory (STAI)-Trait scale for personality, and (iv) World Health Organization Quality of Life assessment

instrument-Bref (WHOQOL-Bref) for QOL. All outcome measures will be assessed after treatment in the shock room (baseline), 3, 6, 9, and 12 months after injury. However, ASD and personality will only be measured at baseline (see Table 1).

Acute Stress Disorder and Post Traumatic Stress Disorder

The MINI-Plus[21] and the IES-R[29] assess ASD and PTSD symptoms. Since both instruments are often used (together) in clinical practice, we will use both in the current study.

The MINI-Plus is a short-structured interview, based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), and it will be used to assess ASD and PTSD symptoms[21]. The items are dichotomous because symptoms are present or absent. The DSM-5 is a classification of mental disorders with associated criteria designed to facilitate more reliable diagnoses of these disorders compared to the DSM-IV. It is a standard reference for clinical practice in the field of mental health[21]. For diagnostic criteria for ASD, see Multimedia Appendix 1 and for PTSD, see Multimedia Appendix 2.

The IES-R is a self-report questionnaire to assess symptom severity of ASD and PTSD[29]. It consists of 15 items which measure intrusive re-experiences of the injury and avoidance of injury-related stimuli. The respondent states whether the content of each statement was present during the past 7 days. A 4-point Likert scale will be used ranging from 0 (*not at all*) to 5 (*often*). The cut-off score for a probable diagnosis of PTSD is ≥ 33 and have good diagnostic accuracy[30,31]. The IES-R has good psychometric properties[31] and the Dutch translation of the IES-R has been found to be valid and reliable[32].

Anxiety and Depressive symptoms

The HADS measures anxiety and depressive symptoms[33]. It is a generic questionnaire measuring levels of anxiety (7 items) and depression (7 items) with a 4-point rating scale ranging from 0 (*not at all*) to 3 (*very much*). Subscale values ≥11 for one of the subgroups are observed as an indication for a psychological disorder, as this cut-off score provides the lowest proportion of false positives (5% for anxiety and 1% for depression)[33]. The questionnaire is shown to be reliable and valid[33].

Personality

Personality will be assessed using the NEO-FFI [34] and the STAI-Trait scale [35]. The 60-item NEO-FFI measures the Big Five personality domains: (1) Neuroticism, (2) Extraversion, (3) Openness to experience, (4) Agreeableness, and (5) Consciousness from the five factor model[34]. Each statement is rated on a five-point rating scale ranging from 1 (*strongly disagree*) to 5

(*strongly agree*), resulting in dimension scores between 12 and 60. The psychometrics has been extensively assessed and the internal consistency, test-retest reliability, and validity are acceptable to good[36].

TABLE 1. Overview of self-report questionnaires

Study and related questionnaires	Domain	Outcome measures	Time point for retrieval
Focus group study			
Patients' experiences	N/A	Primary outcome	N/A
IES-R	PTSD	Secondary outcome	Shortly after meeting
HADS	Anxiety Depressive symptoms	Secondary outcome	Shortly after meeting
Sociodemographic questions	Educational level Living situation Paid job	Secondary outcome	Shortly after meeting
Observational study			
MINI-Plus	ASD PTSD	Primary outcome	Baseline 3 months 6 months 9 months 12 months
IES-R	ASD PTSD	Primary outcome	Baseline 3 months 6 months 9 months 12 months
HADS	Anxiety Depressive symptoms	Secondary outcome	Baseline 3 months 6 months 9 months 12 months
NEO-FFI	Personality	Secondary outcome	Baseline
STAI-Trait	Personality	Secondary outcome	Baseline
WHOQOL-Bref	QOL	Secondary outcome	Baseline 3 months 6 months 9 months 12 months

Abbreviations: N/A: Not applicable, IES-R: Impact of Event Scale-Revised, PTSD: posttraumatic stress disorder, HADS: Hospital Anxiety and Depression Scale, ASD: acute stress disorder, NEO-FFI: NEO Five-Factor Inventory, STAI: State Trait Anxiety Inventory, WHOQOL-Bref: World Health Organization Quality of Life assessment instrument-Bref, QOL: quality of life.

The STAI (short form) consists of 20 items for measuring state anxiety (10 items) and trait anxiety (10 items)[35]. In this study, only the STAI-Trait scale will be used. This scale describes the person's tendency to experience feelings of anxiety and stress. The STAI-Trait scale has a four-point rating scale ranging from 1 (*almost never*) to 4 (*almost always*). The Dutch version of the STAI is a reliable and valid instrument[37].

Quality of Life

QOL will be measured with the WHOQOL-Bref[38]. This 26-item questionnaire is a short version of the WHOQOL-100 and assesses four domains (Physical health, Psychological health, Social relationships, and Environment) as well as one general facet "Overall QOL and General Health". The questions in the domains are derived from the 24 facets of the WHOQOL-100, with one item from each of the facets. Each item is rated on a five-point rating scale. Higher scores indicate better QOL[38,39]. The WHOQOL-Bref has good psychometric properties as prior research shows that the WHOQOL-Bref is a reliable and valid instrument[39-42].

Additional Assessments

Socio-demographic information (i.e., sex, age, marital status, and education level) will be obtained from patients at baseline. Clinical information, including date of trauma treatment, ISS, type of trauma mechanism (e.g., traffic accident or fall), type of injury (e.g., fracture), trauma treatment (e.g., operation or medication), consult or treatment from medical psychology (yes/no and which type of treatment), hospital stay (yes/no), in case of hospital stay, admission to intensive care unit, and duration of hospital stay will be abstracted from the patients' medical records. Possible logistic problems will also be recorded.

Statistical Analysis

Focus Groups

The recorded focus groups are analyzed using open, axial, and selective coding technique[25,26]. Open coding is used to identify different domains: physical, psychological, social, and environmental. Then, axial and selective coding is conducted to determine different themes. These codes consist of single words or short sentences. Two reviewers independently reviewed and coded each of the transcripts and ensured data saturation. Atlas.ti is used for analyzing the transcripts[43]. In addition, patient characteristics, PTSD, anxiety and depressive symptoms, and responses on the questionnaires were analyzed using descriptive statistics in SPSS version 22.

TABLE 2. Overview of statistical analysis

Baseline analysis and aims	Independent variables	Dependent variables	Analyses
Patient characteristics	Sociodemographics	N/A	Frequencies Descriptives
	Clinical variables	N/A	Frequencies Descriptives
	Psychological variables	N/A	Frequencies Descriptives
Comparison of patient characteristics	Participants versus nonparticipant	Sociodemographics Clinical variables Psychological variables	Continuous data: Independent t-test Mann-Whitney U Categorical data: Chi-square Fishers' exact test
	Completers versus noncompleters	Sociodemographics Clinical variables Psychological variables	Continuous data: Independent t-test Mann-Whitney U Categorical data: Chi-square Fishers' exact test
	Participants being discharged versus being in the hospital	Sociodemographics Clinical variables Psychological variables	Continuous data: Independent t-test Mann-Whitney U Categorical data: Chi-square Fishers' exact test
Aim 2: Course of ASD and PTSD	Time	ASD PTSD	Repeated measures latent class analysis
Aim 3: Risk profile	ASD PTSD	Sociodemographics Clinical variables Psychological	Repeated measure latent class analysis
Aim 4: Effect of ASD	ASD	PTSD Anxiety Depressive symptoms QOL	Linear Mixed models repeated measures

Abbreviations: N/A: Not applicable, ASD: acute stress disorder, PTSD: posttraumatic stress disorder, QOL: quality of life.
Note: The dependent and independent variables for aim 1 could not be provided, because this aim focuses on qualitative data.

Observational Study

The patient characteristic will be studied using descriptive statistics. Then, the baseline characteristics (i.e., sociodemographic, clinical, and psychological variables) of participants versus nonparticipants, participants who complete versus drop out during follow-up, and participants who are discharged versus being in the hospital after treatment in the shock room will be compared using an independent t-tests and a Chi-square tests. Non-normal continuous data will be analyzed with Mann-Whitney U tests or Fisher's exact tests.

Repeated measures latent class analysis will be used to analyze the courses (i.e., time is independent variable) of ASD and PTSD (dependent variables). Moreover, to examine if these different courses of ASD and PTSD (independent variable) could be characterized by socio-demographic (e.g., sex, age, education level, and living situation) and clinical (e.g., type of trauma, ISS, Glasgow Coma Score, being hospitalized, being treated on the intensive care unit, complications during treatment, and treated by a medical psychologist or psychiatrist), and psychological (e.g., anxiety, depressive symptoms, and personality) variables (dependent variables). As a result, each class will represent a different course of ASD and PTSD. By focusing on the characteristics of the different classes, a risk profile will, consequently, be developed to determine which patients are at risk for ASD or PTSD. Sociodemographic and clinical variables are examined as moderating effect, while psychological variables are studied as mediating effects.

Linear mixed models, repeated measures, will be used to examine the effect of ASD (independent variable) on PTSD, anxiety and depressive symptoms, and QOL domains (dependent variables) over time (see Table 2).

The ISS, type of injury and type of trauma mechanism (e.g., traffic accident or fall) will be used as covariates.

RESULTS

Data collection and analysis for the focus group study are completed. Results will be reported in 2018. Enrollment of participants for the observational study began in November 2016. Data collection will be completed by the end of 2018. The study results will then be reported in 2019.

DISCUSSION

This is the first multi-method study in trauma patients that examines psychological consequences after injury, using both a qualitative focus group study design as well as an observational prospective design. In the focus group study, the aim was to interview patients about their experiences on the injury, treatment, and rehabilitation. Since it is unknown if and in what way patients' experiences contribute to the development of psychological problems and disorders. The observational study will examine the course of ASD and PTSD. As ASD after injury is less studied and it is unknown how ASD and PTSD develop over time up to 12 months after injury. Moreover, as a result from all outcome measures, a risk profile of patients may be determined to predict which patients are at risk for developing ASD or PTSD. Altogether, this study will provide information concerning which patients to include in further research that focuses on psychological intervention.

Several factors related to the design and execution must be taken into account. First, response bias may occur in the focus group study. Patients may decline participation because they are not interested in discussing their experiences, or it might be too confronting to talk about their experiences and psychological problems. Second, it is known that the population of trauma patients has a broad variety of trauma mechanisms and injuries. Therefore, it might be difficult to generalize to the whole trauma population. However, concerning the observational study, almost all trauma patients being treated in the shock room will be included from two different Level-1 trauma centers so data saturation can be reached. These centers are located in different provinces and cities in the Netherlands. Therefore, a representative population in the observational study can be included. Third, patients with severe injuries might be less capable to complete the baseline questionnaire almost directly after injury due to being treated at the intensive care unit. Patients will, therefore, be asked to fill in the date of completing the questionnaire and if they needed any help. Then, the time between injury and measurement can be analyzed. This provides information on what time severely injured patients are capable to complete the baseline questionnaire.

In conclusion, this study is exploratory in nature and it will contribute to the need for information on psychological consequences after injury. Then, awareness in clinicians about the consequences can be created so they are able to act more effective and patient-oriented care can be provided.

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Chapter 4

PATIENTS' EXPERIENCES AND WELLBEING AFTER INJURY: A FOCUS GROUP STUDY

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ABSTRACT

Background: Injury can have physical, psychological and social consequences. It is unclear which factors have an impact on patients' wellbeing after injury. This study aimed to explore, using focus groups, patients' experiences and wellbeing after injury and which factors, impede or facilitate patients' wellbeing.

Methods: Trauma patients, treated in the shock room of the Elisabeth-TweeSteden Hospital, the Netherlands, participated in focus groups. Purposive sampling was used. Exclusion criteria were younger than 18 years old, severe traumatic brain injury, dementia, and insufficient knowledge of the Dutch language. The interviews were recorded, transcribed verbatim, and analyzed using coding technique open, axial, and selective coding, based on phenomenological approach.

Results: Six focus groups (3 to 7 participants) were held before data saturation was reached. In total, 134 patients were invited, 28 (21%) agreed to participate (Median age: 59.5; min. 18 – max. 84). Main reasons to decline were fear that the discussion would be too confronting or patients experienced no problems regarding the trauma or treatment. Participants experienced difficulties on physical (no recovery to pre-trauma level), psychological (fear of dying or for permanent limitations, symptoms of posttraumatic stress disorder, cognitive dysfunction), social (impact on relatives and social support) wellbeing. These are impeding factors for recovery. However, good communication, especially clarity about the injury and expectations concerning recovery and future perspectives could help patients in surrendering to care. Patients felt less helpless when they knew what to expect.

Conclusions: This is the first study that explored patients' experiences and wellbeing after injury. Patients reported that their injury had an impact on their physical, psychological, and social wellbeing up to 12 months after injury. Professionals with the knowledge of consequences after injury could improve their anticipation on patients' need.

INTRODUCTION

In 2017, mortality rates from injury were the highest in Dutch persons younger than 35 years of age compared to other ages[1]. Due to trauma registration and implementation of specialized trauma care, the quality of trauma care improved and survivorship increased[1-6]. Nevertheless, patients who were less satisfied with general health and recovery after injury needed more medical care, they had a longer hospital stay, and they visited the hospital more often[7]. This resulted in an increase in costs of care. In the Netherlands, the total costs of injuries were €3.5 billion annually[6,8].

After experiencing a single traumatic event (e.g., fall or car accident), survivors will go through a process of medical treatment and rehabilitation: from the ambulance or trauma helicopter to the shock room, possible hospital stay, and finally rehabilitation[9]. The shock room is situated at the emergency department and, for severely injured patients, it is the interface between prehospital management and inpatient care[10]. Adverse physical (e.g., problems on wound repair and pain)[11-13], psychological[14,15], and social (e.g., broken marriages and difficulties in resumption to work)[16,17] outcomes may occur after injury. Patients can experience anxiety[18], depressive symptoms[18,19], acute stress disorder (ASD)[20], and posttraumatic stress disorder (PTSD)[14,18,21,22] after injury. These consequences can arise almost directly after injury or months or years later[23-25]. Even though they are often not recognized, they can have an impact on patients' wellbeing. Yet, it is unclear which factors have an impact on patients' experiences and wellbeing after injury, treatment and recovery. For that reason, qualitative research is needed to evaluate patients' experiences after injury and which factors impede or facilitate patients' wellbeing.

Although patients' perspectives after injury have previously been explored, they evaluated one type of injury (e.g., traumatic brain injury (TBI) or burn injuries)[26,27] or one type of trauma mechanism (e.g., motor vehicle accident)[28,29]. Therefore, results cannot be generalized to the entire trauma population. Research is focused on recovery from different types of injury (e.g., multi trauma, spinal cord injury, and TBI)[29] will provide a broader overview than currently available.

To our knowledge, no focus group study was previously conducted that focused on a process of trauma care (i.e., treatment short after injury, in the shock room and hospital, and rehabilitation) and patients' wellbeing[30,31]. Therefore, this study aimed to explore patients' experiences and wellbeing after injury, treatment, and rehabilitation. Moreover, factors that impede or facilitate patients' wellbeing were evaluated.

MATERIAL AND METHODS

Study design

A focus group study design was used to evaluate the aims of this study. Focus groups, a commonly used method of qualitative research[32,33], were held, because they facilitate an in-depth exploration of a person's perspective through group interaction. Moreover, memories could be triggered by a comment from another participant[32,33]. Otherwise, they can also be triggered by sharing and comparing participants' own experiences[34].

This study is part of a mixed-method study. The protocol of this mixed-method has been published elsewhere[35].The medical ethical committee Brabant (METC Brabant) approved the study (project number NL55386.028.15). This study is also registered in the Netherlands Trail Register (number NTR6258). All participants gave written informed consent. Participation was voluntarily and, except for an exit ticket for the parking lot, no financial reward was given.

Participants and procedure

Eligible patients who experienced an injury, were treated in the shock room of the ETZ Hospital (Elisabeth-TweeSteden Hospital), Tilburg, the Netherlands. These patients were registered in the Brabant trauma registry and a researcher (EV) received a database from this registry. In addition to being treated in the shock room, another inclusion criterion was being aged 18 years or older. Persons were excluded if they had severe TBI (i.e., Glasgow Coma Score ≤ 8), dementia, or insufficient knowledge of the Dutch language (verbal and in writing). Patients' medical records were reviewed on eligibility. Eligible patients received an information letter and were invited to participate in the study. Then, EV contacted the patients, by telephone, to explain the purpose of the study and to ask for their participation. Patients who were willing to participate in a focus group discussion received additional information about the date, time, and location.

To attain a variety of experiences and a representative sample of the heterogeneous trauma population, patients were divided into three groups: (i) Injury Severity Score (ISS) < 16 (one single injury or mild/moderate injurie(s)), (ii) ISS ≥ 16 (i.e., severe multiple injuries), and (iii) mild or moderate TBI (i.e., Glasgow Coma Score ≥ 9). Six to ten patients were invited to participate in each group. In addition, patients were selected based on sex and age. The researcher (EV) invited equal numbers of male and female patients and a variety of ages for each group in order to attain a variety of experiences and a representative sample of the trauma population. In this way, the presence of maximum variability within the primary

data could be warranted, the maximum variation sampling could be clearly set out, and trauma patients with all kind of trauma mechanism and injuries could be included. The purposive sampling method was used[32,33].

In order to obtain reliability and validity[36,37], a manual was developed. The purpose of the focus groups, diversity of study population, and the procedure of the focus groups itself (e.g., introduction by the moderator, questions for participants (e.g., data collection), and finishing the discussion) were set out in this manual. Clear research questions were needed to obtain relevant answers (i.e., validity) and to ensure that the study is replicable (i.e., reliability)[37]. All focus groups had the same structure and were audio-recorded. Two reviewers (EV and BDO) independently reviewed the transcripts to ensure that data saturation (i.e., no new information was found during discussions) was reached. Moreover, to strengthen validity and comprehensiveness, this study was conducted and reported according to the consolidated criteria for reporting qualitative research (COREQ) checklist for qualitative research[36].

Data collection

The focus group meetings took place in a conference room at the hospital. The focus groups were led by a moderator (EV) and an assistant (MT). The moderator started the focus group by giving an introduction of the moderators and the purpose of the focus group meeting. Then, the patients were asked to share their experiences, by answering the main questions "Which experiences after injury impressed you the most?" and "Can you describe the consequences of injury on your life?"". Then, follow-up questions were asked by the moderator to obtain how these experiences impede or facilitate patients' wellbeing, for example; "Could you describe your feelings after injury, hospitalization, and rehabilitation?". In addition, in order to stimulate conversation flow and involve other participants in the discussions, follow-up questions were asked, for instance, "Does someone (i.e. another participant) recognize these experiences, consequences, or feelings?" and "In what way do you experience changes in wellbeing?". Using this method, the moderator made sure that every participant had the opportunity to interact in the discussion and that participants were motivated to talk with each other[32,36]. Participants' experiences were clustered on a flipchart on the basis of the trauma procedure; (i) moment of injury, (ii) treatment from medical staff from the ambulance or the trauma helicopter, (iii) treatment in the shock room, (iv) hospital stay, (v) moment of discharge, and (vi) period after discharge and/or rehabilitation. Also, the assistant moderator took field notes, handled logistics, and monitored the audio recording equipment[32].

At the end of each focus group, participants provided information on sociodemographics (i.e., age, sex, marital status, and education level). In addition, they completed the self-report questionnaires; Impact of Event Scale revised (IES-R) for measuring PTSD and the Hospital Anxiety and Depression Scale (HADS) for measuring anxiety and depressive symptoms.

The 22 items IES-R measures symptoms severity of intrusion, avoidance, and hyperarousal. It uses a 5-point Likert scale ranging from 0 (*not at all*) to 4 (*extremely*)[38]. The cut-off score for a probable diagnosis of PTSD is ≥ 33. The IES-R, as well as the Dutch version, has good psychometric properties[38,39].

The HADS assess anxiety (7 items) depressive symptoms (7 items) and uses a 4-point rating scale ranging from 0 (*not at all*) to 3 (*very much*). Cut-off scores of ≥11 for one of the subscale were regarded as a psychological complaint. The questionnaire is shown to be reliable and valid[40] and has good psychometric properties[41].

Data analysis

The focus group meetings were analyzed using a phenomenological approach[42]. The recorded focus groups were transcribed verbatim. Then, data analysis proceeded stepwise using the open, axial, and selective coding technique[32,33]. First, open coding was used to identify experiences and consequences of injury on patients' wellbeing: physical, psychological, and social wellbeing. In addition, moments in time of trauma treatment or recovery, which were related to patients' experiences were explored. Then, axial and selective coding was used to interpret and explain patients' experiences by determining different themes and subthemes (level 1 and level 2) based on physical, psychological, and social wellbeing. These codes consisted of short sentences or single words, for example, 'ASD symptom' (i.e., theme (level 1) in psychological wellbeing) and 'nightmares' (i.e., subtheme (level 2) of ASD in psychological wellbeing), or 'dependent of care' (i.e., theme in social wellbeing), 'loss of control' (i.e., subtheme level 1 in social wellbeing) and 'reassurance to hear voice of relative' (i.e., subtheme level 2 in social wellbeing).

Two researchers (EV and BDO) independently coded and analyzed each of the transcripts Using the computer program Atlas.ti was. Demographics and responses on the questionnaires were analyzed chi-square tests and independent t-tests using SPSS version 24.

RESULTS

After six focus groups data saturation was reached. The duration of the meetings varied between 60 to 90 minutes. In total, 135 patients were invited of which 28 (21%) agreed to participate (Figure 1).

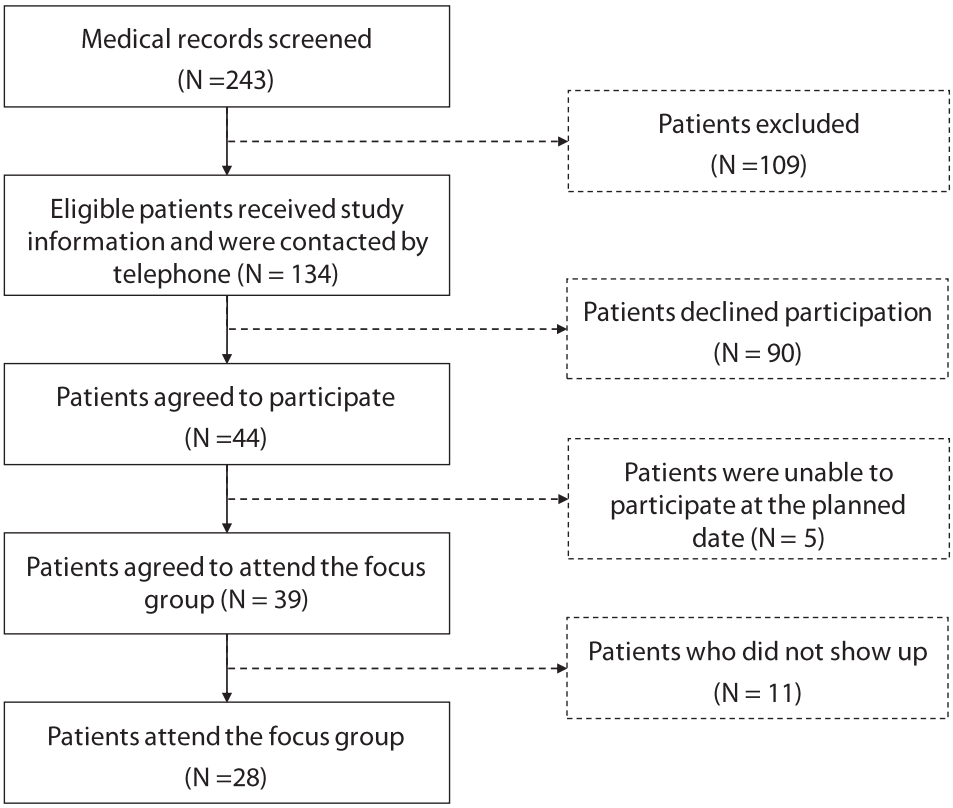

FIGURE 1. Flowchart of patient inclusion

The main reasons for declining participation were that patients indicated that they did not have enough time to participate (22%) or they did not experience any problems after injury (9%). In contrast, a subgroup declined, because participation was too confronting for them (19%). They were afraid that sharing experiences with others could be a trigger for re-experiencing their trauma. The six groups consisted of three up to seven participants (Table 1). The median age was 59.5 (min. 18 – max. 84) and the mean ISS was 11.8 (SD = 9.9).

Based on the IES-R, six (27%) focus group patients had a possible diagnosis of PTSD 12 months after injury. Patients with a possible diagnosis scored different on the subscales. For example, one patient scored *moderately* (score: 2) on avoidance and *extremely* (score: 4) on intrusion and hyper arousal, whereas two other patients scored *quite a bit* (score 3) on all subscales. With regard to the HADS[40], five (22%) patients were anxious and four (17%) had depressive symptoms 12 months after injury. Four patients (17%) showed symptoms of PTSD, anxiety and depression.

TABLE 1. Participants' characteristics

Age*	58.1 ± 16.1
Sex	
Male (N, %)	20 (71%)
Female (N, %)	8 (29%)
Living situation	
Alone (N, %)	5 (19%)
With parents (N, %)	2 (8%)
With a partner, no children (N, %)	11 (42%)
With a partner and children (N, %)	7 (27%)
Alone, with children (N, %)	1 (4%)
Educational level	
Low (N, %)	4 (15%)
Middle (N, %)	13 (50%)
High (N, %)	9 (35%)
Paid job	
Yes (N, %)	13 (50%)
No (N, %)	13 (50%)
Type of trauma	
Fall (N, %	18 (64%)
Accident (N, %)	10 (36%)
ISS score *‡	11.8 ± 9.9
ISS < 16 (N, %)	13 (57%)
ISS ≥ 16 (N, %)	10 (43%)
Time between trauma and focus group (m) *	7.9 ± 3.5
IES score *	21.2 ± 22.0
Avoidance *	0.9 ± 0.8
Intrusion *	1.0 ± 1.2
Hyperarousal *	1.1 ± 1.2
HADS anxiety *	5.8 ± 5.5
No anxiety (N, %)	15 (68%)
Doubtful (N, %)	2 (9%)
Anxiety (N, %)	5 (23%)
HADS depressive symptoms *	5.0 ± 5.3
No symptoms (N, %)	16 (70%)
Doubtful symptoms (N, %)	3 (13%)
Depressive symptoms (N, %)	4 (17%)

** The means and standard deviations are provided, unless stated otherwise. ‡ISS scores could be calculated only for patients who were hospitalized after treatment in the shock room and not for patients who were discharged after treatment in the shock room. Abbreviations: ISS = Injury severity score; m = months; IES = Impact of event scale; HADS = hospital anxiety and depression scale*

During the focus group discussions, seven patients described symptoms of PTSD during rehabilitation, such as having (severe) sleeping problems or nightmares, or re-experiencing trauma. Two of these patients were diagnosed with PTSD by a registered health psychologist, of which one patient (veteran) was diagnosed with PTSD before injury. The other patient developed PTSD as a result of her trauma. This patient also had limited physical (e.g., pain) and psychological functioning (e.g., concentration problems) in such a way that she lost her job and needed to stop her education.

Physical wellbeing

Table 2 shows the major themes and subthemes of physical wellbeing after injury.

Patients reported not being recovered to the pre-trauma functional level, because physical limitations were still present after 12 months.

TABLE 2. Major themes and subthemes of physical wellbeing

Major theme	Subtheme level 1	Subtheme level 2	Moment of procedure
Physical limitations	Inability to communicate	-	Shock room
	No recovery to pre-trauma function	-	Rehabilitation
	Adaptation to physical limitations	Pain, headache or stiffness	Rehabilitation
	Coping	Desire for quick recovery	Rehabilitation
		Intervention by medical staff	Rehabilitation
		Need to slow down	Rehabilitation
Energy level	Activities requires a lot of effort		Rehabilitation

"The physician said that my complaints would diminish over time. However, I still cannot walk well and I am in pain every day. I lost my job and I had to quit my education. Most difficult is that I am only 18 years old and I have lost everything (Female, ISS < 16)".

Patients experienced that the time they needed to recover from activities was much longer than they expected to be. They had to take small steps during rehabilitation, because they experienced physical limitations (e.g., pain or fatigue). Especially severely injured patients (ISS ≥ 16) stated that they ignored physical limitations, because they were motivated to work hard and fully recover as soon as possible.

"I wanted to recover as quickly as possible, but I was hampered by others (rehabilitation specialist or psychotherapists). It was very difficult to cope with that, because I wanted to make progress instead of doing nothing (Male, ISS < 16)".

However, the rehabilitation specialist or physiotherapist often instructed them to slow down in order to respect their physical boundaries. Patients stated that rehabilitation, in this phase, could be frustrating.

"I had to adapt all the time during rehabilitation, because I was not physically capable to rehabilitate the way I hoped and thought I could (Male, ISS < 16)".

Yet, looking back on this rehabilitation phase, patients acknowledged that the rehabilitation specialist, physiotherapist, and nurses played an important role by guiding the patients how they could recognize, adapt, and cope with their physical boundaries. Moreover, health care professionals (HCPs) educated patients how to balance activities and rest, because activities takes a lot of energy. In this way, patients were able to keep their limitations in mind so they did not cross their boundaries.

"It takes a lot of effort to do the things I like to do (Female, ISS < 16)".

Psychological wellbeing

Table 3 shows the major themes and subthemes related to psychological wellbeing after injury.

Severely injured patients experienced a fear of dying short after injury, during treatment in the ambulance, and in the shock room.

"Then just after injury, I saw blood spouting from my leg. I thought that I had an arterial bleeding and was convinced that I would die within a few minutes (Female, ISS ≥ 16)".

During hospitalization and recovery, patients realized that they survived the injury. The previously experiences fears, like fear of dying, were followed by a fear for permanent physical limitation.

"The perspective of ending up in a wheelchair was difficult, because I am a fanatic sportsman (Male, ISS ≥ 16)".

TABLE 3. Major themes and subthemes of psychological wellbeing

Major theme	Subtheme level 1	Subtheme level 2	Moment of procedure
Fear/anxiety	Going to die	-	Injury
	Severe injury	Worse physical outcome	Injury
	Lack of clarity about the cause of trauma	-	Shock room
	No memories	Nightmares	ICU
	Future perspective	-	In hospital
Helplessness	-		Shock room
	Motivation for recovery	-	Rehabilitation
Uncertainty	Lack of clarity about treatment	-	Shock room
	Future perspective	-	In hospital
			Rehabilitation
Processing trauma	Severity of the injury	-	Shock room
	Realizing that one survived	-	In hospital
	Trust in a positive outcome	-	In hospital
	Acceptance	Difficulties with acceptance	Rehabilitation
	Mentally unstable	-	Rehabilitation
Coping	Avoidance	Fear of falling	Rehabilitation
		Facing emotions	Rehabilitation
	Relapse to an old addiction (*e.g., smoking/drinking*)	-	In hospital Rehabilitation
	Feelings of revenge	-	Rehabilitation
ASD symptoms	Nightmares	-	In hospital (*e.g., ICU*)
	Flash backs	-	In hospital
PTSD symptoms	Re-experiencing trauma	-	Rehabilitation
	Being mentally unstable	-	Rehabilitation
	Sleeping problems	-	Rehabilitation
Subjective personality changes	Easier satisfied	-	Rehabilitation
	Response shift	-	Rehabilitation
	No memories of personality before trauma	-	Rehabilitation
Emotion changes	Intensified	-	Rehabilitation
Behavioral changes	Being more careful	-	Rehabilitation
Cognitive function	No memories about injury	-	Injury
			Shock room
	Memory difficulties	-	Rehabilitation

TABLE 3. Continued

Major theme	Subtheme level 1	Subtheme level 2	Moment of procedure
	Mental fatigue	-	Rehabilitation
	Forgetful	-	Rehabilitation
	Reduction in information processing speed	-	Rehabilitation
	Difficulties with recognition of persons	-	Rehabilitation
	Concentration difficulties (*e.g., reading*)		Rehabilitation
	Resumption of work		Rehabilitation

Abbreviations: ICU: Intensive care unit; ASD: acute stress disorder; PTSD: Posttraumatic stress disorder

The fear for permanent physical limitations caused uncertainty about the future. Patients did not know what to expect. In addition, patients who were sedated, were unconscious, or had posttraumatic amnesia during treatment in the ambulance and shock room, described that they were confused and anxious about what had actually happened.

"My anxiety emerged during treatment in the shock room. I mainly had questions about the cause of my injury, for instance: 'What did I experienced?' and 'What has happened to me'? (Male, ISS ≥ 16)".

"The most impressive memory was when I woke up on the ICU after three days of being unconscious. I thought I had a nightmare, but my nightmare was in fact reality (Male, ISS ≥ 16)".

Then, during hospital stay and after being discharged, patients described symptoms of ASD during hospitalization and/or PTSD during rehabilitation.

"During the first weeks after injury, I had a lot of nightmares about my leg amputation (Female, ISS ≥ 16)".

"When I am sad, I see the white car approaching me and I re-experience the injury again (Female, ISS ≥ 16)".

In contrast, patients stated that feelings of helplessness and being dependent of others were difficult experiences to cope with. Especially severely injured patients (ISS ≥ 16) discussed that they were motivation to recover, because they wanted to be autonomous instead of feeling helpless.

"I did not want to feel helpless. Therefore, I was very motivated to recover (Male, ISS ≥ 16)".

In addition to patients' frustrations, angriness, and other negative feelings, they also stated that they experienced adverse and favorable outcomes concerning their (subjective) personality, emotions, and behavior. Changes in (subjective) personality are describe by the participant selves and not determined by a questionnaire. Patients felt satisfied with these changes.

"The trauma changed me. Before my injury, I was quite a reserved person, but now I am more open and kind (Male, ISS ≥ 16)".

"My emotions became more intense. For example, when I am happy, I am happier than I used to be (Male, ISS ≥ 16)".

"Due to trauma, I became easier satisfied instead of being a perfectionist (Female, ISS < 16)".

Patients often had no memories about their injury and treatment in the ambulance. The first memories emerged during treatment in the shock room or during hospitalization. Patients reported mental fatigue during rehabilitation. Moreover, they experienced (in some cases) permanent cognitive problems with recognition of persons, concentration (e.g., reading), reduction in information processing speed, and being forgetful. They also experienced mental fatigue.

"It just feels like I am ten years older. My mental speed is reduced. I am not the person who I used be (Male, ISS ≥ 16)".

Cognitive dysfunction resulted in problems with resumption of work.

"I would like to have a job, however, I have to accept that I am not able to work anymore, because I am not able to concentrate and cannot even read a book (Male, ISS < 16)".

To deal with psychological consequences (e.g., anxiety, changes in subjective personality, and cognitive dysfunction, Table 3), some patients described to use an avoidance coping strategy during hospitalization and/or rehabilitation. As they avoided trauma-related physical activities. They had a fear of falling.

"My bike is still there but I do not look at it anymore (Male, ISS < 16)".

Patients tended to tone down the impact of their trauma by thinking: 'It is just an injury'. However, looking back on the trauma procedure, they acknowledged that they should not underestimate the impact of their trauma.

Social wellbeing

Table 4 shows the major themes and subthemes of social wellbeing after injury, including experiences that are related to the environment.

Patients' injury had an impact on their family, because their family feared that the patient would not survive the physical trauma.

"The impact of my trauma is bigger for my family than for myself (Male, ISS ≥ 16)".

This fear often resulted in partners who became overanxious during rehabilitation.

"My wife pleases me not to go on the bike by saying: "Go find another hobby" (Male, ISS < 16)".

In addition, a patient acknowledged that his injury, the fact that he became dependent of others had negatively influenced his marriage.

"I was angry all the time because of physical limitations I became dependent of others. It was difficult for my wife to cope with my angriness. Due to my rehabilitation, I felt a little bit better, because limitations decreased (Male, ISS < 16)".

Patients experienced a loss of control when they had difficulties with being dependent of care from family and health care providers.

"It was frustrating to be dependent of care (e.g., need help by taking a bath), because I found it difficult to be naked, but I had no choice (Female, ISS < 16)".

Although being dependent of others can be difficult, patients were grateful with the help they received from others. Moreover, patients thought that support of relatives and friends could help them to recover.

"When I got out of bed I was not able to walk. In a period of time, I have learned to walk again step by step with the support of others. In the future, I will ride my bike again (Male, ISS < 16)".

TABLE 4. Major themes and subthemes of social wellbeing

Major theme	Subtheme level 1	Subtheme level 2	Moment of procedure
Impact on relatives	Fear that patient would be dead	-	Injury Shock room
	Panic	-	Injury
	Overanxious	-	Rehabilitation
	Relationship problems	-	Rehabilitation
Dependent of care	Loss of control	Reassurance to hear voices of relatives	Injury
Social support	Help from neighbors	-	Rehabilitation
	No one to fall back on	-	Rehabilitation
	Need for social interaction	-	Rehabilitation
Communication health care provider ↔ patient	Reassurance by nurse	Surrender to care	Shock room
	Lack of clarity about injury severity	Need for further explanation	Shock room
	Lack of clarity about patients' treatment		Shock room
		No time to respond because of treatment protocol	Shock room
	Feel not taken seriously	-	In hospital
	Lack of clarity about future expectations	Need for further explanation	Rehabilitation
Take self-initiative to receive medical care	-	-	In hospital
			Rehabilitation
Communication health care providers → relatives	No update about treatment	-	In hospital
Communication between medical staff	No information transfer	-	In hospital
Communication hospital → GP	No information transfer	-	Rehabilitation
Communication hospital ↔ authorities	No information transfer	-	Rehabilitation
Communication authorities ↔ patient	No information transfer	-	Rehabilitation
Media attention	Negative effect of incorrect information	-	Injury

TABLE 4. Continued

Major theme	Subtheme level 1	Subtheme level 2	Moment of procedure
	Prejudices from others resulting from false information	-	Rehabilitation
Practical problems	Insurance	Financial problems	Rehabilitation
		Claim for damages	

Abbreviations: ↔: between; →: from – to; GP: General practitioner

Moreover, patients felt reassured when they heard voices of relatives shortly after injury. Especially elderly patients (i.e., > 70 years old), who were dependent of relatives' care before injury, reported that the need for the right social support is crucial. These patients experienced more difficulties with social support, because they had a limited social network and in some cases (almost) no one to fall back on compared with younger participants.

"I am all alone after losing my wife a few years ago (Male, ISS ≥ 16)".

"I need a lot of help from my neighbors, because my children live far away (Female, ISS < 16)".

Almost every participant thought that communication could be improved between medical staff in hospital, general practitioners, authorities, and patients. Since almost every patient provided an example of not being well or incorrectly informed by a HCP. For instance, during hospitalization, patients needed more information about their treatment or prognosis of recovery.

"If they (physicians) explained the consequences of my brain injury more clearly, then I would be more able to cope with the consequences (Male, ISS≥16)".

Patients illustrated that medical staff could reassure them during treatment. In addition, they could also clarify patients' injury severity and inform them about their treatment, prognosis, and future outcomes. However, during hospital stay, patients felt that there was limited time for information transfer. Furthermore, they had to take on one's own initiative for receiving care. Patients thought that good communication could facilitate recovery during hospital stay and recovery.

"I had to ask everything, including my medication, because I did not receive the care I needed (Male, ISS < 16)".

"I had to wait a while to be referred for rehabilitation. So, I was the one who arranged physiotherapy during that period, because I wanted to recover (Male, ISS ≥ 16)".

Patients described that lack of clarity about their injury severity and trauma treatment emerged during treatment in the shock room.

"It (shock room) was very hectic, because different physicians were present. Also, I went back and forth to several rooms for different examinations. I had no idea what happened during treatment (Male, ISS ≥ 16)".

At that moment, patients experienced a lack of communication between themselves and HCPs since there was no time to communicate.

"One of the medical staff asked me: "Can we cut your clothes?" But before I could answer, I lay in my naked butt (Male, ISS < 16)".

Patients felt that they were not being taken seriously due to a lack of communication. If information was provided, some patients did not completely understand it. Medical jargon was often used. In addition, multiple physicians were involved in patients' treatment, but they did not introduce themselves or explained what they were doing. Patients felt a loss of control in this overwhelming situation. Therefore, due to a lack of information transfers, patients reported that being well reassured short after injury and during treatment in the shock room could help them to surrender to medical care.

"The nurse was very kind to me. She told me: "It is going to be ok and we will take good care of you." (Female, ISS < 16)".

Moreover, patients reported miscommunication between authorities (e.g., hospital and general practitioners or hospital and rehabilitation specialists).

"I assumed that my GP was informed by the hospital about my injury. Unfortunately, he did not receive any information (Male, ISS < 16)".

Patients described that the media attention negatively affected patients' social interactions after injury, because the media provided false information.

"Within half an hour there was some story on the news about two seriously injured people, but that was incorrect. This news caused a lot of gossip in town (Male, ISS < 16)".

After being discharged and during rehabilitation, patients reported having problems with practical issues, such as problems with finance, health insurance, or difficulties with the re-examination for their driver's license. Although patients were dependent on authorities, they needed to take own initiative to solve these problems.

"I am frustrated because the claim for damages has been rejected (Male, ISS ≥ 16)".

DISCUSSION

This study aimed to explore and describe patients' experiences and wellbeing after injury, treatment, and rehabilitation. Moreover, factors that impede or facilitate patients' wellbeing were examined. Patients explained that they did not recovered to their pre-injury functional level up to12 months after injury. One of the reasons could be the presence of PTSD, anxiety, and depressive symptoms 12 months after injury, which is in line with previous studies[28,43]. Moreover, patients experienced feelings of helplessness, a fear of dying, and/or a fear for a worse outcome short after injury and during treatment in the shock room. They illustrated that feelings of loss of control occurred, because treatment in the shock room was explained as overwhelming and patients needed to surrender to care. Also, patients stated that they needed more information about the injury and treatment when they were in the ambulance and shock room, especially when they did not remember their injury. In some cases, it can be difficult to inform the patient when rapid screening and treatment in the shock room is crucial for survival. In this life-threatening phase, the main goal is fast recognition and prompt treatment of severe injuries[10] by 'treat first what kills first' (i.e., ABCDE-method in trauma treatment)[44]. This has shown to be essential for long-term outcomes[10]. Nevertheless, patients illustrated that reassurance by a physician or nurse could help them to surrender to medical care. Moreover, in line with other studies, nurses could help them to cope with feelings of insecurity[30,45].

Furthermore, this study showed that patients had to deal with adverse changes in physical (i.e., pain, stiffness), emotional, cognitive functioning[46], and (subjective) personality[47,48]. For instance, memory impairment, loss of autonomy, and problems in work, marriage and income, could play an important role as obstructive indicators for these changes[46]. In line with the literature, changes in personality could be related to TBI[48-50], while patients' perception on positive changes in (subjective) personality or emotions might be a result from a change in internal standards or values, i.e., response shift[47]. Furthermore, satisfaction with care improved if a health care provider was interested and involved in patients' care

and recovery[28,51]. Especially during rehabilitation, when patients struggled with resumption to work and financial stress, the need for positive support from their employer or authorities was high[26,29,52].

In addition, patients stated that good communication regarding treatment and rehabilitation is imperative and it needs further improvement[28]. Lack of clarity about patients' treatment or prognosis, emerged when patients were not well, insufficient, or incorrectly informed by the doctor about expectations and consequences of injury on their wellbeing (i.e., physical, psychological, and social). Moreover, patients felt that they were not being heard by HCP. There is a need for further explanation about the outcome of recovery on all domains. One of the reasons for lack of clarity or insufficient information transfer was that patients could not remember the provided information as a result of cognitive deficits from injury. Another reason could be found in limited time to contact between patients and HCPs, which can be a result of high workload and time pressure[53]. Furthermore, patients had to take self-initiative for receiving care (e.g. asking about their own medication), which could be frustrating when they were dependent of others. Miscommunication could be due to a lack of connection or expectations in communication[51]. For example, the content of communication from a trauma surgeon could be oriented on medical or physical outcomes whereas patients' content was focused on personal (i.e., emotional of psychological) needs[51]. Another reason for the presence of miscommunication could explained by the concept of testimonial injustice (i.e., gaining knowledge by being told by others)[54], which is part of epistemic injustice[55].

To our knowledge, this is the first study that explored patients' perspectives on injury, treatment in the shock room and hospital, and rehabilitation using a focus group design. This provided knowledge insight which experiences were present on a specific moment after injury. For instance, after being treated in the shock room, a fear of dying during treatment in the shock room could change in anxiety for permanent physical limitations during hospitalization of rehabilitation. Moreover, the focus has been on psychological consequences and functioning. These topics were under evaluated in the field of trauma research. Moreover, trauma patients with different types of injuries (e.g., fractures, upper and/or lower extremity injuries, traumatic amputation, and TBI) and trauma mechanism (motor vehicle accident, fall, and collision) were included. The qualitative design of this study facilitated an in-depth exploration about patients' experiences. In-depth discussions were stimulated, because participants shared their perspectives. Finally, the focus groups were led by the same moderator and conducted in the same standardized manner. The focus groups were conducted using a reliable and valid methodology which resulted

in robust data with group data saturation[32,33,42]. To facilitate validity, all participants were capable to answer the research questions. They also provided a whole range of responses to the research questions to attain reliability.

Nevertheless, some limitations must be taken into account. First, the low response rate (21%) probably implied response bias[56]. In line with the literature[56,57], patients who declined participation were not interested, because they did not have any physical or psychological problems after trauma. Other patients explained that participation was too difficult, because they could be faced with their psychological problems (e.g., re-experiencing the trauma) when they were triggered by the group discussion . They did not want that. Another limitation was that one of the six focus group consisted of only three participants, because two other patients did not show up. Although this small number could influence the quality of the group dynamic[58], all three participants participated in the discussions in a way that group interaction occurred. This is in line with the literature, which illustrate that smaller focus groups could allow participants to open up about their experiences instead of larger groups[59]. Nevertheless, larger groups can facilitate more in-depth exploration of a persons' perspectives and ideas. Third, selection bias could have occurred, because participants needed to be capable provide informed consent form. Otherwise, without consent, persons could not participate in this study. Our study population consisted of mainly Caucasian participants since sufficient knowledge of the Dutch language was an inclusion criterion.

Results from this qualitative study obtained several implications for future research and clinical practice. Since only patients participated in this study, future research could focus on how trauma care and patients' recovery can further be improved by studying HCPs' (e.g., trauma surgeon, emergency doctor, rehabilitation specialist, etc.) perspectives, their expectations and their role in providing health care. In addition, health care providers must be aware that, in addition to medical traumas, patients can suffer from psychological traumas (e.g., ASD and PTSD) and impaired wellbeing directly or months after injury. Nevertheless, HCPs' contribution in care might affect patients' recovery, because satisfaction with care could facilitate recovery. In order to predict who is at risk for psychological problems and disorders, patients can be screened almost directly after injury using the Injured Trauma and Survival Screen (ITSS)[60] or the Psychosocial Screening Instrument for physical Trauma patients (PSIT)[61]. Then, patients can be prevented from physical, psychological, and social consequences by providing early psychological treatment during hospitalization to improve patients' wellbeing[62].

CONCLUSION

Patients reported that their injury had an impact on their physical, psychological, and social wellbeing after injury. These consequences were present up to 12 months after injury. HCPs with the knowledge on physical, psychological, and social consequences could, according to patients, improve anticipation on patients' needs. This might contribute to patients' satisfaction with health care.

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Chapter 5

PSYCHOLOGICAL RISK FACTORS THAT CHARACTERIZE TRAJECTORIES OF POSTTRAUMATIC STRESS DISORDER AFTER INJURY: A STUDY USING LATENT CLASS ANALYSIS

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ABSTRACT

Purpose: Our aims were to identify different longitudinal trajectories of posttraumatic stress disorder (PTSD), to establish a risk profile based on patients' sociodemographic, clinical, and psychological characteristics, and to study the effect of acute stress disorder (ASD) on PTSD during the 12 months after trauma.

Methods: Patients completed questionnaires after inclusion and at 3, 6, 9, and 12 months afterward. Trajectories were identified using repeated measures latent class analysis (RMLCA). The risk profile was based on a ranking of importance of each characteristic using Cohen's d effect sizes and odds ratios. The impact of ASD on PTSD was examined using logistic regression analyses.

Results: Altogether, 267 patients were included. The mean age was 54.0 (SD=16.1), 62% were men, and the median injury severity score was 5.0 [2.0-9.0]. The prevalence rates of ASD and PTSD were approximately 21.7% at baseline, and 36.1% of trauma patients exhibited PTSD at 12 months after injury. Five trajectories were identified: (1) no PTSD symptoms, (2) mild, (3) moderate, (4) subclinical, and (5) severe PTSD. These trajectories seemed to remain stable over time. Compared with patients in other trajectories, patients with (subclinical) PTSD were younger and scored higher on anxiety, depressive symptoms, neuroticism, and trait anxiety. Patients with ASD were significantly at risk for developing PTSD (OR = 7.82; 95% CI: 3.73-14.23).

Conclusions: Psychological factors primarily characterized PTSD trajectories during 12 months post-trauma. Healthcare providers who are aware of these findings could identify patients at risk for PTSD and refer them for patient-centered interventions.

INTRODUCTION

The number of Dutch patients who are treated in the emergency department (ED) after injury has increased in recent years, from approximately 68,000 in 2010 to approximately 78,000 in 2018[1]. Injury patients have reported impaired functioning and psychological problems and disorders. These consequences occurred directly, months, or years later[2]. Moreover, symptoms of posttraumatic stress disorder (PTSD) are a major barrier to recovery up to 24 months after injury[3]. Several risk factors for PTSD after injury have been found, including female patients, younger age[4,5], admission to the intensive care unit (ICU), anxiety, and depressive symptoms[6-8]. Injury patients who are diagnosed with acute stress disorder (ASD) have a higher risk of developing PTSD[9,10]. However, these studies did not take ASD into account as a prognostic factor. Therefore, it is still unknown what the effect of ASD on PTSD is and whether patients with or without ASD develop PTSD. Personality traits (e.g., neuroticism and extraversion), possible predictors of PTSD, have not yet been examined in injury patients. Only one study revealed that personality traits predicted quality of life in orthopedic patients[11].

In the last decade, the development of PTSD has been increasingly studied using repeated measures latent class analysis (RMLCA)[5,7,12]. However, trajectories have mostly been evaluated in a subset of the trauma population[13,14]. Research is needed that will consider a variety of causes of trauma exposure as well as single and multiple severe injuries[5]. The follow-up period and measurements in recent studies have often been limited[14,15], or investigations have used a cross-sectional design[16,17]. Hence, multiple measurements during a longer follow-up period are needed.

To our knowledge, no study has established a risk profile for PTSD after trauma based on sociodemographic, clinical, and psychological aspects. Thus, this study aimed to identify distinct trajectories of PTSD up to 12 months after injury. Further, patients' sociodemographic, clinical, and psychological characteristics were scrutinized for each trajectory, allowing to develop a risk profile and to determine which patients are at risk for PTSD. Finally, the effect of ASD on PTSD over time was studied to determine the odds of developing PTSD given an earlier ASD diagnosis.

METHODS

Participants

Trauma patients aged 18 or older treated in the trauma room between November 2016 and November 2017 at Elisabeth-TweeSteden (ETZ) Hospital were asked to participate in this

study. The ETZ Hospital in Tilburg, the Netherlands, is a level-1 trauma center in the province of Noord-Brabant. The exclusion criteria were severe traumatic brain injury (i.e., Glasgow coma score [GCS] ≤ 8), dementia, or insufficient knowledge of the Dutch language (verbally and in writing).

Study design and procedure

Patients were asked to participate by either the emergency doctor or the researcher (EV). Patients signed two informed consents. First, in the ED after receiving treatment in the shock room and being informed by the doctor. Then 1-5 days later, patients again confirmed participation to make sure that they had sufficient time to consider participation in the study. As soon as they were lucid, previous unconscious patients were informed and asked to participate. All obtained information was destroyed for patients who did not sign the second informed consent and declined further participation.

This study is part of a mixed-method study. The study protocol has been published elsewhere[19]. This study (protocol number: NL55386.028.15) has been reviewed and approved by the Medical Ethical Committee Brabant (METC Brabant) on December 4, 2015. The study has been registered in the Netherlands Trial Registry (number NTR6258). To strengthen validity and comprehensiveness, this study was conducted and reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist[20]. Participation was voluntarily and no financial reward was given.

Data collection

Sociodemographic information (i.e., sex, age, living situation, education level, and employment) was obtained from patients at baseline (after confirming their participation). Using their medical records, clinical information was prospectively gathered, including the type of trauma mechanism (e.g., motor vehicle accident), type of injury (e.g., spinal cord injury), injury severity score (ISS), GCS, surgery (yes/no), hospital stay (yes/no), ICU admission, length of stay, psychiatric history (yes/no), and consultation or treatment by a medical psychologist (yes/no).

The patients completed a baseline questionnaire on sociodemographics, ASD, PTSD, anxiety, depressive symptoms, and personality. Clinical information was retrieved from the patients' medical records. PTSD was further assessed at 3, 6, 9, and 12 months after injury[18].

Since the MINI International Neuropsychiatric Interview (MINI-Plus) and the Impact of Event Scale-Revised (IES-R) for diagnosing ASD and PTSD are often used (together) in clinical practice, they employed both in this study. However, the IES-R has a higher sensitivity than the MINI-Plus. Therefore, the results from the IES-R are considered the most important. The

IES-R is a self-report questionnaire to assess the symptom severity of PTSD; it consists of 22 items that gauge intrusive re-experiences[20]. It contains a 4-point Likert scale ranging from 0 (*not at all*) to 4 (*often*). The cutoff score for the diagnosis of PTSD is ≥ 33 and shows good diagnostic accuracy[21,22]. The Dutch translation has good psychometric properties [23] and is reliable and valid in various trauma populations[24].

The MINI-Plus is a short-structured interview based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-5); the researcher (EV) conducted the interviews to assess ASD at baseline and PTSD symptoms at follow-up[25]. For ASD, the MINI-Plus contains 14 dichotomous items (i.e., the absence or presence of symptoms) and 20 dichotomous items for PTSD. Patients can be diagnosed with ASD if at least nine symptoms are present in any of the five categories (e.g., intrusion, negative emotions, dissociation, avoidance, and arousal). In contrast, PTSD is indicative when at least one or two symptoms are present in each domain (i.e., intrusion ≥ 1, avoidance ≥ 1, negative emotion ≥ 2 and ≥ 2 arousal).

The HADS is a generic questionnaire that measures anxiety and depressive symptoms[26]; it determines levels of anxiety (7 items) and depression (7 items) with a 4-point rating scale ranging from 0 (*not at all*) to 3 (*very much*). The scores for both subscales range from 0 to 21. The cutoff score for disorder is ≥ 11[26]. The questionnaire is reliable and valid in patients with traumatic brain injury[27].

The 60-item NEO Five Factor Inventory (NEO-FFI) measures the Big Five personality domains: (1) neuroticism, (2) extraversion, (3) openness to experience, (4) agreeableness, and (5) conscientiousness based on the five-factor model[28,29]. Each statement is rated on a five-point rating scale ranging from 1 (*strongly disagree*) to 5 (*strongly agree*). Scores in each domain range between 12 and 60. The psychometrics (i.e., internal consistency, test-retest reliability, and validity) are acceptable to good in injury patients[30].

The State-Trait Anxiety Inventory (STAI) (short form) consists of 20 items for measuring state anxiety (10 items) and trait anxiety (10 items)[31]. In this study, only the STAI-Trait scale was used, which describes a person's tendency to experience feelings of anxiety and stress. The STAI-Trait scale has a four-point rating scale ranging from 1 (*almost never*) to 4 (*almost always*). The Dutch version of the STAI is a reliable and valid instrument in the general population[31].

Data analysis

Missing item-level data of the IES-R and the HADS at a particular time point were imputed with individual subscale means at that time point, according to the half-rule whereby at least half of the items were answered[20,32].

Baseline characteristics of participants versus nonparticipants were compared using independent t-tests and chi-square tests. Non-normally continuous data were analyzed with Mann-Whitney U tests or Fisher's exact tests.

The software Latent Gold (version 5.1)[33] was used to conduct RMLCA to identify the number of non-observed (latent) trajectories in the courses of PTSD (dependent variable). Latent trajectory classes were estimated using the continuous ASD and PTSD scores. The absence or presence of an ASD or PTSD diagnosis as a predictor in all other analyses. Time was modeled as a categorical predictor with five measurements, allowing for the estimation of nonlinear PTSD trajectories over time. Missing values on the dependent variables were handled through full information maximum likelihood estimation, preventing listwise deletion by harnessing patient data at all available time points. The number of parameters (NPar) and the log-likelihood (LL) were used to calculate the Bayesian information criterion (BIC)[34] to determine the number of trajectories that best fit the data based on the rule that lower BIC values indicate a better model fit[35]. Class membership was determined using Latent Gold's model class assignment procedure, and patients were assigned to the trajectory with the highest membership probability. The trajectories were labeled based on the course of PTSD scores across time. Chi-square tests and ANOVAs were used to determine the sociodemographic, clinical, and psychological characteristics of each identified PTSD trajectory. Bonferroni-Holm correction was used to adjust the significance level for the large number of performed statistical tests[36].

For all significant (based on Bonferroni-Holm correction) continuous characteristics, Cohen's d effect sizes were calculated to determine which characteristics most strongly influenced class membership[37]. Odds ratios were used as effect sizes for categorical variables. For each trajectory, the three characteristics with the largest effect sizes were reported. While comparing trajectories, the trajectory of subclinical PTSD symptoms served as the reference class and was compared with the class of patients with no symptoms (i.e., "No PTSD symptoms trajectory") and the class of patients with the worst PTSD symptoms (i.e., "severe trajectory"). Then, a risk profile was developed to determine which patients are at risk for PTSD.

Logistic regression analyses were used to examine the effect of ASD (absent versus present) on PTSD (absent versus present) at 3, 6, 9, and 12 months afterward. The first block (i.e., Model 1) included PTSD. ASD was subsequently included in the second block (i.e., Model 2). Crossover using Venn diagrams were designed to scrutinize the number of patients with ASD or PTSD at baseline and PTSD at 3, 6, 9, and 12 months later. The data imputation, patients' sociodemographic traits, and responses to the questionnaires were analyzed using SPSS version 24.

RESULTS

In total, 267 patients were included at baseline (27% response rate, see Figure 1).

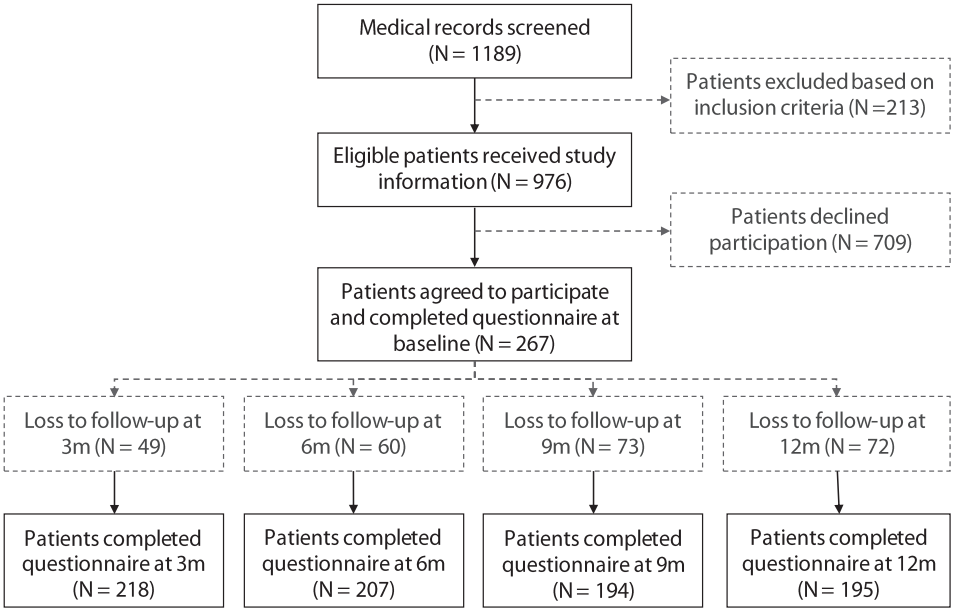

FIGURE 1. Flowchart of study population.
Abbreviations: N: Number

The mean age was 54.0 (SD=16.1), and 61.8% of the patients were male. The number of injuries was higher among participants than nonparticipants. Moreover, compared with nonparticipants, participants showed more spinal cord injuries, thorax or abdominal injuries with a combination of other injuries and more multitrauma or burn wounds. In addition, participants more often experienced trauma as cyclists. Participants more frequently had an isolated head injury than nonparticipants, whereas nonparticipants more often had multitrauma than participants (see Table 1).

TABLE 1. Characteristics of the total cohort, participants who completed the baseline questionnaire and non-participants who were excluded from analysis.

	Total cohort (N=973)	Participants (N=267)	Non-participants (N=706)	p-value
Age (years)*	50.7 ± 20.0	54.0 ± 16.1	49.5 ± 21.2	**<.001**
18-44†	358 (368)	61 (22.8)	297 (42.1)	
45-64†	353 (36.3)	133 (49.8)	220 (31.2)	
65-74†	131 (13.5)	52 (19.5)	79 (11.2)	
≥75†	131 (13.5)	21 (7.9)	110 (15.6)	
Sex				.882
Female	368 (37.8)	102 (38.2)	266 (37.7)	
Male	605 (62.2)	165 (61.8)	440 (62.3)	
Trauma mechanism				**.014**
Motor vehicle accident	217 (22.3)	61 (22.8)	156 (22.1)	
Motorcycle	98 (10.1)	31 (11.6)	67 (9.5)	
Pedal cycle†	185 (19.0)	64 (24.0)	121 (17.1)	
Pedestrian	20 (2.1)	4 (1.5)	16 (2.3)	
Fall	364 (37.4)	92 (34.4)	272 (38.6)	
Struck by/collision	66 (6.8)	15 (5.6)	51 (7.2)	
Other†	23 (2.4)	0 (0)	23 (3.3)	
Number of injuries*	2.0 [0.0-31.0]	3.0 [2.0-7.0]	2.0 [0.0-11.0]	**<.001**
0-2†	591 (60.7)	116 (43.4)	475 (67.3)	
3-5†	301 (30.9)	107 (40.1)	194 (27.5)	
6-8†	53 (5.4)	23 (8.6)	30 (4.2)	
≥9†	28 (2.9)	21 (7.9)	7 (1.0)	
Type/nature of injury				**<.001**
Isolated head injury†	71 (7.3)	7 (2.6)	64 (9.1)	
Head and other injuries	351 (36.1)	93 (34.8)	258 (36.5)	
Spinal cord injury	100 (10.3)	30 (11.2)	70 (9.9)	
Orthopedic injuries only	131 (13.5)	27 (10.1)	104 (14.7)	
Chest/abdominal alone	51 (5.2)	12 (4.5)	39 (5.5)	
Chest/abdominal and other injuries	66 (6.8)	24 (9.0)	42 (5.9)	

TABLE 1. Continued

	Total cohort (N=973)	Participants (N=267)	Non-participants (N=706)	p-value
Other multi-trauma and burn†	191 (19.6)	74 (27.7)	117 (16.6)	
Other†	10 (1.0)	0 (0)	10 (1.4)	
ISS score*‡	N=609	N=263	N=346	**<.001**
	5.0 [1.0-48.0]	5.0 [2.0-9.0]	6.0 [1.0-48.0]	
1-3	209 (34.3)	111 (42.2)	98 (28.3)	
4-8	157 (25.8)	71 (27.0)	86 (24.9)	
9-15	120 (19.7)	47 (17.9)	73 (21.1)	
≥16	123 (20.2)	34 (12.9)	89 (25.7)	
Glasgow Coma Score*	14.6 ± 1.0	14.7 ± 0.8	14.6 ± 1.1	.156
9-12	45 (4.7)	8 (3.0)	37 (5.2)	
13-15	914 (95.3)	259 (97.0)	655 (92.8)	
Living situation				
Alone		45 (16.9)		
With parents		18 (6.7)		
With a partner, no children		101 (37.8)		
With a partner and children		86 (32.2)		
Alone, with children		15 (5.6)		
Educational level				
Low		49 (19.7)		
Middle		103 (41.4)		
High		97 (39.0)		
Employment				
Employed		159 (59.8)		
Unemployed		108 (40.2)		
Hospitalization		173 (64.8)		
Surgery		43 (25.1)		
Admission to ICU		36 (20.8)		
Length of stay*		3.0 [0.0-29.0]		
1-2 days		76 (28.5)		
3-7 days		54 (20.2)		
8-14 days		21 (7.9)		

TABLE 1. Continued

	Total cohort (N=973)	Participants (N=267)	Non-participants (N=706)	p-value
> 15 days		9 (3.4)		
Psychiatric history[¥]		17 (6.4)		
Treatment by medical psychologist after trauma		4 (1.5)		

**Means ± standard deviations or the median [Min-Max]. Number of patients (percentages) are provided for categorical variables. Missing data was not included in calculating percentages. †A significant difference between the participants and non-participants ‡ISS scores could be calculated only for patients who were hospitalized after treatment in the shock room and not for patients who were discharged after treatment in the shock room. Abbreviations: ICU: Intensive Care Unit; ISS: Injury severity score*

After imputing the data, no differences were found in the number of participants since the missing items continued 12 months after trauma. Missing sum scores for the IES-R ranged from 21 (7.9%) at baseline to 6 (2.8%), 8 (4.0%), 5 (2.6%), and 8 (4.3%) at 3, 6, 9, and 12 months after trauma, respectively. Three (1.1%) missing sum scores for the HADS anxiety and 1 (0.4%) missing sum score for HADS depression were imputed.

Trajectories for PTSD

Five latent trajectory classes best fit the data for both the IES-R and the MINI-Plus based on the lowest BIC value (see Table 2).

TABLE 2. Bayesian information criterion (BIC) values of all models for PTSD over 12 months

Number of classes	MINI-Plus	IES Total score
1	5502.307	10382.0093
2	4939.5225	9834.1391
3	4798.7349	9681.5008
4	4681.7435	9610.3946
5	**4618.9204**	**9553.3564**
6	4636.3007	9562.0865
7	4640.8403	9565.0063
8	4665.2222	9521.1833
9	4690.3747	948.3714
10	4697.8798	9512.1275

The BIC value for the final model is marked in bold.

For both questionnaires, the trajectories were labeled as follows: (1) no PTSD symptoms (i.e., almost no PTSD symptoms present), (2) mild (i.e., PTSD symptoms are present a little), (3) moderate (i.e., PTSD symptoms are moderately present), (4) subclinical (i.e., the presence of symptoms that are almost not severe enough to be diagnosed as PTSD; for example, patients who lack one or two symptom criteria short of the full disorder), and (5) severe (i.e., PTSD symptoms are severely present) (see figures 2a and 2b).

Regarding the IES-R, patients (15.0%) in the severe trajectory showed PTSD because their scores were above the cutoff point (IES-R ≥ 33). Approximately 7.2% exhibited subclinical symptoms (trajectory 4) within the first three months after trauma, followed by PTSD after three months (IES-R mean scores ≥ 33 cutoff) and a decrease in PTSD symptoms to a subclinical level between six and 12 months later.

Approximately 7.1% of the patients showed PTSD because their scores were above the cutoff (MINI-Plus ≥ 9) (trajectory 5) in the 12 months after trauma. In addition, 30.5% of the patients reported subclinical PTSD symptoms, as their scores were just under the cutoff score (trajectory 4). Although patients in this subclinical trajectory suffered from PTSD symptoms, they did not present enough symptoms to be diagnosed with PTSD. PTSD symptoms increased during the first three months, whereas they subsequently decreased up to 9 months after trauma. Then, symptoms increased again up to 12 months after trauma. These PTSD symptoms continued on a subclinical level for 12 months after trauma and did not increase to a full-blown diagnosis (above the cutoff point).

With regard to the IES-R, patients in the severe trajectory were younger and had higher scores for anxiety, depressive symptoms, neuroticism, and trait anxiety than patients in other trajectory classes (see Table 3). Most patients (32.4%) with ASD symptoms at baseline had a moderate trajectory. Although the characteristics of the MINI-Plus were similar to the characteristics of the IES-R, and the differences between trajectories mainly concerned psychological characteristics, the largest number of hospitalized patients (94.1%) was in the mild class (trajectory 2). Patients in the moderate class (trajectory 3) exhibited significantly more depressive symptoms and neuroticism than patients with fewer PTSD symptoms (trajectories 1 and 2). Patients with subclinical PTSD symptoms (trajectory 4) were less likely to have been hospitalized (51.3%) than those with mild PTSD symptoms (trajectory 2, 94.1%). Patients with subclinical (trajectory 4) and severe PTSD symptoms (trajectory 5) scored lower on agreeableness than patients without PTSD symptoms (trajectory 1). No clinical predictors were found for PTSD symptoms over 12 months after trauma.

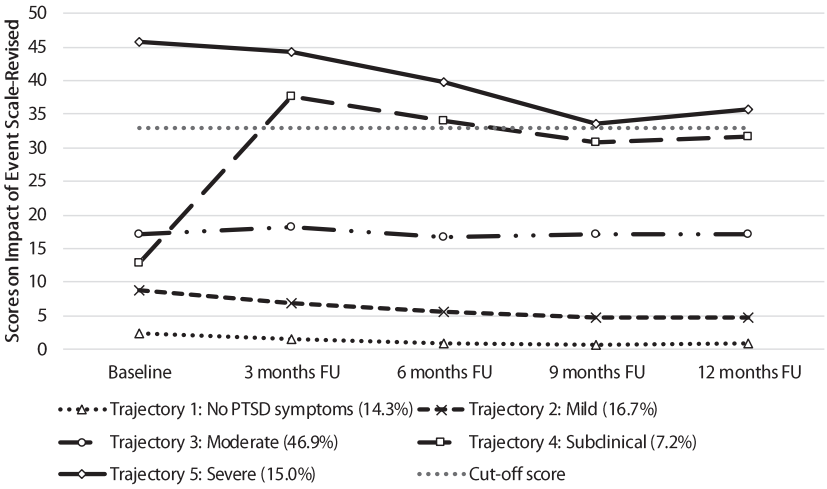

FIGURE 2A. Trajectories of PTSD based on Impact of Event Scale-Revised.
Notes: After using repeated measures latent class analysis, five trajectories were identified over 12-months follow-up: (1) No PTSD symptoms (14.3%), (2) Mild (16.7%), (3) Moderate (46.9%), (4) Subclinical (7.2%), and (5) Severe (15.0%). PTSD was found when patients' mean score was above cut-off point (IES-R ≥ 33).
Abbreviations: FU: Follow up.

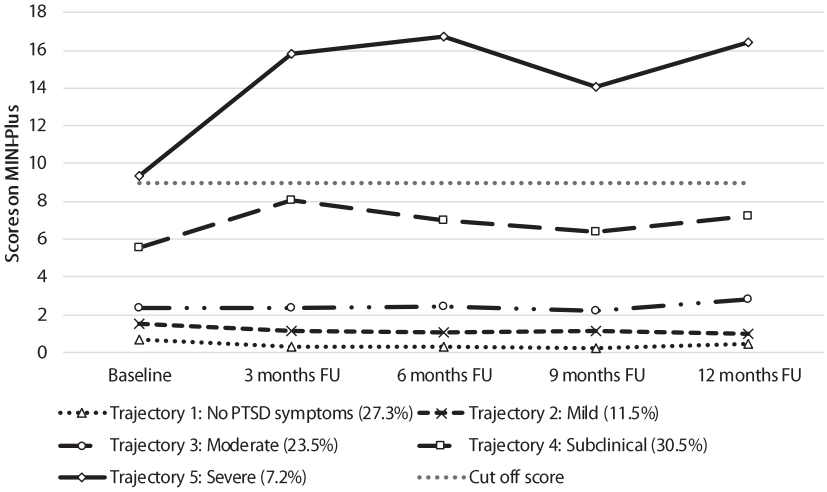

FIGURE 2B. Trajectories of PTSD based on MINI-Plus.
Notes: After using repeated measures latent class analysis, five trajectories were identified over 12-months follow-up: (1) No PTSD symptoms (27.3%), (2) Mild (11.5%), (3) Moderate (23.5%), (4) Subclinical (30.5%), and (5) Severe (7.2%). PTSD was found when patients' mean score was above cut-off (MINI-Plus ≥ 9).
Abbreviations: FU: Follow up.

TABLE 3. Sociodemographic, clinical, and psychological characteristics for the five trajectories, based on the Impact of Event Scale-Revised and the MINI-Plus.

	Impact of Event Scale-Revised					
	Trajectory 1: No PTSD symptoms	**Trajectory 2: Mild**	**Trajectory 3: Moderate**	**Trajectory 4: Subclinical**	**Trajectory 5: Severe**	
Characteristics	**38 (14.3)**	**45 (16.7)**	**125 (46.9)**	**19 (7.2)**	**40 (15.0)**	**p-value**
Age*	59.1 ± 14.8[5]	55.4 ± 14.2[5]	55.4 ± 15.9[5]	54.3 ± 17.8	43.5 ± 15.4[1,2,3]	**<.001**
Anxiety*	3.0 ± 3.5[2,3,4,5]	5.7 ± 3.9[1,5]	7.7 ± 4.7[1,5]	6.8 ± 5.2[1,5]	10.6 ± 3.3[1,2,3]	**<.001**
Depressive symptoms*	3.3 ± 1.8[3,5]	4.3 ± 2.1[5]	5.4 ± 2.5[1,5]	4.8 ± 2.2[1,5]	7.3 ± 2.7[1,2,3,4]	**<.001**
Neuroticism*	22.8 ± 5.2[2,3,4,5]	28.3 ± 7.2[1,5]	28.6 ± 7.7[1,5]	29.3 ± 6.5[1,5]	36.2 ± 7.7[1,2,3,4]	**<.001**
Trait anxiety*	12.9 ± 2.7[3,4,5]	15.8 ± 4.5[5]	16.9 ± 5.2[1,5]	17.1 ± 5.2[1,5]	24.2 ± 6.7[1,2,3,4]	**<.001**
ASD (yes)	5 (4.4)	0 (0)	12 (32.4)[†]	0 (0)	1 (5.6)	**<.001**
Education (high)	18 (50.0)	24 (60.0)	40 (34.8)	5 (26.3)	10 (25.6)	.006
Agreeableness*	42.3 ± 3.7	42.1 ± 5.0	42.2 ± 4.5	41.1 ± 4.3	39.6 ± 4.3	.019
Extraversion*	43.5 ± 6.5	42.3 ± 7.1	42.2 ± 5.9	40.8 ± 6.3	38.9 ± 7.3	.020
Admission to ICU (yes)	6 (26.1)	10 (33.3)	10 (11.5)	4 (33.3)	6 (28.6)	.045
Openness*	35.2 ± 6.1	37.0 ± 6.0	35.5 ± 6.6	32.2 ± 4.7	35.9 ± 5.9	.078
ISS*	9.0 ± 7.4	6.6 ± 6.2	6.1 ± 7.6	5.5 ± 5.1	7.3 ± 7.4	.135
Psychiatric history	2 (5.1)	1 (2.3)	7 (5.6)	1 (5.0)	6 (15.0)	.164
Hospital stay (yes)	23 (59.0)	30 (68.2)	87 (70.2)	12 (60.0)	21 (52.5)	.266
Living together (yes)	34 (87.2)	40 (90.9)	96 (78.7)	18 (90.0)	32 (80.0)	.288
GCS*	14.7 ± 1.0	14.5 ± 1.3	14.7 ± 0.7	14.8 ± 0.6	14.9 ± 0.5	.299
Paid job (yes)	23 (59.0)	30 (68.2)	72 (58.5)	14 (70.0)	20 (50.0)	.428
Table 3. Continued						
Sex (male)	26 (66.7)	27 (61.4)	78 (62.9)	14 (70.0)	20 (50.0)	.495
LOS*	4.4 ± 4.2	5.2 ± 5.6	4.2 ± 4.8	7.0 ± 9.2	5.4 ± 6.5	.538
Conscientiousness*	46.6 ± 4.3	45.8 ± 6.9	45.1 ± 6.2	45.9 ± 6.3	44.5 ± 7.2	.572
Surgery (yes)	5 (21.7)	7 (24.1)	22 (25.3)	3 (25.0)	6 (30.0)	.982

TABLE 3. Continued

	MINI-Plus					
	Trajectory 1: No PTSD symptoms	**Trajectory 2: Mild**	**Trajectory 3: Moderate**	**Trajectory 4: Subclinical**	**Trajectory 5: Severe**	
Characteristics	**73 (27.3)**	**31 (11.5)**	**63 (23.5)**	**81 (30.5)**	**19 (7.1)**	**p-value**
Age*	60.3 ± 14.4[4,5]	54.3 ± 17.1	56.8 ± 16.7[4,5]	48.0 ± 14.1[1,3]	44.1 ± 15.8[1,3]	**<.001**
Anxiety*	4.6 ± 4.5[4,5]	4.3 ± 3.5[4,5]	6.3 ± 4.1[4,5]	9.4 ± 4.2[1,2,3]	11.8 ± 1.9[1,2,3]	**<.001**
Depressive symptoms*	4.1 ± 2.1[4,3,5]	3.5 ± 2.3[4,3,5]	5.4 ± 2.3[1,2,5]	5.9 ± 2.6[1,2,5]	8.7 ± 1.7[1,2,3,4]	**<.001**
Neuroticism*	24.4 ± 7.3[4,3,5]	24.9 ± 4.9[4,5]	28.4 ± 6.3[1,4,5]	33.2 ± 7.2[1,2,3]	38.2 ± 8.4[1,2,3]	**<.001**
Extraversion*	44.0 ± 6.0[4,5]	42.8 ± 5.6[5]	42.4 ± 5.5[5]	39.9 ± 6.9[1]	37.0 ± 7.9[2,3,4]	**<.001**
Trait anxiety*	14.0 ± 4.4[4,5]	14.1 ± 2.8[4,5]	16.3 ± 3.8[4,5]	20.4 ± 5.6[1,2,3,5]	26.7 ± 7.5[1,2,3,4]	**<.001**
ASD (yes)	0 (0)[†]	0 (0)[†]	0 (0)[†]	11 (14.3)	7 (41.2)[†]	**<.001**
Hospital stay (yes)	49 (64.5)	32 (94.1)[†]	39 (65.0)	41 (51.3)[†]	12 (70.6)	**.001**
Agreeableness*	43.0 ± 4.1[4,5]	42.2 ± 4.4	42.2 ± 4.2[5]	40.8 ± 4.6[1]	38.7 ± 5.1[1,3]	**.001**
Conscientiousness*	46.6 ± 5.6	46.4 ± 3.9	46.0 ± 6.0	43.8 ± 7.1	43.4 ± 7.7	.021
Living together (yes)	66 (86.8)	24 (82.4)	48 (80.0)	68 (87.2)	10 (58.8)	.056
Sex (male)	53 (69.7)	23 (67.6)	38 (63.3)	40 (50.0)	11 (64.7)	.118
Education (high)	32 (45.1)	9 (30.0)	26 (45.6)	27 (36.0)	3 (18.8)	.184
Psychiatric history	5 (6.6)	0 (0)	2 (3.3)	8 (10.0)	2 (11.8)	.211
LOS*	3.7 ± 3.6	4.9 ± 7.1	5.9 ± 6.0	5.3 ± 6.0	2.6 ± 1.6	.270
ISS*	6.6 ± 6.2	9.0 ± 7.4	7.3 ± 7.4	6.1 ± 7.6	5.5 ± 5.1	.277
Paid job (yes)	42 (55.3)	20 (58.8)	37 (61.7)	53 (67.1)	7 (41.2)	.293
GCS*	14.8 ± 0.7	14.6 ± 1.0	14.6 ± 0.9	14.7 ± 0.9	14.7 ± 0.8	.520
Openness*	35.6 ± 5.4	33.9 ± 7.8	35.9 ± 5.6	35.8 ± 6.9	35.9 ± 5.7	.601
Admission to ICU (yes)	11 (22.4)	5 (15.6)	8 (20.5)	11 (26.8)	1 (8.3)	.620
Surgery (yes)	11 (22.4)	8 (25.8)	10 (25.6)	12 (29.3)	2 (18.2)	.931

*Number of patients (percentages) are provided for categorical variables. *Means ± standard deviations. Missing data was not included in calculating percentages. [†,1,2,3,4,5]A significant difference between the specified class(es). Note: Using a Holm adjusted significance level, significant p-values for differences in a characteristic between all classes are shown in bold. Ranking of characteristics is based on p-value (low-high).*

Abbreviations: ASD: acute stress disorder, LOS: Length of stay, ISS: Injury severity score, GCS: Glasgow Coma Score, ICU: Intensive Care Unit

Risk profile

The most pronounced differences between patients with subclinical presence of PTSD (trajectory 4) and no PTSD symptoms (trajectory 1) were found for neuroticism, trait anxiety, anxiety, and ASD (see Table 4). Patients in the subclinical trajectory class showed substantially higher scores for neuroticism, trait anxiety, and anxiety than patients without PTSD symptoms. The odds of having ASD were lower for patients without symptoms (trajectory 1) than for patients with subclinical PTSD symptoms. Patients in the subclinical (class 4) and severe (class 5) trajectories differed most prominently in terms of trait anxiety, depressive symptoms, anxiety, and ASD. Patients with subclinical PTSD trajectories had substantially lower scores for trait anxiety, depressive symptoms, and anxiety than patients with severe PTSD trajectories. The odds of having ASD were lower for patients in the severe trajectory class than for patients in the subclinical trajectory class.

We noted the most discernable differences between the subclinical trajectory (class 4; reference group) and no PTSD symptom trajectory (class 1) for ASD, trait anxiety, neuroticism, anxiety, and admission to the hospital (see Table 4). Patients with a subclinical PTSD trajectory had substantially higher scores for trait anxiety and neuroticism, and lower scores on anxiety than patients without PTSD symptoms (trajectory 1). The odds of being hospitalized were lower for patients without PTSD symptoms (trajectory 1) than for patients in the subclinical trajectory. The odds of having ASD were similar for patients with subclinical PTSD symptoms compared to patients without PTSD symptoms.

Patients in the subclinical class showed substantially less depressive symptoms, lower scores on trait anxiety, and neuroticism than patients with severe PTSD trajectories. The odds for being hospitalized and having ASD was less for patients in the subclinical trajectory class than for to patients in the severe trajectory class. No statistically significant differences in patient characteristics were found between the classes with lowest PTSD scores (i.e., no PTSD symptoms, mild, and moderate presence trajectory).

TABLE 4. Risk profile based on the Impact of Event Scale-Revised and the MINI-Plus using Cohens'd effect size and Odds ratio between subclinical trajectory versus no PTSD symptoms and severe trajectory

Characteristics	Cohen's d (Trajectory 4 vs. Trajectory 1)	CI interval (95%)	Cohen's d (Trajectory 4 vs. Trajectory 5)	CI interval (95%)
Impact of Event Scale-Revised				
Age	-.30	[-.86, .25]	.67	[.11, 1.23]
Anxiety	.91	[.33, 1.48]	-.95	[-1.52, -.38]
Depressive symptoms	.77	[.20, 1.34]	-1.01	[-1.58, -.43]
Neuroticism	1.14	[.55, 1.73]	-.94	[-1.52, -.38]
Trait anxiety	1.13	[.544, 1.72]	-1.12	[-1.71, -.54]
ASD	.16	[.01, 2.98]	.68	[.03, 17.35]
MINI-Plus				
Age	-.86	[-1.19, -.53]	.25	[-.25, .75]
Anxiety	1.1	[.76, 1.44]	-.62	[-1.13, -.11]
Depressive symptoms	.74	[.42, 1.07]	-1.13	[-1.65, -.60]
Neuroticism	1.21	[.86, 1.55]	-.67	[-1.18, -.16]
Extraversion	-.63	[-.95, -.30]	.41	[-.09, .19]
Trait anxiety	1.27	[.92, 1.61]	-1.05	[-1.57, -.53]
Agreeableness	-.51	[-.83, .19]	.43	[-.07, .93]
Hospital stay (yes)*	.50	[.26, .97]	.60	[.21, 1.67]
ASD (yes)*	.16	[.00, 8.64]	.27	[.09, .83]

*Trajectory 4: Subclinical is the reference class. *Odds ratios are provided for hospital stay and ASD.*
Abbreviations: vs: versus, CI: confidence interval, ASD: acute stress disorder. Note: A positive Cohen's d indicates a higher mean score for patients in the subclinical trajectory (class 4; reference group) compared to patients in either the no PTSD symptoms trajectory (class 1) or severe trajectory (class 5). Whereas a negative Cohen's d indicates a lower mean score for patients in the subclinical trajectory (class 4; reference group) compared to patients in either the no PTSD symptoms trajectory (class 1) or severe trajectory (class 5). If the 95% confidence interval does not contain the null hypothesis value (zero), the results are statistically significant.

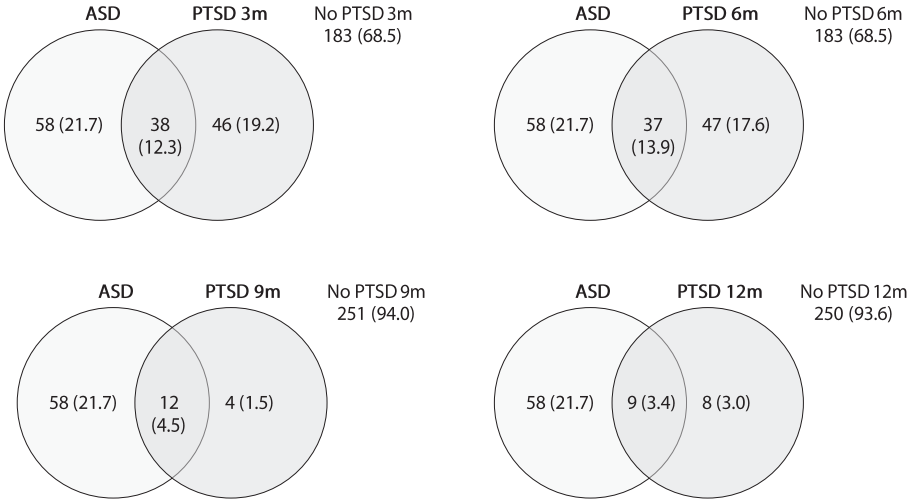

FIGURE 3A. Cross-over, using Venn diagrams, of number of PTSD (at baseline) and PTSD (at 3, 6, 9, and 12 months after trauma) amongst the study population based on the Impact of Event Scale-Revised.
Note: Missing data was not included in calculating numbers and percentages, since Latent Gold is capable in handling missing data.

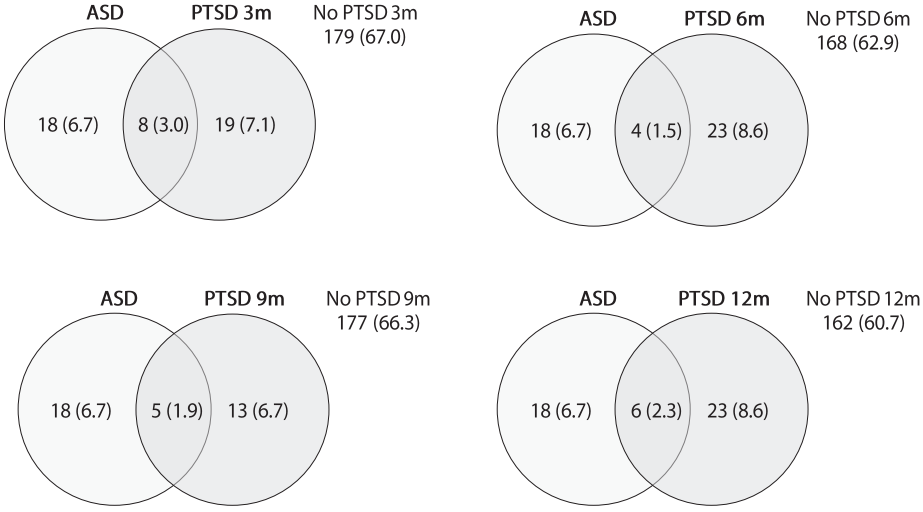

FIGURE 3B. Cross-over, using Venn diagrams, of number of ASD (at baseline) and PTSD (at 3, 6, 9, and 12 months after trauma) amongst the study population based on the MINI-Plus.
Note: Missing data was not included in calculating numbers and percentages, since Latent Gold is capable in handling missing data.

Effect of ASD on PTSD

Figures 3a and 3b show the number and percentage of ASD, PTSD, and ASD+PTSD diagnoses at 3, 6, 9, and 12 months after trauma in the current patient sample. About 21.7% of patients with PTSD (based on the IES-R) at baseline, reported 38 (65.5%), 37 (63.8%), 12 (20.7%), and 13 (36.1%) PTSD symptoms at respectively 3, 6, 9, and 12 months after trauma. The overall model was significant. The odds of developing PTSD during 12 months after trauma were 7.8 times higher for patients with ASD at baseline than they were for patients without ASD at baseline (B = 1.99; $p < 0.001$; OR = 7.82; 95% CI: 3.73, 14.23).

About 7.3% had ASD according to the MINI-Plus at baseline. Of all patients diagnosed with ASD at baseline, 8 (44.4%), 4 (22.2%), 5 (27.8%), and 6 (33.3%) reported PTSD symptoms at respectively 3, 6, 9, and 12 months after trauma. Although a significant overall model was found, the odds of developing PTSD during 12 months after trauma were similar for patients with ASD compared to patients without ASD (B = 0.81; $p = 0.181$; OR = 2.24; 95% CI: 0.69, 7.32).

DISCUSSION

This study aimed to identify distinct trajectories of PTSD up to 12 months after injury and to examine patients' sociodemographic, clinical, and psychological characteristics for each trajectory. We subsequently established a risk profile to scrutinize patients at risk for PTSD. Finally, the effect of ASD on PTSD over time was studied. This study found five PTSD trajectories during the 12 months after injury. A relatively large proportion (22.2% (IES-R) - 37.6% (MINI-Plus)) of the total study population showed (subclinical) symptoms of ASD and PTSD that remained stable 12 months after trauma. Although the prevalence rate of ASD or PTSD at baseline was different for the IES-R and the MINI-Plus, the number of patients with PTSD was comparable at 12 months after trauma. In line with earlier research, no spontaneous recovery or improvement in functioning was found during the 12 months after injury[7,12,38]. Moreover, the mean PTSD scores for the severe trajectory were seriously high (i.e., far above the cutoff point). This could have a negative impact on physiological and physical functioning[3,39,40] since psychological stress can affect wound repair and is related to pain and fatigue[41-45]. Patients with subclinical and severe PTSD symptoms had similar risk profiles with regard to anxiety, trait anxiety, and ASD. However, neuroticism and hospitalization were found only in patients with subclinical PTSD. In contrast, depressive symptoms were found only in patients with severe PTSD symptoms. Most likely, symptoms of PTSD and depression (e.g., negative emotions) overlap; past studies have discovered biological molecular processes between PTSD and major depression[46].

More patients with (subclinical) PTSD were identified using the IES-R than the MINI-Plus (based on the DSM-5). In line with previous results that used the International Classification of Diseases, 11th edition (ICD-11) to indicate PTSD symptom severity in injury patients[47], an increased number of patients with PTSD who would not have been diagnosed by the DSM-5 was noted[47]. Hence, considering our high prevalence rate of subclinical PTSD, future research could examine whether more patients from the subclinical trajectory could be diagnosed with PTSD using the ICD-11. In line with other studies, structured interviews were used to investigate ASD (baseline) and PTSD (follow-up) and a questionnaire to study PTSD (baseline and follow-up). Notwithstanding, they are different tools, and they differ in symptom examination because dissociative symptoms (e.g., depersonalization, derealization, and dissociative amnesia) are emphasized only in ASD and not in PTSD.

Patients with subclinical PTSD symptoms (MINI-Plus, trajectory 4) were less likely to be hospitalized than patients with other trajectories. This could indicate that discharge after treatment in the shock room could be a risk factor for PTSD. In addition, in the case of being hospitalized, the largest prevalence rate (26.8%) of admission to the ICU was found for this trajectory. Patients needed more complex and intensive care than patients in other classes. Thus, the possible presence of postintensive care syndrome (PICS) must be taken into account[48,49].

Psychological trauma after injury is being evaluated in the field of emergency and trauma surgery. Therefore, a major strength of the present study is that it is the first to include personality alongside sociodemographic, clinical, and other psychological features in a risk profile of PTSD after injury. Similar patient characteristics for ASD and PTSD symptoms were found for both questionnaires. Patients with severe PTSD symptoms were younger and scored higher for anxiety, depressive symptoms, neuroticism, and trait anxiety. These aspects might imply symptom severity, showing that patients with more psychological problems and those with anxious and neurotic personalities are at risk for developing ASD and PTSD during the 12 months after trauma. In line with previous studies, we did not detect any clinical predictors (e.g., ISS > 16 or lower GCS)[4,50]. Another strength is that patients were examined on five measurement occasions within 12 months after trauma, which allowed us to identify symptom trajectories over time. As a result, the effect of ASD on PTSD as well as the prevalence rates of patients with ASD at baseline and PTSD 12 months after injury could be determined.

Some limitations must be taken into account. First, this is not a multicenter study since only level-1 trauma centers were involved; these centers mostly treat severely injured patients from the province of Noord-Brabant[1]. Mildly and moderately injured patients are often treated in level-2 or level-3 trauma centers[1]; for example, this province has 11 level-2 or

level-3 hospitals with an ED[1]. Hence, the results may limit the generalizability to the entire trauma population from other rural and urban regions, including mildly and moderately injured people and foreigner (versus indigenous) populations. Additionally, observed differences in the characteristics of responders and nonresponders suggests that selection bias may have occurred.

Second, the response rate was 27%. The main reason for the decline in participation was that patients were not interested, as they did not experience any physical or psychological problems after trauma. In contrast, participation could be difficult because the patients may have been facing other problems or (physical) limitations. Further, concerning dropout rates, it is likely that patients who fully recovered were less interested in completing follow-up measurements than patients who still experienced PTSD symptoms or problems with functioning.

In addition, two kinds of missingness were taken into account. First, missing values on the dependent variable were handled through full information maximum likelihood estimation using Latent Gold software. This method is appropriate when one or two follow-up measurements are missing from a participant. Second, in the case of single missing item scores on the IES-R and the HADS, imputation took place via individual subscale means when at least half of the subscale items were answered[20,32,51]. Unfortunately, overestimation of item variation and a lower Cronbach's alpha of the scale from that item could have occurred[52]. Finally, this study was largely based on self-report questionnaires. Interpretation of an ASD or PTSD diagnosis must be performed with caution.

Our study has implications for daily clinical practice. Clinicians with knowledge of risk profiles can identify and screen patients at an early stage in the ED or department of surgery[53] by using the Psychosocial Screening Instrument for Physical Trauma Patients (PSIT)[54]. HCPs could ask at-risk patients about their needs for additional care in the form of consultation from a social worker or health psychologist. In this way, HCPs are able to positively affect patients' clinical outcomes, and patient-centered care can be offered.

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Chapter 6

PSYCHOLOGICAL RISK FACTORS THAT CHARACTERIZE THE TRAJECTORIES OF QUALITY OF LIFE AFTER A PHYSICAL TRAUMA: A LONGITUDINAL STUDY USING LATENT CLASS ANALYSIS

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Quality of Life Research (2021)

ABSTRACT

Background: The course and corresponding characteristics of quality of life (QOL) domains in trauma population are unclear. Our aim was to identify longitudinal QOL trajectories, determine and predict the sociodemographic, clinical, and psychological characteristics of trajectory membership in physical trauma patients using a biopsychosocial approach.
Methods: Patients completed a questionnaire set after inclusion, and at 3, 6, 9, and 12 months follow-up. Trajectories were identified using repeated measures latent class analysis. The trajectory characteristics were ranked using Cohen's d effect size or phi coefficient.
Results: Altogether, 267 patients were included. The mean age was 54.1 (SD = 16.1), 62% were male, and the median injury severity score was 5.0 [2.0 - 9.0]. Four latent trajectories were found for psychological health and environment, five for physical health and social relationships, and seven trajectories were found for overall QOL and general health. The trajectories seemed to remain stable over time. For each QOL domain, the identified trajectories differed significantly in terms of anxiety, depressive symptoms, acute stress disorder, posttraumatic stress disorder, Neuroticism, trait anxiety, Extraversion, and Conscientiousness.
Discussion: Psychological factors characterized the trajectories during 12 months after trauma. Health care providers can use these findings to identify patients at risk for impaired QOL and offer patient-centered care to improve QOL.

INTRODUCTION

Physical trauma became a major public health problem over the last decade, because an increasing number of patients were treated in the emergency department (ED) after injury[1]. Survivorship increased due to improvement in specialized trauma care[2]. Nevertheless, survivors have reported long-term physical disabilities (e.g., pain and fatigue), psychological problems (e.g., anxiety and depressive symptoms) and disorders (e.g., acute and posttraumatic stress disorder (PTSD))[3-8], and impaired quality of life (QOL; i.e., a subjective and multidimensional concept of person's physical health, psychological state, personal beliefs, social relationships and their relationship to salient features of their environment)[9-13].

These disabilities and disorders were, together with sociodemographic (e.g., older age, female sex, low education) and clinical (e.g., higher injury severity score, hospital stay and ICU admission) characteristics, related to impaired health-related QOL (HRQOL) or health status (HS)[9,12,14-18]. HRQOL is a limited definition of QOL, as it solely focuses on patients' subjective perceptions on health (i.e., physical and mental health), whereas HS refers to the extent of physical, psychological, and social functioning, but without taken patients' satisfaction with functioning into account[19]. Moreover, recent studies, describing latent trajectories, focused on general health[20] and health status (HS)[21-23] and not on QOL. These studies were also based on a subset of the trauma population (e.g., whiplash or traumatic brain injury), instead of a trauma population with multiple injuries.

To our knowledge, no study has been conducted to identify trajectories and predictors for impaired QOL after injury. Repeated measures latent class analysis (RMLCA) can be used to identify a set of distinct longitudinal response patterns (i.e., QOL trajectories). Regression analyses can subsequently be used to examine the sociodemographic and clinical characteristics of patients classified in each trajectory[24]. Therefore, our aims were first to identify latent trajectories representing distinct changes in QOL over a 12-month follow-up and then to determine the sociodemographic, clinical, and psychological characteristics of each identified trajectory using a biopsychosocial approach[25].

METHODS

Patients

Trauma patients treated in the shock room between November 2016 and November 2017 of the ETZ Hospital (Elisabeth-TweeSteden Ziekenhuis), Tilburg, The Netherlands, were asked to participate in this study. This hospital is a Level-1 Trauma Center in the province

of Noord-Brabant. Only patients aged 18 or older were included. Patients were excluded in case of severe traumatic brain injury (i.e., Glasgow Coma Score (GCS) ≤ 8), dementia, or insufficient knowledge of the Dutch language (verbal and writing).

Study design and procedure

Patients were asked to participate by either the emergency doctor or the researcher (EV). Patients signed two informed consents. First, in the emergency department after receiving treatment in the shock room and being informed by the doctor. Then 1 to 5 days later, patients again confirmed participation to make sure that they have had sufficient time to consider participation in the study. Unconscious patients were informed by the researcher and asked to participate as soon as they were lucid. All obtained information was destroyed for patients who declined participation by not signing the second informed consent.

This study is part of a mixed-method study. The study protocol is published elsewhere[26]. This study (protocol number: NL55386.028.15) has been reviewed and approved by the Medical Ethical Committee Brabant (METC Brabant) on December 4, 2015. The study has been recorded in the Netherlands Trial Registry (NTR6258). To strengthen validity and comprehensiveness, this study was conducted and reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist for cohort studies[27]. Participation was voluntarily and no financial reward was given.

Data collection

Sociodemographic information (i.e., sex, age, living situation, education level, and employment) was obtained from patients at baseline. Clinical information, including type of trauma mechanism (e.g., motor vehicle accident), number of injuries, type of injury (e.g., spinal cord injury), injury severity score (ISS), GCS, surgery (yes/no), hospital admission (yes/no), admission to ICU, length of stay, psychiatric history (yes/no), and consult or treatment from health psychologist (yes/no) was abstracted from the patients' medical records.

Data for this study was collected using self-report questionnaires and a structured interview. Patients completed a baseline questionnaire on sociodemographics, QOL, ASD and PTSD, anxiety, depressive symptoms, and personality traits after they confirmed participation. Clinical information was retrieved from patients' medical records. QOL was further assessed during follow-up at 3, 6, 9, and 12 months after injury[26].

QOL was measured with the World Health Organization Quality of Life assessment instrument-Bref (WHOQOL-Bref)[25,28]. This 26-item questionnaire is the short version of the WHOQOL-100 and assesses four domains (physical health, psychological health, social relationships, and environment) as well as one general facet overall QOL and general

Health. Each item is rated on a five-point rating scale. Norm scores[29] were used to indicate and label each trajectory (e.g., physical health; Poor: 9.1, Fair: 12.3, Good: 14.8, Very good: 16.5, Excellent: 18.3). Higher scores indicate better QOL. The WHOQOL-Bref has good psychometric properties[25,30,31] and it is a reliable and valid instrument in trauma patients[32].

The MINI-Plus is a short-structured interview, based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) and it is used to assess ASD at baseline[33]. The items are dichotomous (symptoms: absent or present). The total scores theoretically range from 0 to 14 and indicates symptom severity. Nevertheless, patients can only be diagnosed with ASD if at least nine symptoms are present from each of the five categories (i.e., intrusion, negative emotions, dissociation, avoidance, and arousal). Therefore, in line with the manual instructions, dichotomous scores (disorder: no versus yes) for ASD were used in the analyses.

The IES-R is a self-report questionnaire to assess symptom severity of PTSD. It consists of 22 items which measure intrusive re-experiences (8 items, e.g., Any reminder brought back feelings about it'), hyperarousal (6 items, e.g., 'I felt irritable and angry'), and avoidance (8 items, e.g., 'I avoided letting myself get upset') of injury-related stimuli[34]. The participant stated whether the content of each statement was present during the past 7 days on a 4-point Likert scale ranging from 0 (*not at all*) to 4 (*often*). The total scores theoretically ranged from 0 to 88 and continuous scores were used in the analyses. The IES-R has good psychometric properties[35] and the Dutch translation[36] of the IES-R is reliable and valid in various populations of people experiencing traumatic stress[37].

The Hospital Anxiety and Depression Scale (HADS) was used to measure anxiety and depressive symptoms[38]. It is a generic questionnaire measuring levels of anxiety (7 items) and depression (7 items) with a 4-point rating scale ranging from 0 (*not at all*) to 3 (*very much*). The total scores for both subscale theoretically range from 0 to 21. The questionnaire is reliable and valid in patients with traumatic brain injury[39].

The 60-item NEO Five Factor Inventory (NEO-FFI) was used to measure Big Five personality domains: Neuroticism, Extraversion, Openness to experience, Agreeableness, and Conscientiousness[40,41]. Each of the 60 items is rated on a five-point rating scale ranging from 1 (*strongly disagree*) to 5 (*strongly agree*), resulting in domain scores theoretically ranging between 12 and 60. The psychometrics have been extensively assessed and the internal consistency, test-retest reliability, and validity are acceptable to good in physical trauma patients[42].

The State-Trait Anxiety Inventory (STAI) (short form) consists of 20 items for measuring state anxiety (10 items) and trait anxiety (10 items)[43]. In this study, only the STAI-Trait scale was

used. The STAI-Trait scale has a four-point rating scale ranging from 1 (*almost never*) to 4 (*almost always*), resulting in a total score theoretically ranging from 10 to 40. The Dutch version of the STAI is a reliable and valid instrument in the general population[43].

Statistical analysis

Missing item scores of the WHOQOL-Bref, IES-R and the HADS were imputed with individual subscale means when at least half of the subscale items were answered[34,44,45].

Baseline characteristics (i.e., sociodemographic, clinical, and psychological variables) of participants versus nonparticipants were compared using independent t-tests for continuous normally distributed data, Mann-Whitney U tests for continuous non-normally distributed data, Chi-square tests for categorical data and Fisher's exact tests for categorical data (e.g., ASD) where one or more of the crosstab cells showed expected cell counts less than 5.

The software Latent Gold (version 5.1)[46] was used to conduct a RMLCA, to identify the number of non-observed (latent) trajectories in the courses of each the QOL domain scores (dependent variables). Time was modeled as a categorical predictor with five measurements, allowing for the estimation of non-linear QOL trajectories over time. Missing values on the dependent variables were handled through full information maximum likelihood estimation. The Bayesian Information Criterion (BIC) was used to determine the number of trajectories that best fitted the data, based on the rule that lower BIC values indicate better model fit[24,47]. Class membership was determined using Latent Gold's model class assignment procedure by assigning patients to a trajectory with the highest membership probability. The identified trajectory classes were compared on the sociodemographic, clinical and psychological characteristics using Chi-square tests and ANOVA's. As a result, each class represents a different trajectory of QOL, and each trajectory has its own characteristics. A Bonferroni-Holm correction was used to adjust the significance level for the large number of performed statistical tests[48].

For all significant (based on Bonferroni-Holm correction) continuous characteristics, Cohen's d effect sizes were calculated to determine what characteristics are most strongly related to class membership[49]. Phi coefficients were used to examine the correlation between class membership and categorical characteristics (e.g., ASD). For each domain, three characteristics with the largest effect sizes were reported. While comparing trajectories, Good or Excellent trajectory (i.e., class with highest mean QOL scores over 12 months after injury) served as the reference class and was compared with Poor or Worse (i.e., class with lowest mean QOL scores over 12 months after trauma) QOL trajectory.

RESULTS

In total, 267 patients were included at baseline (27% response rate, see Figure 1).

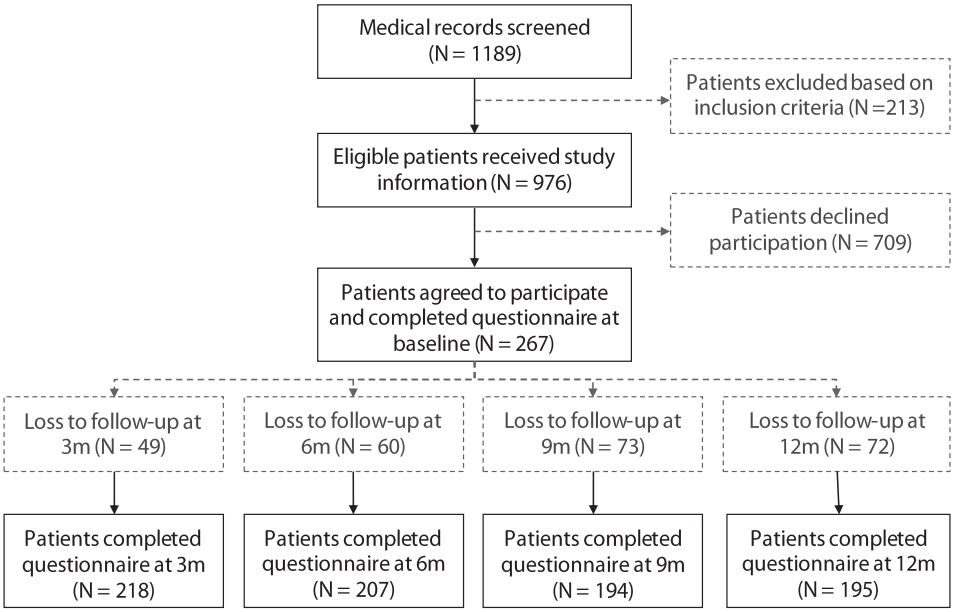

FIGURE 1. Flowchart of study population.
Abbreviations: N: Number

The response rate at three, six, nine, and 12 months follow-up were 81.6%, 77.5%, 72.7%, and 73.0%, respectively. The mean age of participants was 54.0 (SD = 16.1) and 61.8% were male patients. Moreover, participants showed more spinal cord injuries, thorax or abdominal with a combination of other injuries, and multi-trauma or burn wounds than non-participants. With regard to the nature of the injury, participants experienced more often a trauma as cyclist and they more often had an isolated head injury compared to non-participants. Patients' sociodemographic and medical aspects are shown in Table 1.

The missing sum scores for QOL are presented in Supplemental table 1. Concerning the IES-R, 21 (7.9%) missing item scores were imputed, whereas 3 (1.1%) missing item scores for the HADS anxiety and 1 (0.4%) missing item score for HADS depression were imputed.

TABLE 1. Characteristics of the total cohort, participants who completed the baseline questionnaire and non-participants who were excluded from analysis.

	Total cohort (N=973)	Participants (N=267)	Non-participants (N=706)	p-value
Age (years)*	50.7 ± 20.0	54.0 ± 16.1	49.5 ± 21.2	**<.001**
18-44†	358 (36.8)	61 (22.8)	297 (42.1)	
45-64†	353 (36.3)	133 (49.8)	220 (31.2)	
65-74†	131 (13.5)	52 (19.5)	79 (11.2)	
≥75†	131 (13.5)	21 (7.9)	110 (15.6)	
Sex				.882
Female	368 (37.8)	102 (38.2)	266 (37.7)	
Male	605 (62.2)	165 (61.8)	440 (62.3)	
Trauma mechanism				**.014**
Motor vehicle accident	217 (22.3)	61 (22.8)	156 (22.1)	
Motorcycle	98 (10.1)	31 (11.6)	67 (9.5)	
Pedal cycle†	185 (19.0)	64 (24.0)	121 (17.1)	
Pedestrian	20 (2.1)	4 (1.5)	16 (2.3)	
Fall	364 (37.4)	92 (34.4)	272 (38.6)	
Struck by/collision	66 (6.8)	15 (5.6)	51 (7.2)	
Other†	23 (2.4)	0 (0)	23 (3.3)	
Number of injuries*	2.0 [0.0-31.0]	3.0 [2.0-7.0]	2.0 [0.0-11.0]	**<.001**
0-2†	591 (60.7)	116 (43.4)	475 (67.3)	
3-5†	301 (30.9)	107 (40.1)	194 (27.5)	
6-8†	53 (5.4)	23 (8.6)	30 (4.2)	
≥9†	28 (2.9)	21 (7.9)	7 (1.0)	
Type/nature of injury				**<.001**
Isolated head injury†	71 (7.3)	7 (2.6)	64 (9.1)	
Head and other injuries	351 (36.1)	93 (34.8)	258 (36.5)	
Spinal cord injury	100 (10.3)	30 (11.2)	70 (9.9)	
Orthopedic injuries only	131 (13.5)	27 (10.1)	104 (14.7)	
Chest/abdominal alone	51 (5.2)	12 (4.5)	39 (5.5)	
Chest/abdominal and other injuries	66 (6.8)	24 (9.0)	42 (5.9)	
Other multi-trauma and burn†	191 (19.6)	74 (27.7)	117 (16.6)	
Other†	10 (1.0)	0 (0)	10 (1.4)	
ISS score*‡	N=609	N=263	N=346	**<.001**

TABLE 1. Continued

	Total cohort (N=973)	Participants (N=267)	Non-participants (N=706)	p-value
	5.0 [1.0-48.0]	5.0 [2.0-9.0]	6.0 [1.0-48.0]	
1-3	209 (34.3)	111 (42.2)	98 (28.3)	
4-8	157 (25.8)	71 (27.0)	86 (24.9)	
9-15	120 (19.7)	47 (17.9)	73 (21.1)	
≥16	123 (20.2)	34 (12.9)	89 (25.7)	
Glasgow Coma Score*	14.6 ± 1.0	14.7 ± 0.8	14.6 ± 1.1	.156
9-12	45 (4.7)	8 (3.0)	37 (5.2)	
13-15	914 (95.3)	259 (97.0)	655 (92.8)	
Hospitalization				**<.001**
Yes	519 (53.3)	173 (64.8)	346 (49.0)	
No	454 (46.7)	94 (54.3)	360 (51.0)	
Admission to ICU‡				**<.001**
Yes	138 (26.6)	36 (20.8)	102 (29.5)	
No	381 (73.4)	137 (79.2)	244 (70.5)	
Length of stay*	7.2 [0.0-124.0]	3.0 [0.0-29.0]	8.3 [1.0-124.0]	**.010**
1-2 days	204 (21.0)	76 (28.5)	128 (18.1)	
3-7 days	165 (17.0)	54 (20.2)	111 (15.7)	
8-14 days	77 (7.9)	21 (7.9)	56 (7.9)	
> 15 days	60 (6.2)	9 (3.4)	51 (7.2)	
Surgery		43 (25.1)		
Living situation				
Alone		45 (16.9)		
With parents		18 (6.7)		
With a partner, no children		101 (37.8)		
With a partner and children		86 (32.2)		
Alone, with children		15 (5.6)		
Educational level				
Low		49 (19.7)		
Middle		103 (41.4)		
High		97 (39.0)		
Employment				
Employed		159 (59.8)		

TABLE 1. Continued

	Total cohort (N=973)	Participants (N=267)	Non-participants (N=706)	p-value
Unemployed		108 (40.2)		
Psychiatric history[¥]		17 (6.4)		
Treatment by health psychologist after trauma		4 (1.5)		

**Means ± standard deviations or the median [Min-Max]. Number of patients (percentages) are provided for categorical variables. Missing data was not included in calculating percentages. †A significant difference between the participants and non-participants ‡ISS scores could be calculated only for patients who were hospitalized after treatment in the shock room and not for patients who were discharged after treatment in the shock room.*
Abbreviations: ICU: Intensive Care Unit; ISS: Injury severity score

TABLE 2. The number of parameters and the log-likelihood were used to calculate the Bayesian information criterion (BIC) values of all models for quality of life domains over 12 months

N. of classes	NPar	Physical health		Psychological health		Social relationships		Environment		Overall QOL and general health	
		LL	BIC	LL	BIC	LL	BIC	LL	BIC	LL	BIC
1	6	-2789.3	5612.2	-2631.2	5295.9	-2691.3	5416.1	-2525.6	5084.6	-2132.7	4298.9
2	13	-2521.2	5115.0	-2316.4	4705.5	-2448.4	4969.4	-2237.6	4547.8	-1920.5	3913.6
3	20	-2450.2	5012.2	-2222.1	4555.9	-2391.6	4894.9	-2085.0	4281.6	-1830.6	3773.0
4	27	-2415.5	4981.8	**-2153.8**	**4458.5**	-2348.3	4847.5	**-2033.7**	**4218.2**	-1791.9	3734.6
5	34	**-2395.9**	**4981.7**	-2134.4	4458.8	**-2325.0**	**4839.9**	-2014.4	4218.7	-1711.6	3613.1
6	41	-2377.1	4983.3	-2121.1	4471.2	-2310.4	4849.8	-2002.2	4233.5	-1690.9	3610.9
7	48	-2365.2	4998.5	-2111.9	4491.9	-2301.5	4871.2	-1993.5	4255.1	**-1669.0**	**3606.2**
8	55	-2352.3	5011.9	-2106.1	4519.4	-2280.5	4868.4	-1981.6	4270.4	-1651.1	3609.6
9	62	-2339.1	5024.7	-2094.0	4534.3	-2271.2	4888.9	-1973.9	4294.3	-1629.9	3606.3
10	69	-2325.2	5035.9	-2086.7	4558.9	-2261.0	4907.5	-1972.1	4329.8	-1618.9	3623.4

The BIC value for the final model is marked in bold. Abbreviation: QOL: quality of life, N: Number, NPar: number of parameters, LL: log-likelihood, BIC: Bayesian Information Criterion Note: The optimum number of classes are based on the BIC. This is an indicator for model fit (LL) and it takes complexity of de model with number of parameters (NPar) into account. The number of parameters are the same for each class.

Table 2 indicates that four similar latent trajectory classes best fitted the data for psychological health and environment, based on the lowest BIC value criterion.

Five different trajectories best fitted the data for physical health and social relationships. Seven trajectories were found for overall QOL and general health. The labels of the trajectories were based on total mean scores on each domain at baseline, when they seemed to be stable during 12 months after trauma. Otherwise, in case of change in direction, the labels of the trajectories were based on the course of QOL scores across time (e.g., Recovery) and compared with norm scores[29]. Tables 3 to 7 show the sociodemographic, clinical, and psychological characteristics of patients classified in each trajectory. Table 8 shows for each QOL domain the characteristics that most strongly predict the difference between the highest and lowest scoring QOL trajectories over the 12-month follow-up.

Trajectories for physical health

The five trajectories were labelled as Poor, Fair, Good, Very good, and Excellent (Figure 2a).

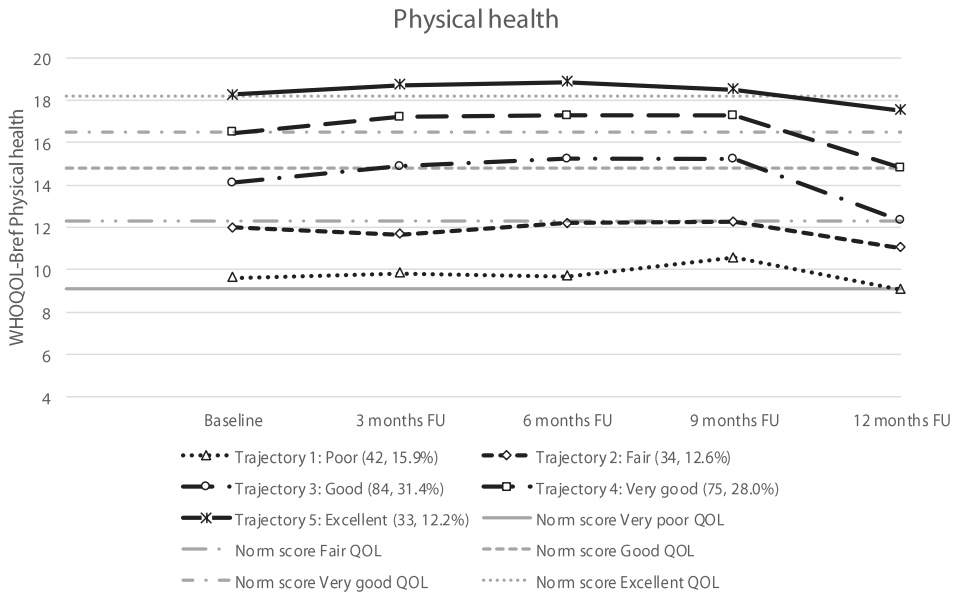

FIGURE 2A. Trajectories of physical health.

Abbreviations: WHOQOL-Bref: World Health Organization Quality of Life assessment instrument-Bref. Note: Class means are shown. A higher score indicates a better quality of life. Number of patients and percentages are shown of the sample included in each class. Norm scores are provided for Very poor QOL, Fair QOL, Good QOL, Very good QOL, and Excellent QOL.

The identified physical health trajectories differed significantly on all investigated psychological characteristics, except for Agreeableness and Openness. Patients in both the Poor and Fair class scored significantly more often on ASD (p = .002) and higher on anxiety, depressive symptoms, PTSD, Neuroticism, trait anxiety, and lower on Extraversion and Conscientiousness compared with the other three trajectories (i.e., Good, Very good, and Excellent). No significant differences were found for sociodemographic and clinical characteristics (see Table 3).

The most pronounced differences between the Excellent trajectory and Poor trajectory were found for PTSD, trait anxiety, and anxiety. Patients with Poor physical health trajectories had substantially higher baseline scores on PTSD, trait anxiety, and anxiety than patients with Excellent physical health. Patients in the Poor physical health trajectory significantly more often had ASD at baseline than patients with Excellent physical health trajectories ((n = 9, 22.5% versus n = 0, 0%, r_{φ} = .27, p = .024).

TABLE 3. Sociodemographic, clinical, and psychological characteristics for the five trajectories of physical health.

	Physical health					
	Trajectory 1: Poor	**Trajectory 2: Fair**	**Trajectory 3: Good**	**Trajectory 4: Very good**	**Trajectory 5: Excellent**	
Characteristics	**42 (15.9)**	**34 (12.6)**	**84 (31.4)**	**75 (28.0)**	**33 (12.2)**	**p-value**
Anxiety*	9.2 ± 3.7[4,5]	10.6 ± 3.2[3,4,5]	6.9 ± 4.8[2,5]	5.4 ± 4.3[1,2]	3.8 ± 4.4[1,2,3]	**<.001**
Depressive symptoms*	6.9 ± 2.7[3,4,5]	6.9 ± 2.5[3,4,5]	5.0 ± 2.6[1,2]	4.3 ± 2.1[1,2]	4.2 ± 2.3[1,2]	**<.001**
Neuroticism*	34.2 ± 8.6[3,4,5]	34.9 ± 8.2[3,4,5]	28.1 ± 7.2[1,2]	26.4 ± 6.5[1,2]	24.8 ± 6.8[1,2]	**<.001**
Trait anxiety*	21.9 ± 7.8[3,4,5]	22.0 ± 5.9[3,4,5]	17.0 ± 5.1[1,2]	14.8 ± 3.8[1,2]	14.0 ± 3.4[1,2]	**<.001**
PTSD*	34.7 ± 21.2[3,4,5]	26.0 ± 16.8[3,4,5]	15.6 ± 14.3[1,2]	10.8 ± 11.7[1,2]	10.2 ± 12.9[1,2]	**<.001**
Extraversion*	38.5 ± 7.1[3,4,5]	38.4 ± 5.9[3,4,5]	42.5 ± 5.3[1,2]	43.6 ± 6.4[1,2]	42.8 ± 7.2[1,2]	**<.001**
Conscientiousness*	44.1 ± 7.5	41.5 ± 6.2[3,4,5]	45.6 ± 5.8[2]	46.5 ± 5.4[2]	47.4 ± 6.0[2]	**<.001**
ASD (yes)	9 (22.5)[†]	3 (10.0)	4 (5.4)	2 (2.6)	0 (0)	**.001**
GCS*	14.8 ± 0.6	14.3 ± 1.5	14.9 ± 0.4	14.7 ± 0.8	14.6 ± 0.9	.022
Hospital stay on the ICU (yes)	4 (16.0)	7 (35.0)	8 (15.1)	16 (31.4)	1 (4.2)	.023
Psychiatric history	7 (17.5)	1 (3.2)	5 (6.0)	2 (2.5)	2 (6.1)	.028
Agreeableness*	40.7 ± 4.5	40.1 ± 4.7	42.1 ± 4.9	42.5 ± 3.9	42.2 ± 4.3	.054
LOS*	5.6 ± 6.0	5.8 ± 6.0	4.5 ± 4.6	5.6 ± 6.7	1.8 ± 1.3	.057
Age*	50.5 ± 16.8	49.5 ± 14.7	56.3 ± 16.2	55.9 ± 15.3	52.5 ± 15.1	.117
Living together (yes)	27 (69.2)	25 (80.6)	71 (86.6)	69 (86.3)	28 (84.8)	.147
Sex (male)	20 (50.0)	16 (51.6)	51 (61.4)	57 (71.3)	21 (63.6)	.147
Paid job (yes)	20 (51.3)	17 (54.8)	50 (60.2)	46 (57.5)	26 (78.8)	.157
Education (high)	12 (32.4)	9 (29.0)	24 (31.6)	34 (46.6)	18 (56.3)	.176
Surgery (yes)	9 (37.5)	7 (35.0)	13 (24.5)	11 (21.6)	3 (13.0)	.275
ISS*	6.8 ± 6.9	8.7 ± 10.0	6.9 ± 7.1	6.9 ± 6.2	4.9 ± 5.2	.327
Hospital stay (yes)	25 (62.5)	20 (64.5)	53 (63.9)	51 (63.8)	24 (72.7)	.898
Openness*	36.4 ± 7.8	36.8 ± 5.0	34.7 ± 6.3	35.0 ±5.5	36.6 ± 6.6	.284

*Number of patients (percentages) are provided for categorical variables. *Means ± standard deviations. Missing data was not included in calculating percentages[†,1,2,3,4,5]. A significant difference between the specified class(es). Using a Holm adjusted significance level, significant p-values for differences in a characteristic between all classes are shown in bold. Ranking of characteristics is based on p-value (low-high). Abbreviations: PTSD: posttraumatic stress disorder, ASD: acute stress disorder, LOS: length of stay, ISS: injury severity score, GCS: Glasgow Coma Score, ICU: intensive care unit*

Trajectories for psychological health

The four identified trajectories were labelled as Poor, Good, Very good, and Excellent psychological health (see Figure 2b).

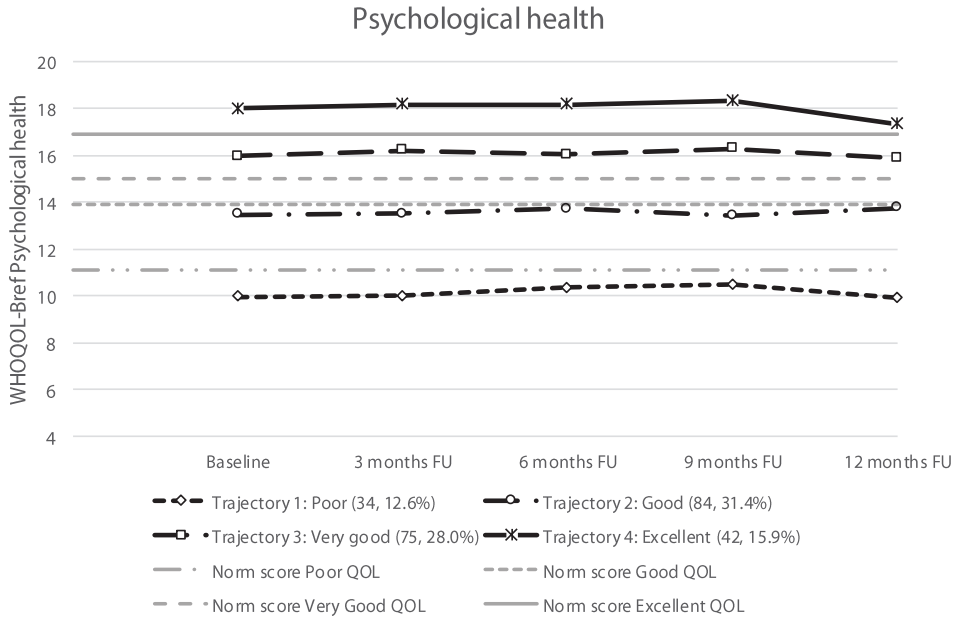

FIGURE 2B. Trajectories of psychological health.
Abbreviations: WHOQOL-Bref: World Health Organization Quality of Life assessment instrument-Bref. Note: Class means are shown. A higher score indicates a better quality of life. Number of patients and percentages are shown of the sample included in each class. Norm scores are provided for Poor QOL, Good QOL, Very good QOL, and Excellent QOL

These trajectories differed significantly on all examined psychological factors, except for Agreeableness and Openness (see Table 4). Sociodemographic and clinical factors did not significantly differ between the psychological health trajectories. Patients with Poor psychological health scored more often on ASD ($p < .001$) and higher on anxiety, depressive symptoms, PTSD, Neuroticism, trait anxiety, and lower on Extraversion and Conscientiousness compared to the other three trajectories (i.e., Good, Very good, and Excellent). Patients in the Very good psychological health trajectory showed significantly less ASD symptoms compared with other trajectories (i.e., Poor and Good).

TABLE 4. Sociodemographic, clinical, and psychological characteristics for the four trajectories of psychological health

	Psychological health				
	Trajectory 1: Poor	**Trajectory 2: Good**	**Trajectory 3: Very good**	**Trajectory 4: Excellent**	
Characteristics	**34 (12.6)**	**84 (31.3)**	**75 (28.0)**	**42 (15.6)**	**p-value**
Anxiety*	11.3 ± 2.5[2,3,4]	9.0 ± 4.2[1,3,4]	4.7 ± 3.8[1,2]	3.9 ± 4.0[1,2]	**<.001**
Depressive symptoms*	8.1 ± 2.1[2,3,4]	5.7 ± 2.4[1,3,4]	4.0 ± 2.1[1,2]	4.2 ± 2.3[1,2]	**<.001**
Neuroticism*	39.1 ± 6.3[2,3,4]	31.3 ± 6.4[1,3,4]	25.8 ± 6.5[1,2]	23.4 ± 5.9[1,2]	**<.001**
Trait anxiety*	26.4 ± 6.5[2,3,4]	18.7 ± 4.6[1,3,4]	14.6 ± 3.1[1,2]	13.2 ± 2.9[1,2]	**<.001**
PTSD*	37.6 ± 21.2[2,3,4]	20.4 ± 14.9[1,3,4]	9.9 ± 11.5[1,2,4]	11.7 ± 13.7[1,2]	**<.001**
Extraversion*	36.0 ± 6.0[2,3,4]	41.4 ± 5.9[1,4]	42.3 ± 5.9[1]	45.0 ± 6.3[1,2]	**<.001**
Conscientiousness*	41.6 ± 7.8[3,4]	44.3 ± 6.1[4]	46.0 ± 5.3[1]	48.3 ± 5.0[1,2]	**<.001**
ASD (yes)	10 (28.6)[†]	7 (7.9)	0 (0)[†]	1 (1.8)	**<.001**
Agreeableness*	39.5 ± 4.7	41.6 ± 4.1	42.1 ± 4.5	42.9 ± 4.6	.004
Psychiatric history	21 (60.0)	53 (57.6)	51 (65.4)	40 (64.5)	.005
Age*	47.6 ± 16.4	52.0 ± 16.4	57.4 ± 15.4	56.5 ± 15.2	.008
Education (high)	8 (23.5)	29 (33.3)	33 (46.5)	27 (47.4)	.010
Living together (yes)	23 (65.7)	76 (84.4)	68 (87.2)	53 (58.8)	.032
Paid job (yes)	17 (48.6)	59 (64.8)	46 (59.0)	37 (59.7)	.421
GCS*	14.9 ± 0.6	14.6 ± 1.0	14.7 ± 0.8	14.8 ± 0.8	.455
ISS*	5.5 ± 6.5	6.9 ± 7.7	6.7 ± 6.6	7.7 ± 6.7	.521
Sex (male)	21 (60)	53 (57.6)	51 (65.4)	40 (64.5)	.717
LOS*	4.5 ± 4.9	5.2 ± 5.4	5.0 ± 6.3	4.0 ± 5.0	.743
Hospital stay (yes)	21 (60.0)	58 (63.0)	51 (65.4)	43 (69.4)	.788
Openness*	35.1 ± 5.5	35.9 ± 6.8	35.3 ± 6.7	35.5 ± 5.2	.904
Surgery (yes)	4 (20.0)	15 (25.9)	13 (26.0)	11 (25.6)	.956
Hospital stay on the ICU (yes)	4 (19.0)	13 (22.4)	10 (19.6)	9 (20.9)	.981

*Number of patients (percentages) are provided for categorical variables. *Means ± standard deviations. Missing data was not included in calculating percentages[†,1,2,3,4]. A significant difference between the specified class(es). Using a Holm adjusted significance level, significant p-values for differences in a characteristic between all classes are shown in bold. Ranking of characteristics is based on p-value (low-high).*

Abbreviations: PTSD: posttraumatic stress disorder, ASD: acute stress disorder, LOS: length of stay, ISS: injury severity score, GCS: Glasgow Coma Score, ICU: intensive care unit

The most pronounced differences between the Excellent (class 4; reference group) trajectory and Poor psychological health trajectory were found for trait anxiety, Neuroticism, and anxiety. Patients with Poor psychological health had substantially higher baseline scores on trait anxiety, Neuroticism, and anxiety than patients with Excellent psychological health. Patients in the Poor psychological health trajectory more often had ASD at baseline than patients with patients with Excellent psychological health (n = 10, 28.6% versus n = 1, 1.8%, $r_{\varphi} = .31$, $p = .007$).

Trajectories for social relationships

The five identified trajectories were labelled as Very poor, Fair, Good, Very good, and Excellent social relationships (see Figure 2c).

These trajectories differed significantly on all investigated psychological characteristics, except for Agreeableness and Openness (see Table 5). The trajectories did not differ in terms of sociodemographic and clinical characteristics. Patient in the Very poor and Fair social relationships trajectory scored more often on ASD ($p < .001$) and significantly higher on anxiety, depressive symptoms, PTSD, Neuroticism, and trait anxiety, and lower on Extraversion and Conscientiousness compared to the other three (i.e., Good, Very good, and Excellent) trajectories.

The most pronounced differences between the Excellent and Very poor social relationships trajectories were found for trait anxiety, Neuroticism, and depressive symptoms. Patients with Very poor trajectories scored substantially higher on trait anxiety, Neuroticism, and depressive symptoms than patients with Excellent trajectories. Patients with Very poor social relationships trajectories had more often ASD than patients with patients with Excellent social relationships (n = 3, 37.5% versus n = 0, 0%, $r_{\varphi} = .45$, $p = .014$).

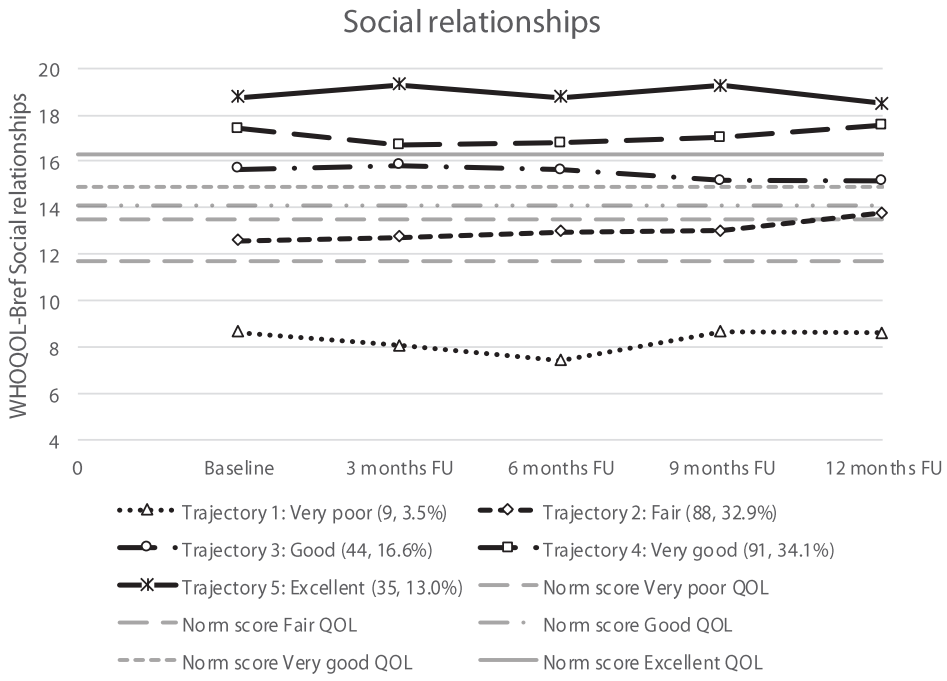

FIGURE 2C. Trajectories of social relationships.

Abbreviations: WHOQOL-Bref: World Health Organization Quality of Life assessment instrument-Bref. Note: Class means are shown. A higher score indicates a better quality of life. Number of patients and percentages are shown of the sample included in each class. Norm scores are provided for Very poor QOL, Fair QOL, Good QOL, Very good QOL, and Excellent QOL.

TABLE 5. Sociodemographic, clinical, and psychological characteristics for the five trajectories of social relationships.

	Social relationships					
	Trajectory 1: Very poor	**Trajectory 2: Fair**	**Trajectory 3: Good**	**Trajectory 4: Very good**	**Trajectory 5: Excellent**	
Characteristics	**9 (3.5)**	**88 (32.9)**	**44 (16.6)**	**91 (34.1)**	**35 (13.0)**	**p-value**
Anxiety*	12.3 ± 2.3[3,4,5]	8.8 ± 4.5[3,4,5]	6.3 ± 4.4[1,2]	5.4 ± 4.4[1,2]	4.8 ± 4.4[1,2]	**<.001**
Depressive symptoms*	8.1 ± 2.4[3,4,5]	5.8 ± 2.6[4,5]	5.4 ± 2.6[1,5]	4.6 ± 2.4[1,2]	3.3 ± 2.0[1,2,3]	**<.001**
Neurotiscism*	40.4 ± 8.0[2,3,4,5]	32.3 ± 7.3[1,3,4,5]	27.7 ± 6.0[1,2]	26.7 ± 7.8[1,2]	23.1 ± 6.6[1,2]	**<.001**
Trait anxiety*	28.3 ± 5.2[2,3,4,5]	10.1 ± 6.3[1,3,4,5]	16.2 ± 4.4[1,2]	16.0 ± 5.3[1,2]	13.1 ± 3.3[1,2]	**<.001**
PTSD*	36.7 ± 21.4[3,4,5]	24.4 ± 18.7[3,4,5]	13.0 ± 12.8[1,2]	13.4 ± 15.1[1,2]	11.2 ± 11.5[1,2]	**<.001**
Extraversion*	33.6 ± 8.7[3,4,5]	39.8 ± 5.9[4,5]	42.6 ± 5.3[1]	43.2 ± 6.3[1,2]	44.7 ± 7.5[1,2]	**<.001**
Conscientiousness*	38.7 ± 10.5[4,5]	44.1 ± 6.4[5]	44.8 ± 4.5	46.9 ± 6.0[1,2]	47.2 ± 4.9[1]	**<.001**
ASD	3 (37.5)[†]	11 (12.9)[†]	1 (2.6)	3 (3.0)[†]	0 (0)	**<.001**
Agreeableness*	40.9 ± 4.6	40.4 ± 4.1	42.2 ± 4.0	42.8 ± 4.6	41.6 ± 5.4	.005
Education (high)	3 (37.5)	23 (26.7)	16 (38.1)	47 (49.5)	8 (44.4)	.053
Age*	45.3 ± 16.7	52.1 ± 15.3	59.5 ± 16.2	54.3 ± 16.4	52.7 ± 15.0	.063
Psychiatric history	2 (25.0)	8 (9.0)	3 (6.8)	3 (2.8)	1 (5.6)	.090
Sex (male)	4 (50.0)	62 (69.7)	30 (68.2)	58 (53.7)	11 (61.1)	.161
ISS*	2.9 ± 2.8	6.9 ± 7.5	8.1 ± 7.8	6.3 ± 6.4	8.6 ± 6.7	.231
Living together (yes)	6 (75.0)	69 (79.3)	41 (93.2)	88 (81.5)	16 (88.9)	.281
Hospital stay (yes)	4 (50.0)	55 (61.8)	33 (75.0)	67 (62.0)	14 (77.8)	.307
Openness*	37.9 ± 4.8	34.7 ± 5.9	36.3 ± 6.5	35.5 ± 6.4	37.2 ± 6.7	.342
Paid job (yes)	3 (37.5)	56 (63.6)	22 (50.0)	66 (61.1)	12 (66.7)	.357
Surgery (yes)	0 (0)	12 (21.8)	11 (33.3)	16 (24.6)	4 (28.6)	.568
GCS*	14.9 ± 0.4	14.7 ± 0.9	14.8 ± 0.4	14.7 ± 0.8	14.6 ± 1.2	.716
LOS*	1.7 ± 1.2	4.9 ± 5.6	4.7 ± 4.5	4.6 ± 5.6	5.8 ± 7.4	.824
Hospital stay on the ICU (yes)	0 (0)	13 (23.6)	7 (21.2)	13 (19.4)	3 (21.4)	.843

*Number of patients (percentages) are provided for categorical variables. *Means ± standard deviations. Missing data was not included in calculating percentages. [1,1,2,3,4,5]A significant difference between the specified class(es). Using a Holm adjusted significance level, significant p-values for differences in a characteristic between all classes are shown in bold. Ranking of characteristics is based on p-value (low-high).*

Abbreviations: PTSD: posttraumatic stress disorder, ASD: acute stress disorder, LOS: length of stay, ISS: injury severity score, GCS: Glasgow Coma Score, ICU: intensive care unit

Trajectories for environment

The four identified trajectories were labelled as Poor, Good, Very good, and Excellent environmental QOL (Figure 2d).

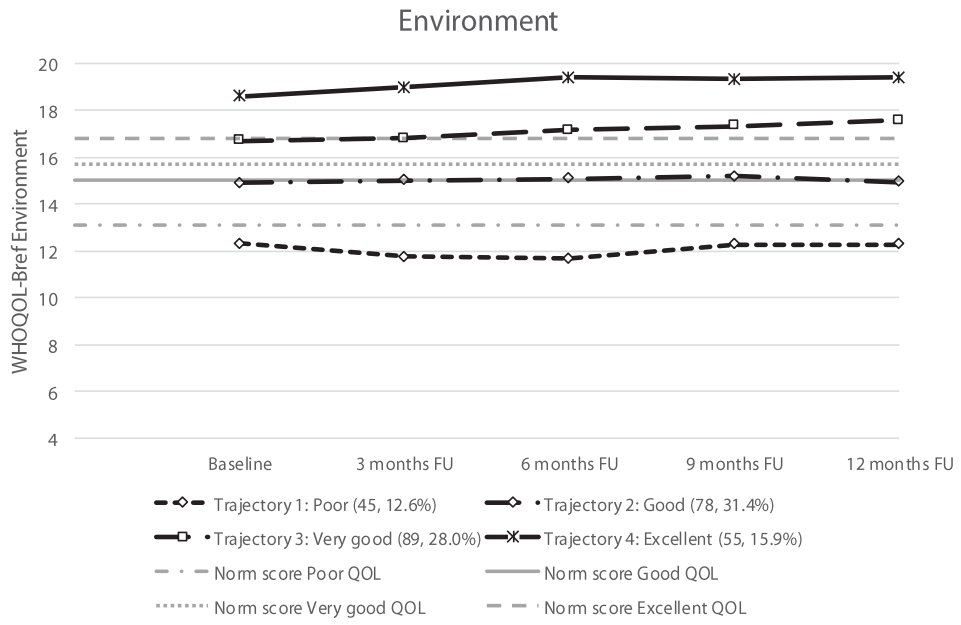

FIGURE 2D. Trajectories of environment.

Abbreviations: WHOQOL-Bref: World Health Organization Quality of Life assessment instrument-Bref. Note: Class means are shown. A higher score indicates a better quality of life. Number of patients and percentages are shown of the sample included in each class. Norm scores are provided for Poor QOL, Good QOL, Very good QOL, and Excellent QOL.

These trajectories differed significantly on all investigated psychological factors, except for Openness (see Table 6). The trajectories did not differ significantly in terms of clinical characteristics. Patients in the Poor environment trajectory scored significantly more often on ASD ($p < .001$) and higher on anxiety, depressive symptoms, PTSD, Neuroticism, trait anxiety, and lower on Extraversion, Conscientiousness, and Agreeableness compared with the other (i.e., Good, Very good, and Excellent) trajectories.

TABLE 6. Sociodemographic, clinical, and psychological characteristics for the four trajectories of environment

	Environment				
	Trajectory 1: Poor	**Trajectory 2: Good**	**Trajectory 3: Very good**	**Trajectory 4: Excellent**	
Characteristics	**45 (16.8)**	**78 (29.0)**	**89 (33.4)**	**55 (20.7)**	**p-value**
Anxiety*	9.7 ± 4.0[3,4]	7.9 ± 4.4[3,4]	6.0 ± 4.6[1,2]	4.3 ± 4.4[1,2]	**<.001**
Depressive symptoms*	7.3 ± 2.5[2,3,4]	5.4 ± 2.5[1,3,4]	4.4 ± 2.4[1,2]	4.2 ± 2.0[1,2]	**<.001**
Neurotiscism*	37.3 ± 7.4[2,3,4]	29.3 ± 7.0[1,4]	26.8 ± 6.8[1]	24.8 ± 6.6 [1,2]	**<.001**
Trait anxiety*	24.3 ± 6.9[2,3,4]	17.4 ± 5.1[1]	15.7 ± 4.3[1]	13.7 ± 3.1[1]	**<.001**
PTSD (IES-R)*	33.5 ± 20.9[2,3,4]	19.0 ± 15.7[1,3,4]	12.3 ± 12.2[1,2]	10.6 ± 13.5[1,2]	**<.001**
Extraversion*	37.9 ± 5.7[2,3,4]	41.9 ± 6.2[1]	42.4 ± 6.1[1]	43.8 ± 7.0[1]	**<.001**
Conscientiousness*	42.2 ± 7.4[2,3,4]	45.3 ± 6.3[1]	45.9 ± 5.1[1]	47.3 ± 5.8[1]	**<.001**
ASD (yes)	11 (24.4)[†]	5 (6.9)	1 (1.3)[†]	1 (1.9)	**<.001**
Agreeableness*	38.6 ± 3.8[2,3,4]	41.8 ± 4.2[1]	42.9 ± 4.3[1]	42.6 ± 4.7[1]	**<.001**
Education (high)	6 (13.6)[†]	18 (25.4)[†]	39 (50.0)[†]	34 (60.7)[†]	**<.001**
Psychiatric history	8 (17.4)	3 (3.8)	5 (5.9)	1 (1.7)	.006
Age*	47.5 ± 16.3	54.2 ± 16.7	55.7 ± 16.6	56.6 ± 13.3	.017
ISS*	4.6 ± 6.9	7.1 ± 7.7	6.8 ± 6.4	8.3 ± 6.8	.065
Paid job (yes)	21 (46.7)	43 (55.1)	55 (64.7)	40 (69.0)	.078
Openness*	35.1 ± 6.4	34.3 ± 6.5	35.9 ± 6.4	37.0 ± 5.4	.078
GCS*	14.9 ± 0.5	14.7 ± 0.7	14.6 ± 1.1	14.7 ± 0.8	.206
Hospital stay (yes)	24 (52.2)	50 (64.1)	59 (69.4)	40 (69.0)	.215
Living together (yes)	33 (73.3)	66 (85.7)	70 (82.4)	51 (87.9)	.220
Hospital stay on the ICU (yes)	3 (12.5)	14 (28.0)	10 (16.9)	9 (22.5)	.365
Sex (male)	26 (56.5)	52 (66.7)	50 (58.8)	37 (63.8)	.628
LOS*	4.5 ± 4.6	5.1 ± 5.4	5.1 ± 6.2	4.0 ± 5.1	.755
Surgery (yes)	5 (21.7)	14 (28.6)	16 (27.1)	8 (20.0)	.769

*Number of patients (percentages) are provided for categorical variables. *Means ± standard deviations. Missing data was not included in calculating percentages. [†,1,2,3,4] A significant difference between the specified class(es). Using a Holm adjusted significance level, significant p-values for differences in a characteristic between all classes are shown in bold. Ranking of characteristics is based on p-value (low-high).*

Abbreviations: PTSD: posttraumatic stress disorder, ASD: acute stress disorder, LOS: length of stay, ISS: injury severity score, GCS: Glasgow Coma Score, ICU: intensive care unit

The most pronounced differences between the Excellent trajectory and Poor trajectory were found for trait anxiety, Neuroticism, and depressive symptoms. Patients in the Poor trajectory scored at baseline substantially higher on trait anxiety, Neuroticism, and depressive symptoms than patients in the Excellent environment trajectory. Patients in the Poor environment trajectory had more often ASD at baseline (n = 11, 24.4%) than patients in the Excellent trajectory (n = 1, 1.9%, r_{φ} = .29, p = .006). More patients in the Excellent environment trajectory were higher educated (n = 34, 60.7%) compared to patients in the Poor trajectory (n = 6, 13.6%, r_{φ} = -.28, p = .002).

Trajectories for overall quality of life and general health

The seven identified trajectories were labelled as Very poor, Recovery, Poor, Fair, Good, Very good, and Excellent class (see Figure 2e).

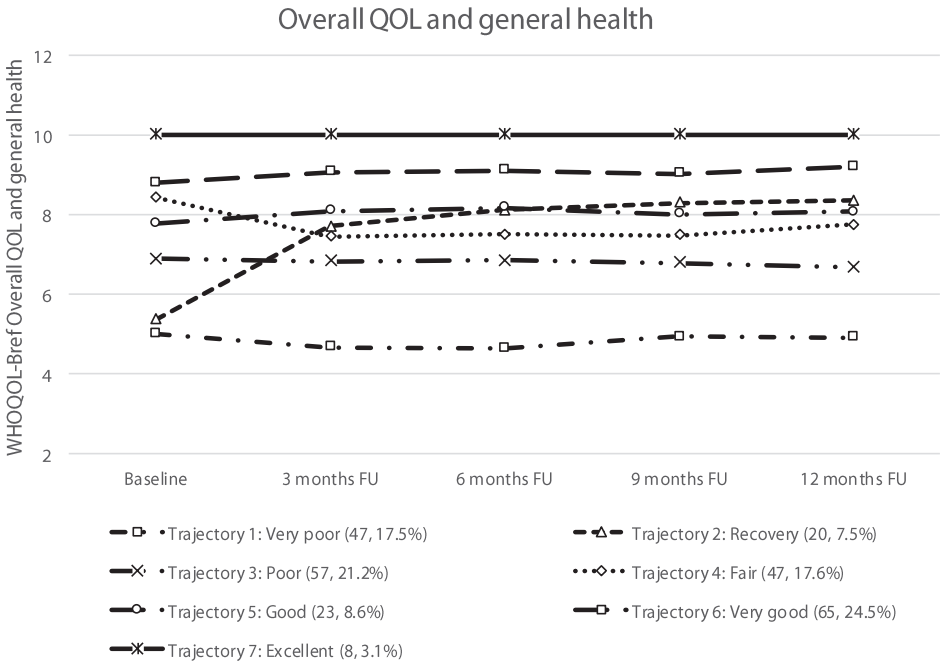

FIGURE 2E. Trajectories of overall QOL and general health.
Abbreviations: WHOQOL-Bref: World Health Organization Quality of Life assessment instrument-Bref, QOL: quality of life. Note: Class means are shown. A higher score indicates a better quality of life. Number of patients and percentages are shown of the sample included in each class.

These trajectories differed significantly on all investigated psychological factors, except for Conscientiousness, Agreeableness and Openness (see Table 7). The trajectories did not significantly differ on the sociodemographic and clinical variables. Patients in the Very poor trajectory scored significantly higher on anxiety, depressive symptoms, PTSD, Neuroticism, trait anxiety, and lower on Extraversion than patients in the other trajectories. Significantly more patients with ASD ($p < .001$) were found in the Very poor (trajectory 1, n = 13, 27.1%) trajectory compared with other trajectories, whereas no patients with ASD were found in the Very good (trajectory 6, n = 0, 0%) class. The Recovery trajectory was the only trajectory in which QOL improved over time, from Very poor QOL at baseline to Good QOL at 12 months after trauma. These patients scored significantly higher on Extraversion and had significantly lower PTSD, Neuroticism, trait anxiety and depression scores at baseline than patients who did not recover during the 12 months follow-up (i.e., Very Poor trajectory). Furthermore, patients in the Recovery trajectory were more often female patients with high education and longer hospital stay, though these results were not statistically significant.

The most pronounced differences between the Excellent trajectory and Very poor trajectory were found for anxiety, depressive symptoms, and trait anxiety. Patients in the Very poor trajectory had substantially higher baseline scores on anxiety, depressive symptoms, and trait anxiety than patients in the Excellent trajectory.

TABLE 7. Sociodemographic, clinical, and psychological characteristics for the seven trajectories of overall quality of life and general health.

	Overall quality of life and general health							
	Trajectory 1: Very poor	**Trajectory 2: Recovery**	**Trajectory 3: Poor**	**Trajectory 4: Fair**	**Trajectory 5: Good**	**Trajectory 6: Very good**	**Trajectory 7: Excellent**	
Characteristics	**47 (17.5)**	**20 (7.5)**	**57 (21.1)**	**47 (17.6)**	**23 (8.6)**	**65 (24.4)**	**8 (3.1)**	**p-value**
Anxiety*	9.6 ± 3.5[4,5,6,7]	7.6 ± 3.6[6]	9.0 ± 4.6[5,6,7]	6.5 ± 5.0[1,6]	5.8 ± 3.8[1,3]	3.7 ± 3.9[1,2,3,4]	3.9 ± 3.8[1,3]	**<.001**
Depressive symptoms*	7.6 ± 2.3[2,3,4,5,6,7]	5.4 ± 2.3[1]	5.2 ± 2.4[1]	4.7 ± 2.7[1]	4.3 ± 2.1[1]	4.1 ± 2.1[1]	4.3 ± 2.0[1]	**<.001**
Neurotiscism*	35.8 ± 7.9[2,3,4,5,6,7]	28.1 ± 7.1[1]	31.3 ± 8.0[1,4,6]	26.2 ± 6.5[1,3]	27.4 ± 4.9[1]	24.7 ± 6.7[1,3]	25.4 ± 7.4[1]	**<.001**
Trait anxiety*	23.4 ± 7.5[2,3,4,5,6,7]	17.5 ± 5.2[1]	19.0 ± 4.7[1,4,5,6,7]	14.6 ± 3.9[1,3]	14.1 ± 2.5[1,3]	14.4 ± 4.0[1,3]	13.6 ± 3.7[1,3]	**<.001**
PTSD*	33.3 ± 21.8[2,3,4,5,6,7]	14.4 ± 14.0[1]	20.2 ± 14.9[1,5,6]	15.7 ± 14.2[1]	8.3 ± 11.3[1,3]	10.9 ± 11.8[1,3]	8.6 ± 12.1[1]	**<.001**
Extraversion*	38.1 ± 6.2[2,6]	44.6 ± 6.0[1]	40.8 ± 5.9	42.1 ± 6.7	42.6 ± 5.0	43.8 ± 6.6[1]	43.7 ± 7.7	**<.001**
ASD (yes)	13 (27.1)[†]	1 (5.6)	1 (1.9)	2 (5.6)	1 (3.8)	0 (0)[†]	0 (0)	**<.001**
Conscientiousness*	43.0 ± 7.2	46.4 ± 6.6	44.2 ± 5.6	45.1 ± 6.7	47.5 ± 3.9	47.0 ± 5.4	46.9 ± 8.1	.004
Psychiatric history	9 (18.8)	1 (5.6)	4 (6.8)	2 (5.3)	0 (0)	1 (1.5)	0 (0)	.007
Education (high)	11 (24.4)	11 (68.8)	14 (24.1)	13 (39.4)	11 (40.7)	32 (52.5)	5 (55.6)	.013
Sex (male)	26 (54.2)	6 (33.3)	37 (62.7)	26 (68.4)	23 (82.1)	43 (64.2)	4 (44.4)	.026
LOS*	5.3 ± 5.3	8.7 ± 6.8	5.6 ± 7.2	3.9 ± 3.1	5.6 ± 7.7	3.0 ± 2.8	2.3 ± 1.5	.035
Age*	50.7 ± 17.2	50.7 ± 13.2	53.1 ± 16.1	60.3 ± 11.5	54.5 ± 17.1	54.7 ± 17.9	52.3 ± 10.8	.176
Agreeableness*	40.3 ± 4.3	41.4 ± 5.0	41.6 ± 5.0	42.1 ± 4.8	41.5 ± 3.5	42.8 ± 4.2	42.7 ± 3.6	.180
Paid job (yes)	22 (46.8)	14 (77.8)	36 (61.0)	21 (55.3)	19 (67.9)	40 (59.7)	7 (77.8)	.235
Hospital stay on the ICU (yes)	8 (25.8)	3 (25.0)	7 (20.0)	3 (10.7)	7 (38.9)	6 (14.0)	2 (33.3)	.260
Living together (yes)	34 (72.3)	16 (88.9)	49 (83.1)	31 (83.8)	26 (92.9)	56 (83.6)	8 (88.9)	.378

TABLE 7. Continued

	Overall quality of life and general health							
Characteristics	**Trajectory 1: Very poor** **47 (17.5)**	**Trajectory 2: Recovery** **20 (7.5)**	**Trajectory 3: Poor** **57 (21.1)**	**Trajectory 4: Fair** **47 (17.6)**	**Trajectory 5: Good** **23 (8.6)**	**Trajectory 6: Very good** **65 (24.4)**	**Trajectory 7: Excellent** **8 (3.1)**	**p-value**
ISS*	6.8 ± 8.3	10.1 ± 7.8	6.3 ± 7.3	6.6 ± 5.5	7.5 ± 7.2	6.2 ± 6.0	7.4 ± 7.9	.541
GCS*	14.6 ± 1.0	14.4 ± 1.3	14.8 ± 0.8	14.8 ± 0.5	14.8 ± 0.5	14.7 ± 0.8	14.6 ± 0.7	.597
Surgery (yes)	7 (23.3)	4 (33.3)	8 (22.9)	8 (28.6)	6 (35.3)	10 (23.3)	0 (0)	.707
Openness*	34.6 ± 6.4	37.1 ± 8.5	35.2 ± 6.1	35.6 ± 5.7	34.8 ± 6.0	36.1 ± 6.0	36.8 ± 7.2	.744
Hospital stay (yes)	43 (64.2)	12 (66.7)	35 (59.3)	28 (73.7)	18 (64.3)	43 (64.2)	6 (66.7)	.906

*Number of patients (percentages) are provided for categorical variables. *Means ± standard deviations. Missing data was not included in calculating percentages.* [1, 1,2,3,4,5,6,7] *A significant difference between the specified class(es). Using a Holm adjusted significance level, significant p-values for differences in a characteristic between all classes are shown in bold. Ranking of characteristics is based on p-value (low-high).*

Abbreviations: PTSD: posttraumatic stress disorder, ASD: acute stress disorder, LOS: length of stay, ISS: injury severity score, GCS: Glasgow Coma Score, ICU: intensive care unit

TABLE 8. Cohens d effect sizes and Phi coefficients between Excellent and (Very) Poor QOL trajectories for all quality of life domains and overall QOL and general health

	Physical health		Psychological health		Social relationships		Environment		Overall QOL and general health	
Characteristics	**Cohens' d (Excellent vs. Poor)**	**CI interval (95%)**	**Cohen's d (Excellent vs. Poor)**	**CI interval (95%)**	**Cohen's d (Excellent vs. Very poor)**	**CI interval (95%)**	**Cohen's d (Excellent vs. Poor)**	**CI interval (95%)**	**Cohen's d (Excellent vs. Very poor)**	**CI interval (95%)**
Anxiety	1.34	[.83, 1.85]	2.17	[1.60, 2.74]	1.84	[1.01, 2.66]	1.28	[.85, 1.71]	1.61	[.80, 2.42]
Depressive symptoms	1.07	[.58, 1.55]	1.76	[1.23, 2.29]	2.31	[1.43, 3.18]	1.38	[0.95, 1.82]	1.46	[.66, 2.26]
Neuroticism	1.20	[.70, 1.69]	2.58	[1.97, 3.19]	2.51	[1.61, 3.41]	1.79	[1.33, 2.26]	1.33	[0.54, 2.12]
Trait anxiety	1.26	[.76, 1.76]	2.72	[2.10, 3.35]	4.07	[2.95, 5.19]	2.05	[1.57, 2.54]	1.38	[.58, 2.17]
PTSD	1.36	[.85, 1.86]	1.48	[.97, 1.99]	1.83	[1.00, 2.66]	1.33	[0.89, 1.76]	1.19	[.41, 1.97]
Extraversion	-.60	[-1.07, -.14]	-1.46	[-1.97, -.95]	-1.43	[-2.23, -.64]	-.91	[-1.33, -.50]	-.87	[-1.64, -.11]
Conscientiousness	-.48	[-.94, -.02]	-1.05	[-1.53, -.56]	-1.34	[-2.12, -.55]	-.78	[-1.19, -.37]	-	-
Agreeableness	-	-	-	-	-	-	-.93	[-1.34, -.51]	-	-
	r_φ	**p-value**	r_φ	**p-value**	r_φ	**p-value**	r_φ	**p-value**	r_φ	**p-value**
ASD (yes)*	.27	.024	.31	.007	.45	.014	.29	.006	.18	.203
Education (high)*	-	-	-	-	-	-	-.28	.002	-	-

*Excellent trajectory is the reference class. *Phi coefficients are provided for ASD and education. -No significantly differences were found for Conscientiousness in Overall QOL and general health, Agreeableness in physical, psychological, social, and overall QOL and general health, and education in physical, psychological, social, and overall QOL and general health. Abbreviations: QOL: quality of life, vs: versus, CI: confidence interval, ASD: acute stress disorder. Note: A positive Cohen's d indicates a higher mean score for patients in the Poor or Very poor trajectory (class 1) compared to patients in the Excellent trajectory (class 4, 5, or 7; reference group). Whereas a negative Cohen's d indicates a lower mean score for patients in the Poor or Very poor trajectory (class 1) compared to patients in either the Excellent trajectory (class 4, 5, or 7; reference group). If the 95% confidence interval does not contain the null hypothesis value (zero), the results are statistically significant.*

DISCUSSION

To our knowledge, this is the first study that examined QOL trajectories and determined sociodemographic, clinical, and psychological characteristics of trajectory membership in physical trauma patients using a biopsychosocial approach. An overall finding is that psychological, but not sociodemographic or clinical aspects, defined trajectories. Furthermore, four latent trajectories were found for psychological health and environment, five for physical health and social relationships, and seven trajectories for overall QOL and general health. This study showed that patients at risk for impaired QOL can be identified at baseline based on symptoms of anxiety, depressive symptoms, acute stress disorder, posttraumatic stress disorder, Neuroticism, and trait anxiety and in general not on sociodemographic or clinical characteristics.

Although earlier research focused on improvement of HRQoL or HS[18,21,22,50], the present study is the first to examine recovery on QOL domains. A Recovery trajectory was not found for the separate domains, but only for overall QOL and general health. At baseline, these patients had significantly less PTSD, depressive symptoms, Neuroticism, and trait anxiety than patients who did not improve their QOL during 12-months follow-up. Patients in the Recovery trajectory also showed significantly higher scores on Extraversion (at baseline) than patients in other trajectories. Finally, patients showing a Recovery trajectory were more often female patients, higher educated, and had a longer hospital stay, than patients from other QOL trajectories. However, these results failed to reach statistical significance. Even though these latter findings should be interpreted with caution, they may be interesting areas of future research.

Previous research identified psychological characteristics (e.g., anxiety, depressive symptoms, and PTSD) for impaired QOL[4,9,16], which were also relevant in this study. Compared to other trajectories, Very poor or Poor trajectories were characterized by ASD at baseline. This was also confirmed by the result that experiencing ASD symptoms is strongly related to impaired QOL[51]. A high score on the MINI-Plus does not necessarily mean that someone is diagnosed with ASD, because such a diagnosis requires the presence of symptoms on all domains (i.e., intrusion, negative emotions, dissociation, avoidance, and arousal). Therefore, ASD was used as a dichotomous variable. However, the other characteristics were used as continuous variables, because they indicate symptom severity. In addition, information about the relation between ASD on QOL is scarce, possibly because ASD is a relatively new diagnosis and less studied compared to PTSD[52]. Therefore, more research is needed that examines ASD in relation to QOL. Moreover, in line with previous studies, the association between personality traits and QOL was confirmed[53-55]. Regarding Very poor or Poor trajectories in all domains, patients scored higher on Neuroticism, trait anxiety and lower on Extraversion

compared to other trajectories. Different results were found for Conscientiousness and Agreeableness. Surprisingly, except for high education in environment trajectory, no sociodemographic (e.g., female sex) and clinical characteristics were found as risk factors for impaired QOL, which is contrary with earlier research[12,15,17,18].

A major strength and study implication is that it identified patients at risk for impaired QOL. This knowledge will help clinicians to screen patients in an early stage, for example on the emergency department or department of surgery, by using the Psychosocial Screening Instrument for physical Trauma patients (PSIT)[56]. In addition, the trajectories seemed to be stable during 12 months after trauma. However, RMLCA evaluates characteristics of individuals and not whether a change in development of symptoms is statistically significant. Therefore, interpretation of the course of trajectories can be evaluated using repeated measures ANOVA or mixed models ANOVA (in case of > two groups). The fact that most identified trajectories did not involve change over time suggests that QOL at baseline is almost the same 12 months after trauma. Therefore, patients can also be asked about their QOL almost directly after trauma as this implies QOL 12 months post-trauma. Then, patients can be treated to prevent a psychological disorder. Concerning trajectories of social relationships, patients seemed to rate their social relationships better than the norm scores. A reason could be that trauma patients, who are dependent on others, rate their QOL better when they experienced being supported by their relatives than patients who are not dependent of others and receive less support. Unfortunately, Hawthorn et al. (2006) did not provide norm scores for overall QOL and general health[29]. However, trajectories for overall QOL and general health were indicated based on the labels provided for the other domains. Also, to the best to our knowledge, this was the first study that examined QOL domains after a physical trauma. Because of inconclusive results regarding recovery trajectories, more research is needed that examines in QOL domains. Also, pre-injury HRQOL[57] or HS[58,59] was likely to be a predictor of post-trauma HRQOL and HS. It is still unclear whether pre-injury QOL could be a predictor for post-trauma QOL. In addition, future research could also focus on sociodemographic and clinical characteristics to determine which characteristics mostly influence QOL trajectories and to clarify inconsistent results.

Some limitations must be taken into account. First, as this hospital is a level-1 trauma center, only severely injured patients were included[1]. This may limit the generalizability to other severely injured patients from other level-1 trauma centers or less severely injured patients from level-2 or 3 hospitals. Also, the observed differences in characteristics of responders and non-responders suggests that selection bias might have occurred. Second, the response rate was 27%. Main reasons to decline participation, was that patients were not interested, because they did not experience any physical or psychological problems after trauma. In contrast, participation could be difficult, because patients could be faced

with their problems or (physical) limitations. Furthermore, concerning our dropout rates, it is likely that patients who were fully recovered were probably less interested to complete follow-up measurements compared to patients who still experienced problems with functioning. This could also be the reason for the sparse data in the cross tables comparing the ASD diagnoses between the trajectory classes. Since this sparsity resulted in extremely large odds ratios, we expressed these associations using the phi coefficient. In addition, two kinds of missingness were taken into account. First, missing values on the dependent variables (i.e., WHOQOL-BREF) were handled through full information maximum likelihood estimation using Latent Gold software. This method is appropriate when one or two follow-up measurements are missing from a participant. The second method focussed on single missing item scores of the IES-R and the HADS, which were imputed with individual subscale means when at least half of the subscale items were answered[34,44,45]. However, overestimation of item variation and a lower Cronbach's alpha of the scale from that item could occur[60]. Furthermore, the risk factors for QOL were interpreted in terms of correlation and this interpretation did not imply causation[61]. Another limitation is that this study was largely based on self-reported questionnaires. A PTSD diagnosis could not solely rely on self-report questionnaire, as a consultation from a health psychologist or psychiatrist is needed to be diagnosed with PTSD. Therefore, interpretation of such a diagnosis must be done with caution. Finally, no significant changes in trajectories were observed during 12 months post injury. Since the strength of RMLCA is to identify how many patterns of responses (i.e., trajectories of QOL) are present in the data and how these patterns are characterized over multiple time points[24]. Therefore, instead of screening patients on risk factors (e.g., ASD, anxiety, depressive symptoms, or personality traits), HCPs could ask them about their needs, perspectives, and satisfaction with QOL almost directly after trauma (at baseline). Future research could focus on the need and the impact of further additional care, from a social worker or registered health psychologist, on patients' recovery and QOL[62].

CONCLUSION

The present study demonstrates that psychological characteristics influence the development of QOL during 12 months after trauma. These findings can enable health care providers to identify patients at risk of impaired QOL. Then, they can offer patient-centered care and, subsequently, patients' QOL after trauma could be improved.

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SUPPLEMENTAL TABLE 1. Missing sum scores on each quality of life domain for every measurement during 12 months follow-up.

Domains	Baseline	3 mo FU	6 mo FU	9 mo FU	12 mo FU
Physical health	2 (0.7%)	53 (19.9%)	61 (22.8%)	74 (27.7%)	76 (28.5%)
Psychological health	0 (0%)	54 (20.2%)	61 (22.8%)	74 (27.7%)	75 (28.1%)
Social relationships	1 (0.4%)	55 (20.6%)	62 (23.2%)	74 (27.7%)	76 (28.5%)
Environment	1 (0.4%)	53 (19.9%)	61 (22.8%)	74 (27.7%)	75 (28.1%)
Overall QOL and general health	0 (0%)	54 (20.2%)	62 (23.2%)	74 (27.7%)	75 (28.1%)

Number of missing domain scores with percentages are presented. Abbreviations: mo: months, FU: follow-up, QOL: quality of life

Chapter 7

PHYSICAL TRAUMA PATIENTS WITH SYMPTOMS OF ACUTE STRESS: A PILOT FEASIBILITY STUDY WITH EYE MOVEMENT DESENSITIZATION AND REPROCESSING (EMDR)

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ABSTRACT

Background: Eye Movement Desensitization and Reprocessing (EMDR) therapy is an effective treatment for injury patients with posttraumatic stress disorder (PTSD). EMDR in injury patients with acute stress disorder (ASD) has not been examined. Therefore, this study examined the feasibility of providing EMDR in injury patients with (subclinical) ASD during hospitalization. Secondly, changes in ASD scores between baseline and one month post-injury were evaluated.

Methods: Trauma patients who were treated in the shock room of the ETZ Hospital (Elisabeth-TweeSteden Ziekenhuis), Tilburg, The Netherlands, were asked to participate. Participants completed a baseline questionnaire on sociodemographics and ASD during hospitalization. EMDR was offered to patients with (subclinical) ASD. ASD was also measured directly after ending EMDR and one month after injury. Average changes in ASD between baseline and one month post-injury were evaluated with repeated measures ANOVA. Reliable Change Index (RCI) was subsequently used to determine, for each participant, whether ASD changes were statistically significant.

Results: In total, 29 trauma patients participated in this feasibility study (response rate = 31.5%). Six patients (20.7%) reported (subclinical) ASD at baseline, of whom two received EMDR. In total, 20 participants completed the follow-up questionnaire one month after injury. Except for employment status, no other significant differences were found between participants or between participants and non-participants. Although no significant change in ASD scores were found between baseline and one month post-injury, the RCI indicated an individual significant decrease of ASD in four participants between baseline and one month after injury. Two of these patients received EMDR.

Discussion: About a fifth of the patients in this pilot study reported (subclinical) ASD. Due to contra-indications and logistic problems, only two patients received EMDR. Although professionals believe in a positive effect of EMDR, logistic aspects of screening patients on ASD and providing EMDR as part of standard care needs further evaluation. Therefore, this study provides several implications for future research and clinical practice.

INTRODUCTION

Because of an aging population and an increase in traffic accidents, the number of patients who were treated at an emergency department in the Netherlands increased from 68,000 in 2010 to 78,000 in 2018[1]. Therefore, specialized multidisciplinary trauma care was implemented[2] and resulted in an improved survivorship after injury[3]. Nevertheless, survivors reported unfavourable physical (e.g., problems on wound repair and pain)[4-6], psychological (e.g., anxiety, depressive symptoms, acute stress disorder (ASD) and posttraumatic stress disorder (PTSD)[7-13], and social (e.g., broken marriages and difficulties in resumption to work)[14,15] outcomes.

Research showed that 25% of trauma patients had ASD during hospital admission, 30% had PTSD one month after injury, and 49% showed a delayed onset of PTSD six months after trauma[16,17]. For that reason, the National Health and Medical Research Council (NHMRC) stated that psychological care, especially individual trauma-focused cognitive behavioral therapy, after a traumatic event should be considered when patients show signs of ASD or PTSD[18,19]. In line with these guidelines, physical trauma patients with ASD or PTSD have been treated in studies using a broad range of psychological interventions[18-21], including (components of) cognitive behavioral therapy (CBT)[22,23], such as (in vivo) exposure[24] and Eye Movement Desensitization and Reprocessing (EMDR)[25,26].

EMDR is a therapy that focuses on four memory components that are stored as a traumatic image, body sensation, associated cognition, and/or affect[25,27]. This treatment stimulates the intrinsic information processing system to restore the targeted traumatic memory as a contextual memory[28]. Exposure in vivo or imaginary (types of CBT) and EMDR are effective treatments and they are the treatments of choice for patients with PTSD[18,20,21]. However, EMDR requires less therapy sessions than exposure or other components of CBT[27]. The health care costs for EMDR will, subsequently, likely be less compared to CBT.

According to new guidelines of the International Society of Traumatic Stress studies, EMDR is an effective treatment for ASD[21]. Nevertheless, existing studies about EMDR treatment for physical trauma patients with ASD are still scarce[17]. Moreover, patients with subclinical ASD can also be treated, because a subclinical disorder is associated with levels of distress and impaired functioning similar to that of a full disorder and affects patients' recovery[29]. Furthermore, treatment with EMDR at an emergency department was effective in patients with acute stress symptoms after injury[30]. Yet, to our knowledge, no study examined EMDR in physical trauma patients with symptoms of ASD before. Therefore, the aim was to evaluate the feasibility of providing EMDR in trauma patients with (subclinical) symptoms of ASD who were admitted to the hospital. Moreover, changes in ASD scores between baseline, directly

after ending EMDR, and one month post-injury were examined. This provides insights in the possibility of performing a psychological intervention in a clinical hospital setting as part of standard care. When this is feasible, it may prevent patients from developing PTSD.

METHODS

Participants

Physical trauma patients who were treated in the shock room and admitted to the Elisabeth-TweeSteden Hospital (ETZ), Tilburg, The Netherlands, were asked to participate in this feasibility study. Eligible patients were treated in the shock room and aged 18 or older. Patients were excluded from participation in case of severe traumatic brain injury (i.e., Glasgow Coma Score ≤ 8), cognitive decline (e.g., dementia) or insufficient knowledge of the Dutch language (verbal and writing). Patients with a contraindication for EMDR (e.g., substance abuse disorder) did not receive EMDR.

Study design and procedure

This is an intervention study with a prospective cohort design (see Figure 1).

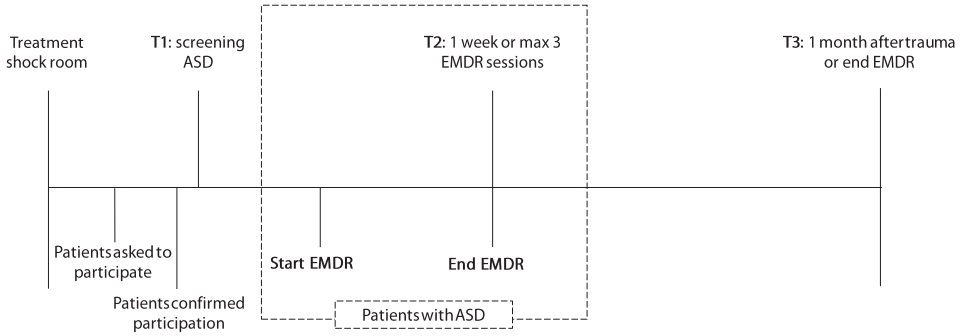

FIGURE 1. Timeline study procedure.
Abbreviations: ASD: acute stress disorder, EMDR: Eye Movement Desensitization and Reprocessing. Note: T1: measurement at baseline, T2: measurement after ending EMDR treatment, T3: measurement one month after trauma or ending or EMDR treatment.

All patients who were admitted to the hospital after an injury and treatment in the shock room were asked to participate by a (specialized) nurse as part of standard care. If a patient was not approached within a week after injury, the researcher (EV) invited the patient to participate. Previous unconscious patients were informed and asked to participate as soon

as they were lucid. Patients who were willing to participate signed an informed consent form and completed the baseline questionnaire. Patients who were discharged before being asked to participate were contacted by phone and willing patients received the informed consent form and the questionnaire at home.

Patients completed a baseline questionnaire with questions on sociodemographics and ASD almost directly after injury during hospitalization. EMDR was offered as soon as possible in case of (subclinical) ASD symptoms scores. Patients with (subclinical) ASD completed the ASD questionnaire directly after ending EMDR and one month after injury. In addition, patients with a contra-indication for EMDR as well as patients without ASD symptoms at baseline completed the ASD questionnaire one month after injury. Patients did not receive a financial compensation.

This study has been approved by the Medical Ethics Committee Brabant (METC Brabant); protocol number: NL66194.028.18 on November 13, 2019. The study was also recorded in the Netherlands Trial Registry, number NTR7228. The study has been performed in accordance with the ethical standards in the 1964 Declaration of Helsinki and with relevant regulations of the US Health Insurance Portability and Accountability Act (HIPAA).

Treatment

The EMDR therapist used bilateral stimulation. First, the patient was asked about the traumatic experience of the injury. When the focus was on the four memory components (i.e., image, body sensation, associated cognition, and/or affect), the psychologist started the stimulation using eye movements alone or in combination with sums or finger taps. The therapist used restricted questioning together with bilateral stimulation to unblock the intrinsic information processing system[21,31]. In this study, eye movements or a combination of eye movements with sums or finger taps were used, because this technique is more effective than solely finger taps or sums[32,33]. A combination of stimuli was used to optimize the cognitive load of the working memory. In general, this is often the case in intellectual persons.

The treatment was performed by health psychologists of the department of Medical Psychology who are also EMDR therapists and specialized in treating physical trauma patients in the ETZ Hospital. The most recent version (2019) of the Dutch EMDR protocol was used[31]. As the focus was on the injury, the intervention contained one to three EMDR sessions, 45 minutes per session, within five days after trauma and was provided on a ward in the hospital. Patients with symptoms of ASD, who were discharged, received EMDR at the department of Medical Psychology. EMDR treatment was ended when the Subjective Units of Distress (SUD) scale was equal to zero or when a patient received three EMDR sessions.

The SUD is used to measure the level of intensity of distress and is designed as a Likert scale ranging from 0 (i.e., no emotion or distress) to 10 (i.e., maximum emotion or distress). The health psychologists reported to the researcher the number of sessions and when the treatment was finished.

Evaluation feasibility

In order to evaluate the feasibility of providing EMDR on a hospital ward as part of standard trauma care, the following data were recorded: number of potentially eligible patients, number of patients who received the questionnaire from a HCP, number of patients who received the questionnaire from the researcher, number of patients with (subclinical) ASD and the number of patients who received and completed EMDR treatment, number of patients who completed the questionnaire during hospital admission and one month follow-up, and the number of patients without ASD, but who received additional care (e.g., psychiatrist or health psychologist). Logistic problems were also recorded.

Data collection

Sociodemographic information (i.e., sex, age, living situation, education level, and employment) was obtained from patients at baseline. To assess ASD the IES-R was used. This is a self-report questionnaire to assess symptom severity of ASD. It consists of 22 items to measure intrusive re-experiences (8 items, e.g., "Any reminder brought back feelings about it"), hyperarousal (6 items, e.g., "I felt irritable and angry"), and avoidance of injury-related stimuli (8 items, e.g., "I avoided letting myself get upset when I thought about it or was reminded of it")[34]. It contains a 4-point Likert scale ranging from 0 (*not at all*) to 4 (*often*). The cut-off score for subclinical ASD is ≥ 22 and the cut-off score for ASD is ≥ 33. The IES-R has good diagnostic accuracy[35,36]. The Dutch translation has shown to be reliable and valid in various trauma populations[37,38].

Clinical information, including type of trauma mechanism (e.g., motor vehicle accident), type of injury (e.g., spinal cord injury), Injury Severity Score (ISS), Glasgow Coma Score (GCS; range 9 - 15), surgery (yes/no), hospital stay (yes/no), admission to ICU, length of hospital stay, psychiatric history (yes/no), and former consultation or treatment by a psychologist (yes/no) was retrieved from the patients' medical records or the Dutch trauma registry[1].

Statistical analysis

Missing data on the IES-R at a particular time point was imputed with individual subscale means at that time point, according to the half-rule that at least half of the items were answered[34]. If more than half of the items were missing, the total score for that participant was considered missing.

Patient characteristics were studied using descriptive statistics. Then, the sociodemographic and clinical variables of participants versus non-participants were compared using independent t-tests (normally distributed continuous characteristics), Mann-Whitney U test (non-normally distributed continuous characteristics), Chi-square tests (categorical characteristics) or Fisher's exact test (categorical characteristics with expected cell counts lower than 5). A repeated measures ANOVA was performed to determine the average change in ASD scores between baseline and one month post-injury. Finally, the Reliable Change Index (RCI) was used to determine for each participant whether the change in ASD score between the two measurements was statistically significant[39].

RESULTS

Participant characteristics

Patients' sociodemographic and clinical characteristics are shown in Table 1.

Except for significant differences between participants with regard to employment status, no differences were found between participants or between participants and non-participants. Significantly more male participants had a paid job compared to the female participants.

Two or three missing items were imputated for two participants on the IES-R one month after injury (Time 3). As one other participant answered only one item from the IES-R at Time 3, the total score for that participant was considered missing.

TABLE 1. Characteristics of the total cohort, participants who completed the baseline questionnaire and non-participants who were excluded from analysis.

	Total cohort (N=92)	Participants (N=29)	Non-participants (N=63)	p-value
Age (years)*	57.1 ± 21.3	58.8 ± 19.3	56.4 ± 22.3	.609
18-44	24 (26.1)	7 (24.1)	17 (27.0)	
45-64	29 (31.5)	9 (31.0)	20 (31.7)	
65-74	14 (15.2)	8 (27.6)	6 (9.5)	
≥75	25 (27.2)	5 (17.2)	20 (31.7)	
Sex				.641
Female	33 (35.9)	9 (69.0)	24 (38.1)	
Male	59 (64.1)	20 (31.0)	39 (61.9)	
Trauma mechanism				.227
Motor vehicle accident	14 (15.2)	1 (3.4)	13 (20.6)	
Motorcycle	10 (10.9)	2 (6.9)	8 (12.7)	
Pedal cycle	16 (17.4)	6 (20.7)	10 (15.9)	
Pedestrian	2 (2.2)	1 (3.4)	1 (1.6)	
Fall	42 (45.7)	17 (58.6)	25 (39.7)	
Struck by/collision	3 (3.3)	0 (0)	3 (4.8)	
Other	5 (5.4)	2 (6.9)	3 (4.8)	
Number of injuries*	3.7 ± 3.1	4.6 ± 4.2	3.4 ± 2.3	.122
	[0-15]	[0-15]	[0-10]	
0-2	43 (46.7)	12 (41.4)	31 (49.2)	
3-5	29 (31.5)	8 (27.6)	21 (33.3))	
6-8	13 (14.1)	4 (13.8)	9 (14.3)	
≥9	7 (7.6)	5 (17.2)	2 (3.2)	
Injury Severity Score*	14.1 ± 9.5	13.7 ± 7.6	14.4 ± 10.3	.748
	[1-50]	[1-32]	[1-50]	
1-3	3 (3.3)	2 (6.9))	1 (1.6)	
4-8	11 (12.0)	4 (13.8)	7 (11.1)	
9-15	35 (38.0)	10 (34.5)	25 (39.7)	
≥16	28 (30.4)	10 (34.5)	18 (28.6)	
Missing¥	15 (16.3)	3 (10.3)	12 (19.0)	
Glasgow Coma Score*	14.1 ± 1.9	14.1 ± 2.1	14.1 ± 1.8	.986
9-12	9 (9.8)	2 (6.9)	7 (11.1)	
13-15	74 (80.4)	23 (79.3)	51 (81.0)	
Missing	9 (9.8)	4 (13.8)	5 (7.9)	

TABLE 1. Continued

	Total cohort (N=92)	Participants (N=29)	Non-participants (N=63)	p-value
Admission to ICU				.873
No	56 (60.9)	18 (62.1)	38 (60.3)	
Yes	36 (39.1)	11 (37.9)	25 (39.7)	
Length of stay on ICU*	1.5 ± 3.7	1.0 ± 1.7	1.8 ± 4.4	.389
	[0-30]	[0-6]	[0-30]	
Length of stay in hospital*	9.9 ± 10.5	9.6 ± 8.0	10.1 ± 11.4	.835
	[1-60]	[1-36]	[1-60]	
1-2 days	17 (18.5)	6 (20.7)	11 (17.5)	
3-7 days	27 (29.3)	7 (24.1)	20 (31.7)	
8-14 days	31 (33.7)	9 (31.0)	22 (34.9)	
> 15 days	17 (18.5)	7 (24.1)	10 (15.9)	
Living situation				.671
Alone		6 (2.7)		
With parents		3 (10.3)		
With a partner, no children		12 (41.4)		
With a partner and children		8 (27.6)		
Educational level				.924
Low		9 (31.0)		
Middle		11 (37.9)		
High		8 (27.6)		
Missing		1 (3.4)		
Employment				.014
Employed		14 (48.3)		
Unemployed		15 (51.7)		
Psychiatric history		1 (3.7)		
History consult from health psychologist		3 (11.1)		

**Means ± standard deviations or the median [Min-Max]. Number of patients (percentages) are provided for categorical variables.*

Abbreviations: ICU: Intensive Care Unit. Note: Solely participants completed questions concerning living situation, educational level, employment status, psychiatric history, and history consult from health psychologist.[¥] The Injury Severity Score could only be calculated for patients who were included during November 2019 and March 2020 and not between July 2020 and September 2020, as these number were not yet available in the trauma registry.

Feasibility

In total, the researcher invited 92 patients to participate in this study. Two eligible patients were asked by a nurse. Moreover, HCPs informed the researcher (EV) about three possible eligible patients and, subsequently, requested the researcher to ask the patients to participate instead of the HCPs. In total, 29 physical trauma patients participated in this feasibility study (see Figure 2). The response rate at baseline was 31.5%.

Six patients (20.7%) reported (subclinical) ASD at baseline. Two of them received EMDR treatment. Three other patients were not treated with EMDR, since they had a contra-indication (i.e., ASD related to another psychological or physical trauma) for EMDR. Two patients experienced ASD symptoms that were not related to the injury, while the other patient was known with substance abuse. Finally, one patient was discharged and admitted to a revalidation center in another urban region. This patient was, therefore, not able to receiving EMDR from a health psychologist from our hospital. The two patients who received EMDR treatment completed the questionnaire directly after ending EMDR as planned.

In total, 20 participants, including treated patients, patients with a contra-indication, and participants without ASD at baseline, completed the ASD questionnaire one month after trauma. The response rate was 69.0% one month after injury. Four patients showed subclinical ASD at one month after trauma, of which one already received EMDR treatment. This patient' ASD symptoms fluctuated from a decrease directly after ending EMDR treatment to an increase of symptom during the month after ending the treatment. After informing the other three participants about their scores, one patient was referred to a health psychologist to receive further treatment while the other two did not need a referral for consultation or treatment. Nine patients (one who received EMDR treatment) were lost to follow-up. In addition, three patients without ASD used additional care from a health psychologist during hospital stay. A psychiatrist was involved in one case during hospital admission.

Acute stress disorder during the first month after trauma

Repeated measures ANOVA showed that, averaged across all participants, there was no significant change in ASD scores between baseline and one month after injury (Total mean scores at baseline: 14.2 ± 16.3 and one month after trauma: 11.1 ± 11.3, $p = .160$). However, the RCI indicated for participants 1 and 17 a significant decrease of ASD between baseline and directly after ending EMDR treatment. Moreover, the RCI indicated for participants 9 and 29 a significant decrease of ASD between baseline and one month after injury (see Figure 3 and Table 2).

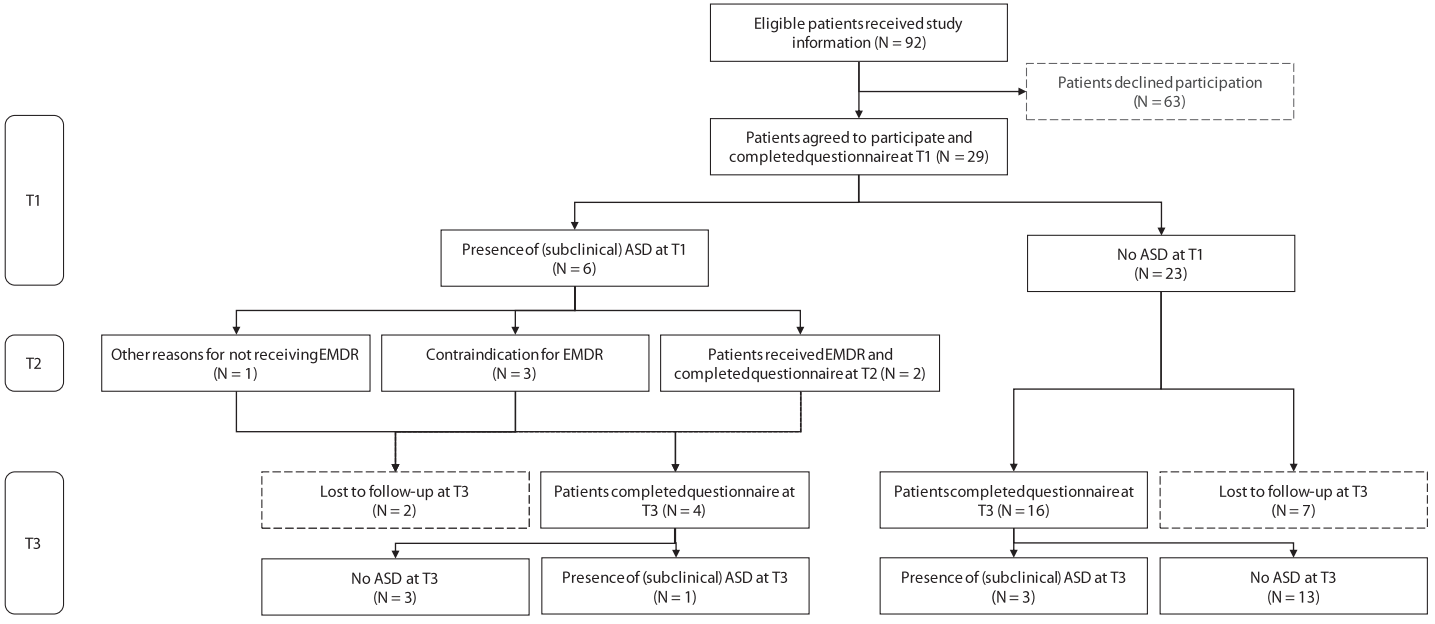

Figure 2. Flow diagram of participation in the study.

Abbreviations: ASD: acute stress disorder, EMDR: Eye Movement Desensitization and Reprocessing. Note: T1: measurement at baseline, T2: measurement after ending EMDR treatment, T3: measurement one month after trauma or ending EMDR treatment.

TABLE 2. Reliable Change Index analysis for each participant that completed the questionnaires at baseline, directly after finishing EMDR, and one month after injury

Participant	T1	T2	T3	Difference	RCI
1*	67	37	43	-24	-3.4
2	5		2	-3	-.4
4	2		7	5	.71
8	9		12	3	.43
9*	15		0.1	-14.9	-2.1
10	12		2	-10	-1.4
11	9		13	4	.57
12	3.6		6	2.4	.34
13	32		26	-6	-.9
14	30		26	-4	-.6
15	1		0	-1	-.1
16	11		19	8	1.1
17*	61	5		-56	-2.1
19	12		5	-7	-1.0
20	8		9	1	.1
23	3		10	7	1.0
24	1		3	2	.3
26	21		25	4	.6
27	7		1	-6	-.9
28	0		3	3	0.5
29*	36		11	-25	-4.1
Cronbach's α	.940	.974	.934		
Variance	360.7	512	140.0		
SD	19.0	22.6	11.8		
R	.7				
Rel. Difference	-1..6				

** Participants 1, 9, 17, and 29 showed an significant decrease of ASD, which was measured with the Impact of Event Scale-Revised. Abbreviations: T1: baseline; T2: directly after ending EMDR treatment; T3: one month after injury; RCI: Reliable Change Index; α: alpha; SD: standard deviation; r: Pearson correlation coefficient between T1 and T3 scores; Rel: reliability. Note: RCI Value > 1.96 indicates significant increase, whereas < -1.96 indicates significant decrease.*

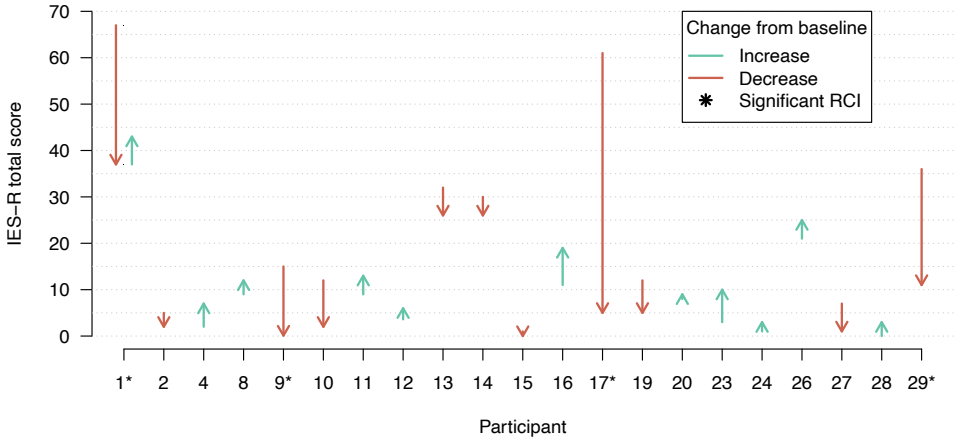

Figure 3. Arrow plot showing the change in total scores of acute stress disorder for each participant from baseline to one month after trauma.
Abbreviations: ASD: acute stress disorder; IES-R: Impact of Event-Scale. Note: The course of the arrow indicate for each patient whether there is a decrease (downward pointing arrow) or increase (upward pointing arrow) of ASD symptoms. An asterisk indicates whether a patient showed significant individual change according to the reliable change index. Participants 1 and 17 received EMDR treatment.

DISCUSSION

The aim was to examine the feasibility of providing EMDR in physical trauma patients with symptoms of ASD during hospitalization. Moreover, changes in ASD scores between baseline, directly after ending EMDR, and one month post-injury were evaluated. This provided insight into the possibility of performing EMDR in a clinical hospital setting as part of standard care.

Only two eligible patients were asked by a nurse. Six out of 29 participants (20.7%) reported (subclinical) ASD at baseline. Two of these patients received EMDR treatment, because four other patients had a contra-indication for EMDR and one other patient was discharged and admitted to a revalidation center in another urban region. The RCI indicated a significant decrease of ASD, in the two patients who received EMDR, between baseline and directly after ending EMDR treatment. Unfortunately, there were not enough participants who needed EMDR to evaluate the effect of EMDR on (subclinical) ASD.

During presentations about the study and conversations between HCPs (doctors and nurses) and the researcher, most HCPs stated they were convinced of the effectiveness of EMDR as short intensive treatment to decrease ASD symptoms and improve recovery. Yet, during the

inclusion period, nurses responded that it was difficult to ask and screen patients because of the workload and time pressure[40]. Moreover, maybe not all HCPs were capable to identify patients with ASD symptoms, because of limited knowledge about ASD symptoms and other psychological consequences after injury. Furthermore, not every nurse or doctor was able to attend one of the presentations, because they were scheduled during a workday and not all HCPs worked that specific day. Therefore, the researcher send news updates about the study. Despite these efforts, the researcher did not receive feedback from HCPs in the form of questions about eligible participants or patients who were willing to participate. Research, for instance using a qualitative study design, could focus on what is needed so that HCPs are able to screen and identify injury patients with ASD as part of standard care.

The design of the feasibility study entail several limitations and strengths that needs to be acknowledged. The first limitation is that the low response rate probably implied response bias[41]. To optimize the low response rate, though not in line with the aim of providing EMDR during hospitalization, patients who were discharged before being asked to participate were contacted by phone and willing patients received the informed consent form and the questionnaire at home. Participation could be too difficult when patients were critically injured and not fully recovered from injury[41]. Patients with cognitive decline, from a mild or moderate brain injury, could not be asked shortly after trauma[42]. On the one hand, their brain injury and cognition needed to recover before they were capable to decide whether they were willing to participate. On the other hand, capable patients with brain injury were discharged as soon as possible so they could further rehabilitate in a revalidation clinical. Moreover, the number of treated patients was too low to compare scores between baseline, the second measurement (i.e., directly after ending EMDR), and one month follow-up. Finally, interpretation of a probable ASD diagnosis must be done with caution[20]. Since solely a self-reported questionnaire was used and not a combination of a questionnaire and structured interview from a health psychologist or psychiatrist.

A major strength was that a psychological intervention design was used in a clinical trauma setting as part of standard care. The impact of an injury on psychological consequences and functioning are under evaluated in trauma research and clinical practice. Moreover, patients with a single as well as multiple and severe injuries participated in this study. Since several health psychologists were involved in this study, patients with (subclinical) ASD could be seen and treated within 24 hours after patients' confirmation (i.e., signing informed consent) to participate.

Results provide directions for future research and clinical implications for daily practice. Even though some promising results from EMDR treatment short after trauma[30], especially severely injured patients were not capable to be screened on ASD symptoms and

treated with EMDR short after trauma. Therefore, future research could focus on the most appropriate time to screen patients on ASD and treat them with EMDR by taken patients' injury severity and other patient-related factors into account. Then, personalized therapy or shared decision making can be provided and implemented during therapy.

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Chapter 8

GENERAL DISCUSSION

AIMS AND MAIN FINDINGS OF THE DISSERTATION

Because of an aging population and an increase in traffic accidents and severe injuries, more patients were treated on the emergency department (ED), in the Netherlands, last decade[1,2]. About a third of physical trauma patients reported (subclinical) acute stress disorder (ASD) during hospital admission, 25% reported posttraumatic stress disorder (PTSD) one month after injury and 42% reported PTSD six months after injury[3,4]. In addition to psychological disorders, patients reported adverse physical and social consequences as well as impaired quality of life (QOL) up to six years after trauma. Short and intensive treatment with Eye movement desensitization and reprocessing (EMDR) could be effective to prevent patients from experiencing psychological disorders[5-7].

The gaps in the literature and aims for each chapter were outlined in **Chapter 1**. The ASD and PTSD literature was first systematically searched for courses, risk factors, and psychological treatments (**Chapter 2**). Results demonstrated that ASD and PTSD have different courses across time and that patients can develop PTSD without having (had) ASD. These courses fluctuated during recovery and could, because of natural remission[8,9] or psychological treatment, decrease throughout the year. The onset of PTSD was in the majority of cases within three months after trauma, except for patients with a delayed onset (i.e., onset > 6 months after trauma)[10,11]. Several sociodemographic (e.g., being female and younger age), medical (e.g., pre-existing disability, comorbidity, and pain), psychosocial (e.g., ASD, anxiety, depressive symptoms, financial problems, low social support, and living alone) risk factors were found. PTSD could be prevented by providing early treatment within the first two weeks after trauma. Trauma patients were treated with Cognitive Behavioral Therapy (CBT), EMDR, psychoeducation, supportive counseling, or a combination of treatments (e.g., hypnosis and CBT). CBT was mostly examined compared to other psychological treatments. In addition, CBT was the most effective treatment for PTSD after injury, as patients who had CBT reported less PTSD symptoms compared with patients who received psychoeducation, supportive counseling, or a combination of treatments without EMDR. Although EMDR was examined in only one study, it was an effective treatment for reducing PTSD symptoms after injury.

Then, the protocol, describing the design of a focus group study and the design of an observational prospective cohort study in physical trauma patients, was provided in **Chapter 3**. The aim of the focus group study was to evaluate patients' perspectives on injury, treatment and recovery (**Chapter 4**). Patients with mild as well as severe injury reported that they did not fully recovered with regard to their pre-injury wellbeing at 12 months after trauma. On the one hand, patients stated that this might be related to difficulties on psychological (e.g., fear of dying or for permanent limitations), social (e.g., impact on relatives

and social support), and environmental health (e.g., financial problems). On the other hand, patients who experienced problems in communication between health care providers' (HCPs) or authorities and themselves reported more problems in recovery. In contrast, but in line with previous research[12,13], HCPs care seemed to be associated with patients' satisfaction with care and recovery, since patients who were reassured during treatment in the shock room could better surrender to care and cope with feelings of insecurity. Patients started processing trauma, not during hospital admission, but after they were discharged and needed to rehabilitate from injury (**Chapter 4**). In addition, the aim of the observational cohort study was to evaluate trajectories of PTSD (**Chapter 5**) and QOL (**Chapter 6**) and their corresponding characteristics during 12 months after trauma. Five trajectories of PTSD were found in physical trauma patients up to 12 months after injury (**Chapter 5**). Symptoms of PTSD remained stable during 12 months after trauma and no recovery of PTSD symptoms was found[14-16]. The (subclinical) PTSD trajectories showed a peak in prevalence rates of PTSD symptoms about three months after trauma (**Chapter 5**). In addition, the symptom severity of PTSD was seriously high to negatively affect patients' physiological (e.g., immune system and HPA and HPT-axis related hormones) and physical functioning[17-19]. Four latent trajectories were found for Psychological health and Environment, five for Physical health and Social relationships, and seven trajectories were found for Overall QOL and general health. Although mainly all QOL trajectories remained stable over time, one trajectory recovered from very poor to good overall QOL during 12 months after trauma (**Chapter 6**). A risk profile could subsequently be determined to examine patients at risk for PTSD or identify patients who experienced impaired QOL. Patients with subclinical and severe PTSD symptoms had similar risk profiles regarding trait anxiety, anxiety, and ASD. However, neuroticism and admission to the hospital were found only in patients with subclinical PTSD. In contrast, depressive symptoms were found only in patients with severe PTSD symptoms. Comparable psychological variables characterized QOL trajectories as well during 12 months after trauma (**Chapter 6**). However, differences between PTSD and QOL trajectories were found in clinical and personality characteristics. Younger age and being admitted to the intensive care unit (ICU) characterized (subclinical) PTSD trajectories, whereas being female, high education, conscientiousness, and agreeableness characterized QOL trajectories. Especially, neuroticism and trait anxiety had the strongest effect size in relation to PTSD and QOL.

Finally, the aim of **Chapter 7** was to evaluate the feasibility of providing EMDR treatment in patients with ASD who were hospitalized after a physical trauma, as part of standard care. In total, 29 trauma patients participated in this feasibility study. Even though six (20,7%) patients had (subclinical) ASD during hospital admission, only two underwent EMDR treatment and completed the questionnaire after ending their treatment. No overall significant changes in ASD scores between baseline and one month post-injury were found. However, when

focusing on individual changes, four participants showed a significant decrease of ASD between baseline and one month after injury. Unfortunately, there were not enough participants to evaluate the effect of EMDR on (subclinical) ASD. The results showed that HCPs did not screen every patient on symptoms of ASD. Only two patients were approached by a nurse and 90 patients were approached by the researcher. We hypothesized that HCPs were not able to screen, identify patients with ASD symptoms, or ask them to participate, because they had to deal with a high workload or limited knowledge about ASD symptoms and other psychological consequences. However, various solutions could support HCPs to overcome these difficulties and balance the workload[20].

METHODOLOGICAL CONSIDERATIONS OF THE DISSERTATION

The nature and design of the TraP-study entail several limitations and strengths that needs to be acknowledged. The first limitation is that this was no multicenter study, because only one level-I trauma center was involved. This hospital mostly treats severely injured patients from the province of Noord-Brabant. Mild and moderate injured patients are often treated in a level-II or level-III trauma center, for example, this province counts 11 level-II or level-III hospitals with an Emergency Department (ED)[2]. One other level-I trauma center, which is located in another urban region, was not able to include participants, due to lack of time and limited capable professionals (e.g., trauma nurses) who could ask patients to participate. Therefore, results may limit the generalizability to the entire trauma population from other rural and urban regions, including mild and moderate injured[2].

Second, the low response rate probably implied response bias[21]. The response rate in the focus group study, the observational prospective cohort study, and the feasibility study, was about 21%, 27%, and 32% respectively. In line with the literature[21,22], one of the reasons for declining participation, was that participation could be too difficult. Patients could be faced with their psychological problems when they were trigged by a focus group discussion or when they completed a self-report questionnaire. They did not want that. In addition, patients were less interested to participate or complete all follow-up moments, when they did not experience any physical or psychological problems related to their injury. Subsequently, overestimation of psychological problems and disorders could occur at follow up measurements. In addition, participation can be challenging when patients are critically injured and not fully recovered from injury[21]. This could be a reason for the low response rate regarding the observational study, because the baseline questionnaire contained 70 items more compared to other follow-up measurements. However, the time to complete the follow-up questionnaires decreased from 15 minutes at baseline to 5 to 10 minutes at follow-up. In order to increase the response rate, patients who were discharged

and/or not been asked to participate during hospital stay at follow-up, were approached by telephone and they received the questionnaire within the first month after trauma when they agreed to participate. When participants did not complete a follow-up questionnaire, they were approached by telephone and motivated to complete the questionnaire[22,23].

Another limitation was that selection bias could occur, since sufficient knowledge of the Dutch language was an inclusion criterion. Moreover, observed differences in number of injuries and type of injuries were found in the observational cohort study between responders and non-responders (**Chapter 5** and **6**). Also, less severely injured patients participated in this study compared to non-responders. Therefore, it is likely that critically injured patients who were admitted to the ICU were too badly wounded during hospital stay and after discharge, because some of them needed surgery or they experienced cognitive declines from injury, for example concentration problems or memory loss. Nevertheless, these patients are the ones needing the extra care in terms of psychological after care.

A fourth limitation is that, even though trajectories of PTSD and QOL seemed to be stable during 12 months after trauma, repeated measures ANOVA or mixed models ANOVA (in case of > two groups) are needed to examine differences in courses over time. Since latent class analysis especially examines characteristics of trajectories and not whether a change is statistically significant[24,25].

Finally interpretation of a probable diagnosis must be done with caution[26], because this study was largely based on self-reported questionnaires. In addition, the risk factors for PTSD and QOL were interpreted in terms of correlation, which do not imply causation[27].

A major strength of this thesis was that three different study designs were used to examine the aims of the thesis. First, our focus group study, which is a qualitative design, was the first study that explored patients' perspectives from injury, treatment in the shock room and hospital, and rehabilitation. Since patients' experiences throughout a longitudinal period from injury, treatment up to rehabilitation were explored, information was gained about which factors were present on a specific moment after trauma and how these factors developed over time.

Second, concerning the observational cohort study, a relatively large proportion of severely injured patients were included and completed the follow-up measurements. Moreover, this was one of the first studies that included personality together with sociodemographic, clinical, and other psychological characteristics in a risk profile of PTSD and QOL. Based on results from the risk profiles, HCPs are now able to screen and identify, patients at risk for PTSD or impaired QOL short after injury. Patients at risk can be referred for psychological

aftercare, to prevent them for developing psychological disorders and to improve their QOL. Also, to the best to our knowledge, this was the first study that examined QOL domains after a physical trauma compared to health-related QOL (HRQOL) or health status (HS). Moreover, this observational design had five measurements in 12 months after trauma. This resulted in detailed trajectories of PTSD symptom severity and QOL after injury.

Third, an intervention design was used to examine the feasibility of providing EMDR after a physical trauma in a clinical setting as part of standard care. Psychological consequences and functioning after a physical trauma have been under evaluated in the field of trauma research and clinical practice. Results, from the focus groups and observational cohort study, provide clinical implications for daily practice that leads to straightforward applications that can be implemented.

IMPLICATIONS FOR FUTURE RESEARCH

The results from this thesis have several implications for future research. First, results suggested that HCPs play an important role in patients' recovery and satisfaction with care (Chapter 4). To further improve trauma care and patients' recovery, HCPs' perspectives, expectations, and their role in providing health care should be studied. This provides knowledge about what factors are related to trauma care and which factors can be improved and optimized.

Second, since only trajectories of PTSD, and not ASD, were examined, it is still unknown what the trajectories of ASD are and which trauma patients develop ASD. Since ASD can only be observed within the first month after trauma, a study with several follow-up measurements within the first month after injury will provide information on courses of ASD symptoms. Experience Sampling Method (ESM), a structured data collection technique, can be used to observe and identify patients with symptoms of ASD within the first month after trauma[28,29]. It can be implemented as a Mobile Health (mHealth) smartphone application[30-32], in which participants respond to randomly timed short repeated measurements over the course of time, for example several times a day within the first month after trauma[33]. To decrease the burden of questioning patients can be monitored using ESM in combination with computer adaptive testing (CAT)[34]. CAT is a valid tailored-made technique that adapt to a persons' answer on a questionnaire[35-37]. As this method is short and precise, it requires less items to screen patients on psychosocial problems or disorders after trauma[35]. In our case, a patient can be screened by exploring symptoms on a specific domain of ASD. If a patient does not experience symptoms on that domain, then the patient can subsequently be asked about the other domains. Patients with symptoms of ASD can be referred to a registered health psychologist for early psychological treatment to prevent them for developing PTSD.

Third, concerning PTSD trajectories, the largest prevalence rate (26.8%) of patients who were admitted to the ICU was found in patients with subclinical PTSD. Patients in this trajectory needed more complex and intensive care compared to patients from other trajectories. Therefore, a possible presence of post intensive care syndrome (PICS) must be taken into account in patients with subclinical PTSD who were admitted to the ICU, because PICS is associated with PTSD[38,39]. PICS is a relatively new diagnosis and it is defined as: 'The disability that remains in surviving the critical illness. This comprises of impairment in cognition, psychological health, and physical function of the ICU survivor'[40]. Moreover, acute psychological reactions in the ICU were the most pronounced risk factors for developing mental problems and disorders after injury[41]. Yet, more research is needed to evaluate the relationship between PICS and PTSD in severely injured patients[42].

Before EMDR can be implemented as part of standard care in hospitalized trauma patients, HCPs (e.g., trauma surgeons and nurses) must be aware of the presence of ASD short after injury and they need to be able to screen patients on ASD as part of standard care. Therefore, research should evaluated what is needed so that HCPs are able to screen and identify injury patients with ASD as part of standard care. Subsequently, the effectiveness of EMDR can be compared, in a randomized controlled trial, with other CBT techniques, such as imaginary exposure, in vivo exposure, or cognitive restructuring[6,43,44]. Since these treatments are all considered the treatment of choice for patients with PTSD, the research question could, on the one hand, focus on which treatment is most effective and short in physical trauma patients. On the other hand, the research question could focus on patient-related factors and patient specific care. Moreover, although some promising results from EMDR treatment short after trauma were found[6], especially severely injured patients cannot be capable to be screened on ASD and treated with EMDR[45]. Therefore, future research should focus on the most appropriate time to screen patients on ASD and treat them with EMDR by taken patients' injury severity into account.

It is still unclear whether EMDR is feasible as part of standard care in other patient populations. In this hospital, all kinds of chronically ill patients can be treated with EMDR by a registered health psychologist when they experience psychological problems or disorders during hospitalization. The feasibility of providing EMDR could be evaluated in patients with different kind of diseases and/or psychological problems or disorders. In addition, less patients were able to successfully be treated with EMDR, because they were discharged to their own home or a revalidation clinic before treatment had started or was ended. Future research could focus on the feasibility and efficacy of providing online EMDR treatment compared with face-to-face treatment[46,47]. Especially, since the Covid-19 pandemic, online EMDR was implemented and provided[48], but scientific evidence concerning the efficacy of online EMDR is still lacking.

Finally, results from both studies are difficult to generalize to the entire trauma population from other rural and urban regions, because only one hospital was involved in the observational and feasibility study. This could be a reason for the low response rates in the observational study and feasibility study. Therefore, concerning the feasibility study, more research with larger sample sizes from other trauma centres are needed to examine the effect of EMDR shortly after trauma[6]. The generalizability could be enhanced by a multicenter study design[49], resulting in different rural and urban regions, other level-1, level-2, and level-3 hospitals, and a larger number of (multicultural) participants with a broader variety of type of trauma, injury severity, and number of injuries.

IMPLICATIONS FOR CLINICAL PRACTICE

The medical field of emergency and trauma surgery is mainly focused on patients' physical recovery instead of physical as well as psychological traumas. Therefore, *HCPs* need to be aware of psychosocial consequences and pay more attention to these concerns. This can be implemented in care by asking about symptoms of anxiety, depressive symptoms, ASD within one month after injury, PTSD after one month post-trauma, and about perspectives and satisfaction with functioning and QOL. In this way, the HCP is able to identify risk factors for PTSD or impaired QOL. To support the focus on psychosocial problems, they can be alerted by using a pop-up psychological screening form, for example the Psychosocial Screening Instrument for physical Trauma patients (PSIT)[50]. Yet, HCPs often need to deal with a high workload. However, a recent study showed that determining patients' characteristics is relevant in balancing and eventually reducing nurses' workload[51]. For that reason, we argue for a central role of a specialized trauma nurse or trauma case manager. This HCP could be appointed to also coordinate psychosocial screening during hospital stay and rehabilitation, to observe patients' need in aftercare, and to be a point of contact for patients and the multidisciplinary trauma care team. Then, in case of presence of a psychological disorder, patients can be referred for psychological treatment. The procedure of multidisciplinary treatment will contribute to better trauma care during hospital stay and rehabilitation.

Promising international results have been found in the use of aftercare clinics in severely injured patients[40,52]. The continuity of care, in the way that patients are followed-up after hospital stay, contributed to patients' physical and psychological recovery. Although aftercare clinics are mainly used in ICU patients, we expect that physical trauma patients as well as their family will benefit from the support of the aftercare clinic.

During recovery, patients could be faced with limited progression or they can experience impaired physical functioning. Especially, when no medical reasons are found for these limitations or impairments, a doctor, nurse, or physiotherapist could support patients by focusing on patients' strengths and what they are capable of instead of focusing on what their limitations are. This is supported by a quote from the focus group study. A patient, who was critically injured and hospitalized for weeks, stated: 'you should not focus on your limitations, but you need to look at what you are capable of'. This severely injured patient fully recovered. This citation is an example of "positive psychology", which is focused on positive experiences and individual traits, and the institutions that facilitate their development[53]. The focus is on human strengths and wellness instead of mental illness and pathology[54] by the approach of 'building up what is strong rather than correct what is wrong'[53]. Positive affect, hope, optimism, and resilience are commonly used constructs in this field. These qualities are related to less psychological stress and endorse better adjustment and engagement to treatments[55]. Then, even though physical or psychological limitations may be present, with support from HCPs, patients' psychological consequences decrease and QOL improve[56,57].

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APPENDICES

NEDERLANDSE SAMENVATTING

De laatste decennia zijn meer ongevalsslachtoffers op de spoedeisende hulp in Nederland behandeld. Dit komt door vergrijzing, een toename in aantal verkeersongevallen en meer patiënten met een ernstig en/of meervoudig letsel. Ongeveer een derde van de ongevalsslachtoffers heeft een (subklinische) acute stress stoornis (ASS) tijdens ziekenhuisopname, 25% van de ongevalsslachtoffers rapporteert klachten van een posttraumatische stress stoornis (PTSS) een maand na het ongeval en 42% heeft PTSS zes maanden na het ongeval. Daarnaast ervaren patiënten negatieve lichamelijke en sociale gevolgen en een verminderde kwaliteit van leven (KvL). Deze klachten kunnen tot zes jaar na het ongeval aanwezig zijn. Kortdurende en intensieve behandeling met Eye movement desensitization and reprocessing (EMDR) zou effectief kunnen zijn om psychologische stoornissen, zoals ASS en PTSS, te voorkomen.

Hoofdstuk 1 beschrijft verschillende onderzoek hiaten en doelen voor elk hoofdstuk. Als eerste hebben we een systematische literatuurstudie verricht. Deze studie is gericht op het beloop, risico factoren en psychologische behandelingen van ongevalsslachtoffers met ASS en PTSS (**Hoofdstuk 2**). Resultaten laten zien dat ASS en PTSS verschillende trajecten hebben. Patiënten kunnen PTSS ontwikkelen, zonder dat ze eerst ASS hebben ervaren. De gevonden trajecten fluctueerden tijdens revalidatie en konden, vanwege natuurlijk herstel of psychologische behandeling, afnemen binnen het eerste jaar na het ongeval. PTSS ontstond bij de meerderheid van de patiënten binnen de eerste drie maanden na het ongeval. Daarnaast was er een groep patiënten, die PTSS pas na zes maanden na het ongeval ontwikkelde. Verschillende sociodemografische (bijv. vrouwelijk geslacht, alleenstaand en jongere leeftijd), medische (bijv. onderliggende aandoeningen, co-morbiditeit en pijn) en psychosociale (bijv. ASS, angst, depressieve symptomen, financiële problemen en lage sociale steun) risico factoren zijn gevonden. Ongevalsslachtsoffers zijn behandeld met Cognitieve Gedragstherapie (CGT), EMDR, psycho-educatie, ondersteunende counseling of middels een combinatie van behandelingen, zoals hypnose gecombineerd met CGT. CGT was de meest onderzochte therapie in vergelijking met andere psychologische behandelingen. Daarnaast lijkt CGT de meeste effectieve therapie voor PTSS na een ongeval te zijn. Patiënten, die CGT hebben gekregen, rapporteren minder PTSS klachten in vergelijking met patiënten die psycho-educatie, ondersteunende counseling of een combinatie van behandelingen (met uitzondering van EMDR) hebben gehad. Ondanks dat EMDR slechts in een studie was onderzocht, blijkt het wel een effectieve behandeling te zijn voor patiënten met PTSS na een ongeval. Ook zijn er minder behandelsessies nodig in vergelijking met CGT.

Hoofdstuk 3 beschrijft vervolgens het protocol van de focusgroepen studie en de observationele prospectieve cohortstudie. Het protocol geeft de onderzoeksopzet en procedure voor beide studies weer.

In de focusgroepen studie delen ongevalsslachtoffers hun ervaringen met betrekking tot het ongeval, behandeling en herstel (**Hoofdstuk 4**). Door middel van groepsdiscussies zijn hun ervaringen en welzijn na het ongeval geëxploreerd. Daarnaast is bestudeerd welke factoren het welzijn belemmeren of bevorderen. Patiënten beschrijven verschillende problemen op lichamelijk welzijn. Zo zijn patiënten met zowel milde als ernstige letsels niet volledig hersteld 12 maanden na het ongeval. Bovendien beschrijven patiënten consequenties op psychologisch welzijn, zoals angst om dood te gaan of angst voor permanente lichamelijke beperkingen. Ook ervaren ze veranderingen in (subjectieve) persoonlijkheid, gedrag en cognitieve klachten, zoals geheugen- of concentratieproblemen. Patiënten omschrijven ook symptomen van posttraumatische stress stoornis als gevolg van hun ongeval. Problemen met het sociale welzijn is zichtbaar in de impact van het ongeval op familie, de behoefte sociale steun en financiële problemen als gevolg van hun ongeval. Deze lichamelijk, psychologische en sociale consequenties belemmeren het welzijn van de patiënten. Daarentegen kan goede communicatie het welzijn bevorderen. Patiënten illustreren dat helderheid over het ongeval, prognose en verwachtingen over het herstel en toekomstperspectief, hen kan helpen om zich over te geven aan de behandelingen. Patiënten voelen zich minder hulpeloos wanneer ze weten wat ze kunnen verwachten. Dit draagt bij aan tevredenheid met de traumazorg en het herstel (**Hoofdstuk 4**).

Het doel van de observationele cohortstudie is het beloop, door middel van latente trajecten, van PTSS symptomen (**Hoofdstuk 5**) en KvL (**Hoofdstuk 6**) te bestuderen tot 12 maanden na het ongeval. Daarnaast zijn bijbehorende karakteristieken van de trajecten onderzocht, zodat er een risicoprofiel ontwikkeld kon worden voor patiënten met een verhoogd risico op het ontwikkelen van PTSS en patiënten met een verminderde KvL. Er zijn vijf trajecten voor PTSS na het ongeval gevonden (**Hoofdstuk 5**). De PTSS trajecten lijken stabiel te zijn gedurende 12 maanden na het ongeval. Er is geen (natuurlijk) herstel gevonden. Ongeveer drie maanden na het ongeval lijkt er een piek in prevalentie van (subklinische) PTSS te zijn. Bij patiënten met PTSS was de aanwezigheid van de PTSS symptomen dusdanig ernstig dat ze een negatieve invloed op het fysiologisch, hormonaal en lichamelijk functioneren kunnen hebben (**Hoofdstuk 5**).

Voor de verschillende domeinen van KvL (**Hoofdstuk 6**), zijn vier latente trajecten gevonden voor 'psychologische gezondheid' en 'omgeving', vijf trajecten voor 'fysieke gezondheid' en

'sociale relaties' en zeven trajecten voor 'algehele KvL en gezondheid'. Ondanks dat bijna alle trajecten stabiel zijn, is er een traject gevonden, die herstel van slechte na goede KvL laat zien (**Hoofdstuk 6**).

Na deze analyses is een risicoprofiel bepaald. Patiënten met subklinische en ernstige PTSS symptomen hebben ongeveer eenzelfde risicoprofiel, die bestaat uit angst als karaktereigenschap, toestandsangst en ASS. Karaktereigenschappen, zoals Neuroticisme en ziekenhuisopname zijn alleen gevonden bij patiënten met subklinische PTSS. Daarentegen zijn depressieve symptomen alleen gevonden bij patiënten met ernstige PTSS klachten (**Hoofdstuk 5**). De KvL trajecten laten vergelijkbare profielen zien (**Hoofdstuk 6**). Neuroticisme en angst als karaktereigenschap zijn het sterkst gerelateerd aan PTSS en verminderd KvL. Echter, de risicoprofielen tussen PTSS en KvL trajecten zijn verschillend met betrekking tot klinische eigenschappen. Zo waren patiënten met een jongere leeftijd en opname op de intensive care (IC) kenmerkend voor (subklinische) PTSS trajecten, terwijl vrouwelijk geslacht, hoger opleidingsniveau, Consciëntieusheid en Vriendelijkheid kenmerken voor KvL trajecten zijn.

Tot slot beschrijft **Hoofdstuk 7** een haalbaarheidsstudie met EMDR. In dit hoofdstuk is onderzocht of het haalbaar is EMDR aan te bieden, als onderdeel van de standaard traumazorg, aan patiënten met ASS. Deze patiënten zijn in het ziekenhuis opgenomen na een ongeval. In totaal participeren 29 patiënten in deze studie. Zes (20.7%) patiënten hebben (subklinische) ASS tijdens ziekenhuisopname, waarvan slechts twee patiënten daadwerkelijk EMDR hebben gekregen. Er zijn over het algemeen geen significante verschillen in ASS symptomen gevonden tussen de metingen op baseline (d.w.z. start deelname) en een maand na het ongeval. Echter, als we ons richten op individuele scores, dan is bij vier participanten een significant afname in ASS symptomen te zien tussen baseline en een maand na het ongeval. Helaas, nemen niet voldoende patiënten deel aan de studie om het effect van EMDR op (subklinische) ASS te evalueren. De resultaten demonstreren echter wel dat zorgverleners niet elke patiënt op ASS hebben gescreend. Slechts twee patiënten waren door een verpleegkundige benaderd en 92 patiënten zijn door de onderzoeker (EV) benaderd. Onze hypothese is dat het, door verschillende redenen, voor zorgverleners niet mogelijk is om patiënten te screenen, hen met ASS te identificeren of hen te vragen te participeren in de studie. Dit kan te maken hebben met een hoge werkdruk, minimale of beperkte kennis over ASS symptomen en andere psychologische gevolgen na een ongeval. Uit verschillende studies blijkt dat er verschillende oplossingen zijn, die kunnen helpen om met deze moeilijkheden om te gaan.

LIST OF PUBLICATIONS

Published articles

Visser, E., Den Oudsten, B.L., Gosens, T., Lodder, P., De Vries, J. (2021) Psychological risk factors that characterize the trajectories of quality of life after a physical trauma: a longitudinal study using latent class analysis. *Quality of Life Research* (2021). https://doi.org/10.1007/s11136-020-02740-x

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Submitted articles

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DANKWOORD

Nelson Mandela, de meest bekende persoon uit mijn geboorteland Zuid-Afrika, sprak de wijze woorden: "*A winner is a dreamer who never gives up*". Ik moest toen denken aan de vele patiënten, die ik tijdens mijn onderzoek heb gesproken. Daarnaast herkende ik mezelf er heel erg in. Promoveren was een droom, die ik koesterde sinds ik de master Medische Psychologie deed. Toen ik, tijdens mijn promotieonderzoek, ernstig ziek bleek te zijn was het afronden van mijn promotie niet meer zo vanzelfsprekend. Ik heb ervaren hoe het, als patiënt, is om van de een op de andere dag overgeleverd te zijn aan de kennis en kunde van artsen en dat goede zorg zo belangrijk is voor het behandel- en hersteltraject. Dat ik nu dan toch het laatste, en mijn inziens, het belangrijkste hoofdstuk schrijf is iets waar ik op dat moment alleen maar van kon dromen. Ik knijp mezelf dan ook in de arm tijdens het schrijven van mijn dankwoord, die voor mij extra bijzonder is geworden.

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Eva

ABOUT THE AUTHOR

Eva Visser was born in Pietersburg, South-Africa on October 10, 1986. After graduating Senior general secondary education (HAVO) at Mgr. Frencken College, Oosterhout, in 2005, she completed the first two years of Bachelor of Nursing at Avans Hogeschool, Breda, in 2007. She started her Bachelor degree in Psychology and Health at Tilburg University and obtained this Bachelor in 2010. Subsequently, Eva obtained her Master's degree in Medical Psychology at the same institution (2012). Between March 2013 and August 2015, she worked as a junior researcher at the department of Neuropsychology, Tilburg University. In August 2015 she started her PhD study at the department of Trauma TopCare, Elisabeth-TweeSteden Hospital (ETZ), Tilburg, which resulted in this thesis lying before you. This research project was performed in close collaboration with the Department of Medical and Clinical Psychology at Tilburg University. After working as a psychologist at the Department of Medical Psychology at ETZ Hospital, Eva is currently working at Revant Revalidatiecentrum in Breda.