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## Factors associated with posttraumatic stress symptoms in a prospective cohort of patients after abdominal sepsis: a nomogram

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**Abstract** *Objective:* To determine to what extent patients who have survived abdominal sepsis suffer from symptoms of posttraumatic stress disorder (PTSD) and depression, and to identify potential risk factors for PTSD symptoms. *Design and setting:* PTSD and depression symptoms were measured using the Impact of Events Scale–Revised (IES-R), the Post-Traumatic Symptom Scale 10 (PTSS-10) and the Beck Depression Inventory II (BDI-II). *Patients and participants:* A total of 135 peritonitis patients were eligible for this study, of whom 107 (80%) patients completed the questionnaire. The median APACHE-II score was 14 (range 12–16), and 89% were admitted to the ICU. *Measurements and results:* The proportion of patients with “moderate” PTSD symptom scores was 28% (95% CI 20–37), whilst 10% (95% CI 6–17) of patients had “high” PTSD symptom scores. Only 5% (95% CI 2–12) of the patients expressed severe depression symptoms. Factors

associated with increased PTSD symptoms in a multivariate ordinal regression model were younger age (0.74 per 10 years older,  $p = 0.082$ ), length of ICU stay (OR = 1.4 per doubling of duration,  $p = 0.003$ ) and having some (OR = 4.9,  $p = 0.06$ ) or many (OR = 55.5,  $p < 0.001$ ) traumatic memories of the ICU or hospital stay. *Conclusion:* As many as 38% of patients after abdominal sepsis report elevated levels of PTSD symptoms on at least one of the questionnaires. Our nomogram may assist in identifying patients at increased

risk for developing symptoms of PTSD.

**Keywords** Peritonitis · Sepsis · Posttraumatic stress disorder · PTSD · Depression · Intensive care · IES-R · PTSS-10 · BDI-II

**Abbreviations** *APACHE-II:* Acute Physiology and Chronic Health Evaluation II · *ARDS:* Acute respiratory distress syndrome · *APS:* Acute Physiology Score · *DSM-IV:* Diagnostic and Statistical Manual of Mental Disorders–Fourth

Edition · *ICU:* Intensive care unit · *IQR:* Interquartile range · *IES-R:* Impact of Events–Revised Questionnaire · *N:* Number of patients · *n. a.:* Not applicable · *OR:* Odds ratio · *PTSD:* Post-traumatic stress disorder · *PTSS-10:* Post-Traumatic Stress Syndrome 10-Questions Inventory · *SCID:* Standardized Clinical Interview Diagnosis · *SD:* Standard deviation · *95% CI:* 95% Confidence intervals

## Introduction

Posttraumatic stress disorder (PTSD) is the development of psychological and physical symptoms following exposure to one or more traumatic events [1, 2]. PTSD symptoms include intrusive recollections (re-experiencing the trauma in flashbacks, memories or nightmares); avoidant and numbing symptoms (including diminished emotions and avoidance of situations that are reminders of the traumatic event); and hyperarousal (including increased irritability, exaggerated startle reactions or difficulty sleeping or concentrating) [3]. PTSD symptoms have a major impact on life, illustrated by the fact that the patients have a reduced quality of life [4] and frequently suffer from depression [5].

Events that typically trigger the development of PTSD include exposure to violent events such as rape, domestic violence, child abuse, war, accidents, natural disasters and political torture, all of which include a threat to life [6–8]. Increasingly PTSD has also been found in patients who have survived a major, life-threatening disease and patients who have spent a significant amount of time in an intensive care unit (ICU) [9–13]. Severe peritonitis (or abdominal sepsis) is such a disease where typically an episode of acute and severe illness [14, 15] is followed by a lengthy ICU stay and a long recovery period that often includes multiple surgical and non-surgical interventions [16–22]. This combination of factors could make this patient group particularly vulnerable for developing PTSD symptoms. To date, little is known about the presence and severity of PTSD and possible risk factors in patients recovering from severe peritonitis [15].

Therefore, our aims were to determine the presence and level of symptoms of PTSD in patients surviving abdominal sepsis. In addition, we searched for demographic and disease-related factors associated with higher levels of PTSD symptoms. Identification of such factors may be important to determine possible targets of intervention

and to select patients for psychological assessment interviews.

## Methods

### Study design

Our study was embedded in an ongoing randomized clinical trial (the RELAP Trial) evaluating two surgical treatment strategies for patients with secondary peritonitis after the initial emergency laparotomy. Patients were enrolled between December 2001 and February 2005 in two academic medical centers and seven regional teaching hospitals in The Netherlands. All patients were followed up for 12 months after initial (index) laparotomy.

The study was approved by the medical ethics committee of the Academic Medical Center, Amsterdam. All patients gave informed consent to participate in this study.

### Study population

Patients were eligible for the RELAP trial if they had a clinical diagnosis of secondary peritonitis requiring emergency laparotomy and an Acute Physiology and Chronic Health Evaluation II (APACHE-II) score above 10. Further details of the study population can be found elsewhere [23].

### Data collection

All self-administered PTSD questionnaires were distributed by mail to patients who survived at least 12 months following initial emergency laparotomy, with a reminder by phone within 2 weeks in the case of no response. After

1 month without response a new questionnaire including a reminder letter was sent.

#### Instruments assessing the level of PTSD symptoms

We used two instruments with good psychometric characteristics [24, 25] for measuring PTSD symptoms in research settings: the Post-Traumatic Stress Scale 10 [26] and the Impact of Event Scale–Revised [27, 28].

The *Post-Traumatic Stress Syndrome Scale 10* (PTSS-10) was originally designed to diagnose PTSD according to the Diagnostic and Statistical Manual of Mental Disorders III (DSM-III) criteria in victims of natural disasters [14]. The PTSS-10 is now a widely used self-report questionnaire assessing symptoms related to PTSD, particularly in critically ill and ICU patients [4, 11, 12]. The PTSS-10 consists of 10 items, each of which ranges from 1 point (none) to 7 points (always). The total score ranges from 10 to 70, with higher scores indicating more symptoms; scores of 35 or above are considered indicative of PTSD [11, 29].

The *Impact of Events Scale–Revised* (IES-R) is one of the most commonly used self-report questionnaires for determining PTSD symptomatology following a trauma [27]. The IES-R consists of 22 items, each ranging from 0 (no problems) to 4 (frequent problems), with the total score ranging from 0 to 66. Scores above 24 points are generally considered indicative of PTSD, with higher scores indicating more symptoms [28]. The IES-R has been developed based on DSM-IV criteria and therefore has three distinct subscales, the avoidance subscale (eight questions), the intrusion subscale (eight questions) and the hyperarousal subscale (six questions) [28, 30], and is one of the most frequently used self-report questionnaires in both the clinic and in PTSD research [27].

#### Potential risk factors

Potential risk factors were selected from previous studies [31] examining factors for increased mortality and morbidity [17–22, 32, 33] in secondary peritonitis supplemented with specific factors mentioned in the PTSD literature [6, 9–11, 14, 34, 35]. We divided these factors into three distinct categories.

*General patient characteristics* included age, gender and the presence of major comorbidity (cardiovascular disease; COPD; renal failure; diabetes; malignancy).

*Disease characteristics and postoperative course* included severity of disease measured at the time of initial laparotomy using the APACHE-II score. As several components of the APACHE-II score are already considered in a univariate analysis (namely age and comorbidity); we chose to replace the APACHE-II score with the APS score as a potential predictor of PTSD [36]. The APS comprises

only the acute components of the APACHE-II score, without age and comorbidity. Postoperative characteristics included administration of hydrocortisone during ICU stay [13, 37], development of acute respiratory distress syndrome (ARDS), [4, 12, 20], number of relaparotomies, duration of ICU and hospital stay, the development of a disease-related major morbidity during 6 months' follow-up [23] and an enterostomy present after 6 months' follow-up.

*Traumatic memories of ICU/hospital stay* were assessed using the four-item adverse experiences questionnaire, which captures four types of traumatic memories of the stay in the ICU or hospital ward: nightmares, fear and panic, pain, and difficulty in breathing [13]. Patients scored the frequency of traumatic memories of their stay in the ICU or hospital ward using a four-point scale of 0 (never), 1 (sometimes), 2 (regularly) or 3 (often), administered concurrently with the PTSS-10 and IES-R questionnaires after at least 12 months' follow-up. These were subsequently summed and classified into three graded categories of traumatic memories: 0 (no traumatic memories), 1–4 (some traumatic memories), more than 4 (many traumatic memories).

We also collected data on whether patients had experienced other traumas or whether a close family member or friend had experienced a trauma within the previous 3 years. We used questions 29 and 30 from the Life Stressor Checklist–Revised [38], administered at the same time as the PTSS-10, IES-R and Beck Depression Inventory II (BDI-II) questionnaires. Responses were given dichotomously as yes or no, and patients were subsequently asked to specify the event type [38]. These questions were asked to determine to what extent the PTSD symptomatology found in this patient group was due to their peritonitis or to other traumatic events.

#### Data analysis

We used two instruments aimed at measuring the presence and severity of PTSD symptoms in our population, each with their own cut-off value. Combining data from two instruments measuring the same construct (PTSD symptoms) may lead to a more robust classification of patients. To preserve the natural ordering of patients who scored below the cut-off value on both questionnaires ('low-scoring patients'), patients scoring above the cut-off on only one of these questionnaires ('moderate scoring patients') and patients scoring above the cut-off on both questionnaires ('high-scoring patients'), we applied ordinal regression modeling. The proportion of patients in each of these three categories is presented with 95% confidence intervals (95% CI) using the method of Wilson [39].

Potential predictors for PTSD symptoms were analyzed using an ordinal logistic regression model. This ordinal regression model is an extension of the binary

logistic model and is appropriate when a continuous trait is grouped into several categories by using cut-offs [40].

All potential predictors for PTSD symptoms were first examined in univariate ordinal regression models. Factors with a  $p$ -value of less than 0.1 were entered in a multivariate ordinal logistic regression model. If variables within a group of predictors were strongly correlated, only the factor with the strongest univariate relationship and/or most relevant clinical interpretation was added to the model. Because the literature on PTSD and ICU studies shows them to be clinically relevant, age and gender were always included in the multivariate model regardless of the strength of their associations [34].

In addition, a factor comprised of other non-related traumas that the patient had experienced within the previous 3 years was included in the final model to assess its potential confounding role.

The fit and validity of the model was evaluated by checking the discriminatory properties (overlap in risk scores of patients with different outcomes), the proportional odds assumption (test for parallel lines) and calibration (closeness in expected and observed numbers of patients evaluated by an extension of the Hosmer–Lemeshow goodness-of-fit statistic).

Calibration was checked by comparing expected and observed number of patients in each of the three outcome categories across deciles of expected risk and tested

for significance by using an extension of the Hosmer–Lemeshow goodness-of-fit statistic [41].

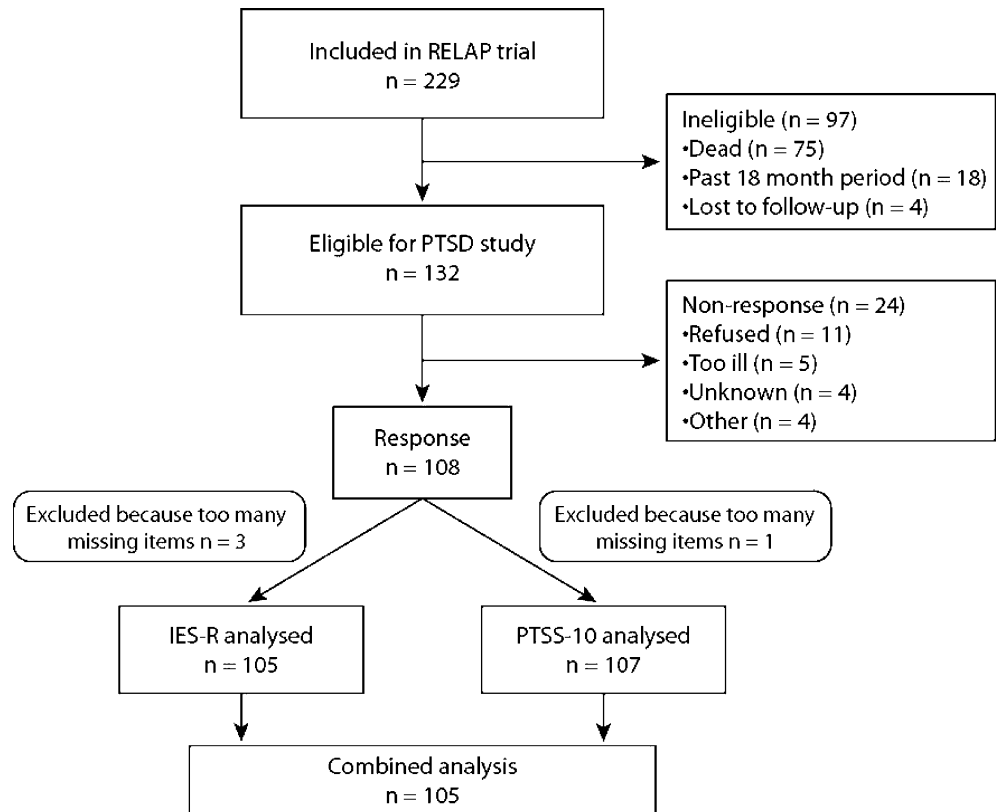
**Nomogram:** A nomogram was developed to visualize the prognostic strength of the different factors from the multivariate model in a single diagram. A nomogram allows readers to calculate an expected distribution of PTSD symptomatology ('low-scoring', 'moderate-scoring' and 'high-scoring' patients) based on a specific profile of a patient. The number of points for each predictor was based on the original coefficient from the multivariate ordinal model. The total number of points derived by specifying values for all predictors was used to calculate the expected probabilities that a patient would be a 'low-scoring patient', a 'moderate-scoring patient' or a 'high-scoring patient'.

Analyses were performed using SAS software version 9.1 (SAS Institute Inc., Cary, NC, USA).

## Results

Of the total of 132 patients eligible for this study, 108 (80%) patients responded to the questionnaire (Fig. 1). On average the responses were provided approximately 12.5 months following initial emergency laparotomy. There were no significant differences in any of the

**Fig. 1** Flowchart summarizing inclusion and response



patient or disease characteristics between respondents and non-respondents.

The median age of patients was 66.8 years and 54% were male. Patients were severely ill, with a median APACHE-II score of 14 and a median APS score of 6, and 5% had a major comorbidity (Table 1). Ninety-six patients (89%) were admitted to ICU: their median ICU-stay was 7 days, and these patients were mechanically ventilated for a median of 5 days. Patients were hospitalized for a median period of 28 days (IQR 19–55 days). Fifty-one percent of patients also underwent

another trauma in the 3 years prior to filling in the PTSD questionnaires.

#### Prevalence of PTSD symptoms

The proportion of ‘moderate-scoring’ PTSD patients was 28% (95% CI 20–37%), whilst 10% (95% CI 6–17%) of patients were ‘high-scoring’ patients (Table 1). Detailed information on depression and PTSD symptoms is presented in the electronic supplementary material (ESM).

**Table 1** Association between severity of PTSD symptoms (three categories) and patient, disease operative and postoperative characteristics: results from univariate ordinal regression models

	Overall	PTSD symptoms <sup>a</sup> (n = 107)			Univariate ordinal regression <sup>b</sup> p-value
		None to mild (n = 66)	Moderate (n = 30)	High (n = 11)	
<b>General patient characteristics</b>					
Median age (IQR)	66.8 (57–73)	70.2 (60–74)	58.7 (47–72)	57.8 (49–65)	0.004
Male gender (%)	54%	53%	53%	64%	0.847
Major comorbidity present (%) <sup>c</sup>	53%	55%	50%	55%	0.670
<b>Peritonitis and postoperative characteristics</b>					
<b>Initial</b>					
Median APS score (IQR)	6 (4–8)	6 (4–8)	7 (5–9)	8 (3–8.5)	0.271
Hydrocortisone in first 14 days in ICU (median days)	2 (0–7)	1.5 (0–8)	1 (0–8)	5 (1–7)	0.749
ARDS	6%	3%	10%	9%	0.192
One or more relaparotomies	67%	70%	63%	64%	0.515
Admitted to ICU	89%	85%	93%	100%	0.110
Median length of ICU stay (IQR)	7 (4–15)	7 (4–12)	7 (4–19)	9 (6–16)	0.042
Median ventilation time (IQR)	5 (1–8)	4 (1–7)	5 (1–10)	7 (4–13)	0.073
Median length of hospital stay (IQR)	28 (19–55)	26 (18–47)	31 (23–60)	56 (19–72)	0.102
<b>Follow-up</b>					
Disease-related major morbidity at 6-month follow-up	15%	9%	27%	18%	0.068
Enterostomy at 6-month follow-up	51%	47%	55%	70%	0.183

IQR, Interquartile range; <sup>a</sup> Three graded outcomes: none to mild, moderate and high; two patients’ data are based on only one completed questionnaire; <sup>b</sup> All models were checked for parallel lines to see if an ordinal test for significance was appropriate; <sup>c</sup> Major comorbidity included cardiovascular disease, COPD, renal failure, diabetes and malignancy

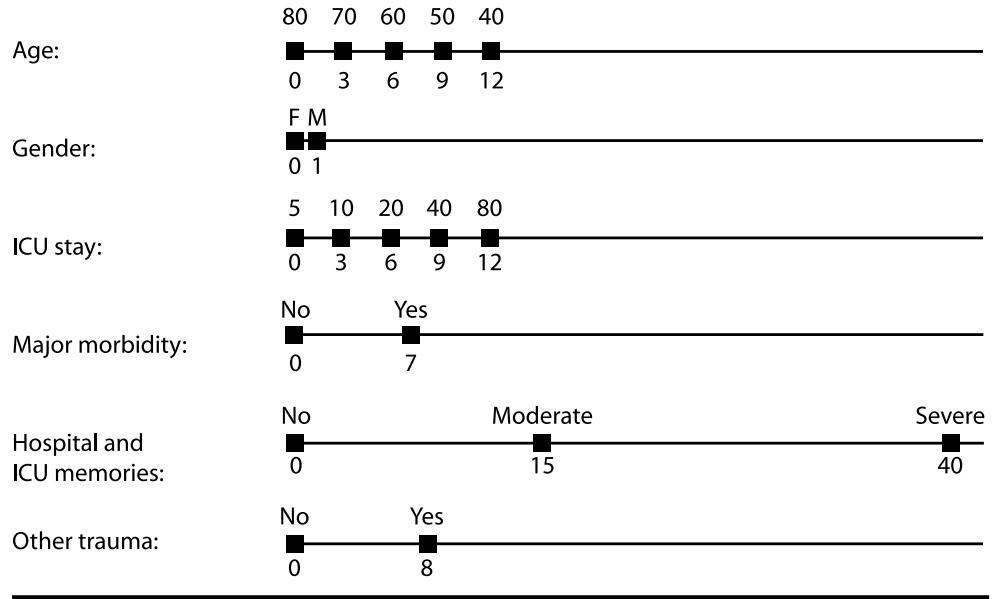
**Table 2** Association between severity of PTSD symptoms (three categories) and other traumatic experiences following peritonitis

	PTSD symptoms (n = 105)			Univariate ordinal regression p-value
	None to mild (n = 64) <sup>a</sup>	Moderate (n = 30) <sup>a</sup>	High (n = 11)	
<b>Traumatic memories of ICU or hospital stay</b>				
Nightmares	39%	61%	82%	0.002
Fear and panic	24%	61%	100%	<0.001
Pain	67%	70%	82%	0.002
Difficulty breathing	33%	76%	100%	<0.001
<b>Traumatic memories</b>				
None (0)	41%	50%	9%	<0.001
Moderate (1–4)	7%	47%	47%	
Severe (> 4)	0%	18%	82%	

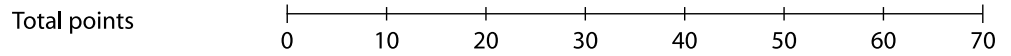
<sup>a</sup> Two patients not included in final analysis due to missing data on traumatic memories during ICU or hospital stay

**Fig. 2** Nomogram for prediction of severity of PTSD symptoms in patients with secondary peritonitis. Graded outcome categories are: none to mild (negative on both instruments), moderate (positive on one instrument), and severe (positive on both instruments)

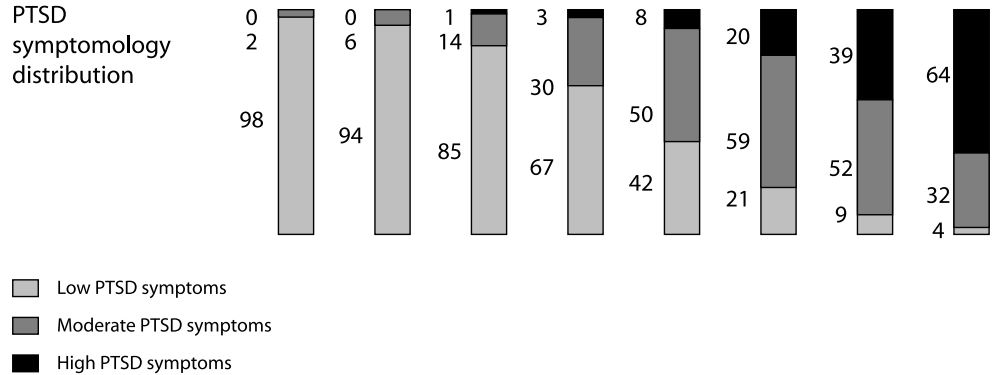
**Section 1:**



**Section 2:**



PTSD symptomology distribution



**Instructions:**

From **section 1** of the nomogram, locate the age of the patient on the axis. Determine how many points the patient receives. Repeat this for each factor in section 1. Sum the points for all predictors.

From **section 2**, locate this sum score on the total points axis. Draw a line straight down to the bar graphs. These bars indicate the estimated probability of that patient having 'no to mild' PTSD symptoms (negative on both instruments), 'moderate' PTSD symptoms (positive on one instrument) and 'high' PTSD symptoms (positive on both instruments).

**Predictive factors**

Results from the univariate analysis are presented in Table 1 and Table 2, and descriptive details can be found in the ESM.

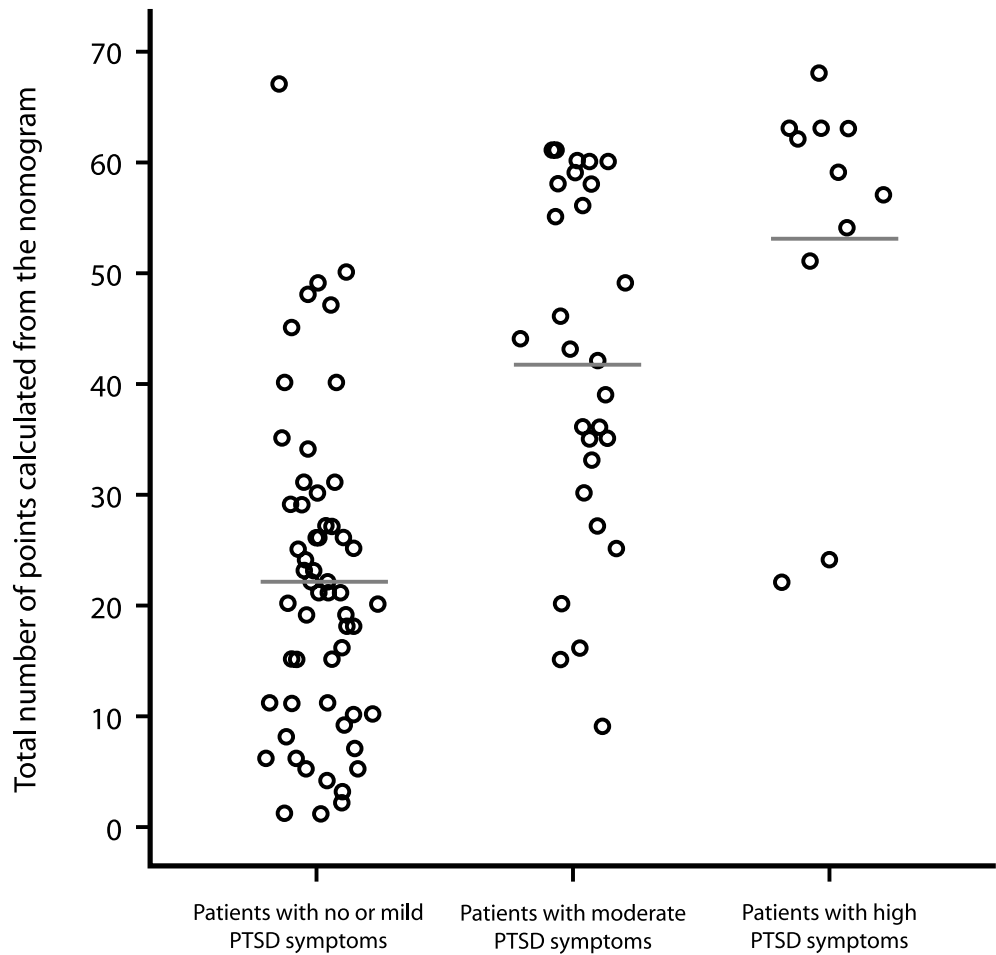
The final multivariate model included age, gender, length of ICU stay, disease-related morbidity during the 6-month follow-up, traumatic memories of the ICU or hospital stay and other traumatic factors within the previous 3 years (Table 3).

**Table 3** Association between severity of PTSD symptoms and patient, disease operative and postoperative characteristics and other traumatic experiences following peritonitis in a multivariate analysis

	Final model ( <i>n</i> = 105) <sup>a</sup>			<i>p</i> -value
	OR	95% CI Lower	Upper	
Ten years increase in age	0.74	0.53	1.04	0.084
Female	0.9	0.94	2.3	0.822
Length of ICU stay (log2 transformed)	1.4	1.1	1.7	<0.003
Major disease-related morbidity during 6-month follow-up (including index hospital admittance)	2.1	0.61	7.11	0.238
Traumatic memories of ICU or hospital stay				
Moderate (1–4)	4.9	0.95	24.9	0.058
Severe (> 4)	55.5	9.4	328.0	<0.001
Other trauma within previous 3 years	2.4	0.94	6.3	0.085

<sup>a</sup> This multivariate ordinal analysis included a test for parallel lines (*p* = 0.694)

**Fig. 3** Distribution of total points from nomogram (risk score) for the prediction of the severity of PTSD symptoms with use of the risk factors taken from the multivariate ordinal model. PTSD categories are graded according to severity: none to mild (negative on both instruments), moderate (positive on one instrument), severe (positive on both instruments)



In our final model, increasing age was associated with a lower likelihood of PTSD symptomatology (OR = 0.74 per 10 years increase in age, *p* = 0.084). Gender was not predictive of PTSD symptoms (OR = 0.90, *p* = 0.82). Disease-related morbidity at the 6-month follow-up (OR = 2.1, *p* = 0.24) was no longer independently predictive of PTSD symptoms. Memories of the ICU/hospital stay (patients that reported some memories: OR = 4.9, *p* < 0.057; patients that reported many memories:

OR = 55.5, *p* < 0.001) were the most prominent independent risk factor for increased PTSD symptomatology. Length of ICU stay was also significantly predictive in the development of PTSD symptomatology in the multivariate model (OR = 1.4, *p* = 0.004). The relative strengths of these relationships are visualized in the nomogram (Fig. 2). In this nomogram, one can calculate for the individual patient given his/her risk profile the probability that he/she will score either no to mild, moderate or

high PTSD symptoms according to the PTSS-10 and IES-R.

The proportional odds assumption was not violated as indicated by a  $p$ -value of 0.694 for the test of parallel lines. Calibration of the model (closeness between predicted and observed probabilities) was good, with a  $p$ -value of 0.987 for the goodness-of-fit test for ordinal models. A graphical impression of the model's discriminative ability is shown in Fig. 3. This figure shows that the mean risk score is significantly different between all three PTSD symptom severity categories ( $p < 0.001$ ), although there is some substantial overlap in the risk scores between patients from different categories of PTSD symptom severity.

## Discussion

The proportion of patients with 'high-scoring' PTSD symptomatology 12 months after peritonitis was 10%, and the number of 'medium-scoring' patients (28%) was in line with earlier studies measuring PTSD symptoms in critically ill patients who had been admitted to ICU [9–13, 15, 42]. The prevalence of PTSD recorded in the general population varies between 0.9% and 2.9% (the ESEMEd study) [7, 43, 44].

From our study, the following observations can be made. Firstly, the development of PTSD symptoms is not directly related to the severity of the disease at presentation. The APS score at baseline was not predictive for the development of PTSD symptoms. The APS measures the severity of disease score solely on the weight of the acute clinical features and does not incorporate age and comorbidity [36].

The development of PTSD symptoms was, however, predominantly related to a more complicated course of secondary peritonitis. Longer ICU and hospital stays and major disease-related morbidity during the 12-month follow-up were associated with more PTSD symptoms. In concordance with earlier studies [15, 34], the strongest predictor of having PTSD symptoms following abdominal sepsis was having traumatic memories and experiences during their initial hospital or ICU stay. These results suggest that the presence of traumatic memories is one of the most relevant aspects for the development of PTSD-related symptoms. Earlier studies also found that subjective interpretation of the intensive care experience emerged as a consistent predictor of adverse emotional outcome in both the short and the long term [13, 34].

Age plays a critical role in the development of PTSD symptoms. Younger patients are much more likely to develop and report such symptoms. This finding confirms the results of an earlier, retrospective study of a different cohort of patients 4–10 years after hospital admission for severe peritonitis [15]. These findings suggest that older patients are more able to adapt to the limitations that are associated with experiencing such a major disease, most

likely because they have already experienced a co-morbid illness and health-related problems. In contrast to some other studies, gender did not play a role in the development of PTSD symptoms [34].

Patients with abdominal sepsis suffering from ARDS did not report more PTSD symptomatology than those without ARDS. In earlier ICU studies, ARDS patients reported considerable PTSD symptoms [12, 45]. In our cohort of abdominal sepsis patients we found different predictive factors for PTSD than those found in the ARDS patients [10, 12, 15]. Secondary peritonitis in itself may have been severe enough, with ICU admission and extended mechanical ventilation days, to cause PTSD symptoms; therefore, the added risk by ARDS may be moot. Lack of power may also be a factor, because the proportion of patients developing ARDS in this study was modest.

We did not find an association between hydrocortisone administration during ICU stay and PTSD symptoms within this peritonitis cohort, as has been demonstrated for other critically ill patient groups [13, 37, 46, 47]. Hydrocortisone did not protect against developing PTSD symptoms, whereas other studies have found that administration of hydrocortisone during ICU can lead to a reduction in PTSD symptoms after discharge. In this study corticosteroid use during only the first 14 days of ICU was included in our analyses. The effect of prolonged use of hydrocortisone or late-stage use during conditional adrenal insufficiency cannot be excluded.

Unfortunately, due to the acute and life-threatening nature of secondary peritonitis, it was not possible to collect baseline information on PTSD or data on earlier psychological disorders. However, as recommended in a recent review by Griffiths and colleagues [48], to account for possible earlier traumas we considered information pertaining to comorbid diseases. Furthermore, we collected data on other, non-disease-related traumatic events that had occurred within the previous 3 years. These non-disease-related events were indeed associated with having more PTSD symptoms, and altered the initial ORs of the other factors to the extent that we considered it a moderate confounder.

Timing plays an important role in collecting data on PTSD symptoms in critically ill and ICU patients [48]. We set the period for the recording of PTSD symptoms at 12 months for a very specific reason; in this severely ill patient group, we did not want to record patient recovery. Past studies have shown that critically ill patients develop PTSD symptoms only after their physical recovery period has passed, hence with a delayed onset [9].

Although these self-report questionnaires are frequently used, the diagnostic value of such instruments in relation to a DSM-IV diagnosis obtained by a structured interview is still being researched and discussed [49]. Some studies have reviewed the diagnostic value of the questionnaires, but in general these studies were



methodologically limited [11, 29, 50]. In this study we did not include a structured clinical interview for establishing a definite DSM-IV criteria diagnosis of PTSD, although this is highly recommended in clinical psychology. However, we feel that the use of questionnaires is more feasible in the ICU [48], and patients who report many symptoms on these self-report questionnaires [51] can subsequently be referred to an appropriate mental healthcare provider [50].

In this study we have tried to learn from two questionnaires, one commonly used and validated in particular for critically ill patients, together with one of the most frequently used screening instruments for PTSD, the IES-R. The prevalence of PTSD symptomatology in the present study was based on whether or not a patient scored above the cut-offs of the IES-R and the PTSS-10. We employed the two questionnaires as complementary for the detection of PTSD symptoms and not to compare results deduced from both questionnaires separately [49]. Combining the results of both questionnaires in our analysis was anticipated to lead to a more robust assessment of the factors associated with more PTSD symptoms. Although these two instruments aim to measure the presence of PTSD symptoms, their concordance in classification of patients was not perfect, with 30 patients (28%) being positive on one questionnaire but not on the other. This demonstrates the difficulty in measuring PTSD symptoms by questionnaire, but also means that both questionnaires are informative in their own right. Combining the two instruments may therefore lead to a more robust classification of patients based on their level of PTSD symptoms and may be a more useful tool in screening patients following ICU stay, while potentially reducing biases due to instrument variation [52].

We assessed traumatic experiences during ICU/hospital stay based on the patients' recollections (after 1 year). The patients' perceived traumatic experience may well have contributed to the development of PTSD symptoms, but it is also possible that having PTSD symptoms influenced their perceptions. Future studies should aim to prospectively quantify traumatic experiences during or shortly after ICU stay to draw more causal conclusions, even though this might be difficult in patients with such a lengthy recovery period [9, 48, 53, 54].

In the clinical setting, there is a continuing debate on whether to intervene in the more acute peritraumatic psychological processes or in a later phase, when symptoms or prodromes of PTSD are observed. By improving our understanding of which factors play an important role in the development of PTSD, we can better prevent PTSD symptoms in high-risk patients and decide when best to intervene. The aim of our predictive model is for it to be used by treating physicians, following the acute episode and phase of secondary peritonitis in which survival and physical recovery are the main concerns, to recognize high-risk PTSD patients. This relatively simple

model can aid the surgeon, for instance, during the first outpatient visit in determining which patients are at higher risk for the development of PTSD symptoms. However, before this nomogram can be used to actually predict PTSD symptomatology in clinical practice, it must be externally validated in another cohort of patients with secondary peritonitis.

In conclusion, 10% of peritonitis patients report 'high' PTSD symptomatology and another 28% 'moderate' PTSD symptoms. Factors that were related to more PTSD symptoms included younger age, traumatic memories of the period of hospitalization and length of ICU stay. Knowledge of these predictive factors is required to increase awareness, and to develop tailored early treatment options for these high-risk patients our nomogram may assist in identifying patients with PTSD symptoms.

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#### **Appendix: RELAP trial clinical centers and investigators of the Dutch Peritonitis Study Group**

All investigators are from departments of surgery unless specified as clinical epidemiology and biostatistics (E), intensive care (I) or medical psychology (MP).

O. van Ruler, K. R. Boer (E), J. B. Reitsma (E), C. W. Mahler, E. A. Reuland, J. W. O. van Till, B. C. Opmeer (E), P. M. M. Bossuyt (E), M. J. Schultz (I), M. A. Sprangers (MP), H. Obertop, D. J. Gouma, C. A. J. M. de Borgie (E), M. A. Boermeester: Academic Medical Center, Amsterdam; E. P. Steller, P. Tanis, H. Hart (I): Sint Lucas Andreas Hospital, Amsterdam; M. F. Gerhards, M. Guijt, H. M. Oudemans (I): Onze Lieve Vrouwe Gasthuis, Amsterdam; K. Bosscha, E. Ritchie, M. Vermeer: Bosch Medical Centre, Den Bosch; P. W. de Graaf, B. van Etten, C. Haazer, E. Salm (I): Reinier de Graaf Hospital, Delft; B. Lamme, E. J. Hesselink, H. Rommes (I): Gelre Hospitals, Lukas Hospital, Apeldoorn; R. J. Oostenbroek, L. te Velde, G. Govaert, H. H. Ponsen (I): Albert Schweitzer Hospital, Dordrecht; H. G. Gooszen, M. K. Dinkelman, L. P. H. Leenen (I): University Medical Centre Utrecht; E. G. J. M. Pierik, K. W. W. Lansink, J. Bakker (I): Isala Clinics, Zwolle.

Key staff and steering committee at coordinating center of RELAP trial: O. van Ruler (investigator), E. A. Reuland (data management), C. W. Mahler (investigator), J. B. Reitsma (epidemiologist), C. A. J. M. de Borgie (epidemiologist), K. R. Boer (quality of life investigator), B. C. Opmeer (economist), M. A. Boermeester (principal investigator, project supervisor) from the Department of Surgery, Academic Medical Center Amsterdam, The Netherlands.

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