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CLINICAL RESEARCH ARTICLE

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Predicting treatment outcome for complex posttraumatic stress disorder using the personalized advantage index

Karine Frost [a,b], Chris M. Hoeboer [c,d], Asle Hoffart [a,b] and Peter Sele [a,b]

[a]Research Institute, Modum Bad Psychiatric Hospital, Vikersund, Norway; [b]Department of Psychology, University of Oslo, Oslo, Norway; [c]Department of Psychiatry, Amsterdam UMC, Location University of Amsterdam, Amsterdam, The Netherlands; [d]Amsterdam Public Health, Mental Health, Amsterdam, The Netherlands

ABSTRACT

Background: Ample studies have demonstrated the effectiveness of psychotherapy for posttraumatic stress disorder (PTSD). However, large individual variation in treatment outcome remains unsolved and treatment options for complex posttraumatic stress disorder (CPTSD) are debated. There is a need for exploring methods for matching patients with treatment they will most likely benefit from.

Objective: To develop a personalized advantage index (PAI) based on relevant clinical and demographic predictors of outcome from exposure therapy and skills-training for CPTSD.

Method: Data from a previous randomized controlled trial (RCT) in 92 patients with a CPTSD diagnosis was used to compare Prolonged Exposure (PE; $n = 32$) and Skills Training in Affective and Interpersonal Regulation (STAIR; $n = 60$). Outcome measures were clinician-assessed and self-reported PTSD symptoms. Predictors of outcome in PE and STAIR were identified separately from sixty-one candidate variables using random forest and bootstrap procedures. Relevant predictors were then used to calculate PAI and retrospectively identify optimal versus suboptimal treatment in a leave-one-out cross-validation approach.

Results: In PE, somatoform dissociation, depression, suicidal ideation, and reduced physical health predicted worse outcome. In STAIR, interpersonal problems, total PTSD symptom severity, intrusions, elevated guilt, and psychoticism predicted worse outcome, while being a witness to trauma predicted better outcome. Allocation to optimal treatment according to the PAI was associated with large improvements in clinician-assessed (Cohen's $d = 0.83$) and moderate improvement in self-rated (Cohen's $d = 0.60$) PTSD symptoms as compared to allocation to suboptimal teatment.

Conclusions: Using the PAI in personalizing psychological treatment for CPTSD is a promising approach to improve treatment benefits. Further research on larger samples and external validation of the PAI is needed.

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KEYWORDS

Complex PTSD; prolonged exposure; skills training; personalized psychotherapy; treatment selection, machine learning; personalized advantage index

PALABRAS CLAVE

TEPT complejo; exposición prolongada; entrenamiento en habilidades; psicoterapia personalizada; selección de tratamiento; aprendizaje automático; índice de ventaja personalizada

HIGHLIGHTS

- The present study aimed to assess the potential for improving psychotherapy outcome by applying machine learning methods in treatment selection.
- Different baseline variables predicted the outcome of exposure treatment and skills training for patients with complex posttraumatic stress disorder.
- The study demonstrated the utility of the machine learning method personalized advantage index in predicting differential treatment outcomes.

Predicción del resultado del tratamiento para el trastorno de estrés postraumático complejo mediante el índice de ventaja personalizada

Antecedentes: Numerosos estudios han demostrado la eficacia de la psicoterapia para el trastorno de estrés postraumático (TEPT). Sin embargo, la gran variabilidad individual en los resultados del tratamiento sigue siendo un desafío sin resolver, y las opciones terapéuticas para el trastorno de estrés postraumático complejo (TEPT-C) continúan siendo debatidas. Es necesario explorar métodos que permitan asignar a los pacientes el tratamiento con el que tengan mayor probabilidad de beneficiarse.

Objetivo: Desarrollar un índice de ventaja personalizada (PAI, por sus siglas en inglés) basado en predictores clínicos y demográficos relevantes del resultado terapéutico en la terapia de exposición y el entrenamiento en habilidades para el TEPT-C.

Método: Se utilizaron datos de un ensayo clínico aleatorizado (RCT) previo con 92 pacientes diagnosticados con TEPT-C, en el que se compararon la Exposición Prolongada (PE; $n = 32$) y el Entrenamiento en Habilidades para la Regulación Afectiva e Interpersonal (STAIR; $n = 60$). Las medidas de resultado incluyeron síntomas de TEPT evaluados tanto por clínicos como autoinformados por los pacientes. Se identificaron predictores de resultado en PE y STAIR por separado a partir de 61 variables candidatas, utilizando procedimientos de bosque aleatorio y remuestreo bootstrap. Posteriormente, los predictores relevantes se emplearon para calcular el PAI determinando retrospectivamente la asignación a un tratamiento óptimo o subóptimo mediante un enfoque de validación cruzada dejando uno fuera.

Resultados: En PE, la disociación somatomorfa, la depresión, la ideación suicida y una salud física reducida predijeron peores resultados. En STAIR, los problemas interpersonales, la gravedad total de los síntomas de TEPT, las intrusiones, la culpa elevada y el psicoticismo

CONTACT Karine Frost karine.frost@modum-bad.no Research Institute, Modum Bad Psychiatric Hospital, Postbox 33, Vikersund, N-3370, Norway; Department of Psychology, University of Oslo, Oslo, Norway

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predijeron peores resultados, mientras que haber sido testigo de un trauma predijo mejores resultados. La asignación al tratamiento óptimo según el PAI se asoció con mejoras significativas en los síntomas de TEPT evaluados por clínicos (*d* de Cohen = 0.83) y mejoras moderadas en los síntomas autoinformados (*d* de Cohen = 0.60) en comparación con la asignación a un tratamiento subóptimo.
Conclusiones: El uso del PAI en la personalización del tratamiento psicológico para el TEPT-C es una estrategia prometedora para mejorar los beneficios terapéuticos. Se requiere investigación adicional con muestras más grandes y validación externa del PAI.

1. Introduction

Complex posttraumatic stress disorder (CPTSD) was included in the 11th revision of the International Classification of Diseases (ICD-11; World Health Organization, 2019) to address the multifaceted symptoms often observed in connection with childhood relational trauma. In addition to the PTSD core symptoms (intrusions, avoidance, and exaggerated perceptions of threat), CPTSD includes problems in affect regulation, beliefs about oneself as diminished, defeated or worthless, accompanied by feelings of shame, guilt or failure related to the traumatic event, and difficulties in sustaining relationships and in feeling close to others (WHO, 2019). CPTSD is a debilitating condition with persisting afflictions, stressing the need to improve health and life functioning for this group (Maercker et al., 2022).

Choice of treatment for CPTSD is debated and includes proposals of treatments models that are inherently different in both treatment foci and therapeutic approach. The comparison of trauma-focused treatments to non-trauma-focused skills-training interventions is at the heart of this debate. While treatment studies on patients formally diagnosed with CPTSD are scarce, research has supported the effectiveness of trauma-focused treatments for childhood abuse-related PTSD (CA-PTSD; Ehring et al., 2014; McLean et al., 2022). Patients with CPTSD seem to benefit equally from treatment compared to patients with 'basic' PTSD (Hoeboer et al., 2021a), but about 50% of PTSD-patients still report substantial symptoms after treatment (Cuijpers et al., 2024; Ehring et al., 2014). With regards to CPTSD, primarily phase-based treatment has been proposed as an alternative approach to improve outcomes (Cloitre et al., 2010). Phase-based treatments combine non-trauma focused skills-training or stabilization with trauma-focused treatment in a sequential procedure (Cloitre et al., 2002), but skills-training or stabilization are also used as stand-alone interventions in clinical practice (e.g. Bækkelund et al., 2021). Studies comparing phase-based and trauma-focused interventions have generally found large and comparable effects (Oprel et al., 2021; Raabe et al., 2022; Sele et al., 2023; Van Vliet et al., 2021), and thus the potentially added benefits from stabilization appear questionable (Darby et al., 2023). However, within all interventions there is considerable variance on an individual level, and it is possible that non-responders could benefit from alternative treatments. Individual variation in treatment response elucidates the need for expanding our knowledge on what works for whom to personalize treatment to the individual patient (Cohen et al., 2021). There is unharvested potential for improving outcomes by identifying predictors that could help match patients to treatment, thereby improve the decision-making processes leading to the choice of one treatment model over another for individual patients with CPTSD.

A recent meta-analysis of outcome-predictors in trauma-focused psychotherapy for PTSD (Keyan et al., 2024) identified five broad predictor categories: fear biology factors, clinical factors, demographic factors, psychiatric comorbidities, and trauma characteristic. Importantly, factors biologically related to fear conditioning and factors not involving fear mechanisms seem both related to outcome. Given the complex interaction of various predictors, Keyan and colleagues (2024) argue for the use of data-driven approaches to support clinical judgement in personalizing treatment for patients with PTSD.

Previous research has supported increased effectiveness of treatment for depression based on machine learning methods (Delgadillo et al., 2022; Nye et al., 2023). Among these methods, DeRubeis and colleagues (2014) developed the Personalized Advantage Index (PAI) to identify the optimal treatment approach for individual patients. The PAI identifies optimal and suboptimal treatment for each individual from pre-treatment variables and calculates the relative advantage of the optimal treatment over the suboptimal treatment. This approach holds a potential for offering tailored treatment choices for individual patients, enhance treatment efficacy, and reduce the trial-and-error process in finding the best treatment fit.

Two studies have supported the potential utility of the PAI approach in PTSD patients with various traumas (Deisenhofer et al., 2018; Keefe et al., 2018), while Held and colleagues (2023) failed to find significant differences in outcomes based on PAI recommendations in a sample of veterans with PTSD. The PAI has also been utilized to compare treatments for CA-

PTSD specifically. Using data from a previous RCT, Hoeboer and colleagues (2021b) applied the PAI to compare the predicted outcomes of phase-based treatment (STAIR + PE) and exposure therapy (PE). Patients assigned to their optimal treatment, as indicated by the PAI, showed greater improvement in PTSD symptoms compared to those assigned to suboptimal treatment. In contrast, Bremer and colleagues (2023) failed to find significant differences between optimal and suboptimal treatment when comparing Eye Movement Desensitization and Reprocessing (EMDR) and phase-based treatment (STAIR + EMDR). Differences in sample size, study design, and available pretreatment variables might have contributed to the divergent findings. For instance, in the study by Bremer and colleagues (2023), the same amount of trauma-focused treatment was provided in the two treatment conditions, leading the authors to hypothesize that trauma-focused treatment by itself is sufficient to elicit symptom reduction possibly explaining the lack of difference.

These mixed findings point to external validation studies in different samples as an essential next step to evaluate the clinical usefulness of the PAI approach. Van Bronswijk and colleagues (2021) tested the generalizability of PAIs for treatment of depression from two studies using cross-trial prediction, but the evidence did not support the validity of PAIs across samples. Likewise, Tait and colleagues (2024) evaluated the PAI from the study conducted by Deisenhofer and colleagues (2018) in an external sample treated either with trauma-focused cognitive–behavioural therapy or EMDR. Again, comparing two trauma-focused treatments failed to elicit significant results, possibly indicating that the mechanisms of change in the two approaches are similar. Consequently, no interactions exist between predictors and the choice between the two. The significant PAI findings from the original study could be a result of overfitting, meaning that a model fits too closely to its training data and performs poorly in other samples. The choice of machine learning method for model development, using a measure of depression as outcome, and the lack of PTSD symptom measures and trauma-related variables could have limited the development of the PAI model in the original study. Accordingly, the authors recommended that future research should use a PTSD measure as the outcome, test different modelling methods, and apply bootstrapping in predictor selection (Tait et al., 2024). In sum, divergent findings across PAI studies may be related to insufficient power because of small sample sizes, differences in the dosage of the compared treatments, differences in the variables that are collected and can be included as potential treatment predictors, differences in the machine learning methods that are used to identify relevant predictors, or differences in the outcome measures being used. Notably, previous studies on PTSD have rarely compared trauma-focused treatments with non-trauma-focused treatments. It is possible that the emphasis on comparing similar treatment modalities has contributed to the lack of significant findings.

There is a need for expanding our knowledge on which treatments are optimal for CPTSD, and how to personalize these treatment approaches given the individual variation within the group. Moreover, PAI studies using PTSD-measures as an outcome and rigorous method choice in predictor selection have been encouraged. The present study aimed to use recommended machine learning approaches to identify predictors of treatment outcome of PE and STAIR assessed by PTSD-measures, using data from a previous RCT in patients with CPTSD (Sele et al., 2023). We aimed to investigate whether the PAI could identify the optimal treatment for each individual participant, and whether the relative advantage of receiving optimal treatment over suboptimal treatment would be significant. This would indicate a potential additional benefit of using the PAI when making treatment choices.

2. Materials and methods

The present study used data from an RCT comparing phase-based, exposure and skills-training therapy for childhood-abuse-related CPTSD (Sele et al., 2023). 92 patients were recruited from referrals to a residential treatment clinic and randomly assigned to phase-based treatment where Skills Training in Affective and Interpersonal Regulation (STAIR) was followed by Narrative Therapy (SNT), Prolonged Exposure (PE), or STAIR (Cloitre et al., 2002; Foa et al., 2007). For detailed descriptions of the patient sample, procedures, treatments, and outcome measures, see Sele et al. (2023).

2.1. Participants

Participants were patients referred to a national clinic in Norway offering residential treatment of childhood-abuse-related disorders. The inclusion criteria were similar to the established criteria at the clinic: age 18–65 years, exposure to childhood trauma, CPTSD diagnosis according to the ICD-11 criteria (World Health Organization, 2019), and PTSD diagnosis according to the DSM-5 criteria (American Psychiatric Association, 2013). Exclusion criteria were complex dissociative disorder, substance abuse during the last three months, psychosis, acute suicidality, severe somatic illness, severely disturbed group functioning, current life crisis (e.g. ongoing divorce process or lawsuit), and mental disability.

2.2. Procedures

The RCT was approved by the Norwegian Ethical Committee (REK/2017/655) and pre-registered at

ClinicalTrials.gov (NCT03509844). Predictor variables were collected at a four-day assessment admission prior to treatment start and at pre-treatment when the study interventions commenced. The current study used outcome assessed at 10 weeks, corresponding to the end of treatment in PE and STAIR and to the end of phase 1 in SNT. At this point, the treatments provided to patients in the SNT condition was equivalent to the treatment provided to patients in the STAIR condition and we therefore collapsed STAIR and SNT participants into one group. This left two groups who had received either STAIR or PE, each over a period of 10 weeks (PE: $n = 32$; STAIR: $n = 60$).

2.3. Treatment

STAIR is a skills-training intervention to improve affective and interpersonal regulation (Cloitre et al., 2002). In this study, STAIR was provided as a 12-session group programme supported by concurrent individual sessions. PE was delivered according to the standard protocol, with 8–16 individual sessions (Foa et al., 2007). Treatment enhancements (e.g. milieu therapy, supportive consultations, medical assistance, and organized physical exercise) were similar in both conditions.

3. Measures

3.1. Outcome measures

The primary outcome was PTSD symptom severity, assessed with the Clinician Administered PTSD Scale (CAPS-5; Weathers et al., 2018) and the PTSD Checklist for DSM-5 (PCL-5; Weathers et al., 2013).

The CAPS-5 is a semistructured interview of PTSD symptoms matching the DSM-5 diagnostic criteria. The CAPS-5 consists of 20 questions rated on a scale from 0 (no complaints) to 4 (invalidating complaints), giving a total sum score from 0 to 80 with higher scores indicating higher symptom severity. The CAPS-5 is considered the gold standard for diagnosing PTSD and evaluation symptom severity, showing strong interrater and test-retest reliability and convergent validity to other PTSD measures, and satisfactory discriminant validity (Weathers et al., 2018). In this study, the baseline Cronbach's $\alpha = 0.73$, indicating acceptable internal consistency.

The PCL-5 (Weathers et al., 2013) is a self-report questionnaire for PTSD consisting of 20 symptom items which corresponds to the DSM-5 diagnostic criteria. Items are scored on a five-point Likert scale from 0 (not at all) to 4 (extremely), giving a total sum score from 0 to 80 with higher scores indicating higher symptom severity. Studies of the PCL-5 has shown satisfactory findings of internal consistency, and convergent and discriminant validity (Blevins et al., 2015). The baseline Cronbach's $\alpha = 0.84$ in the current study indicated good internal consistency.

3.2. Predictor variables

CAPS-5 data was collected at pre-treatment. All other potential predictors were collected at a preceding 4-day assessment admission corresponding to the timepoint when the choice of treatment approach in the clinic ordinarily is made. Predictors were chosen from research on predictors for PTSD, clinical experience, and available data in the RCT within the following domains: demographics, trauma background, self-reported psychiatric symptoms, and clinician-assessed psychiatric symptoms and disorders (for details, see Table 1).

4. Data analysis

4.1. Data preprosessing

Data was analysed using SPSS version 29.0.1.0 (IBM Corp., 2023) and R Statistical Software (v4.4.0; R Core Team, 2024). Subscale scores were included to maximize the clinical utility. The correlations between all scales were explored to avoid multicollinearity. Measures correlating > .80 were omitted (Kuhn & Johnson, 2013) and included the following: PCL-5 cognition and mood, IIP-64 self-sacrificing, and the SCL-90 R subscales obsessive-compulsive, depression, anxiety, alienation, and interpersonal sensitivity.

The data was inspected for missing values. Following standard procedures at the clinic, the full Alcohol Use Disorders Identification Test (AUDIT; Saunders et al., 1993) and Drug Use Disorders Identification Test (DUDIT; Berman et al., 2016) questionnaires were only administered to respondents who endorsed an initial screening question eliciting ongoing problematic alcohol or substance use. Substance abuse was an exclusion criterion in the RCT. Consequently, the missing rate for the DUDIT was high (94.6%) and therefore removed from the analysis. Missing data from the 4-day assessment admission for the PCL-5 ($n = 12$, 13%) and SCL-90 ($n = 1$, 1.1%) were imputed with pre-treatment scores collected when the study intervention started from the corresponding person. The scores did not differ significantly (PCL-5 total assessment admission: $M = 2.71$; $SD = .51$ vs pre-treatment: $M = 2.72$; $SD = 0.52$; SCL-90 total assessment admission: $M = 170.66$; $SD = 50$ vs. pre-treatment: $M = 173.01$; $SD = 54.65$). We used person-mean imputation for all variables when missing items were maximum 2 per questionnaire and all measures were included as mean scores, except CAPS-5 (which had no missing). The RCT data included weekly PCL-5 measures throughout the treatment period. 36 (39.1%) PCL-5

post-treatment scores were missing. If available, the last observation in the weekly data was carried forward from week 9 (16 scores, 17.4%), or subsidiary substituted with scores from week 11 (9 scores, 9.8%). Data from week 11 were used for four group-members in the SNT group. This left 11 participants (12%) missing PCL-5 scores at post-treatment. (For details on missing data, see supplementary Table 1)

The remaining missing data was imputed using the R package missForest (Stekhoven & Bühlmann, 2012). The missForest provides an estimate of the imputation error based on the out-of-bag error estimate of random forest. The normalized root mean squared error (NRMSE) gives a value for the continuous variables, and the proportion of falsely classified (PFC) for the categorical variables. The Dissociation Experiences Scale-II (DES-II; Bernstein & Putnam, 1986) items returned too high NRMSE value and were therefore omitted. To incorporate a measure on dissociation, we included the CAPS-5 subscales depersonalization and derealization and completed the imputation. The NRMSE was .19 and the PFC was .29, indicating acceptable levels of imputation error. We compared these results with a second dataset including the best performing DES-II subscale (amnesia). The NRMSE was .38 and the PFC was .31, exceeding recommended imputation error levels (Stekhoven & Bühlmann, 2012). We therefore continued with the first dataset.

After data preprocessing, a total of 61 variables was used for model building. See Tables 1 and 2 for an overview of the final predictors included in the analyses.

4.2. Outcome

Change in CAPS-5 and PCL-5 scores from pre-treatment to post-treatment were used as outcome variables in all analyses. Change scores were calculated by subtracting pre-treatment scores from post-treatment scores with more negative scores indicating better outcomes.

4.3. Predictor selection with Boruta

Predictor variables were selected separately for PE and STAIR using the R package Boruta (Kursa & Rudnicki, 2010). The relevance of a predictor is determined by assessing its performance against 'shadow' predictors, created separately by randomly shuffling the values of the original predictors. The Boruta is based on random forest classification using different bagging samples of the dataset to develop multiple trees. Z-scores are used to calculate the importance of shadow and original variables by dividing the average loss of accuracy of classification caused by random permutations of the variable between samples by its standard deviation. A variable is considered a relevant predictor and stored as a hit in a vector when its Z-score is higher than the Z-score of the maximum shadow variable. The Boruta procedure was repeated for a maximum of 10,000 iterations or until all variables were categorized. We ran the Boruta ten times for all conditions and retained variables which turned out relevant five times or more in the following bootstrap procedure.

4.4. Predictor selection using bootstrap procedure

The Boruta runs a risk of overfitting the data. The comparisons with the shadow features are performed multiple times for each feature, and the Boruta is based on Random Forest which can overfit during importance calculation. The PAI is calculated with a linear combination of variables. Following recommendations from recent PAI research (Bremer et al., 2023; Tait et al., 2024), we conducted an additional variable selection procedure with a bootstrapped model to prevent overfitting and secure inclusion of the best variables for a linear outcome prediction (Kursa & Rudnicki, 2010). We ran a bootstrapped model using the R package bootStepAIC (Rizopoulos, 2022) which selects the model with the best fit.

4.5. Personalized advantage index

Predictions of the treatment outcome were calculated with a regression model including the final set of predictors in a leave-one-out cross-validation approach in which the predicted outcome for a patient in the test set is based on a training set which includes all other patients. Each patient had predictions for both PE and STAIR conditions. The PAI was calculated using the final set of predictors by subtracting the predicted outcome in STAIR from the predicted outcome in PE. A positive PAI thus indicated a relative advantage of STAIR, and a negative PAI indicated a relative advantage of PE. Patients were defined as having received optimal treatment when they had been randomized to the treatment recommended by the PAI and defined as having received suboptimal treatment if they had been randomized to the non-recommended treatment. Two separate sets of analyses were conducted using the CAPS-5 and the PCL-5 as the defined outcome.

5. Results

Independent samples t-test was used to compare the observed decrease in interview rated and self-reported PTSD symptoms from pre-treatment to post-treatment in the PE condition (CAPS-5: $M = -10.43$; $SD = 12.59$, PCL-5: $M = -12.36$; $SD = 16.31$) versus the STAIR condition (CAPS-5: $M = -3.38$; $SD = 8.03$, PCL-5: $M = -6.60$; $SD = 10.50$). Levene's test revealed significant differences in the groups' variances.

Table 1. Potential predictors for PE and STAIR.

	Potential predictors	Measure	
Demographics	Age		
	Gender		
	Married/cohabitant		
	Education level		
	Employment		
	Years of active treatment		
Trauma background	Life threatening disease	Stressful Life Events Screening Questionnaire (SLESQ)	Goodman et al. (1998)
	Life threatening accident		
	Robbery/assault with physical power/ weapon		
	Sudden death of a close person		
	Penetrating sexual assault		
	Fondling		
	Childhood sexual abuse		
	Adult sexual abuse		
	Emotional abuse		
	Threatened by weapon		
	Witness to trauma		
	Seriously harmed or life-threatening situation		
	Frightened or very helpless		
	Number of trauma categories		
	Age at first trauma experience		
	Perpetrator parent		
Self-reported psychiatric symptoms	PCL-5 total score	PTSD Checklist for DSM-5	Weathers et al. (2013)
	PCL-5 intrusion		
	PCL-5 hyperarousal		
	PCL-5 avoidance		
	PCL-5 cognition and mood		
	BDI-II total score	Beck's Depression Inventory-II	Beck et al. (1996)
	SDQ-20 total score	Somatoform Dissociation Questionnaire-20	Nijenhuis et al. (1996)
	SCL-90-R total score	Symptom Checklist-90-Revised	Vaurio (2011)
	SCL-90 R somatization		
	SCL-90 R hostility/anger		
	SCL-90 R phobic anxiety		
	SCL-90-R paranoid ideation		
	SCL-90 R psychoticism		
	SCL-90 R additional		
	SF-36 physical function	36-item Short From Health Survey	Ware and Sherbourne (1992)
	SF-36 role limitation physical		
	SF-36 pain		
	SF-36 general sickness experience		
	SF-36 energy and fatigue		
	SF-36 social function		
	SF-36 role limitation emotional		
	SF-36 mental health		
	IIP-64C total score	Inventory of Interpersonal Problems	Horowitz et al. (2013)
	IIP-64C domineering/controlling		
	IIP-64C vindictive/self-centered		
	IIP-64C cold/distant		
	IIP-64C socially inhibited		
	IIP-64C non-assertive		
	IIP-64C intrusive/needy		
	AUDIT	Alcohol Use Disorders Identification Test	Saunders et al. (1993)
Clinician-assessed psychiatric symptoms and disorders	CAPS-5	Clinician Administered PTSD Scale	Weathers et al. (2018)
	CAPS-5 derealization		
	CAPS-5 depersonalization		
	Number of diagnoses	Mini-International Neuropsychiatric Interview	Sheehan et al. (1998)

Accordingly, the Welch's test was applied, demonstrating that CAPS-5 symptoms declined significantly more in PE compared to STAIR, ($t(44.899) = -2.869$, $p = .006$), with no significant differences for PCL-5 ($t(45.077) = -1.808$, $p = .077$).

5.1. Variable selection

Different variables were identified as important predictors of outcome in STAIR and PE, and when defining outcome using the CAPS-5 versus the PCL-5 change scores. The SCL-90 R additional subscale was among the relevant predictors. Since it is a composite scale of various symptoms, an exploratory analysis of the subscale was conducted revealing which items were the relevant predictors. The analysis was repeated with the additional subscale replaced by the constituting items.

Variables dropped in the subsequent bootstrap procedure are found in Tables 3 and 4.

Table 2. Descriptive information about potential predictors for PE and STAIR.

Predictors [1]	Possible range of Predictor Scores Min-Max	Prolonged Exposure ($n = 32$)	STAIR ($n = 60$)
Demographics			
Age, mean (*SD*)		40.6 (8.9)	41.4 (9.6)
Female, *n* (%)		25 (78.1)	49 (81.7)
Married/cohabitant, *n* (%)		21 (65.6)	40 (66.7)
High school level education, *n* (%)		22 (68.8)	43 (71.7)
College level education, *n* (%)		9 (28.1)	20 (33.3)
Employed, yes, *n* (%)		11 (34.4)	26 (43.3)
Years of active treatment, *n* (%)		7.4 (4.5)	6.3 (2.7)
Trauma background			
SLESQ type of trauma			
Life threatening disease, *n* (%)		2 (6.3)	7 (11.7)
Life threatening accident, *n* (%)		2(6.3)	12 (20.0)
Robbery/assault with physical power/weapon, *n* (%)		7 (21.9)	18 (30.0)
Sudden death of a close person, *n* (%)		16 (50)	28 (46.7)
Penetrating sexual assault, *n* (%)		28 (87.5)	48 (80.0)
Fondling, *n* (%)		19 (59.4)	28 (46.7)
Childhood sexual abuse, *n* (%)		21 (65.6)	45 (75.0)
Adult sexual abuse, *n* (%)		20 (62.5)	24 (40.0)
Emotional abuse, *n* (%)		29 (90.6)	49 (81.7)
Threatened by weapon, *n* (%)		6 (18.8)	15 (25.0)
Witness to trauma, *n* (%)		22 (68.8)	36 (60.0)
Seriously harmed or life-threatening situation, *n* (%)		2 (6.3)	5 (8.3)
Frightened or very helpless, *n* (%)		20 (62.5)	49 (81.7)
Number of trauma categories, mean (SD)		3.9 (1.6)	4,1 (2.0)
Age at first trauma experience, mean, (*SD*)		5.8 (3.1)	5.4 (3.5)
Perpetrator parent, yes, *n* (%)		22 (68.8)	50 (83.3)
Clinician-assessed psychiatric symptoms and disorders			
CAPS-5[2] sum (*SD*)	0–80	46.1 (8.2)	42.9 (7.5)
CAPS-5 derealization mean (*SD*)	0–4	0.6 (1.1)	0.6 (0.9)
CAPS-5 depersonalization mean (*SD*)	0–4	1.3 (1.1)	1.0 (1.3)
Number of diagnoses (MINI) mean (*SD*)		3.2 (1.8)	2.9 (1.3)
Self-reported psychiatric symptoms[1]		**Mean (*SD*)**	**Mean (*SD*)**
PCL-5 total score	0–4	2.8 (0.5)	2.7 (0.5)
PCL-5 intrusion	0–4	2.9 (0.9)	2.8 (0.7)
PCL-5 hyperarousal	0–4	2.5 (0.5)	2.4 (0.5)
PCL-5 avoidance	0–4	3.2 (0.8)	3.1 (0.8)
PCL-5 cognition and mood	0–4	2.8 (0.7)	2.8 (0.7)
BDI-II total score	1–4	1.6 (0.5)	1.6 (0.4)
SDQ-20 total score	1–5	1.6 (0.5)	1.5 (0.5)
SCL-90-R total score	0–4	2.0 (0.7)	1.9 (0.5)
SCL-90 R somatization	0–4	2.3 (0.9)	2.1 (0.8)
SCL-90 R hostility/anger	0–4	0.6 (0.7)	0.6 (0.5)
SCL-90 R phobic anxiety	0–4	1.8 (1.0)	1.5 (0.9)
SCL-90-R paranoid ideation	0–4	1.6 (0.8)	1.4 (0.7)
SCL-90 R psychoticism	0–4	1.1 (0.7)	0.9 (0.6)
SCL-90 R additional	0–4	2.4 (0.7)	2.1 (0.7)
SF-36 physical function	1–3	2.4 (0.5)	2.5 (0.4)
SF-36 role limitation physical	1–5	3.2 (1.4)	3.2 (1.3)
SF-36 pain	1–6	3.9 (1.3)	3.9 (1.2)
SF-36 general sickness experience	1–5	3.3 (0.7)	3.4 (0.5)
SF-36 energy and fatigue	1–6	3.6 (0.7)	3.7 (0.4)
SF-36 social function	1–5	3.1 (0.7)	3.0 (0.4)
SF-36 role limitation emotional	1–5	2.7 (1.2)	2.9 (1.1)
SF-36 mental health	1–6	3.6 (0.6)	3.8 (0.5)
IIP-64C total score	0–4	1.8 (0.5)	1.8 (0.4)
IIP-64C domineering/controlling	0–4	0.6 (0.4)	0.7 (0.4)
IIP-64C vindictive/self-centered	0–4	1.1 (0.5)	1.1 (0.5)
IIP-64C cold/distant	0–4	1.6 (0.7)	1.8 (0.6)
IIP-64C socially inhibited	0–4	2.3 (0.9)	2.3 (0.7)
IIP-64C non-assertive	0–4	2.8 (0.9)	2.8 (0.8)
IIP-64C intrusive/needy	0–4	1.1 (0.6)	1.0 (0.5)
AUDIT	0–4	0.6 (0.5)	0.5 (0.4)

Notes: STAIR = Skills Training in Affective and Interpersonal Regulation, Min = minimum, max = maximum, MINI = Mini-International Neuropsychiatric Interview, PCL-5 = PTSD Checklist for DSM-5, BDI = Beck's Depression Inventory-II, SDQ-20 = Somatoform Dissociation Questionnaire-20, SCL-90 R = Symptom Checklist-90 Revised, CAPS-5 = Clinician-Administered PTSD Scale, SF-36 = 36 Item Short-Form Survey, IIP-64C = Inventory of Interpersonal Problems-64C, SLESQ = Stressful Life Events Screening Questionnaire, AUDIT = Alcohol Use Disorders Identification Test, *SD* = standard deviation, *n* = sample size. [1] On all measures higher scores on predictors signify higher symptom severity except SF-36 scores where higher scores indicate better functioning. [2] CAPS-5 no missing and reported in sum score.

Table 3. Results from Boruta and subsequent bootstrap procedure for potential predictors of PE.

	CAPS			PCL		
	Boruta		Bootstrap	Boruta		Bootstrap
Predictors	Number of Hits (%)	Important	Important	Number of Hits (%)	Important	Important
Demographics						
Age	0	No	No	0	No	No
Gender, female	0	No	No	0	No	No
Married/cohabitant, yes	0	No	No	0	No	No
Finished high school, yes	0	No	No	0	No	No
Finished college, yes	0	No	No	0	No	No
Employed, yes	0	No	No	0	No	No
Years of active treatment	0	No	No	0	No	No
Trauma background						
SLESQ type of trauma:						
Life threatening disease	0	No	No	0	No	No
Life threatening accident	0	No	No	0	No	No
Robbery/assault with physical power/weapon	0	No	No	0	No	No
Sudden death of a close person	0	No	No	0	No	No
Penetrating sexual assault	0	No	No	0	No	No
Fondling	0	No	No	0	No	No
Childhood sexual abuse	0	No	No	0	No	No
Adult sexual abuse	0	No	No	0	No	No
Emotional abuse	0	No	No	0	No	No
Threatened by weapon	0	No	No	0	No	No
Witness to trauma	0.69	Yes	No	0	No	No
Seriously harmed or life-threatening situation	0	No	No	0	No	No
Frightened or very helpless	0	No	No	0	No	No
Number of trauma categories	0	No	No	0	No	No
Age at first trauma experience	0	No	No	0	No	No
Perpetrator parent, yes	0	No	No	0	No	No
Self-reported psychiatric symptoms						
PCL-5 total score	0	No	No	0	No	No
PCL-5 intrusion	0	No	No	0	No	No
PCL-5 hyperarousal	0	No	No	0	No	No
PCL-5 avoidance	0	No	No	0	No	No
BDI-II total score	0	No	No	0.71	Yes	Yes
SDQ-20 total score	0.78	Yes	Yes	0.50	Tentative	No
SCL-90-R total score	0.96	Yes	No	0.91	Yes	No
SCL-90 R somatization	0.01	No	No	0.61	Yes	No
SCL-90 R hostility/anger	0	No	No	<0.01	No	No
SCL-90 R phobic anxiety	0	No	No	<0.01	No	No
SCL-90-R paranoid ideation	0	No	No	0	No	No
SCL-90 R psychoticism	0	No	No	0	No	No
SCL-90 Q19	0	No	No	0	No	No
SCL-90 Q44	0	No	No	0	No	No
SCL-90 Q59	0.84	Yes	Yes	<0.01	No	No
SCL-90 Q60	0	No	No	0	No	No
SCL-90 Q64	0	No	No	0	No	No
SCL-90 Q66	0	No	No	0	No	No
SCL-90 Q89	0	No	No	0	No	No
SF-36 physical function	<0.01	No	No	0.67	Yes	Yes
SF-36 role limitation physical	0	No	No	0	No	No
SF-36 pain	<0.01	No	No	0	No	No
SF-36 general sickness experience	0.47	Yes	No	0	No	No
SF-36 energy and fatigue	0	No	No	0	No	No
SF-36 social function	<0.01	No	No	0	No	No
SF-36 role limitation emotional	0	No	No	0	No	No
SF-36 mental health	0.65	Yes	No	0.57	Yes	No
IIP-64C total score	0.54	Yes	No	0	No	No
IIP-64C domineering/controlling	0	No	No	0	No	No
IIP-64C vindictive/self-centered	0	No	No	0	No	No
IIP-64C cold/distant	0	No	No	0	No	No
IIP-64C socially inhibited	0	No	No	0	No	No
IIP-64C intrusive/needy	0	No	No	<0.01	No	No
AUDIT	0	No	No	0.57	Yes	No
Clinician-assessed psychiatric symptoms and disorders						
CAPS-5	0	No	No	0	No	No
CAPS-5 derealization	0	No	No	0	No	No
CAPS-5 depersonalization	<0.01	No	No	0	No	No
Number of diagnoses (MINI)	0	No	No	0	No	No

Table 4. Results from Boruta and subsequent bootstrap procedure for potential predictors of STAIR.

	CAPS			PCL		
	Boruta		Bootstrap	Boruta		Bootstrap
Predictors	Number of Hits (%)	Important	Important	Number of Hits (%)	Important	Important
Demographics						
Age	0	No	No	0	No	No
Gender, female	0	No	No	0	No	No
Married/cohabitant, yes	<0.01	No	No	0	No	No
Finished high school, yes	0	No	No	0	No	No
Finished college, yes	0	No	No	0	No	No
Employed, yes	0	No	No	0	No	No
Years of active treatment	0	No	No	0	No	No
Trauma background						
SLESQ type of trauma						
Life threatening disease	0	No	No	0	No	No
Life threatening accident	0	No	No	0	No	No
Robbery/assault with physical power/weapon	0	No	No	0	No	No
Sudden death of a close person	0	No	No	0	No	No
Penetrating sexual assault		No	No	0.03	No	No
Fondling	0	No	No	<0.01	No	No
Childhood sexual abuse	0	No	No	0	No	No
Adult sexual abuse	0	No	No	0	No	No
Emotional abuse	0	No	No	0	No	No
Threatened by weapon	0	No	No	0	No	No
Witness to trauma	0	No	No	0.75	Yes	Yes
Seriously harmed or life-threatening situation	0	No	No	0	No	No
Frightened or very helpless	0	No	No	0	No	No
Number of trauma categories	0	No	No	0	No	No
Age at first trauma experience	0	No	No	0	No	No
Perpetrator parent, yes	0	No	No	0	No	No
Self-reported psychiatric symptoms						
PCL-5 total score	0	No	No	0.05	No	No
PCL-5 intrusion	0	No	No	0.71	Yes	Yes
PCL-5 hyperarousal	0	No	No	0	No	No
PCL-5 avoidance	0	No	No	0	No	No
BDI-II total score	0	No	No	0	No	No
SDQ-20 total score	<0.01	No	No	0	No	No
SCL-90-R total score	0	No	No	0.67	Yes	No
SCL-90 R somatization	0	No	No	0	No	No
SCL-90 R hostility/anger	0	No	No	0	No	No
SCL-90 R phobic anxiety	<0.01	No	No	0.17	No	No
SCL-90-R paranoid ideation	0	No	No	0	No	No
SCL-90 R psychoticism	<0.01	No	No	0.79	Yes	Yes
SCL-90 Q19	0	No	No	0	Yes	No
SCL-90 Q44	0	No	No	0	No	No
SCL-90 Q59	0	No	No	0	No	No
SCL-90 Q60	0	No	No	0	No	No
SCL-90 Q64	0	No	No	0	No	No
SCL-90 Q66	0	No	No	0	No	No
SCL-90 Q89	0	No	No	0.66	Yes	Yes
SF-36 physical function	0	No	No	0	No	No
SF-36 role limitation physical	0	No	No	0	No	No
SF-36 pain	0.04	No	No	<0.01	No	No
SF-36 general sickness experience	0	No	No	0	No	No
SF-36 energy and fatigue	0	No	No	0	No	No
SF-36 social function	0	No	No	0	No	No
SF-36 role limitation emotional	0	No	No	0	No	No
SF-36 mental health	0.49	Tentative	No	0	No	No
IIP-64C total score	0.79	Yes	Yes	0	No	No
IIP-64C domineering/controlling	0	No	No	0	No	No
IIP-64C vindictive/self-centered	0	No	No	0	No	No
IIP-64C cold/distant	0	No	No	0	No	No
IIP-64C socially inhibited	0	No	No	0	No	No
IIP-64C intrusive/needy	0	No	No	0	No	No
AUDIT	0	No	No	0	No	No
Clinician-assessed psychiatric symptoms and disorders						
CAPS-5 total score	0	No	No	0.98	Yes	Yes
CAPS-5 derealization	0	No	No	0	No	No
CAPS-5 depersonalization	0	No	No	0	No	No
Number of diagnoses (MINI)	0	No	No	0	No	No

Table 5. Final prediction models of PE and STAIR with calculated change in CAPS-5 score from pre-treatment to 10 weeks as the outcome variable.

PE	Estimate	Std. Error	*t*-value	*p*
SDQ-20 total	7.03	3.89	1.81	.081
SCL-90 Q59	4.48	1.41	3.17	.004 **
STAIR				
IIP-64 total	7.65	2.52	3.03	.004 **

Note: Cross-validation approach gave a small individual variation in the prediction models.

Tables 5 and 6 display the predictor variables included in the final prediction models.

5.2. PAI

PAI using CAPS-5 as outcome resulted in RMSE = 10.99 in the PE condition and RMSE = 7.65 in the STAIR condition. One third of the patients ($n = 33$) were randomized to what PAI indicated was their optimal treatment. This group improved more on the CAPS-5 from assessment admission to post-treatment ($M_{improvement} = -11.00$; $SD_{improvement} = 12.02$) compared to the two thirds of the patients ($n = 59$) randomized to their non-optimal treatment ($M_{improvement} = -2.94$; $SD_{improvement} = 8.05$; $F(1, 90) = 10.69$, $p = .002$). The standardized mean difference between optimal and suboptimal treatment reciprocates a large effect size (Cohen's $d = 0.83$).

PAI using PCL-5 resulted in RMSE = 13.67 in the PE condition and RMSE = 9.47 in the STAIR condition. About one third of the patients ($n = 40$) were randomized to what PAI indicated was their optimal treatment. Patients randomized to optimal treatment improved more on the PCL-5 ($M_{improvement} = -12.85$; $SD_{improvement} = 13.39$) compared to patients randomized to their suboptimal treatment ($M_{improvement} = -5.34$; $SD_{improvement} = 11.86$; $F(1, 90) = 4.22$, $p = .043$). The standardized mean difference between optimal and suboptimal treatment reciprocates a medium effect size (Cohen's $d = 0.60$) (see Figure 1).

Within patients treated with PE, the PAI predictions indicated that one in five (18.7%, using the CAPS-5 and the PCL-5 as outcomes) would have profited more from treatment if they had received STAIR instead. Within patients treated with STAIR, the PAI predictions indicated that approximately four in five (88.3% based on the CAPS-5, and 76.7% based on the PCL-5) would have improved more from PE. The PAI thus identified groups within both conditions predicted to have better outcomes if they had received the alternative treatment.

Table 6. Final prediction models of PE and STAIR with calculated change in PCL-5 score from pre-treatment to 10 weeks as the outcome variable.

PE	Estimate	Std. Error	*t*-Value	*p*
BDI total	10.59	5.33	1.99	.057
SF-36 physical	−11.29	5.26	−2.15	.040 *
STAIR				
CAPS total	0.26	0.17	1.57	.122
PCL-5 intrusion	2.96	1.69	1.74	.087
Witness to trauma	−7.38	2.40	−3.08	.003 **
SCL-90 Q89	1.52	1.03	1.48	.146
SCL-90 psychoticism	3.20	2.26	1.42	.162

Note: Cross-validation approach gave a small individual variation in the prediction models. Note that SF-36 scores indicate better functioning.

6. Discussion

The current study aimed to identify predictors of treatment outcome in skills-training and prolonged exposure treatment for CPTSD using the PAI approach and evaluate the relative advantage of receiving optimal over suboptimal treatment. Different predictors were identified as relevant for skills-training and exposure. The PAI depicted significant difference between optimal and suboptimal treatment both using CAPS-5 and PCL-5 as outcome, indicating that patients randomized to their optimal treatment improved significantly more compared to patients randomized to their suboptimal treatment. The difference amounted to large and medium effect size using CAPS-5 and PCL-5 as outcomes, respectively. About two thirds of the patients had been randomized to their suboptimal treatment. This implies a potential improvement in outcomes if the treatment choice had been based on the PAI recommendation instead of random allocation.

This study demonstrates the potential utility of the PAI approach. However, the present results should be interpreted cautiously, and additional studies are needed before actual treatment recommendations can be made. With that in mind, a discussion of the relevant predictors follows.

In the PE-condition, using CAPS-5 as outcome, somatoform dissociation and suicidal ideation predicted worse outcome. Symptoms of somatoform dissociation include lack of body awareness or bodily feelings, insensitivity for pain, inhibitions of movement, or experiencing sensations in absence of stimuli. Reducing emotional discomfort, somatoform dissociation might lead to disengagement from trauma related emotions essential for emotional processing. Research on the relationship between somatoform dissociation and exposure therapy is scarce, but somatoform dissociation did not predict outcome in a study of intensive short-term treatment combining PE and EMDR (Zoet et al., 2021). The joint effects of EMDR and PE, or the intensive treatment format, may have relieved somatoform dissociative symptoms more effectively than PE provided alone in the present study, tentatively explaining the lack of predictive value of somatoform dissociation. Research on suicidal ideation as a predictor of PTSD treatment outcomes remain limited, possibly due to the uncertainty surrounding the inclusion of patients with

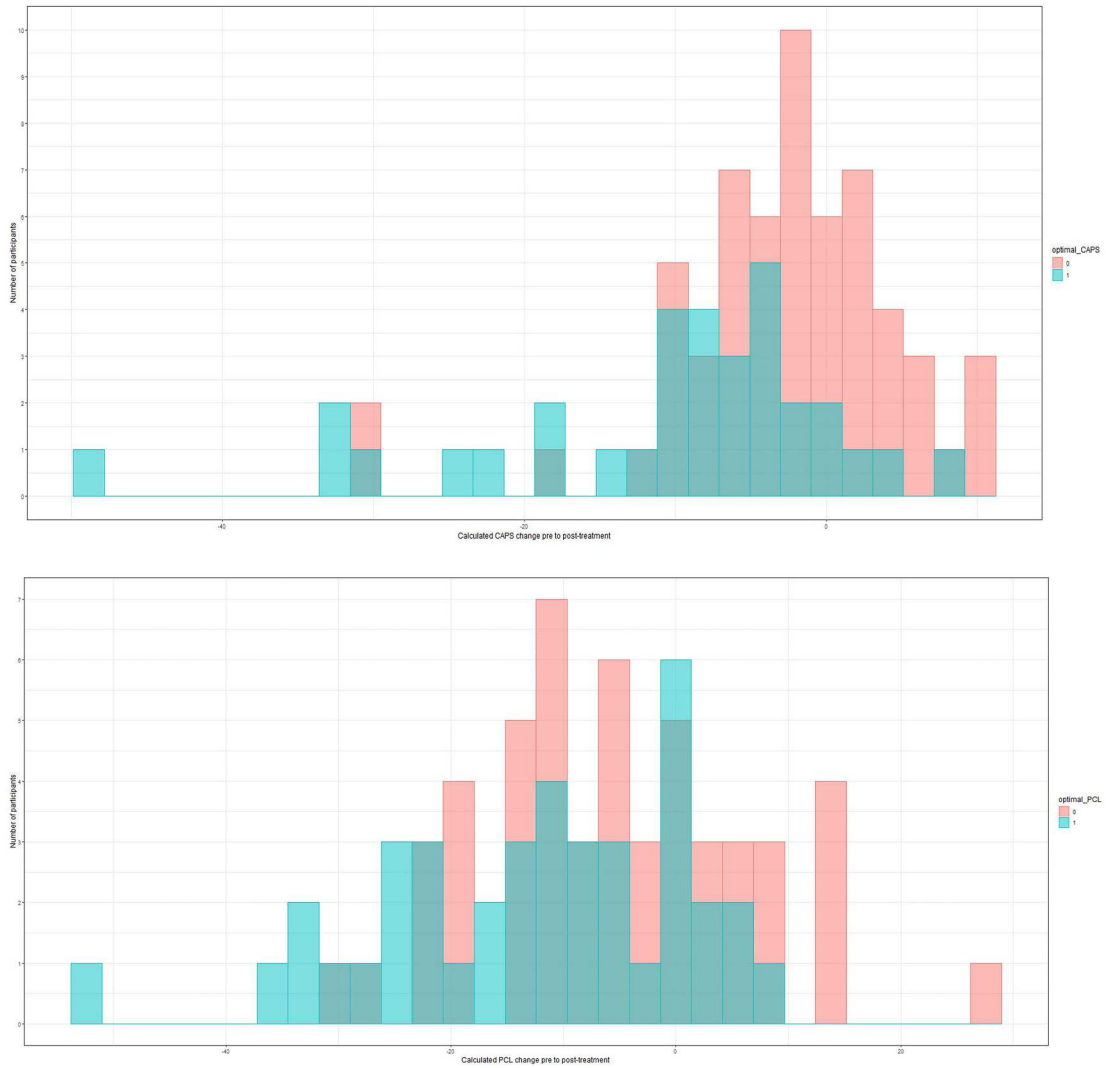

Figure 1. Distribution of calculated change in CAPS-5 and PCL-5 scores from assessment to 10 weeks for patients randomized to their optimal (blue) treatment versus suboptimal (red) treatment.

suicidal ideation in clinical trials for PTSD (Brooks et al., 2021). Our findings align with a study comparing cognitive therapy to imaginal exposure for chronic PTSD, in which heightened suicide risk predicted poorer treatment outcome irrespective of treatment (Tarrier et al., 2000). Contrary to the present finding, suicidal ideation did not predict the outcome of Cognitive Processing Therapy for active duty military personnel (Resick et al., 2017).

In the PE condition, using PCL-5 as outcome, severe depressive symptoms and reduced physical functioning (e.g. having trouble walking stairs, or trouble dressing oneself) predicted worse outcome. Depression and dysphoric emotions involve diminished access to other emotions which might limit the effect of exposure therapy. Dysphoric and numbing symptoms are associated with executive function impairments, possibly interfering with the voluntary engagement with trauma memories (Keyan et al., 2024). Several studies have reported high baseline depressive symptoms as predictor of poorer treatment outcome (Barawi et al., 2020; Dewar et al., 2019; Hoeboer et al., 2021b). Physical impairment is indicative of the more complex symptom constellation associated with CPTSD, often requiring the inclusion of several foci in therapy, and possibly contributing to a more challenging route to recovery. Impaired functioning has been found to predict poorer T-F psychotherapy response (Keyan et al., 2024). Previous research on military veterans has indicated an association between reduced physical functioning and lower odds of psychotherapy retention (Duan-Porter et al., 2021). Overall, the symptoms predicting worse outcome of PE in the present study support the hypothesis that a primary focus on emotional processing in trauma-focused therapies could explain the limited effects of these approaches for some patients (Keyan et al., 2024).

In the STAIR condition, using CAPS-5 as outcome, higher levels of relational difficulties predicted worse outcome. STAIR addresses relational issues specifically and is therefore assumed to fit patients with relational problems. The present finding challenges this notion. Although targeting lack of skills, STAIR does

not address the link between these difficulties and trauma history. Working directly with this link is proposedly essential in treating PTSD, which in case can illuminate our findings. Sotsky and colleagues (1991) provides an alternative explanation, suggesting that different therapeutic modalities rely on different learning techniques, with each modality requiring an adequate capacity in the corresponding functional domain to facilitate recovery. Conceivably, patients with less relational difficulties might gain more from STAIR, while more severe relational difficulties might diminish the effect. Our findings are in line with a previous study by Hoeboer and colleagues (2021b) where interpersonal problems predicted reduced outcomes in phase-based treatment (STAIR + PE) but not in PE alone for CA-PTSD.

In the STAIR condition, using PCL-5 as outcome, more severe PTSD symptoms, and particularly intrusions, predicted worse outcome. STAIR's lack of focus on intrusions and other PTSD symptoms might elucidate this finding, possibly indicating that patients with higher PTSD scores and severe intrusive symptoms would benefit more from treatments targeting these symptoms directly. Our findings are in line with two former studies comparing STAIR, PE, and their combination, in CA-PTSD (Cloitre et al., 2016; Hoeboer et al., 2021b), while other studies on various trauma populations have not found that PTSD scores predict outcome (Barawi et al., 2020).

In the STAIR condition, using PCL-5 as outcome, feelings of guilt predicted worse outcome. STAIR addresses emotional issues specifically and is therefore assumed to fit patients struggling with emotional problems. A possible explanation may the lack of connection between guilt and explicit work on trauma history. Or alternatively, a lack of capacity in the relevant functional domain (Sotsky et al., 1991). Research on guilt as a predictor of STAIR or similar skills-training programmes is scarce, while research on trauma-focused methods have reported either no predictive relationship (Barawi et al., 2020), that higher pre-treatment guilt predicts greater reduction in PTSD symptoms (Clifton et al., 2017; Rizvi et al., 2009), or that guilt also mediates change in PTSD symptoms during treatment (Øktedalen et al., 2015).

In the STAIR condition, using PCL-5 as outcome, psychoticism predicted worse outcome. Symptoms such as hearing voices, having severely disturbed thoughts, and experiencing profound feelings of loneliness are particularly debilitating. More severe symptom compilation might require an even more tailored approach to treatment (Herzog et al., 2021). A previous study identified psychoticism as predicting worse outcome of PTSD inpatient treatment (Herzog et al., 2021). The treatment consisted of a combination of trauma-focused therapy and skills training in groups. The group sessions included a focus on alternative social skills and managing emotions, which are key components in STAIR. Sotsky and colleagues (1991) hypothesized that for a therapeutic modality to be effective, a certain level of capacity within the corresponding functional domain must be present. Consequently, patients with high scores on the psychoticism subscale may experience a reduced effect from the STAIR skills training due to limited emotional and relational capacity. Additionally, severely distressing thought content could impair patients' learning ability, making it challenging to fully benefit from the psychoeducation provided in STAIR.

In the STAIR condition, using PCL-5 as outcome, being a witness to trauma predicted better outcome regardless of whether the patient had any other direct traumatic experiences. Focusing particularly on relational struggle, STAIR might serve as a more useful approach for the general, relational effect associated with being a witness to trauma. Being a witness to trauma is, to our knowledge, not formerly reported as a predictor.

Finding different predictors in a clinician-administered and self-reported PTSD-measure (i.e. CAPS-5 and PCL-5) might elicit concern about the validity of the predictors, underlining the need for cautious interpretation and external validation. The identification of depression, baseline PTSD severity, and sleep disturbances predicting worse outcome is, however, supported by a recent meta-analysis (Keyan et al., 2024) while we did not replicate the findings regarding social support, gender, alcohol abuse, pain, early trauma, and more trauma load reported by Keyan and colleagues (2024). Depression and interpersonal problems identified as relevant predictors are in line with Hoeboer and colleagues' study (2021b) comparing treatments similar to the present study, with data from a CA-PTSD sample.

The present study found a significant difference between optimal and suboptimal treatment according to PAI. Our findings should be interpreted with caution since the PAI-procedure is applied to the sample from which the prediction models the PAI-procedure is based on were developed. Furthermore, the models have not been validated in independent data. However, the present finding is in line with previous research comparing treatments with different amounts of trauma-focused methods for CA-PTSD (Hoeboer et al., 2021b). The mixed findings among studies using the PAI approach may be related to the treatments being compared, as exemplified by studies involving treatments with an equivalent number of trauma-focused interventions (Bremer et al., 2023). The clinical utility of the PAI approach in recommending treatments for CPTSD may lie in identifying characteristics that predict greater benefit from trauma-focused versus non-trauma-focused approaches, rather than distinguishing between various trauma-focused

options. Within each treatment condition, subgroups predicted to have better outcomes if allocated to the other treatment condition were identified. Thus, despite PE performing better than STAIR on a group level, the PAI identified a subgroup within the PE condition predicted to have better outcomes if treated with STAIR. The finding demonstrates the PAI's potential of identifying possible subgroups deviating from the treatment effect of a larger group, backing the possible clinical utility of the PAI as a decision-support tool in treatment selection.

6.1. Strengths and limitations

The strengths of the present study include the use of data from an RCT on patients diagnosed with ICD-11 CPTSD. This study is one of few investigating the utility of the PAI approach using PTSD measures as the outcome, hence contributing to the limited knowledge on predictors of CPTSD treatment outcomes. The data includes both clinician-assessed and self-reported measures, and a wide range of possible predictors are used. The analysis-method includes a thorough process for predictor selection and cross-validation techniques.

The small sample size of 92 participants is an important limitation of the study. There are no clear guidelines considering sample size when applying machine learning, however a simulation study suggested $n = 300$ patients per treatment group as necessary to reliably discover predictors of differential treatment response (Luedtke et al., 2019). Small sample size implies increased risk of overfitting the model, thereby complicating generalizability. The implications of the study should therefore be restricted to preliminary investigation of the utility of using PAI when making treatment choices. The choice of using the Boruta for predictor selection on a small sample is debated. In comparing various predictor selection algorithms on different sample sizes, Bain and colleagues (2022) found random forest algorithms to perform poorly on smaller samples. Therefore, the use of alternative predictor selection algorithms could have led to the identification of other predictors. The exclusion of patients with severe co-morbidity limits the generalizability of our finding to sub-populations. Another limitation is the possible impact on the analyses from the PE condition generally doing better in the RCT.

6.2. Conclusions

The present study found relevant predictors for PE and STAIR treatment for patients with CPTSD. It demonstrated the utility of the PAI in predicting differential treatment outcomes based on the identified predictors, supporting the potential of using machine learning methods for improving treatment outcomes for CPTSD. Experts within the field of personalization and precision medicine underline the importance of finding ways to successfully implement precision methods (Deisenhofer et al., 2024), bridging the often perceived gap between the research world and the realities, limitations, and possibilities of the everyday clinical work. The present study is limited to a demonstration of the PAI's utility on the sample from which it is developed. Further research is needed to test the PAI on considerably larger samples, to examine the external validity of PAIs by evaluating the models in independent samples, and to assess the potential benefits of using the PAI prospectively in clinical settings.

Author contribution statement

Karine Frost: Conceptualization, study design, data curation, formal analysis, interpretation, writing – original draft, visualization.

Chris Hoeboer: Methodology, formal analysis, interpretation writing – reviewing and editing.

Asle Hoffart: Study design, interpretation, writing – reviewing and editing.

Peter Sele: Conceptualization, study design, methodology, formal analysis, interpretation, writing – reviewing and editing.

Disclosure statement

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Data availability statement

The data that support the findings of this study are available from the corresponding author (K. F.), upon reasonable request.

ORCID

Karine Frost http://orcid.org/0009-0007-8241-5013
Chris M. Hoeboer http://orcid.org/0000-0002-5991-1963
Asle Hoffart http://orcid.org/0000-0002-8042-8570
Peter Sele http://orcid.org/0000-0002-7188-7900

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