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RESEARCH ARTICLE

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In rape trauma PTSD, patient characteristics indicate which trauma-focused treatment they are most likely to complete

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Background: Dropout rates for effective therapies for posttraumatic stress disorder (PTSD) can be high, especially in practice settings. Although clinicians have intuitions regarding what treatment patients may complete, there are few systematic data to drive those judgments.

Methods: A multivariable model of dropout risk was constructed with randomized clinical trial data (n = 160) comparing prolonged exposure (PE) and cognitive processing therapy (CPT) for rape-induced PTSD. A two-step bootstrapped variable selection algorithm was applied to identify moderators of dropout as a function of treatment condition. Employing identified moderators in a model, fivefold cross-validation yielded estimates of dropout probability for each patient in each condition. Dropout rates between patients who did and did not receive their model-indicated treatment were compared.

Results: Despite equivalent dropout rates across treatments, patients assigned to their model-indicated treatment were significantly less likely to drop out relative to patients who did not (relative risk = 0.49 [95% CI: 0.29–0.82]). Moderators included in the model were: childhood physical abuse, current relationship conflict, anger, and being a racial minority, all of which were associated with higher likelihood of dropout in PE than CPT.

Conclusions: Individual differences among patients affect the likelihood they will complete a particular treatment, and clinicians can consider these moderators in treatment planning. In the future, treatment selection models could be used to increase the percentage of patients who will receive a full course of treatment, but replication and extension of such models, and consideration of how best to integrate them into routine practice, are needed.

KEYWORDS
behavior therapy, CBT/cognitive behavior therapy, clinical trials, empirical supported treatments, PTSD/posttraumatic stress disorder, trauma, treatment

1 | INTRODUCTION

Approximately 20% of posttraumatic stress disorder (PTSD) patients who receive psychotherapeutic treatment in a clinical trial do not complete their treatment, with few differences observed for the average patient between therapies in meta-analytic estimates (Imel, Laska, Jakupcak, & Simpson, 2013). However, in treatment of chronic PTSD, active, trauma-focused treatments may in fact have higher dropout rates compared to control treatments, potentially indicating patient aversion to trauma-focused interventions (Bisson, Roberts, Andrew, Cooper, & Lewis, 2013). Dropout rates appear to be higher in naturalistic settings, ranging from 38 to 68% (Garcia, Kelley, Rentz, & Lee, 2011; Kehle-Forbes, Meis, Spoont, & Polusny, 2016; Wang et al., 2005).

Dropout is a serious problem for the population of people with PTSD, because its untreated course is especially poor (Bradley, Greene, Russ, Dutra, & Westen, 2005; Perkonigg et al., 2005). Relative to, for example, switching from one medication to another, it can be more difficult for a patient to switch from one psychotherapy to another (Markowitz & Milrod, 2015). Moreover, patients who have dropped out of one treatment may not return to any type of treatment.

Although general examinations of dropout rate can inform whether any given treatment is likely to be completed by the average patient, they do not inform whether a patient's individual characteristics may predispose them to complete or not complete a particular therapy. Patients likely differ from each other in their ability to tolerate or engage in one treatment, versus another, such that a matching

of patients with treatments would result in lower attrition rates (Zilcha-Mano et al., 2016). For example, some clinicians are concerned that patients with past childhood abuse are more likely to drop out of exposure-focused therapies, due to concerns about symptom worsening (van Minnen, Hendriks, & Olff, 2010). However, temporary symptom exacerbation is both relatively uncommon (Foa, Zoellner, Feeny, Hembree, & Alvarez-Conrad, 2002; Larsen, Wiltsey Stirman, Smith, & Resick, 2016), and has not been found to predict dropout in these treatments (Kehle-Forbes et al., 2016; Larsen et al., 2016).

Indeed, there have only been a few tests of this or any other theories concerning patient characteristics that might predict greater retention in one treatment relative to another, comparing patients with different characteristics (Cloitre, 2015). In one study comparing interpersonal psychotherapy (IPT) to prolonged exposure (PE) for PTSD, patients with comorbid depression exhibited a higher dropout rate in PE, relative to IPT, whereas this was not the case for patients without comorbid depression (Markowitz et al., 2015). In another, patients with higher levels of anger were more likely to drop out of PE than cognitive processing therapy (CPT) (Rizvi, Vogt, & Resick, 2009).

Importantly, no investigation of patient characteristics and differential dropout in PTSD has included a test of whether and how a set of factors may combine to predict differential retention or engagement. Whereas, in principle, single patient-level moderators of dropout could inform clinically meaningful recommendations for treatment selection, if there exist multiple moderators, and they are not strongly correlated with one another, a patient could have a mix of characteristics that both recommend them for or against a particular treatment (Cohen & DeRubeis, 2018).

To address this clinically relevant knowledge gap (Cloitre, 2015) and to illustrate methodologies of treatment selection that may ultimately result in better patient engagement and outcomes (DeRubeis et al., 2014; Wallace, Frank, & Kraemer, 2013; Zilcha-Mano et al., 2016), we conducted a comprehensive moderator analysis from a clinical trial comparing CPT (Resick & Schnicke, 1993) and PE (Foa, Hembree, & Rothbaum, 2007) in a sample of women with PTSD who were survivors of rape (Resick, Nishith, Weaver, Astin, & Feuer, 2002), to assess comparative risk of dropout between treatments. Given that CPT and PE are efficacious treatments for PTSD, clinical tools that could be used to maximize a patient's likelihood of completing treatment should prove to be valuable to patients as well as to care systems.

2 | METHODS

2.1 | Patients

Patients were women who qualified for a DSM-IV diagnosis of PTSD through a standardized, reliable, and masked trauma interview (Resick, Jordan, Girelli, Hutter, & Marhoefer-Dvorak, 1988). Patients were included if they had experienced a completed rape in childhood or adulthood, they were at least 3 months posttrauma, and, if on medication, they reported that they were stabilized on a current dose ($n = 48$; 30.1%) by client self-report.[1] At least one other major trauma victimization, apart from the index rape, was reported by 86% of those in the sample (mean = 6.4, $SD = 4.9$). On average, 1.4 of those other trauma victimizations were classified as sexual in nature and 5.0 were nonsexual (e.g., physical assault). Exclusion criteria included current psychosis, substance dependence, illiteracy, instability of psychiatric medication dosages, and acute risk of harm to one's self or others.

Participants were randomized to PE, CPT, or a waitlist for 6 weeks. Following the wait, the delayed treatment participants were randomly assigned to either CPT or PE. Further details on trial methodology and patient sample can be found in the primary outcome publication (Resick et al., 2002).

2.2 | Treatments

2.2.1 | Cognitive processing therapy

CPT is a primarily cognitive therapy. The treatment is delivered over 12 sessions for 50–60 min each and, for the sample used in the current study, it followed the original manual as written by Resick and Schnicke (1993). CPT includes psychoeducation, an impact statement, training in identifying thoughts and emotions, two assigned written accounts of the traumatic event that are reviewed in the subsequent session and then read daily between sessions, and cognitive restructuring with regard to beliefs about the meaning of the event and the implications of the trauma for one's life. The second half of the treatment focuses on disruptions in beliefs about safety, trust, power/control, esteem, and intimacy, which may have resulted from the traumatic exposure.

2.2.2 | Prolonged exposure

PE is based upon emotional processing theory, which suggests that PTSD symptomatology is maintained primarily by avoidance of trauma cues, and by negative cognitions about the self, the world, and one's reaction to the trauma. The nine-session PE protocol includes four components: education and explanation of rationale for PE, breathing retraining, behavioral exposures, and imaginal exposures (Foa et al., 2007). The majority of the sessions (sessions 3–9) involve imaginal exposure of the traumatic event for 45–60 min of the 90-min session.

2.3 | Measures

Twenty potential moderator variables were selected for this exploratory analysis, representing participant demographics, interpersonal and crime history, PTSD symptomatology, comorbid symptomatology (e.g., depression symptoms), and cognitive-personality features of the patient (e.g., trauma cognitions). Counting subscores of measures, there were over 50 baseline variables we could have potentially chosen. We decided to limit ourselves to 20 variables to balance Type-I and Type-II error in this exploratory moderator analysis. First, we wanted to include variables that may be particularly relevant to the procedures of a given treatment, such as trauma-related cognitions in CPT. Moreover, in light of concerns from some clinicians that trauma-focused treatments may be more difficult to tolerate for repeatedly traumatized individuals (van Minnen et al., 2010), we included number of additional sex crime exposures and measures assessing abuse in both one's current romantic relationship and during childhood.[2] Second, depression (Markowitz et al., 2015), anger (from

TABLE 1 Baseline variables selected as potential moderators

Demographics
Age
Race (Caucasian/Minority)
Years of education
Quick test—Estimated IQ (Ammons & Ammons, 1962)
Years since index rape
Interpersonal history
Assessing Environments-III, Physical Punishment Scale—Severity of Childhood Physical Abuse (Rowan, Foy, Rodriguez, & Ryan, 1994)
Sexual Abuse Exposure Questionnaire—Severity of Childhood Sexual Abuse (Rowan et al., 1994)
Conflict Tactics Scale—Abuse by Current Partner (Straus, Hamby, Boney-McCoy, & Sugarman, 1996)
Total sex crime exposures
Psychiatric symptoms
Clinician-Administered PTSD Scale Total Score (Blake et al., 1995)
Posttraumatic Symptom Scale (PSS) (Foa, Riggs, Dancu, & Rothbaum, 1993)—Avoidant symptoms
PSS—Arousal symptoms
PSS—Re-experiencing symptoms
BDI-II Depression (Steer, Ball, Ranieri, & Beck, 1999)
Dissociative Experiences Scale (Carlson & Putnam, 1993)
Cognitive features
Beck Hopelessness Scale (Beck, Weissman, Lester, & Trexler, 1974)
State-Trait Anger Expression Inventory (Trait) (Spielberger, Sydeman, Owen, & Marsh, 1999)
Trauma-Related Guilt Inventory (TRGI)—Total Trauma Cognitions (Kubany et al., 1996)

this trial dataset; Rizvi et al., 2009), and race (Lester, Artz, Resick, & Yinong, 2010) have been identified in previous PTSD trials as being relevant for predicting dropout rates in trauma-focused treatments. Finally, many of the variables were chosen because they are relatively easy to collect in practice (e.g., age; time since index trauma) or are routinely collected in the process of diagnosing PTSD (e.g., elevations in particular PTSD symptom clusters), because an eventual goal would be to deploy treatment selection strategies in clinical practice

Selected variables are described in Table 1. All observer-based measures were obtained by trained study personnel who were masked to treatment condition, and inter-rater reliability was established for all measures (Resick et al., 2002).

Because 11 patients dropped out during the waiting list period, prior to being informed of their assignment to treatment, their data could not inform a model of differential dropout, leaving 160 patients from the intention-to-treat sample who were informed of their treatment randomization.[3]

2.4 | Analyses

2.4.1 | Missing baseline data

Missing values ranged from 0 to 11 (trauma cognitions), with the median level of missingness among measures with missing values being 3. Explorations of missing data patterns relationships between degree of missingness and the criterion of treatment dropout. Therefore, a single-dataset random forest imputation strategy was undertaken (Stekhoven & Bühlmann, 2012), using all available pretreatment and outcome data.

2.4.2 | Variable selection

All analyses were conducted in the *R* statistical computing language. Initial moderator variable selection was performed using a bootstrapped, random forest variant of model-based recursive partitioning (MoB) (Garge, Bobashev, & Eggleston, 2013). MoB takes a basic parametric model, and attempts to detect variables along which splits into two subgroups lead to significantly different model behavior on either side of the split. It has been applied previously in moderator investigations in psychiatry (Driessen et al., 2016; Zilcha-Mano et al., 2016). The extension of this model employs MoB within bootstrapped resamplings of the dataset. For each bootstrap, the resulting tree is tested on the out-of-bag sample, which is held out of a given tree construction. A variable's ability to predict out of bag is compared to the ability of randomly permuted data to make the same prediction. Variables with a prediction statistic higher than that of the absolute value of the moderator with the most negative predictive value (i.e., in which the permuted data are superior to the real data) are retained (Strobl, Boulesteix, Kneib, Augustin, & Zeileis, 2008). Twenty thousand bootstrapped replicates were run (minimum 10 patients at $P < .10$ per split; random 10 variables per node).

The variables that emerged from the MoB procedure were placed into a bootstrapped variant of an Akaike information criterion-based backward selection model (Austin & Tu, 2004). Terms representing interactions with treatment condition ("prescriptive" variables) as well as terms representing main effects of individual variables that predicted dropout regardless of condition ("prognostic" variables) that were retained in at least 60% of the bootstrapped replicates (k = 20,000) were included in the final model, per Austin and Tu's (2004) recommendations. Combined, the two-step bootstrap filtering partially protects against overfitting by ensuring that any given variable is predictive across bootstrapped replications of the data structure, and predicts significantly better than the noise of the dataset itself (i.e., via permutation test) (Chekroud et al., 2016; Davidson & Hinkley, 1997; Koutsouleris et al., 2016). Any variable that survived the two-step variable selection process was included in the final model.

2.4.3 | Treatment selection model

Logistic regression models predicting treatment completion were used to ascertain the statistical significance of each of the selected moderator variables individually, when each was included in a model that also contained treatment condition and the interaction. An omnibus logistic model was also fit in which all moderator variables, and their interactions with treatment, were simultaneously included.

To estimate the degree to which assigning patients to a specific treatment on the basis of the outputs of the logistic model would yield superior treatment completion rates, the Personalized Advantage Index (PAI) approach was implemented. In this approach, multiple

predictors and moderators are combined in a statistical model that is then used to predict for each patient, which treatment they would be more likely to complete. An index that reflects the magnitude of the predicted advantage is also given by the method (DeRubeis et al., 2014). A stratified fivefold cross-validation scheme was used to estimate the predictive value of the final logistic model indicated by the variable selection process (Kohavi, 1995). For any given patient, estimates of the probability of treatment completion for each treatment were output from a model that used data from the fourfolds of the fivefold model in which their data were *not* included. The difference between the two model-predicted probabilities of completing each treatment was calculated, resulting in a signed (positive or negative) score, indicating which of the treatments was determined to be "optimal" for that patient (i.e., the treatment in which they were predicted to be less likely to drop out).

To test the validity and potential utility of the set of predictions, logistic regressions were performed to compare the rates of treatment completion between patients who had been randomized to the treatment predicted by the PAI model to be their "optimal" treatment in terms of retention, as compared with patients randomized to the treatment predicted to be their "nonoptimal" treatment. Following DeRubeis et al. (2014), and on the understanding that PAI values close to zero are weak indicators of the relative advantage of one treatment over another, we also compared the optimal versus nonoptimal dropout rates in the subset of patients whose PAIs were among the highest 60% in absolute value.

3 | RESULTS

3.1 | Dropout rates

The average baseline data for PE and CPT patients can be found in Table 2. There were no significant between conditions in baseline values for any moderator variables.

Of 30.6% of patients dropped out of the trial after randomization to one of the active treatment conditions, including those who did not attend any sessions (30.9% in PE; 30.4% in CPT; $P = .947$). Of patients in the minimal attention condition, 23.4% dropped out prior to being re-randomized to an active treatment condition. Their data were not used in these analyses.

3.2 | Variable selection for dropout model

Four moderator variables (prescriptive variables: childhood physical abuse, current relationship abuse, trait anger, and race) were retained across both sets of bootstrap methods (see supplement for model selection output). Considered in separate logistic regressions, each moderator variable was statistically significant in predicting treatment completion in an interaction with treatment (*P*s ranging from .018 to .001). Two variables that predicted dropout regardless of condition (prognostic variables: years of education and estimated IQ score) were also retained in the final model.

TABLE 2 Demographic and clinical characteristics of patient sample

	Cognitive processing therapy ($n = 79$)	Prolonged exposure ($n = 81$)
Age	31.4 (9.6)	32.5 (10.3)
Race (% Caucasian)	58 (73.4)	57 (70.4)
Years of education	14.6 (2.3)	14.2 (2.3)
Estimated IQ	98.1 (8.5)	98.6 (9.9)
Years since index rape	8.6 (8.9)	8.4 (7.9)
Total sex crime exposures	2.4 (2.6)	2.5 (3.3)
CAPS	75.0 (18.2)	74.6 (19.2)
PSS—Avoidance	12.8 (4.6)	12.5 (4.3)
PSS—Re-experiencing	6.7 (3.1)	6.7 (3.2)
PSS—Arousal	10.1 (2.8)	10.1 (3.4)
BDI-II	23.5 (10.2)	23.4 (8.3)
BHS	9.6 (5.5)	9.7 (5.4)
DES	19.9 (13.1)	23.5 (16.6)
TRGI—Total*	1.8 (0.8)	2.1 (0.9)
STAXI—Trait Anger	20.7 (5.8)	21.5 (5.7)
Childhood sexual abuse	1.1 (1.7)	1.4 (1.9)
AE-III—Childhood physical abuse*	3.6 (2.0)	4.1 (2.5)
CTS—current partner	0.9 (3.6)	0.8 (2.3)

AE-III = Assessing Experiences III; BDI-II = Beck Depression Inventory; BHS = Beck Hopelessness Scale; CAPS = Clinician-Administered PTSD Scale; CTS = Conflict-Tactics Scale; DES = Dissociative Experiences Scale; PSS = Posttraumatic Symptom Scale; STAXI = State-Trait Anger Expression Inventory; TRGI = Trauma-Related Guilt Inventory.
*$P < .10$.

3.3 | Final treatment selection model

In the combined model that included the all moderator variables interacting with treatment, their main effects, and the prognostic variables, two moderator variables remained statistically significant: intimate partner abuse, and race.

Patients were more likely to complete CPT, relative to PE, the higher their scores on the measure of current relationship abuse (log odds = −1.08 [95% CI: −2.20 to −0.13], $SE = 0.52$, $P = .037$) (see Fig. 1). Within CPT, higher scores on the relationship abuse measure were not significantly related to retention in treatment (log odds = 0.36 [95% CI: −0.20 to 0.99], $SE = 0.29$, $P = .220$). In PE there was a nonsignificant trend toward current relationship abuse predicting a decreased likelihood of treatment completion (log odds = −0.72 [95% CI: 0.11–0.75], $SE = 0.40$, $P = .093$).

Racial majority/minority membership interacted with treatment to predict dropout (log odds = 1.96 [95% CI: 0.17–3.88], $SE = 0.94$, $P = .037$; see Fig. 2). Whereas there was no statistically significant relationship between race and dropout in the CPT subgroup (log odds = 0.39 [95% CI: −0.80 to 1.56], $SE = 0.60$, $P = .517$), in PE Caucasian patients were more likely to stay in treatment, relative to minority patients (log odds = 2.35 [95% CI: 0.98–3.87], $SE = 0.72$, $P = .001$).

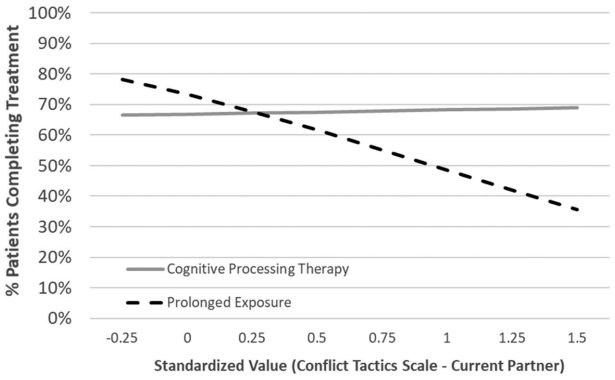

FIGURE 1 Modeled probability of patient dropout as a function of increasing reports of current relationship abuse, with other model values set to sample mean and race to Caucasian. The CTS-CURP differentially predicted dropout in CPT as compared to PE ($P = .037$)

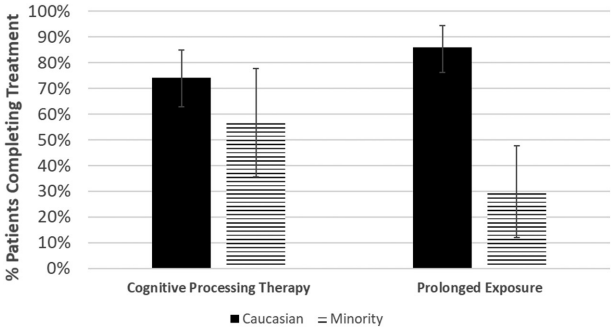

FIGURE 2 In the final model, there was a significant interaction between treatment condition and race in predicting dropout ($P = .037$). Actual dropout rates for Caucasian versus minority patients are displayed. Bars represent 95% confidence intervals

The final two moderator variables were retained in the final model due to their repeated inclusion by the bootstrapped variable selection process and because they yielded nonsignificant trends ($P < .10$) in the final model. For reports of childhood physical abuse (log odds = −0.83 [95% CI: −1.80 to 0.07], $SE = 0.47$, $P = .078$) as well as reports of feelings of anger (log odds = −0.90 [95% CI: −1.94 to 0.07], $SE = 0.51$, $P = .075$), increasing levels predicted dropout within PE but not CPT.

Patients who had a higher estimated IQ based on the quick test (Ammons & Ammons, 1962) were significantly more likely to complete treatment (log odds = 0.60 [95% CI: 0.10–1.13], $SE = 0.26$, $P = .021$), irrespective of treatment received. Individuals who had completed more years of education were more likely to complete treatment, at the level of a nonsignificant trend (log odds = 0.45 [95% CI: −0.05 to 0.98], $SE = 0.26$, $P = .091$).

3.4 | Dropout PAI

For each patient, the one model that did not include that patient's data (of the five cross-validation prediction models) was used to generate the predictions of that patient's likelihood of dropping out in each treatment. The signed difference between the two predictions

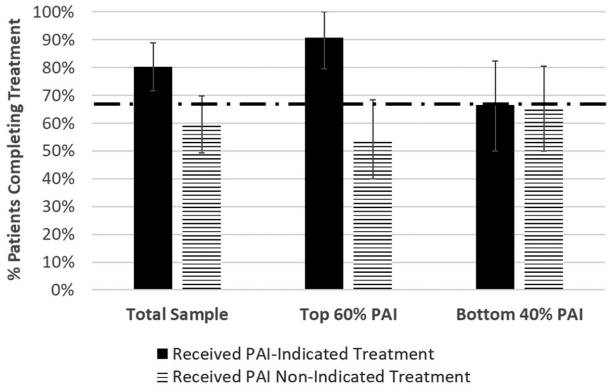

FIGURE 3 Patients who received their indicated treatment were significantly less likely to have dropped out of treatment than those who did not ($P = .005$). By convention (DeRubeis et al., 2014), we additionally divided the sample into patients estimated as having a relatively stronger need for a particular treatment (top 60% PAI magnitude) as compared to those with a relatively weaker estimated need for a particular treatment (bottom 40% PAI magnitude). The dashed and dotted line indicates the average completion rate in the total sample

indicated which was their PAI-indicated treatment vis a vis completion of treatment.

A total of 76 patients (47.5%) were randomized to their model-indicated treatment. PE was the model-indicated treatment for a higher proportion of patients (105, 65.6% vs. 55, 34.4% for CPT). Although the average predicted advantage of receiving the PAI-indicated treatment was not significantly different for patients assigned to PE as compared to CPT (mean PAI score 1.8 vs. 2.1, ns), CPT was associated with a wider range of predicted advantages (standard deviation 1.1 vs. 2.1, $P < .001$), with more high magnitude PAI scores associated with model-indicated assignment to CPT.

Of the 76 patients assigned to their PAI-indicated treatment, 15 (19.7%) dropped out, a rate that differed from the 40.5% rate (34 of 84 patients) who were not assigned to their PAI-indicated treatment (log odds = 1.02 [95% CI: 0.32–1.75], $z = 2.80$, $P = .005$; relative risk of dropout = 0.49 [95% CI: 0.29–0.82], number needed to treat = 4.8 [95% CI: 2.9–14.7]). Figure 3 compares the observed dropout rates for those randomized to their PAI-indicated versus nonindicated treatment. Also displayed are the rates observed among those with the highest 60% (absolute value) on the PAI.

4 | DISCUSSION

In contrast to previous studies in which the relationship between individual patient characteristics and dropout have been examined separately, this study employed a novel methodology to identify each individual study participant's optimal treatment, based on their values on a set of characteristics. Employing machine-learning and bootstrapping methodologies, we detected several robust moderators of dropout between PE and CPTs, two first-line treatments for PTSD. In the context of a randomized controlled trial of PE and CPT for patients with rape-related PTSD, dropout rates were nearly identical. However,

when we constructed and applied a cross-validated multivariable moderation model, it yielded predictions that distinguished which of the two treatments a given patient was most likely to complete, at a level well above chance. These findings suggest that the application of such modeling approaches may, in the future, be used successfully to identify an optimal treatment for each patient and thus decrease the likelihood that patients will terminate treatment before they are able to derive benefit.

Four moderators of dropout between CPT and PE were detected in this study, each of which was statistically significant when considered on its own, and two of which were significant in an omnibus model with all moderators included (race and relationship abuse as measured by the CTS). Although the nature of a moderator can suggest particular mechanisms for differential treatment tolerance, we cannot be certain from these data alone why these moderators had their observed influences. For example, both childhood physical abuse and current relationship abuse predicted dropout more in PE as compared to CPT. A common mechanism for these two variables driving dropout in PE could be that memories of past or ongoing trauma may become activated, perhaps especially during imaginal exposures for the index rape. These patients may find that it is difficult to tolerate exposure exercises (cf. Cloitre et al., 2010) or individuals with these experiences may be more likely to continue to avoid in an effort to cope with distressing memories and feelings. The moderating role of race to predict PE dropout could be due to any number of factors (Cloitre, 2015), including that cultural differences may influence the perceived credibility of exposure-focused treatments or of their delivery by exclusively (in this trial) Caucasian clinicians. It also may be that minority stress or the covariation of race with other sociodemographic variables accounted for this relationship. As relatively little systematic research exists on why patients drop out of trauma-focused treatments for PTSD, or how these reasons can be addressed, our findings may point toward fruitful avenues for such research.

The ability to match patients with treatments that may be optimal in terms of engagement may reduce therapist concerns about potentially poor fits of evidence-based treatments for PTSD, as well as concerns that patients may not be able to tolerate certain treatments (Osei-Bonsu et al., 2017; Zubkoff, Carpenter-Song, Shiner, Ronconi, & Watts, 2016). If these findings are replicated in future studies, the potential reach and effectiveness of trauma-focused PTSD treatments could be significantly increased. Such models could inform decision-support tools, similar to those used in other areas of medicine (Goldstein et al., 2002), that would augment clinical decision making, and could be used in conjunction with other efforts to increase patient-centered, shared decisions about appropriate PTSD treatments (Mott, Stanley, Street, Grady, & Teng, 2014).

4.1 | Limitations

Several limitations concerning the sample and methodology of this study must be recognized. Sexual assault is an especially common primary trauma among PTSD patients (Breslau et al., 1998), but it is not clear whether patterns observed in this population will generalize to other primary trauma populations, such as combat-related PTSD. Although many variables relevant to PTSD were included in this study, several potentially important ones were not, including biological markers and patient preference (Feeny, Zoellner, Mavissakalian, & Roy-Byrne, 2009). Inclusion of a broader range of predictors would be expected to enhance the ability of a model to make these predictions, although the use of self-reported measures may make deployment of treatment selection in routine clinical practice more feasible.

In particular, all selected variables predicted more dropout in PE rather than CPT, which may indicate that we did not include variables important for predicting dropout in CPT specifically. Notably, three of the four selected variables (all but anger) had skewed distributions in our sample—such that the modal patient was not African American, was not exposed to childhood physical abuse, and was not experiencing current relationship abuse. This may have led to the unbalanced rate of PAI recommendations suggesting PE over CPT, reflecting an excess of small PE predictions near the indifference point who did not evidence any benefit from receiving their optimal treatment (see Fig. 3, bottom 40% PAI).

It should also be noted that some of the patients classified as dropouts in this study may have benefitted from their treatment before they dropped out (Szafranski, Smith, Gros, & Resick, 2017). If such patients were counted as completers rather than dropouts, a somewhat different pattern of findings might have emerged (Szafranski et al., 2017).

The selection of moderator variables was implemented in the same data-set as model estimations, which could lead to model overfitting and inflated relationships (Fiedler, 2011). However, unlike nearly all moderator investigations in the psychiatric literature, we used a two-step bootstrapped variable selection process incorporating out-of-bag predictions and permutation tests to select variables that are more likely to generalize to a different sample. Moreover, to limit bias in the model coefficients, we estimated the predictive ability of our selected variables using a fivefold cross-validation. When proper statistical controls are applied, even complex clinical interactions can replicate (Chekroud et al., 2016; Koutsouleris et al., 2016; Lorenzo-Luaces et al., 2017). Nevertheless, employing the obtained model in a validation sample is necessary to test to what extent individual variables, as well as the model, generalize outside of the present sample (Hastie, Tibshirani, & Friedman, 2009). At this time, there are no other data from trials comparing CPT and PE for sexual trauma PTSD on which the present model could be tested. However, a large-scale trial comparing CPT and PE for PTSD among veterans (n = 900) is currently underway, which may provide a powerful opportunity to refine, reconstruct, and test the present treatment selection model (Schnurr et al., 2015).

Finally, this study investigated only two of the commonly used and disseminated treatments for PTSD. More recent advances in CPT include making the written account of the trauma an optional element of CPT (Resick, Monson, & Chard, 2017), although in routine practice, many clinicians received training, and are likely implementing, the version of CPT that includes the written account (Chard, Ricksecker, Healy, Karlin, & Resick, 2012). One study suggests that dropout may be lower when the account is not included (Resick et al., 2008). Thus,

future research should include adequately powered investigation of methods to match patients to treatments that include explicit recounting of traumatic events versus those that do not.

4.1.1 | Future directions

The present findings suggest that patient characteristics measured prior to treatment may be leveraged to make clinically useful predictions as to which PTSD treatment a patient is most likely to tolerate and complete, even though most such treatments have similar retention rates on average (Imel et al., 2013). Although the generalizability of the moderators we identified should be explored in future trials, these moderators may nevertheless provide preliminary guidance for clinicians when planning to conduct a more exposure-focused (i.e., PE) versus cognitively focused (i.e., CPT) treatment with rape trauma PTSD patients. Understanding the individual risk factors for dropout unique to a treatment approach—for example, past or ongoing trauma for PE—might also alert clinicians to address proactively the potential reasons for dropout deriving from those risk factors, such as adding affective regulation/interpersonal skills training if a patient is too activated by exposures (Cloitre et al., 2010).

If patients are strongly dissatisfied with or genuinely dissuaded by an initial treatment, they may be demoralized and less likely to attempt another treatment (Markowitz & Milrod, 2015). On the other hand, studies with patients who engaged in and completed trauma-focused treatments indicate that they perceive them to be "worth it in the end" (Hundt, Barrera, Arney, & Stanley, 2017). Thus, identifying ways to increase treatment retention can increase confidence of patients and providers as healthcare systems implement trauma-focused treatments.

Future clinical trials comparing treatments for PTSD should be structured to allow for the generation and testing of treatment selection algorithms. Yet, under current grant funding priorities, it is relatively uncommon for a given randomized comparison of active treatments to be conducted more than once. Large replication trials that either can test previously built treatment selection models, or that comprise sample sizes large enough to power split-sample investigations, are ultimately necessary to support the clinical impact of treatment selection models.

Nonetheless, in clinic settings providing either PE or CPT for rape trauma, it might be possible to test the individual treatment-level predictions from a treatment selection model (e.g., what is the likelihood of this patient dropping out given they are getting PE). On the one hand, this structure does not allow for the key test of whether patients randomized to their indicated treatment have better outcomes than those who are not. On the other hand, insofar as the clinicians and patients are not sorting themselves into treatments based on features in the model (e.g., race), this type of study may enable us to examine the degree to which the features of the model generalize usefully to a new clinical setting for a given treatment. Moreover, sorting biases may be partially remedied by statistical methods such as propensity score matching (Caliendo & Kopeining, 2008).

Overall, further research on moderators of dropout in PTSD will foster the further development of advanced treatment selection models that promise to enhance the clinical impact of already available evidence-based treatments for PTSD in routine clinical practice.

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ETHICAL STANDARDS

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

CONFLICT OF INTEREST

Patricia A. Resick is the developer of one of the two treatments examined in this manuscript (cognitive processing therapy) and an author of both the original therapy manual "Cognitive Processing Therapy for Rape Victims: A Treatment Manual" and the more recent "Cognitive Processing Therapy for PTSD: A Comprehensive Manual."

ENDNOTES

[1] There was no set time for medication stabilization. A psychiatrist was consulted on a case by case basis if an individual reported a recent change in medication. The stabilization period also depended on the medication and the time it took to stabilize the dosage and, where relevant, the blood level of the medication. For example, if someone's dose was recently increased, she might be delayed entry to the study for a shorter time than if she had started a new medication.

[2] Current relationship abuse was measured by the Conflict Tactics Scale (CTS; Strauss et al., 1996), a commonly used measure of abuse in intimate relationships. The CTS asks questions of the frequencies of experiences in several domains, including psychological aggression (e.g., "shouted or yelled at by my partner"), physical assault (slapped by my partner), sexual coercion (my partner insisted on sex when I did not want it [but did not use physical force]), and injuries (I have a sprain, bruise, or small cut because of a fight with my partner). The final score represents a composite of the frequency and severity of the reported experiences.

[3] Patient-reported reasons for unilateral treatment dropout were not available. However, inclusion of purportedly nontreatment-related dropouts would, if anything, *diminish* the statistical power to detect interactions between treatment condition and patient characteristics in predicting dropout, insofar as the reasons for dropout were, for some patients, unrelated to their experience with their treatment (e.g., unrelated illness or planned relocation out of the area).

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