A Randomized Controlled Trial for Identifying the Most Suitable Treatment for Depression Based on Patients' Attachment Orientation

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Objective: Many active treatments exist for major depressive disorder (MDD), but little is known about their differential effects for various subpopulations of patients to guide precision medicine. This is the first randomized controlled trial (RCT) designed to identify differential treatment effects based on patients' attachment orientations. We tested an a priori preregistered hypothesis of the potential moderating effect of patients' attachment orientation on the outcome of supportive therapy (ST) versus supportive-expressive therapy (SET). *Methods:* The RCT was conducted between 2015 and 2021. Individuals with MDD were randomly assigned to 16-week ST or SET. The predefined primary outcome measure was the Hamilton Rating Scale for Depression. Hypotheses were formulated and preregistered before data collection. *Results:* One hundred patients with MDD were enrolled, 57% women, average age 31.2 (SD = 8.25). Data were analyzed using the intention-to-treat approach. Our hypothesis that attachment anxiety is a significant moderator of treatment outcome was supported ($B = -0.09$, $p = .016$): Patients with higher levels of attachment anxiety showed greater treatment efficacy following SET than ST. Although the hypothesis regarding a potential moderating effect of avoidant attachment was not supported, sensitivity analyses revealed that individuals with disorganized attachment orientation (higher scores on both anxious and avoidant attachment) benefited more from SET than from ST ($B = -0.07$, $p = .04$). *Conclusion:* The findings support the clinical utility of patients' attachment orientation in selecting the most suitable treatment for individuals and demonstrate the methodological utility of RCTs predesigned to test theoretically based models of personalized treatment.

What is the public health significance of this article?
This study is the first randomized controlled trial (RCT) predesigned to test the differential effect of treatments based on the patients' pretreatment attachment orientations. The findings demonstrate the ability of attachment orientation to serve as an empirically informed tool for a personalized match between individuals and their most effective treatment.

Keywords: supportive-expressive treatment, short-term psychodynamic treatment, supportive treatment, attachment orientation

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Major depressive disorder (MDD) is the leading cause of disability worldwide, a main contributor to the overall global burden of disease (Friedrich, 2017), and a highly heterogeneous disorder (Goldberg, 2011). Hundreds of active psychosocial treatments for MDD are available, such as cognitive-behavioral therapy (CBT), supportive-expressive therapy (SET), and supportive therapies (ST) (DeRubeis & Strunk, 2017). These treatments differ in their underlying mechanisms, theorized to drive therapeutic change (Crits-Christoph & Connolly Gibbons, 2021) but do not seem to differ in their efficacy of about 50% response rate for the "average patient" (Cuijpers, 2017). Nevertheless, subpopulations of patients are theorized to show great ability to benefit from a given treatment, whereas others are less able to do so and may even deteriorate (DeRubeis

et al., 2014; Snow, 1991). Thus, dozens of studies have searched for moderators of the differential effect of various treatments, such as symptom severity (e.g., Zandberg et al., 2016), affective lability (e.g., Accurso et al., 2016), self-regulatory deficits (e.g., Eddington et al., 2015), interpersonal problems (e.g., Gomez Penedo et al., 2017), and personality disorders (e.g., Barber & Muenz, 1996; for a review, see Bohart & Wade, 2013; Clarkin & Levy, 2004). Despite great advances in the study of moderators of treatment response, currently the vast majority of studies are based on post hoc analyses, rather than a priori preregistered randomized controlled trials (RCTs) designed to test moderation effects. To meet this need, there is a call for RCTs predesigned to test the differential effects of treatments conceptualized as targeting distinct mechanisms of change for distinct subpopulations of patients to advance toward precision medicine (National Institute of Mental Health, 2015).

The interpersonal characteristics of patients, especially their attachment orientations, are among the pretreatment moderators receiving scientific attention (Levy et al., 2018). In the past 40 years, attachment theory has emerged as one of the most important empirically grounded frameworks for understanding individual differences in interpersonal characteristics (Mikulincer & Shaver, 2007). Individual differences in attachment system activation are commonly conceptualized on two orthogonal dimensions of attachment orientation: anxiety and avoidance. Individuals with high levels of attachment anxiety tend to show hyperactivation of the attachment system, as manifested in exaggeration of proximity-seeking tendencies. By contrast, individuals with high levels of attachment avoidance tend to show deactivation of the attachment system, as manifested in inhibition of proximity-seeking tendencies. Individuals showing high levels of both attachment anxiety and attachment avoidance, referred to as having disorganized attachment, were found to be associated with increased psychopathology and poor prognosis (Lyons-Ruth & Jacobvitz, 1999). Theories and clinical writing suggest a promising role for patients' attachment orientation in determining the differential effect of various treatments (Bowlby, 1988; Daly & Mallinckrodt, 2009). Although attachment orientation appears to predict treatment outcome (Levy et al., 2018), the literature on attachment as a moderator is sporadic and mixed. Some studies have shown that both attachment dimensions may moderate treatment outcome (Newman et al., 2015), others showed that only attachment anxiety (Tasca et al., 2006) or only attachment avoidance (McBride et al., 2006) is a significant moderator, and others yet found no moderating effect of patients' attachment orientation (Bernecker et al., 2016; Gois et al., 2014; Tasca et al., 2013).

According to attachment theory, patients may benefit most from a treatment condition that is opposite (contradictory) to their characteristic level of activation of the attachment system (Mallinckrodt, 2010). Thus, patients with higher levels of attachment anxiety are theorized to benefit most from treatments where the main mechanism of change challenges their maladaptive interpersonal behavior of exaggerated proximity seeking (Daly & Mallinckrodt, 2009), such as SET (Luborsky et al., 1995). By contrast, patients with higher levels of attachment avoidance are theorized to benefit most from treatments where the main mechanism of change creates emotional closeness in the therapeutic alliance (Daly & Mallinckrodt, 2009), such as ST

(Leibovich et al., 2019). Although some empirical findings support the contradictory hypothesis of opposites as an index for determining who may benefit most from each treatment (Daly & Mallinckrodt, 2009; O'Connor et al., 2019), all are correlational in nature and cannot serve as evidence-based tools to hasten progress toward precision medicine.

This is the first RCT designed a priori to investigate the moderating effect of patients' attachment orientations on treatment outcome. Its primary aim is to examine prospectively the differential efficacy of ST versus SET for patients with different attachment orientations. Our primary hypothesis is that attachment orientation has a significant moderating effect on treatment condition in predicting outcome. Our preregistered hypotheses were that (a) patients with higher levels of attachment anxiety benefit most from SET, whereas (b) patients with higher levels of attachment avoidance benefit most from ST. Given the accumulating literature highlighting the unique characteristics of disorganized attachment orientation (higher levels on both attachment anxiety and avoidance), we also (c) explored the potential moderating effect of the interaction between attachment anxiety and avoidance. Based on findings documenting greater psychopathology and poorer prognosis for individuals with disorganized attachment orientation (Lyons-Ruth & Jacobvitz, 1999; Reis & Grenyer, 2004; Shorey & Snyder, 2006), as well as conceptual models and empirical findings suggesting alternation between deactivation and hyperactivation of the attachment system in this subpopulation (Mikulincer & Shaver, 2007), it may be expected that these patients would benefit most from SET, which includes both supportive and expressive components. Because of the limited sample size, we regarded this third theory-driven hypothesis as exploratory.

Method

Study Design

Patients were randomly assigned to SET versus ST based on the minimization algorithm (Pocock & Simon, 1975). Factors for balancing were age (≥ 30 vs. < 30), gender (male vs. female), family status (married/cohabiting vs. not married/cohabiting), baseline 17-item Hamilton Rating Scale for Depression (HRSD; Hamilton, 1967; ≥ 20 vs. < 20), baseline attachment avoidance (≥ 3.5 vs. < 3.5 on the avoidance subscale in the Experience in Close Relationships [ECR]; Brennan et al., 1998), baseline attachment anxiety (≥ 3.5 vs. < 3.5 on the anxiety subscale in the ECR), and personality disorders (present vs. absent). Assignment to treatment arm was conducted by an outside institution, not involved in the study. Treatments were face to face until the start of the pandemic, which resulted in 13 patients being treated remotely (Table 1).

Participants

Inclusion Criteria

(a) MDD diagnostic criteria using structured clinical interviews for *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.; *DSM-V*), with scores above 14 on the 17-item HRSD (Hamilton, 1967) at two evaluations, 1 week apart, and current MDD based on the Mini-International Neuropsychiatric Interview (MINI; Sheehan et al., 1998); (b) if on medication, patients' dosage had to be stable

Table 1

Demographic and Clinical Characteristics as a Function of Treatment Condition

Variable	ST (n = 50)	SET (n = 50)	Total (N = 100)	Statistical test	p value
Demographics					
Age, years, M (SD)	31.02 (6.9)	31.5 (9.6)	31.2 (8.25)	$t(98) = -.31$	0.75
Education, years, M (SD)	14.5 (1.9)	13.9 (2.1)	14.2 (2)	$t(98) = 1.26$	0.21
Female	58 (29)	56 (28)	57 (57)	$\chi^2(1) = .41$	1
Income > average	24 (12)	26 (13)	25 (25)	$\chi^2(1) = .97$	.6
Married/cohabitating	16 (8)	16 (8)	16 (16)	$\chi^2(1) = 1.2$	1.2
Employed	76 (38)	60 (30)	68 (68)	$\chi^2(1) = 4.23$	0.050
Religion, Jewish	80 (40)	80 (40)	80 (80)	$\chi^2(1) = 0$	1
Clinical features					
Current medication, yes	14 (7)	14 (7)	14 (14)	$\chi^2(1) = 0$	1
Previous medication, yes	24 (12)	24 (12)	24 (24)	$\chi^2(1) = 0$	1
Previous psychotherapy, yes	52 (26)	40 (20)	46 (46)	$\chi^2(1) = 1.7$	0.23
Comorbidities					
Any disorder	72 (36)	70 (35)	71 (71)	$\chi^2(1) = .19$	.82
Any anxiety disorder	70 (35)	72 (36)	71 (71)	$\chi^2(1) = .05$	1
Any personality disorder	76 (38)	72 (36)	74 (74)	$\chi^2(1) = .2$	.82
Drop-outs	10 (5)	4 (2)	7 (7)	$\chi^2(1) = 1.38$	0.43
Remote treatment, yes	14 (7)	12 (6)	13 (13)	$\chi^2(1) = .08$	1

Note. Values shown as % (n). ST = supportive treatment; SET = supportive-expressive treatment.

for at least 3 months before the start of the study, and patients were asked to maintain stable dosage for the duration of treatment; (c) age between 18 and 60 years; (d) Hebrew language fluency; (e) written informed consent.

Exclusion Criteria

(a) Current high risk of suicide or self-harm (HRSD suicide item >2); (b) current substance abuse disorder; (c) current or past schizophrenia, psychosis, bipolar disorder, or severe eating disorder, requiring medical monitoring; (d) history of organic mental disease; (e) currently in psychotherapy.

Treatments

Patients received 16 50-min sessions of SET (Luborsky et al., 1995), a time-limited psychodynamic therapy adapted for depression. They were randomized to either an SET-focused condition (including the use of expressive techniques, such as interpretation, confrontation, clarification) or an ST-focused condition (including the use of supportive techniques, such as affirmation and empathic validation). For SET, we used the Luborsky et al. (1995) manualized treatment. The supportive condition included all supportive techniques detailed in the manual used by Luborsky et al. (1995), but forbade the use of expressive techniques (Leibovich et al., 2018). The trial protocol (Zilcha-Mano et al., 2018) provides further details about the trial. All procedures were approved by the institutional review board.

Therapists

Therapists acted as their own controls, providing treatment in both conditions. Eight therapists with at least 5 years of expertise in psychodynamic treatment attended a 20-hr training workshop in supportive and expressive techniques. Therapists completed treatment of two pilot cases, one of each treatment condition and demonstrated acceptable treatment adherence before the trial phase.

During the pilot phase and the trial, each therapist received weekly group supervision from two supervisors as well as individual supervision. In all supervisions, extensive use was made of videotaped sessions for feedback. The supervisors were licensed clinical psychologists, with extensive supervision experience. They received supervision concerning the supervision process from an international expert in SET, with more than 20 years of experience in psychodynamic treatment for depression and more than 15 years of experience in SET in RCTs. Two of the therapists did not continue after the training phase (one being offered a full-time position elsewhere and the other demonstrating low levels of adherence).

Six therapists participated in the study. Their mean age was 42.33 (SD = 4.41), and five were female. All were married or cohabitating. Their mean years of experience was 14.41 (SD = 5.42). All therapists had psychodynamic training, two also had CBT training, and one also had biofeedback training. The mean number of patients each therapist treated was 16.66 (SD = 8.45), range 5–31.

Fidelity Check

We used the Penn Adherence–Competence Scale (PACS; Barber & Critis-Christoph, 1996) to assess therapists' adherence and competence. The PACS includes three subscales: general therapeutic behaviors (ICC = .71 for amount and ICC = .76 for quality), the supportive component (ICC = .86 for amount and ICC = .83 for quality), and the expressive component (ICC = .91 for amount and ICC = .83 for quality). Coders were four trained PhDs in clinical psychology or PhD/MA students in clinical psychology. The number of coders per session varied between two and four. For each patient, we randomly selected between one and three sessions from Sessions 4, 6, or 8. These sessions were chosen based on the treatment protocol (Book, 1998; Luborsky et al., 1995). The first one was the session in which, according to the protocol, the core conflictual relationship thems (CCRT) is first presented and discussed with the patient (Session 4). The subsequent sessions were

those in which interpretative work was expected, making sure that no consecutive sessions were chosen. A total of 161 sessions were coded, 80 SET and 81 ST. Interjudge reliability was calculated as two-way mixed with absolute agreement (Shrout & Fleiss, 1979). The research team was supervised by an international expert on the use of PACS, with vast experience in using PACS in RCTs on SET.

Measures

Treatment Outcome

The primary outcome measure was the HRSD (Hamilton, 1967), a 17-item clinically administered measure assessing the severity of depression.

Psychiatric Disorders

The MINI (Sheehan et al., 1998) was administered to assess the presence and severity of depression and comorbid conditions. The Structured Interview for *DSM-IV* Personality (SIDP; Pfohl et al., 1997) was administered to assess the presence of comorbid personality disorders.

Attachment Orientation

The ECR (Brennan et al., 1998), a 36-item self-report measure of assessing the construct of adult general attachment orientation, examines two primary dimensions: avoidance (Cronbach's α = .89) and anxiety (Cronbach's α = .90).

Procedure and Randomization

Applicants were recruited by self-referral, based on advertisements. One hundred patients meeting the study criteria were randomly assigned to one of two treatment conditions, SET or ST, in the Psychotherapy Research Lab clinic. Only the therapists and their supervisors knew the patients' treatment assignment.

HRSD was administered weekly, and ECR, MINI, and SIDP (Pfohl et al., 1997) at baseline. For HRSD and MINI, evaluators were advanced undergraduate, graduate, and PhD students in clinical psychology; for the SIDP, they were graduate and PhD students in clinical psychology. All evaluators were extensively trained and were found to be reliable in the use of the HRSD, MINI, and SIDP. Throughout the trial period, the reliability of the trained evaluators was evaluated weekly. Interjudge reliability was calculated as two-way mixed with absolute agreement (Shrout & Fleiss, 1979): It was .98 for the HRSD (based on 22.6% of the interviews), .97 for the SIDP (based on 37% of the interviews), and 1.0 for the MINI (based on 14% of the interviews) (Figure 1).

Statistical Analyses

We investigated baseline differences between treatment conditions in demographic and clinical characteristics using independent samples *t*-tests for continuous variables and χ^2 tests of independence or Fisher exact tests for categorical variables, applying 10,000 Monte Carlo simulations. We used multilevel models with observations over time, nested within patients nested within therapists, for outcome and moderation analyses. To test the main hypothesis of the study, we used a model with two three-way interactions of time

by treatment condition by attachment orientation (Time × Treatment condition × Attachment anxiety, Time × Treatment condition × Attachment avoidance) along the lower level effects to predict differences in slope of change in outcome (hereinafter referred to as "treatment outcome"). We used model-based simple slope analysis to interpret the interactions, probing them at low (−1 *SD*) and high (+1 *SD*) levels of the moderators (attachment orientation) for each treatment group. As a sensitivity analysis, we tested a four-way interaction between attachment anxiety and avoidance, time and treatment condition, together with all the lower level effects, to assess the potential moderating effect of disorganized attachment (higher levels on both attachment anxiety and avoidance).

We examined categorical rates of response, remission, clinical significance, and reliable change index (RCI) using χ^2 tests for differences between treatment conditions and logistic regression for moderation effects. We conducted categorical analyses with the full intention-to-treat sample, using last observation carried forward (LOCF) for participants who failed to complete treatment. Similarly to previous psychotherapy trials for MDD (e.g., Barber et al., 2012), we used the consensus definition for response at 16 weeks as HRSD score ≤9 or 50% HRSD score reduction *and* HRSD score ≤12 (Frank et al., 1991). We also used the consensus definition of remission as no longer meeting criteria for MDD and HRSD score <8 (Frank et al., 1991). Clinical significance at 16 weeks was defined as HRSD score <14, the clinical cutoff of MDD. RCI above 1.96 was defined as reliable change (Jacobson & Truax, 1992). All analyses were conducted using R (RC Team, 2020).

Power Analyses

To calculate the required sample size for the moderation models, we used an approach based on Monte Carlo simulations, estimated using R code generated from the MLPowSim Software Package, applying 10,000 Monte Carlo simulations, which produce more accurate results for power estimates than other methods for relatively small sample sizes. The power calculation was based on effect sizes reported by Newman, Castonguay, Jacobson, and Moore (Newman et al., 2015) and on previous studies by the authors. Assuming α = 0.05 and 16 repeated measurements of the outcome variable (including missing data), the simulations indicated a required sample size of 99 participants to ensure a power of at least 0.80.

Results

Sample Characteristics

No significant differences were found between treatment conditions for any baseline demographic or clinical characteristics (Table 1).

Exploring Differences Between Treatment Conditions

Primary Outcome

Patients improved significantly over time, $B = -0.68$, $SE = 0.02$, $t_{(1649)} = -34.37$, $p < .0001$. As hypothesized, no significant differences in treatment outcome emerged between the two treatment conditions, $B = -0.04$, $SE = 0.04$, $t_{(1648)} = -1.13$, $p = .26$. Similarly, no differences were found in attrition rate (see Table 1).

Analysis of Response, Remission, Clinical Significance, and RCI

Using LOCF, no difference was found between treatments in rates of response ($\chi^2_1 = 0.01$, $p = .89$) or remission ($\chi^2_1 = 0.37$, $p = .54$). Rates of response were 68% (34/50) in ST and 72% (36/50) in SET. Rates of remission were 54% (27/50) in ST and 50% (25/50) in SET. Clinical significance and RCI also yielded similar results across treatment conditions ($\chi^2_1 = 0.01$, $p = .92$; $\chi^2_1 = 1.99$, $p = .65$, respectively). Rates of clinical significance were 78% (39/50) in ST and 82% (41/50) in SET. Rates of RCI were 96% (48/50) in SET and 90% (45/50) in ST.

Testing the Moderating Effect of Attachment Orientation on Treatment Outcome

The models that were found to have the best fit showed a linear development over time. As hypothesized, anxious attachment orientation significantly moderated the difference in treatment outcome between the two treatments ($B = -0.09$, $p = .016$; Table 2). Post hoc analysis revealed no significant differences in treatment outcome for ST ($B = -0.76$, $p < .001$) and SET ($B = -0.70$, $p < .001$) in patients with low levels of attachment anxiety (Figure 2). For patients with high levels of attachment anxiety, SET showed better treatment outcomes than ST ($B = -0.70$, $p < .001$ vs. $B = -0.56$, $p < .001$ for SET and ST, respectively, $d = .35$). Contrary to our hypothesis, avoidant attachment orientation did not moderate differences in treatment outcome between the two treatments ($B = -0.02$, $p = .57$, $d = .02$). The pattern of results remained the same when controlling for age, gender, and switching to remote treatment due to coronavirus disease (COVID-19).

Sensitivity Analysis Testing the Potential Moderating Effect of Disorganized Attachment

We tested the interaction between attachment anxiety and avoidance as a moderator of the effect of treatment condition on outcome. The interaction effect was significant ($B = -0.07$, $SE = 2.05$, $p = .04$): Patients with higher levels of attachment anxiety and avoidance improved significantly more in SET than in ST (SET: $B = -.80$ vs. ST: $B = -0.54$, $ps < .0001$, $d = .40$). The rest of the anxiety–avoidance combinations did not differ in treatment outcome (ST: $B = -0.55$ to -0.79 vs. SET: $B = -.62$ to -0.72, all $ps < .0001$) (Figure 3). Additional unregistered post hoc analyses appear in the online Supplemental Materials.

Figure 1

Flow of Participants in the Study Comparing Supportive Treatment versus Supportive-Expressive Treatment for Major Depressive Disorder
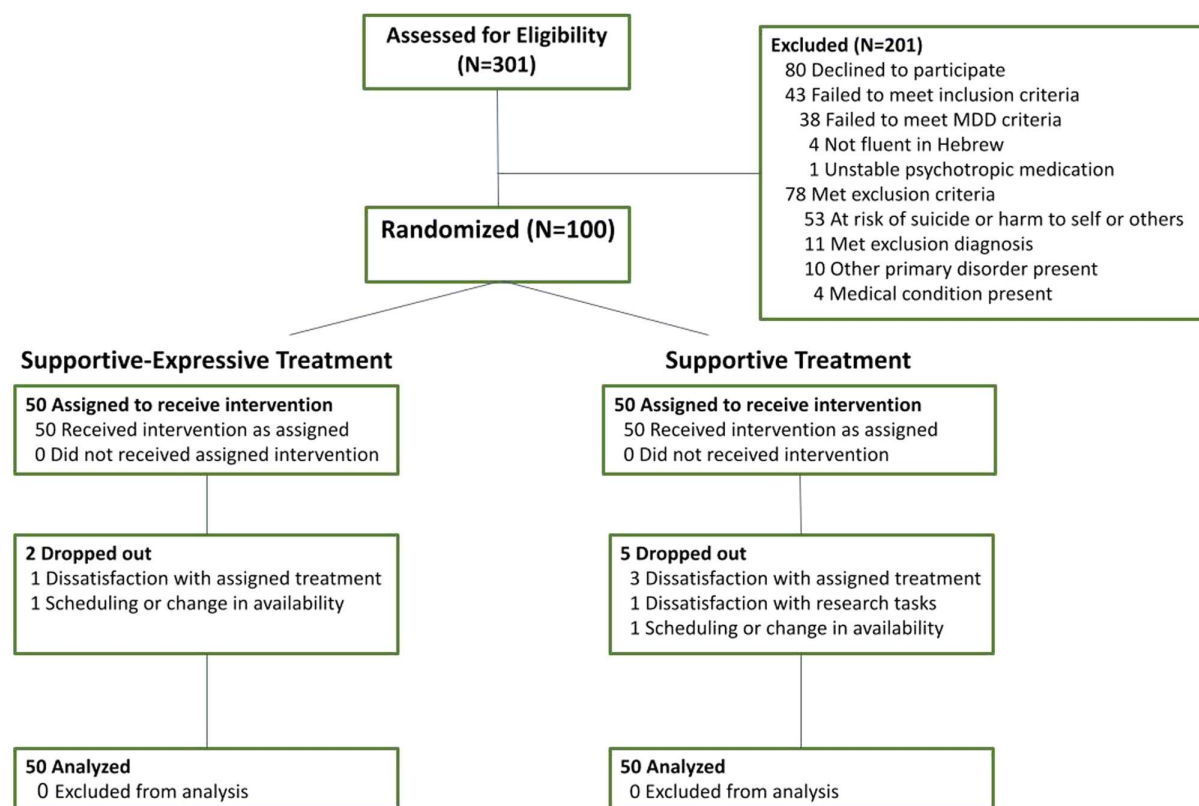
Note. All seven patients who dropped out were lost to follow-up. Otherwise, only one observation was missing, and the rest of the data were complete. The low rate of missing data is due to the fact that the assessments were obtained in person on a platform that does not allow for missing data. See the online article for the color version of this figure.

Table 2

Attachment Orientation as the Moderator of the Effect of Treatment Condition on Treatment Outcome

Predictors	Estimates	CI	t	p
(Intercept)	17.11	8.69 to 25.53	4.02	<0.001***
Time	−0.99	−1.37 to −0.61	−5.14	<0.001***
TxC	−3.45	−14.31 to 7.40	−0.63	0.53
Attachment avoidance	0.01	−1.25 to 1.26	0.01	0.993
Attachment anxiety	0.23	−1.04 to 1.50	0.36	0.719
Time × [TxC]	0.42	−0.08 to 0.92	1.66	0.096
Time × Attachment avoidance	−0.01	−0.07 to 0.05	−0.3	0.762
[TxC] × Attachment avoidance	0.14	−1.59 to 1.86	0.16	0.876
Time × Attachment anxiety	0.09	0.03 to 0.15	3.07	0.002**
[TxC] × Attachment anxiety	0.82	−0.81 to 2.45	1	0.321
Time × [TxC] × Attachment avoidance	−0.02	−0.10 to 0.06	−0.56	0.574
Time × [TxC] × Attachment anxiety	−0.09	−0.17 to −0.02	−2.42	**0.016***

Random effects	Estimates
σ^2	17.20
τ_{00} Patient:Therapist	15.48
τ_{00} Therapist	0.11
ICC	0.48
Marginal R^2/conditional R^2	0.289/0.627

Note. TxC = Treatment condition was coded for supportive-expressive treatment (SET) as the reference; ST = supportive treatment; ICC = intraclass correlation coefficient.
* $p < .05$.   ** $p < .01$.   *** $p < .001$.

Adherence

We tested the difference between the treatment conditions in quality and amount of general therapeutic, ST-focused, and SET-focused adherence using a permutation t-test with 10,000 Monte Carlo permutations. We found no differences between treatment conditions for the amount ($p = .37$) and quality ($p = .90$) of general therapeutic adherence, and the amount ($p = .88$) and quality ($p = .31$) of ST-focused adherence. As expected, SET showed higher levels of adherence than ST in SET-focused adherence ($p < .0001$) and in SET-focused amount ($p < .0001$).

Discussion

This is the first randomized trial predesigned to investigate the value of attachment orientation in determining the differential effect of treatments. The two treatments showed high levels of efficacy as evident by their levels of response, remission, and RCI (Luty et al., 2007). Rates of response were 68% in ST and 72% in SET. Consistent with the literature, no significant differences emerged between the two treatment conditions (Driessen et al., 2010). Results supported our a priori hypothesis of attachment anxiety being a significant moderator. As hypothesized, patients with higher levels of attachment anxiety showed greater treatment efficacy for SET than for ST. Although the hypothesis regarding a potential moderating effect of attachment avoidance was not supported, sensitivity analyses suggest that individuals with disorganized attachment orientation benefited more from SET than from ST. The effect sizes of the two significant effects were large relatively to previously reported moderation effects in psychotherapy (Cohen's $d = 0.35$ and 0.40).

In the absence of one treatment that can cure all patients with MDD (Cuijpers, 2017), the findings demonstrate the great potential of RCTs predesigned to test differential effects of treatments conceptualized as targeting distinct mechanisms of change. In recent years, there has been growing interest in precision medicine (Delgadillo & Lutz, 2020), with most efforts using data-driven approaches and producing important findings (Cohen & DeRubeis, 2018; Lutz et al., 2019). Complementing these data-driven approaches, theory-driven approaches show great promise, especially given the richness of theoretical conceptualization focusing on what works for whom (Barkham et al., 2021). Yet, almost no preregistered RCTs were directly designed to test what works for whom based on the mechanisms underlying different treatments. As was true from the early days of psychiatry and psychotherapy research, such questions are mostly treated today by post hoc nonpreregistered secondary analyses, potentially contributing to the replication crisis in mental health science.

RCTs predesigned to test differential effects of treatments conceptualized as targeting distinct mechanisms of change have the potential to rigorously test how the outcome of treatment can be optimized by identifying the individuals benefiting most from each treatment based on their pretreatment characteristics, in this case, attachment orientation. The findings replicate previously reported secondary analyses of efficacy-based RCTs, demonstrating a moderation effect of attachment orientation (McBride et al., 2006; Newman et al., 2015). The findings are also consistent with the conceptual models and empirical findings of individuals with disorganized attachment showing alternation between deactivation and hyperactivation of the attachment system (Mikulincer & Shaver, 2007) and demonstrate that these individuals benefit most from treatment that combines supportive and expressive components. The results contribute to the ongoing theoretical debate concerning the differential efficacy of various psychotherapeutic approaches for patients with different attachment orientations and to the progress toward personalized selection of the most effective treatment for

Figure 2

Attachment Anxiety as a Moderator of the Effect of Treatment Condition on Treatment Outcome
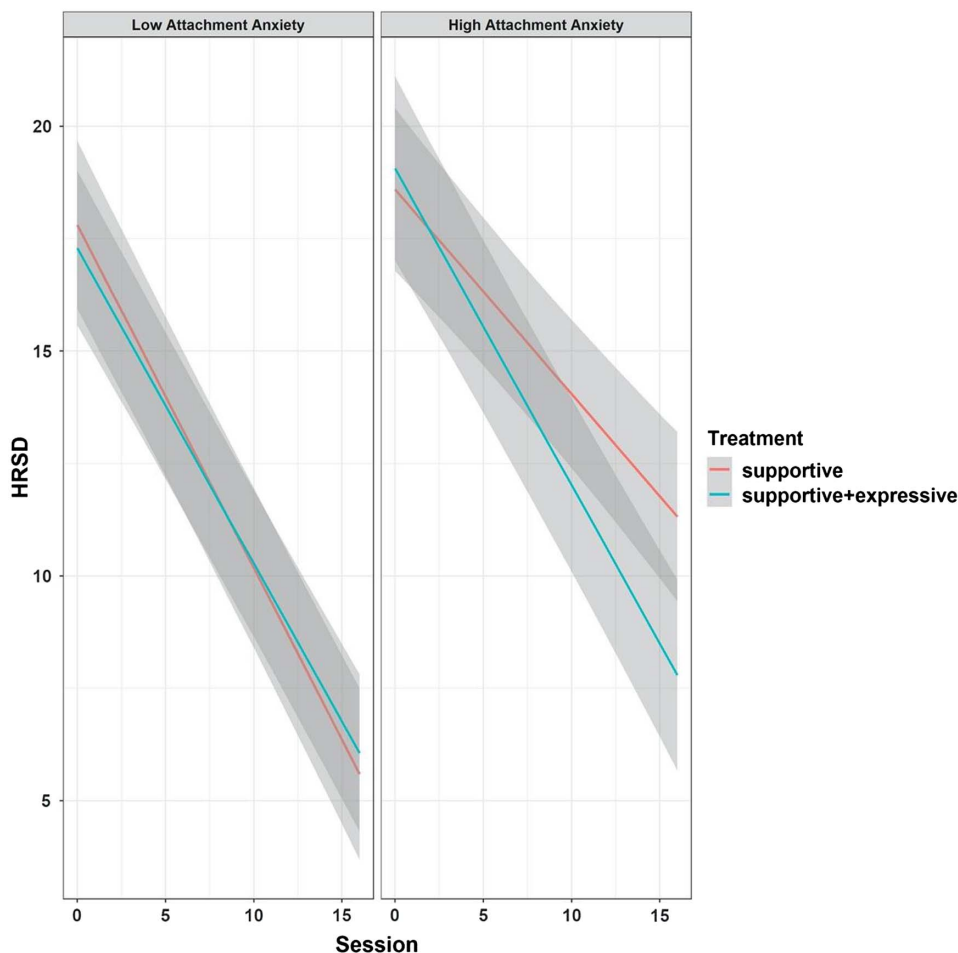
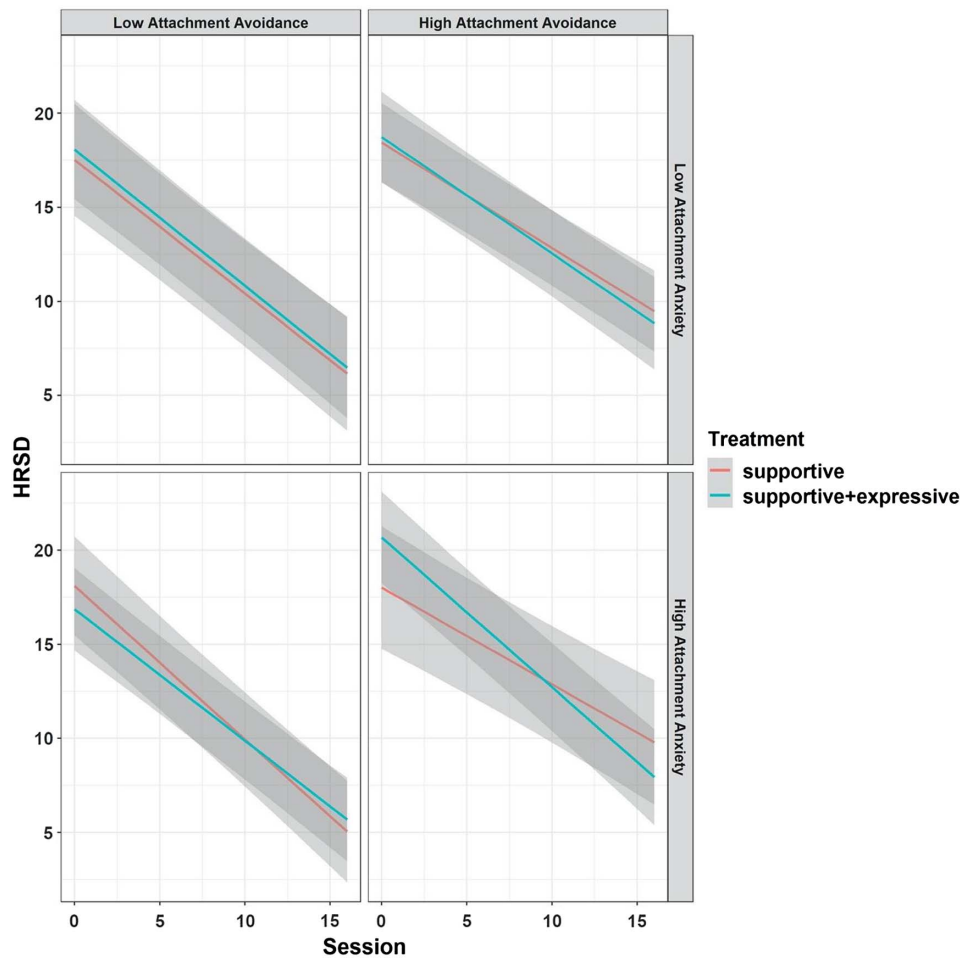*Note.* See the online article for the color version of this figure.

each individual (Cohen & DeRubeis, 2018). This may be the beginning of a new generation of RCTs focusing directly on precision medicine with the aim of optimizing treatments for individuals (National Institute of Mental Health, 2015).

It is intriguing to suggest post hoc explanations for the lack of an effect for attachment avoidance as a moderator of treatment outcome. One potential post hoc explanation is that the baseline avoidance level that characterized the individual before the start of treatment has been reduced over the course of treatment, especially for those who had successful treatments (Levy et al., 2018). The resulting more secure attachment may characterize the patient in general, in all interpersonal relationships, or it may be specific to the attachment formed with the therapists, which may serve as a corrective relational experience for the patient (Castonguay & Hill, 2012). If this post hoc explanation is supported by future research, a more dynamic conceptualization of attachment during treatment may be warranted (Zilcha-Mano, 2020). In this case, it may be suggested that in the progress toward personalized treatment, in addition to personalized treatment assignment based on the individual's pretreatment attachment, it is also necessary to monitor

and adapt treatment on an ongoing basis (Lutz et al., 2019) to the dynamically evolving attachment with the therapist.

The study has several limitations. First, although the sample size was preselected to identify medium and large effects, it was underpowered to detect small effects and precluded us from testing potential effects of the level of fit between patients' and therapists' attachment orientation. For the same reasons, the effect for disorganized attachment, although consistent with theory and clinical work, must be interpreted with caution before receiving further support in future research. Second, future studies are needed to further determine the prospective effect of assigning patients to treatment based on their attachment orientation versus random assignment. Third, the findings are based on attachment orientation as reported by patients. Using other measures may yield different results. Fourth, although consistently with the literature (Fernandez et al., 2021) the switch to remote treatment due to COVID-19 did not affect the results, the sample of remote cases was too small to enable systematic exploration. Fifth, the unique characteristics of the data raise the need to replicate the findings in additional and diverse samples. Specifically, this rigorously conducted study resulted in especially

Figure 3

Disorganized Attachment (High Levels of Attachment Anxiety and Avoidance) as a Moderator of the Effect of Treatment Condition on Treatment Outcome

Note. See the online article for the color version of this figure.

low rates of missing data and dropout compared to the rates documented in the literature (Cooper & Conklin, 2015; Swift & Greenberg, 2014) owing to the highly trained staff and the infrastructure used to collect the data. Thus, replication in naturalistic settings with diverse populations is warranted. In sum, the present study demonstrates the ability of attachment orientation to serve as an empirically informed tool for a personalized match between individuals and their most effective treatment. The study demonstrates the utility of RCTs predesigned to test differential effects of treatments conceptualized as targeting distinct mechanisms of change.

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Appendix

Post Hoc Analyses

The data reported in this manuscript were collected as part of a randomized clinical trial (RCT). This RCT has yielded several manuscripts with separate foci. However, no study to date has used the outcome data of the trial. Similarly, no study used the treatment condition assignment. Thus, there is no overlap with any previous studies.