

Interpersonal Distress as a Criterion for Personalizing Depression Therapy

Juan Martín Gómez Penedo^{1, 2}, Galit Peysachov³, Anna Babl⁴, and Sigal Zilcha-Mano³

¹ Clinical Psychology Department, University of Kassel

² Clinical Psychology and Psychotherapy Department, University of Osnabrück

³ Department of Psychology, University of Haifa

⁴ Clinical Psychology Department, University of Leiden

In this study, we aimed to explore interpersonal distress as a moderator of the effects of supportive treatment (ST) versus supportive expressive treatment (SET) on the therapeutic alliance and outcome in patients with depression. We drew on data from a randomized controlled trial where 100 patients were randomized to receive 16 sessions of either ST or SET. Patients completed a measure of interpersonal problems at baseline. Therapy outcome and the strength of the therapeutic alliance were measured by patient self-report, before and after each session, respectively. We conducted interactive three-level mixed effect models, accounting for the nested structure of the data, with repeated measures nested within patients, nested within therapists. The results showed significant interactive effects of treatment by baseline interpersonal problems on both the evolution of outcome and the alliance. Patients with greater interpersonal problems had a greater reduction in depressive severity and greater improvements in the alliance when treated with SET versus ST. If further replicated, the results of this study suggest that therapists of patients with depression would benefit from evaluating their interpersonal distress at baseline and incorporating this evaluation in their decision-making process regarding the most suitable intervention strategy for each individual patient. To conclude, the results of this study might enhance evidence-based treatment personalization in patients with depression using a parsimonious personalization approach.

Public Significance Statement

This study showed that depressed patients with higher pretreatment interpersonal distress might benefit more from a supportive expressive treatment than a supportive treatment. When treated with supportive expressive treatment (vs. supportive treatment), patients presenting more interpersonal distress tend to have greater reductions in depression severity and greater improvements in the alliance during treatment. The study provides sound but also easy-to-implement information to enhance treatment personalization for patients with depression.

Keywords: interpersonal problems, supportive expressive treatment, supportive treatment, depression, moderation

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Over the last decade, there has been a growing interest in models of treatment personalization and precision in mental health (Deisenhofer et al., 2024; Delgadillo & Lutz, 2020; Lutz et al., 2020; Zilcha-Mano, 2021). These approaches try to enhance treatment outcome by identifying evidence-based subgroups of patients that would benefit from differential interventions or strategies (Cohen & DeRubeis, 2018; Lutz et al., 2022; Moggia et al., 2024). Models such as the Personalized Advantage Index (see, e.g., DeRubeis et al., 2014; van Bronswijk et al., 2021) aim to identify the optimal

treatment by predicting the differential treatment response based on patients' characteristics. Most treatment selection approaches use competitive treatment models (e.g., cognitive behavioral therapy [CBT] vs. psychodynamic therapy) where the differential effects are expected to be more pronounced. However, these algorithms have implementation shortcomings that might reduce their clinical impact: First, a systematized fixed assessment with all the predictors of the algorithms and a process of automatic analysis and prediction, supported by complex technology, is needed. Second, it is uncommon

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Juan Martín Gómez Penedo  <https://orcid.org/0000-0001-7304-407X>

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Correspondence concerning this article should be addressed to Juan Martín Gómez Penedo, Clinical Psychology Department, University of Kassel, Holländische Straße 36-38, 34127 Kassel, Germany. Email: jmgomezpenedo@gmail.com

that therapists are fully trained in more than one treatment approach or that clinics have therapists trained in different approaches (Gómez Penedo et al., 2023).

Compared to data-driven personalization methods such as the Personalized Advantage Index that usually draw on a high amount of predictors, a more parsimonious strategy for identifying the most suitable intervention for each individual patient could focus on studying single theory-driven moderators for treatment selection (Newman et al., 2015; Snow, 1991). Such an approach would imply to select a single theoretically meaningful variable that is easier to assess while being relevant to perform prescriptive inferences. On the one hand, a single-variable strategy might imply less predictive capacity, on the other hand, it would enhance the feasibility to implement it into clinical practice.

A review by Kessler et al. (2017) proposed interpersonal difficulties (i.e., poor social support, relational difficulties, etc.) as a relevant self-report construct to explain heterogeneous results in psychotherapy for patients with depression. The review found several studies supporting relational difficulties as a relevant prognostic variable in the therapy for depression (Denton et al., 2010; Dew et al., 1997; Marquett et al., 2013), while it did not find studies using these difficulties for treatment selection purposes.

In the last years, patients' interpersonal problems have been positioned as a good relational candidate for process and outcome prediction (e.g., Gómez Penedo & Flückiger, 2023; Iovoli et al., 2024). Interpersonal problems are defined as difficulties in relationships with others, in terms of excessive or inhibited behaviors, that produce distress (Horowitz, 2004). Interpersonal problems are divided into eight different subtypes (i.e., domineering, intrusive, self-sacrificing, overly accommodating, nonassertive, socially inhibited, cold, and vindictive) that when aggregated provide an overall measure of interpersonal distress. A recently published meta-analysis demonstrated that patients' interpersonal distress (i.e., overall levels of interpersonal problems) at baseline was a meaningful predictor of treatment outcome (Gómez Penedo & Flückiger, 2023; $r = .13$). Patients with depressive and anxiety disorders having higher interpersonal distress at the beginning of therapy systematically tended to have worse responses to psychotherapy. Interpersonal distress has also been related to relevant psychotherapy processes (i.e., in-session psychotherapy factors; Doss, 2004) such as the therapeutic alliance (Dinger et al., 2013; Renner et al., 2012), a robust and widely established predictor of psychotherapy outcome (Flückiger et al., 2018). A recent meta-analytic synthesis further showed that patients with higher interpersonal distress at intake presented a weaker alliance during therapy (Iovoli et al., 2024; $r = -.12$).

Aiming to develop criteria for treatment adaptations, previous studies have explored specific interpersonal difficulties as a moderator of differential treatment effects. In generalized anxiety disorder, interpersonal problems of being extremely dominant or intrusive predicted differential effects between cognitive and behavioral therapy (Newman et al., 2017). Likewise, among patients with generalized anxiety disorder, interpersonal problems of dominance–submission have been associated with differential treatment effects of CBT versus CBT integrating motivational interviewing strategies (Gómez Penedo et al., 2017). Furthermore, in patients with bulimia nervosa, those with interpersonal problems of low communion/too cold responded better to interpersonal therapy, compared to patients with high communion/too friendly who responded better to CBT (Gómez Penedo et al., 2019).

More important for this study, an article by Probst et al. (2020) showed that specific interpersonal problems moderated treatment effects in patients with depression when comparing mindfulness-based cognitive therapy with group cognitive behavioral analysis system of psychotherapy. While patients with higher problems of being vindictive responded better to mindfulness-based cognitive therapy, patients with higher problems of being nonassertive responded better to cognitive behavioral analysis system of psychotherapy.

Despite the key role attributed to interpersonal factors in psychodynamic theory and treatment (Freud, 1958; Gabbard, 2014; Luborsky et al., 1994), we did not find any previous study analyzing how patients' baseline interpersonal problems might provide information for systematic treatment selection within variations of psychodynamic therapy. However, a series of experimental studies conducted by Høglend et al. (2007, 2008, 2011) on the effect of transference interpretation have provided preliminary evidence to support the relevance of interpersonal functioning for treatment adaptation in psychodynamic therapy. Two studies have shown that patients with low-quality object relations (i.e., worse interpersonal functioning) respond better to a psychodynamic treatment incorporating transference interpretation versus a psychodynamic treatment that avoided their use (Høglend et al., 2008, 2011). More specifically relevant to this study, Høglend et al. (2007) showed that patients with higher interpersonal distress at the beginning of therapy responded better to a psychodynamic treatment where transference interpretations were prescribed compared to a psychodynamic condition in which they were explicitly proscribed. These empirical findings are consistent with the interpersonal theory perspective, proposing that in those patients with depression where interpersonal difficulties play an important role, an approach that would consider those difficulties and target them therapeutically, would be more beneficial (Horowitz, 2004; Horowitz & Vitkus, 1986).

Although the studies conducted by Høglend et al. (2007, 2008, 2011) and colleagues provide preliminary evidence to support the differential effects of a *specific technique* (i.e., using or not transference interpretations with a treatment), the articles did not test differential effects of *whole psychodynamic treatments* as a function of interpersonal difficulties.

In the last decades, supportive–expressive treatment (SET) and supportive treatment (ST) (Luborsky, 1984; Luborsky et al., 1995) have been positioned as two reliable and effective variations of psychodynamic therapies for patients with depression (Leichsenring & Leibling, 2007; Zilcha-Mano et al., 2021). These time-limited psychodynamic treatments adapted for depression share a supportive component aiming at promoting a healthy therapeutic relationship using techniques such as affirmation and empathic validation (see Zilcha-Mano et al., 2018). The main difference between both approaches is that SET incorporates expressive techniques (while ST excludes them) such as interpretation, confrontation, and clarification, which are focused on improving the patients' self-understanding through the interpretation of interpersonal themes (Leibovich et al., 2018; Leichsenring & Leibling, 2007; Zilcha-Mano et al., 2018). Considering this differential component, the benefits of SET versus ST might vary depending on the degree of interpersonal problems presented by the patient. Hence, interpersonal problems may moderate the effects of SET versus ST, informing treatment selection within psychodynamic treatments.

In synthesis, interpersonal distress is considered a relevant variable for psychotherapy process and outcome prognosis. However, there has been scarce-to-null evidence concerning its importance in determining differential treatment effects, particularly in psychodynamic therapy. Compared to more complex approaches for treatment personalization, a recommendation criterion grounded on overall interpersonal distress might provide relevant and easy-to-implement information for clinical practice, with potential specific relevance for psychodynamic treatments where a more SET versus ST approach might be an option.

The Present Study

The aim of the present study was to explore patients' interpersonal distress as a moderator of psychodynamic (i.e., SET vs. ST) treatment effects for depression. We will test differential treatment effects as a function of interpersonal distress on outcome (as measured by the Hamilton Rating Scale for Depression [HRSD], [Hamilton, 1967](#)). Furthermore, considering that the alliance is a robust predictor of psychotherapy outcome (e.g., [Flückiger et al., 2018](#)) and a key factor both in SET and ST (e.g., [Zilcha-Mano et al., 2021](#)), we will also test if interpersonal problems moderate treatment effects on alliance evolution over the course of treatment (as measured by the Working Alliance Inventory [WAI]; [Horvath & Greenberg, 1989](#)). The results of the study could provide a parsimonious criterion to determine if SET versus ST would be more recommendable for patients with depression based on their baseline levels of interpersonal distress. Grounded on the above-described previous literature ([Høgland et al., 2007, 2008, 2011](#)), we hypothesize that patients with greater interpersonal impairment benefit more from SET (i.e., incorporating techniques with an interpersonal focus such as interpretations, clarifications, and confrontations), compared to ST.

Method

To examine the research questions, we used data of a recently completed randomized controlled trial (RCT; [Zilcha-Mano et al., 2018](#)). Consistent with the lack of differences in outcome observed among *bonafide* therapies for depression (see [Barkham & Lambert, 2021](#)), in this RCT no significant differences emerged between SET and ST. However, the main analysis indicated a moderation effect of attachment orientation ([Zilcha-Mano et al., 2021](#)). A data-driven approach implemented on the data also suggested the contribution of interpersonal domineering as a potential moderator ([Zilcha-Mano & Webb, 2024](#)).

Study Design and Procedure

The present study is based on the data of an RCT ([Zilcha-Mano et al., 2018, 2021](#)), with 100 patients being recruited through advertisements offering 16 weekly 50-min sessions of free treatment for depression. Thirteen patients were treated remotely due to COVID-19; all other patients were treated in person. Patients who met the inclusion criteria and did not meet the exclusion criteria were enrolled after signing informed consent forms. The RCT was approved by the ethics committee of the University of Haifa.

Inclusion criteria were as follows: (a) meeting major depressive disorder diagnostic criteria based on the structured clinical interview for the *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.; [American Psychiatric Association, 2013](#)), with scores above 14 on the 17-item HRSD ([Hamilton, 1967](#)) at two evaluations, 1 week apart, and current major depressive disorder based on the Mini-International Neuropsychiatric Interview ([Sheehan et al., 1998](#)); (b) if the patients were on medication, their dosage had to be stable for at least 3 months before entering the study, and they had to be willing to maintain a stable dosage for the duration of the treatment; (c) age between 18 and 60 years; (d) fluency in Hebrew; and (e) provision of written informed consent. Exclusion criteria were as follows: (a) current risk of suicide or self-harm (HRSD suicide item score >2); (b) current substance use disorder; (c) current or past schizophrenia or psychosis, bipolar disorder, or severe eating disorder requiring medical monitoring; (d) history of organic mental disease; or (e) currently in psychotherapy.

Patients

Out of the total sample, 57% were female and the mean age was 31.2 ($SD = 8.25$). The mean level of education was 14.2 years ($SD = 2$). Monthly income was reported as above average (about \$4,212) by 25% of patients, 68% were employed. Patients who reported they were married or cohabitating made up 16% of the sample. Of the patients, 80% were Jewish. From the total sample, 46% had previous psychotherapy, and 24% had previous medication treatment, while 14% were currently on medication. Regarding comorbidities, 71% of the sample presented with a comorbid anxiety disorder, while 74% presented with a comorbid personality disorder.

Therapists

Six therapists participated in the RCT. All therapists had formal training in psychodynamic treatment with at least 5 years of experience in its practice. The therapists attended a 20-hr training workshop in supportive and expressive techniques prior to seeing patients. Before seeing any patient as part of the RCT, eight therapists completed treatment of two pilot patients, one for each treatment type. Of the initial eight therapists, two did not continue after the training phase, one due to low levels of adherence and the other because of a job change to a different institution. The remaining six therapists demonstrated sufficient adherence before beginning the active phase of the RCT. During the pilot phase and the active phase, weekly individual and group supervision was provided to the therapists by two experienced licensed clinical psychologists, who received supervision from an international expert in SET. To avoid nesting of therapists within treatment conditions and for therapists to act as their own control, all therapists provided treatment in both conditions.

Of the six therapists that participated in the RCT, the mean clinical experience was 14.41 ($SD = 5.42$) years. The mean number of patients treated by each therapist was 16.66 ($SD = 8.45$). The mean age of the therapists was 42.33 ($SD = 4.41$), and five of the therapists were female. All therapists were married or cohabitating.

Treatments

One hundred patients were randomized to receive either SET or ST short-term psychotherapy. For the SET condition, a comprehensive treatment protocol was used (Luborsky et al., 1995). For the ST condition, all supportive techniques in the manual were included, excluding the expressive techniques (Leibovich et al., 2018).

Fidelity Check

The Penn Adherence–Competence Scale (Barber & Critis-Christoph, 1996) measures therapists' adherence and competence in three subscales: general therapeutic behaviors, supportive interventions, and expressive interventions. The coders were four trained PhD/MA students in clinical psychology. The number of coders for each session varied between two and four coders. The coders rated between one and three randomly selected sessions (from Sessions 4, 6, and 8) for each patient (161 sessions in total; 80 SET sessions and 81 ST sessions), reaching very good interrater reliability concerning the quantity and quality for each subscale (intraclass correlation coefficient: .71–.91). As expected, there were no significant differences across conditions in the quantity or quality of general therapeutic behaviors or supportive interventions. However, SET presented a significantly higher quantity ($p < .0001$) and quality ($p < .0001$) of expressive interventions (for more details, see Zilcha-Mano et al., 2021).

Measures

Interpersonal Distress

Interpersonal distress was assessed using the Inventory of Interpersonal Problems (IIP-32), which is one of the most widely used questionnaires for the assessment of interpersonal problems (Horowitz et al., 1988). The IIP-32 consists of 32 items in the form of statements about the self that are rated on a 5-point Likert scale ranging from 0 (*not at all*) to 4 (*very much*). The IIP-32 measures dispositional interpersonal difficulty across eight subscales including domineering, intrusive, overly accommodating, self-sacrificing, nonassertive, socially avoidant, cold, and vindictive interpersonal behavior, which can be combined to produce an overall score of interpersonal problems. Although patients completed the IIP at six time points during treatment (at Sessions 1, 2, 4, 8, 12, and 16) for this study, we only used the baseline assessment. Internal consistency for the IIP-32 was 0.87.

Treatment Outcome

Treatment outcome was assessed using the HRSD (Hamilton, 1967), the preregistered main outcome measure of the trial (Zilcha-Mano et al., 2018). The HRSD is a 17-item clinically administered semistructured interview to assess depression severity. This measure is among the most widely used in clinical trials to evaluate treatment outcome in depression. The items have different ranges (i.e., seven items range from 0 to 2, one item from 0 to 3, and nine items from 0 to 4). Higher total scores indicate greater depression severity. Scores of 19 and higher indicate severe depression, scores of 14–18 of moderate depression, scores of 13–8 of mild depression, and scores of 7 and below are considered normal symptoms or clinical

remission (National Collaborating Centre for Mental Health, 2010). All interviews were administered by interviewers that received extensive training and supervision. Internal consistency for the HRSD in the current sample was 0.82.

Alliance

Alliance was assessed using the WAI (Horvath & Greenberg, 1989; Tracey & Kokotovic, 1989). The WAI is one of the most widely spread process measures in the field of psychotherapy research. It has 12 self-report items that are rated on a 7-point Likert scale ranging from 1 (*never*) to 7 (*always*). The overall score is obtained from three subscales: agreement on treatment goals, agreement on treatment tasks, and the emotional bond between the patient and therapist. Patients rated the alliance with their therapists after each session. Internal consistency for the WAI was 0.93.

Analytic Strategies

As the primary analytic strategy, we used multilevel models (Raudenbush & Bryk, 2002). Multilevel models account for the dependency of the observations due to the nested structure of the data (e.g., repeated measures of an outcome variable nested within patients). By estimating variability (i.e., random effects) at the different levels of data organization, this approach allows to conduct prediction models (Snijders & Bosker, 2011), preventing the risk of inflation of both Type I and Type II errors (Van den Noortgate et al., 2005). Furthermore, as multilevel models take information from all the participants of the sample into account when estimating the models, they provide a robust approach to deal with missing data in the repeatedly measured variables, mimicking an intent-to-treat approach (Westra et al., 2016).

Due to the data structure in this study, we ran three-level multilevel models accounting for variability at the repeated measures level (Level 1), the patient level (Level 2), and the therapist level (Level 3). We ran separate models for both depression severity and the therapeutic alliance as outcomes. First, we conducted fully unconditional models (i.e., without any predictor) to determine the percentage of outcome variance explained by the therapists. Second, we ran models with time (defined as sessions and centered at posttreatment) as the only Level 1 predictor, to determine the average rate of change during treatment. Third, we ran conditional models including both treatment conditions (dummy-coded: ST = 0, SET = 1) and total interpersonal distress (z -standardized) as Level 2 predictors of both the intercept and the time effect. Last, we included an interaction term in the models to estimate how interpersonal distress moderates treatment effects on the outcome variables (see equations of the moderation models in the Supplemental Material).

The main hypotheses of the study were tested based on the parameter γ_{130} , defined as the interactive effect of treatment by interpersonal distress on session-by-session reductions/improvements in depressive severity/alliance over the course of treatment. Based on the results of these interactive models for depression and alliance, we also computed simple slopes and regions of significance (Preacher et al., 2006) to determine empirical thresholds for treatment recommendation. To provide effect sizes

for the estimates, we computed standardized coefficients (SC; Lorah, 2018).

Transparency and Openness

Power calculations were performed to determine the sample size of the main RCT (Zilcha-Mano et al., 2021). All patients from the RCT were incorporated in this secondary analysis. All manipulations done and the measures used in the study were reported. To present the quantitative results, we followed Journal Article Reporting Standards (Kazak, 2018). The clinical data used for the study are not publicly available. For data analyses, we used the open environment R, Version 4.3.3 (R Core Team, 2024), and packages *lme4* (Bates et al., 2015) and *lmerTest* (Kuznetsova et al., 2017). The codes for the analyses are available upon request. The design of the RCT was published in the study protocol (Zilcha-Mano et al., 2018). The specific analyses for this study were not preregistered.

Results

Sample Descriptives

Descriptive statistics of the targeted variables of the study at baseline are presented in Table 1. Surprisingly, baseline interpersonal distress was not significantly correlated with either baseline depression severity ($r = -.02, p = .88$) or with initial alliance ($r = -.05, p = .60$).¹ At baseline, a t test showed no significant differences in interpersonal distress between ST and SET, $t(98) = -1.34, p = .18$.

Models for Depression Severity

The results of all the models conducted with depression severity as outcome are fully presented in Table 2.

Unconditional Models

The unconditional three-level model with depression severity as the dependent variable, showed that therapist effects explained

Table 1

Means and Standard Deviations of Interpersonal Distress, Alliance, and Depression at Baseline

Group (<i>N</i>)	<i>M</i>	<i>SD</i>
All sample (<i>N</i> = 100)		
IIP	57.45	14.04
WAI	5.19	0.94
HRSD	20.92	3.72
SET (<i>N</i> = 50)		
IIP	55.58	12.52
WAI	5.23	0.96
HRSD	21.00	3.88
ST (<i>N</i> = 50)		
IIP	59.32	15.30
WAI	5.15	0.93
HRSD	20.84	3.59

Note. IIP = Inventory of Interpersonal Problems; WAI = Working Alliance Inventory; HRSD = Hamilton Rating Scale for Depression; SET = supportive-expressive treatment; ST = supportive treatment.

Table 2

Results of the Unconditional, Time-as-Only-Predictor, Conditional, and Interactive Effect Models With Depression Severity as Outcome

Fixed model effect	Posttreatment depression (π_{0jk})		Session-by-session change in depression (π_{1jk})	
	γ	<i>SE</i>	γ	<i>SE</i>
Fully unconditional				
Intercept	12.34**	.47		
Time model				
Intercept	7.97**	.56	−0.56**	.02
Model comparison		$\chi^2(1) = 524.26, p < .001$		
Conditional model				
Intercept	8.10**	.74	−0.52**	.03
Treatment	−0.27	.95	−0.07	.04
IIP	0.18	.47	−0.03	.02
Model comparison		$\chi^2(4) = 4.09, p = .39$		
Interactive model				
Intercept	8.07**	.74	−0.53**	.03
Treatment	−0.30	.95	−0.07	.04
IIP	0.54	.60	0.02	.03
Treatment × IIP	−0.88	.96	−0.12*	.04
Model comparison		$\chi^2(2) = 7.06, p = .03$		

Note. *SE* = standard error; IIP = Inventory of Interpersonal Problems.
* $p < .01$. ** $p < .001$.

0.5% of outcome variance (intraclass correlation coefficient = .005). The model estimated an average sample HRSD of 12.32 across treatment, $\gamma_{000} = 12.32, SE = .47, 95\% \text{ CI } [11.39, 13.25], t(2.27) = 25.97, p < .001$.

Time-as-Only-Predictor Model

When estimating change during treatment, the model suggested a significant reduction of depression severity, $\gamma_{100} = -0.56, SE = .02, 95\% \text{ CI } [-0.60, -0.52], t(1,446.8) = -25.11, p < .001$. Patients significantly reduced their HRSD levels session-by-session, reducing them on average 0.56 units per session. The inclusion of the time variable significantly improved the model fit when compared to the fully unconditional model, $\chi^2(1) = 524.26, p < .001$.

Conditional Models

The conditional models showed no significant effect of treatment condition on depression severity when adjusting for interpersonal distress, $\gamma_{110} = -0.07, SE = .04, 95\% \text{ CI } [-0.15, 0.01], t(1,446.3) = -1.49, p = .14$, nor a significant effect of interpersonal distress when adjusting for treatment condition, $\gamma_{120} = -0.03, SE = .02, 95\% \text{ CI } [-0.07, 0.02], t(1452.1) = -1.19, p = .24$. The inclusion of the predictors did not significantly improve the model fit when compared with the time-as-only-predictor model, $\chi^2(4) = 4.37, p = .36$.

Interactive Effect Models

The moderation model showed a significant interactive effect of treatment by interpersonal distress on depression severity rates

¹ These results were unexpected considering the findings from several studies showing that interpersonal distress is associated with depressive severity (Altenstein-Yamanaka et al., 2017; Grosse Holtforth et al., 2014; Lemmens et al., 2017) and worse therapeutic alliance (Iovoli et al., 2024).

of change, $\gamma_{130} = -0.12$, $SE = .04$, 95% CI $[-0.21, -0.08]$, $t(1,452.88) = -2.658$, $p = .008$, $SC = -0.02$.² In patients with interpersonal distress levels 1 *SD* above the mean, being treated with SET (vs. ST) was associated with a 0.12 unit greater session-by-session reduction in depression severity. The aggregated standardized effect across the 16 sessions would be equivalent to $d = 0.32$. Figure 1, Panel A illustrates the interactive effect of treatments by interpersonal problems on session-by-session changes in depression severity. The model comparison test showed a significant improvement of model fit when adding the interactive effects to the conditional models, $\chi^2(2) = 7.26$, $p = .03$.

Simple slope analysis showed that among patients treated with ST, the difference between the expected rate of change in HRSD was small when comparing patients with low levels of interpersonal problems (i.e., 1 *SD* below mean; $\gamma_{100} = -0.55$) and patients with high levels of interpersonal distress (i.e., 1 *SD* above mean; $\gamma_{100} = -0.51$). However, when treated with SET, a greater difference was observed between the estimated rates of change in patients with low levels of interpersonal distress level ($\gamma_{100} = -0.50$) and high levels of interpersonal distress ($\gamma_{100} = -0.71$). Ultimately, the calculations of regions of significance showed that the session effect was significant across the whole range of interpersonal distress (i.e., -2.54 to 2.38) for both treatments.

Models for Alliance

The findings of the alliance models are fully presented in Table 3.

Unconditional Models

When running the unconditional three-level model with alliance as the dependent variable, the model had problems of singularity due to the small variability observed at the therapist level (intraclass correlation coefficient $< .001$). Thus, we adjusted the models to two-level models (i.e., repeated measures nested within patients) for the analyses performed with the alliance as outcome. The unconditional two-level model estimated an average sample alliance level across treatment of 5.64, $\gamma_{00} = 5.64$, $SE = .09$, 95% CI $[5.47, 5.81]$, $t(99.8) = 65.75$, $p < .001$.

Time-as-Only-Predictor Model

Patients showed a significant improvement in the alliance over the course of treatment, $\gamma_{10} = .04$, $SE = .003$, 95% CI $[0.04, 0.05]$, $t(1422.7) = 16.53$, $p < .001$. Patients significantly increased their alliance levels during treatment, increasing them on average 0.04 units per session. The model comparison test showed a significantly improved model fit when comparing the time-as-only-predictor model to the fully unconditional model, $\chi^2(1) = 249.97$, $p < .001$.

Conditional Models

The conditional models showed a significant effect of treatment condition on the alliance when adjusting for interpersonal distress, $\gamma_{11} = 0.02$, $SE = .005$, 95% CI $[0.01, 0.03]$, $t(1422.5) = 4.51$, $p < .001$. However, the model did not show a significant effect of interpersonal distress when adjusting for treatment condition, $\gamma_{12} = -0.005$, $SE = .003$, 95% CI $[-0.01, 0.001]$, $t(1426.1) = -1.72$, $p = .09$. The inclusion of the predictors significantly improve the model

fit when compared to the time-as-only-predictor model, $\chi^2(4) = 29.19$, $p < .001$.

Interactive Effect Models

This moderation model also showed a significant interactive effect of treatment by interpersonal distress on alliance improvements during therapy, $\gamma_{13} = 0.01$, $SE = .005$, 95% CI $[0.0002, 0.02]$, $t(1,427.14) = 1.990$, $p = .047$, $SC = 0.01$.³ In patients with interpersonal distress levels 1 *SD* above average, being treated with SET was associated with a .01 unit greater session-by-session improvement in alliance scores during therapy. The aggregated standardized effect across the 16 sessions would be equivalent to $d = 0.16$. The interactive effect of treatment by interpersonal problems on session-by-session improvements in alliance scores is illustrated in Figure 1, Panel B. However, the model comparison did not show a significant improvement of model fit when adding the interactive effects, $\chi^2(2) = 4.47$, $p = .11$.

Simple slope analysis showed that among patients treated with ST, patients with lower interpersonal problem levels had a greater session-by-session increase in the alliance (i.e., 1 *SD* below mean; $\gamma_{10} = 0.04$), compared to patients with higher levels of interpersonal problems (i.e., 1 *SD* above mean; $\gamma_{10} = 0.02$). In SET, the opposite effect was observed, with a greater session-by-session increase in alliance for patients with higher levels of interpersonal problems ($\gamma_{10} = 0.06$), compared to patients with lower levels ($\gamma_{10} = 0.05$). However, the difference was smaller than in the ST. Calculating regions of significance showed that in ST, a nonsignificant improvement over the course of treatment in the alliance was expected for patients with 2 *SD* above the mean in interpersonal distress at baseline (see Figure 2). In SET, the alliance was expected to significantly improve for the whole range of interpersonal distress across the sample (i.e., -2.54 to 2.38).

Discussion

The aim of this study was to evaluate patients' interpersonal distress as a moderator of depressive treatment effects (i.e., ST vs. SET) on psychotherapy outcome and the alliance. The results showed that for patients with depression having more severe interpersonal problems at the beginning of treatment being treated with SET as opposed to ST resulted in a greater reduction in depressive symptoms and greater improvements in the therapeutic alliance during treatment.

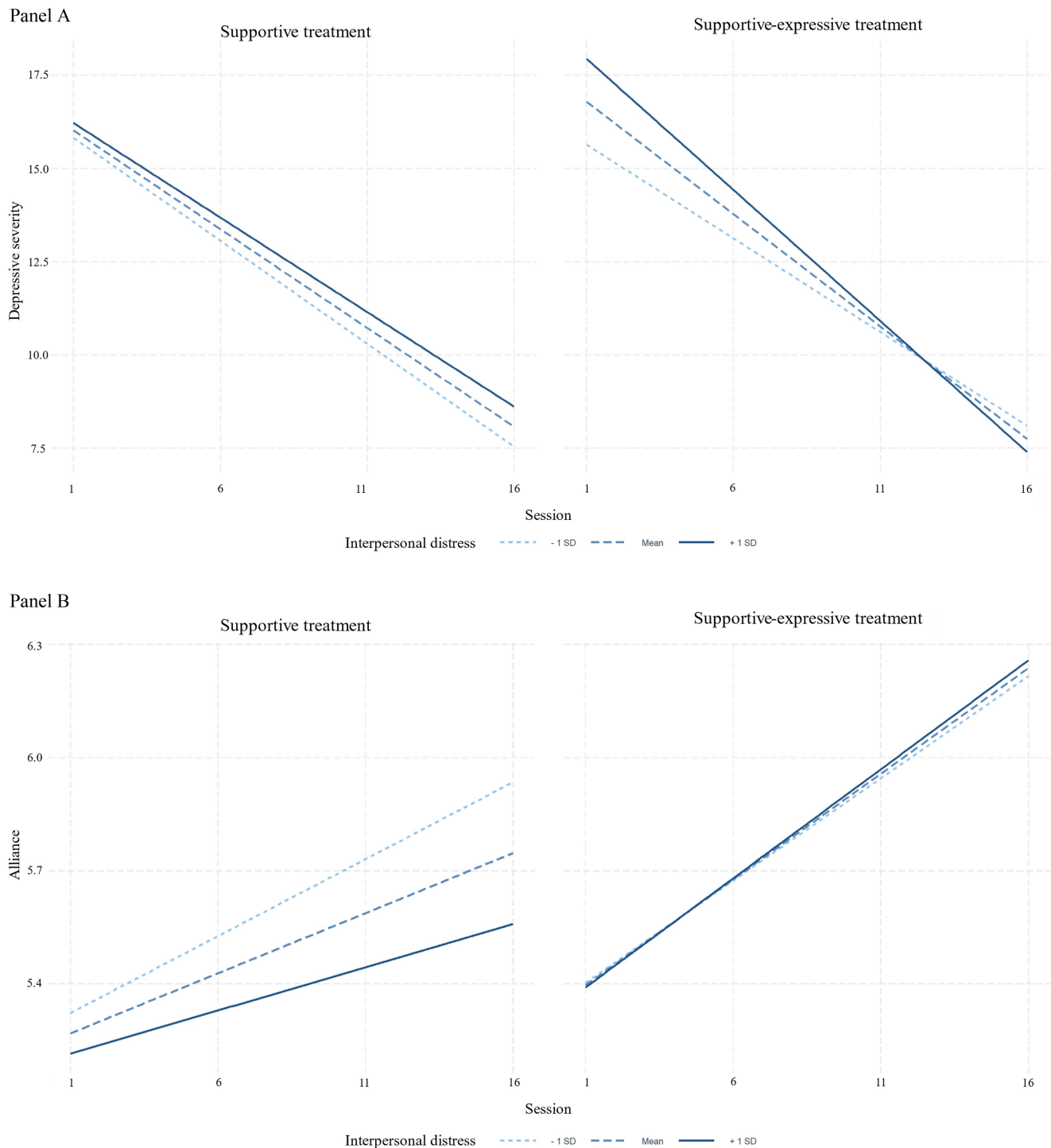
The findings of the study are in line with our hypothesis that patients with greater interpersonal impairments would benefit the most from a more expressive approach, compared to a treatment mainly providing support presenting a small-to-medium aggregated

² Following suggestions that emerged in the peer-review process, as sensitivity analyses, we tested if the interpersonal dimensions of agency and communion moderate treatment effects on outcome. The multilevel models showed no significant interactive effects either of agency, $\gamma_{130} = 0.04$, $SE = 0.04$, 95% CI $[-0.05, 0.13]$, $t(1,453.5) = 0.04$, $p = .91$, or of communion, $\gamma_{130} = 0.06$, $SE = 0.05$, 95% CI $[-0.04, 0.15]$, $t(1,457.1) = 1.20$, $p = .23$, on outcome.

³ Also following peer-review suggestions, as sensitivity analyses we tested if the interpersonal dimensions of agency and communion moderate treatment effects on alliance. The multilevel models showed no significant interactive effects either of agency, $\gamma_{13} = 0.002$, $SE = 0.01$, 95% CI $[-0.01, 0.01]$, $t(1,422.8) = 4.65$, $p = .66$, or of communion, $\gamma_{13} = -0.01$, $SE = 0.01$, 95% CI $[-0.02, 0.004]$, $t(1,424.8) = -1.22$, $p = .22$, on alliance.

Figure 1

Differential Time Effects of Patients' Baseline Interpersonal Distress on Outcome (Panel A) and Alliance (Panel B) by Treatment



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

effect size ($d = 0.32$). These results align with previous experimental research at the intervention level (e.g., Høglend et al., 2008, 2011) suggesting that patients with worse interpersonal functioning broadly speaking have better responses to psychodynamic treatments that

incorporate a fundamental expressive intervention such as transference interpretation. Specifically relevant for this study, Høglend et al. (2007) have shown that patients with higher interpersonal distress responded better to a treatment prescribing (vs. proscribing)

Table 3

Results of the Unconditional, Time-as-Only-Predictor, Conditional, and Interactive Effect Models With Alliance as Outcome

Fixed model effect	Posttreatment alliance level (π_{0jk})		Session-by-session change in alliance (π_{1jk})	
	γ	SE	γ	SE
Fully unconditional				
Intercept	5.64***	.09		
Time model				
Intercept	5.98***	.09	0.04***	.003
Model comparison	$\chi^2(1) = 249.97, p < .001$			
Conditional model				
Intercept	5.74***	.12	0.03***	.004
Treatment	0.48**	.17	0.02***	.005
IIP	-0.10	.08	-0.004	.003
Model comparison	$\chi^2(4) = 29.191, p < .001$			
Interactive model				
Intercept	5.75***	.12	0.03***	.004
Treatment	0.49**	.17	0.02***	.005
IIP	-0.19	.11	-0.01**	.003
Treatment $\times$ IIP	0.21	.17	0.01*	.005
Model comparison	$\chi^2(2) = 4.47, p = .11$			

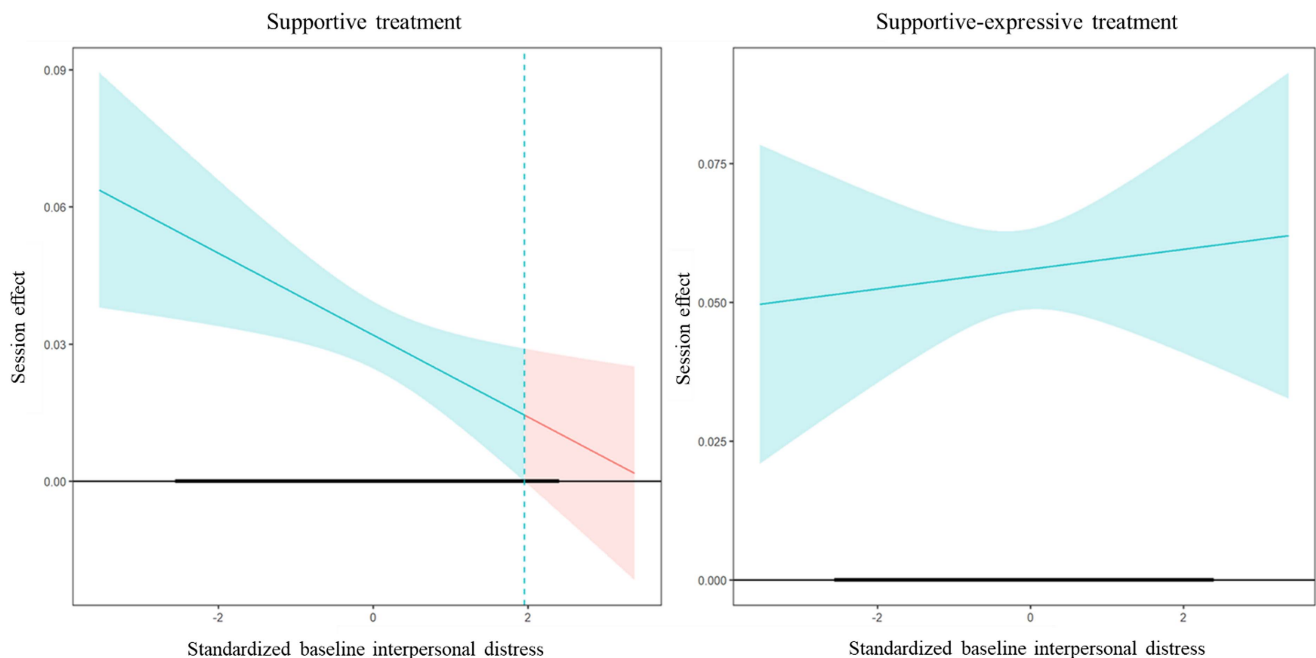
Note. SE = standard error; IIP = Inventory of Interpersonal Problems.

* $p < .05$. ** $p < .01$. *** $p < .001$.

transference interpretation techniques. The current article provides further evidence at the treatment selection level (rather than at the technique level as in the studies from Høglend et al.), suggesting that patients with more interpersonal distress might better be served with an SET approach than an ST approach, alone.

Figure 2

Regions of Significance Calculations for Session Effects on Alliance in Supportive Versus Supportive-Expressive Therapy Based on Patients' Interpersonal Distress at Baseline



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

SET might be more beneficial than ST in cases with more severe interpersonal difficulties because the expressive component of SET specifically targets interpersonal functioning via core conflictual relational themes (Luborsky et al., 1994), being the main focus of the interpretations, confrontations, and clarification techniques (Leibovich et al., 2018). In comparison to ST, SET is oriented toward fostering a deeper exploration of emotions and interpersonal relationships, therefore providing a more conducive environment for patients to address and process their interpersonal distress within the therapeutic relationship (Book, 1998). This approach may enable patients to develop greater insight into their relational patterns and emotional responses, leading to more meaningful therapeutic outcomes (e.g., Benjamin, 2003; Horowitz, 2004).

From a theoretical perspective, interpersonal problems are hypothesized to be connected to patients' depressive symptoms (e.g., Horowitz, 2004; Sullivan, 1953). Empirical research has supported this idea, showing that interpersonal distress is a meaningful covariate of depression severity (Anderson et al., 2018, $r = .38$; Carryer & Greenberg, 2010, $r = .43$; Strand et al., 2018, $r = .39$) and depressive mechanisms such as pathological beliefs (Neelapajjit et al., 2018, $r = .61$), dysfunctional attitudes (Bernholtz, 2013, $r = .67$; Watson et al., 2020, $\rho = .71$), and self-criticism (Dinger et al., 2015, $r = .40$; Watson et al., 2020, $\rho = .75$). Hence, in patients presenting with greater interpersonal problems, an approach like SET could produce corrective interpersonal experiences that might help to reduce patients' interpersonal distress and in turn lead to improvement in their depressive symptoms (Zilcha-Mano et al., 2018). Future research should use moderated mediation models (see, e.g., Hayes, 2017) in order to evaluate if changes in interpersonal problems

mediate treatment effects and if that mediation is moderated by patients' initial levels of interpersonal distress.

Also consistent with our hypothesis, the results of the present study showed that patients with greater interpersonal distress when treated with SET (vs. ST) tended to have a greater improvement in the alliance over the course of therapy, presenting a small aggregated effect size ($d = .16$). Further analyses showed that this difference was mainly due to a lower increase in the alliance for patients with higher interpersonal problems (compared to patients with lower interpersonal problems) when treated with ST, while in SET patient with lower and higher problems presented similar slopes of alliance improvements. The results observed in ST are consistent with recent meta-analytic evidence showing that patients with more interpersonal problems tend to have worse alliance during treatment (Iovoli et al., 2024). This difference in the alliance seems to be canceled out in the SET condition, having an expected similar evolution of the alliance in patients with lower and higher interpersonal distress. The expressive approach might facilitate a deeper interpersonal environment for the exploration of patients' relational patterns. Although this could bring about challenges to the patient–therapist relationship, if adequately handled, it might also produce therapeutic opportunities to strengthen the alliance, ultimately related to outcome (Eubanks et al., 2018). Even though it was not tested in this study, considering the well-established alliance–outcome association (Flückiger et al., 2018), it could be hypothesized that the differential effect of SET on outcome in patients with greater interpersonal problems is partially explained (i.e., mediated) by the strengthening of the alliance during treatment. Future studies might benefit to test this hypothesis within a mediated moderation framework (see, e.g., Hayes, 2017).

In synthesis, both the models to predict outcome and alliance levels converged suggesting that in patients with higher interpersonal problems, an SET approach would be more recommended than an ST approach. Although the size of the effect observed for outcome and alliance were small-to-medium ($d = 0.32$) and small ($d = 0.16$), respectively, they might provide a modest but easy-to-implement and low-burdensome method that could contribute to enhance psychotherapy for depression via treatment personalization. Previous research investigating differential treatment effects has mostly focused on evaluating competitive treatment approaches (e.g., CBT vs. psychodynamic therapy) in which individual therapists are unlikely to be trained to an equal extent (Gómez Penedo et al., 2023). By evaluating variations of psychodynamic treatments, the present study might provide a more scalable but also parsimonious strategy to recommend the most suitable intervention for each individual patient. Similar criteria could be developed within other treatment approaches, such as CBT. Although speculative, it could be hypothesized that the integration of motivational interviewing (Westra et al., 2016) or emotion-focused techniques (Grosse Holtforth et al., 2019) in CBT might be more beneficial for patients with greater interpersonal distress compared to a classical CBT treatment. However, the present study could not provide any evidence to support those hypotheses, and future research would need to be conducted to test them.

Although the present study has several strengths, it also has some limitations which must be taken into account when interpreting the results. First, although the sample size was relatively large compared to other treatment-comparison RCTs in psychotherapy, the sample size

of the study might be small for testing interactive (i.e., moderation) effects. Second, the study only included patients with depression, and therapies were carried out in the outpatient setting. This limits the generalizability of findings to patients with other disorders or in inpatient facilities, which should be taken up in future research. Third, only one other study exists investigating how patients' baseline interpersonal problems might provide information for treatment selection within variations of psychodynamic therapy (Høglund et al., 2007), which makes it difficult to compare the results. Results must thus be interpreted as preliminary and should be replicated in prospective studies and more diverse samples. Future studies should test this straightforward algorithm prospectively in a new sample where patients are allocated to receive either SET or ST based on their interpersonal distress at baseline. The goal is to evaluate whether the algorithm performs consistently and effectively across various settings and circumstances, thereby validating its utility and reliability. Such validation studies are crucial for ensuring the robustness and generalizability of algorithms before they are implemented in clinical practice.

Besides these limitations, our study adds to previous research on treatment selection in that it provides relevant but preliminary information about interpersonal distress as a recommendation criterion in psychodynamic therapy. Nevertheless, more research on different relevant baseline characteristics and their interaction with treatment effects is necessary to enhance the personalization of treatment to the individual patient.

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