



# Interpersonal problems as a predictor of treatment outcome in adult depression: An individual participant data meta-analysis

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## ABSTRACT

**Objectives:** Interpersonal problems are a fundamental feature of depression, but study-level meta-analyses of their association with treatment outcome have been limited by heterogeneity in primary studies' analyses and reported results. We conducted a pre-registered individual participant data meta-analysis (IPD-MA) to examine this

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Treatment  
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IPD

relationship for adult depression. This meta-analytic strategy can reduce variability by standardizing data analysis across primary studies.

**Methods:** We included studies examining the efficacy of five treatments for adult depression and assessing interpersonal problems at baseline. One-stage IPD-MA was conducted with three-level mixed models to determine whether baseline overall interpersonal distress, agency, and communion predicted depressive symptom level at post-treatment, 12-month, and 24-month follow-up. The moderating effect of treatment type was also investigated.

**Results:** Ten studies (including  $n = 1282$  participants) met inclusion criteria. Only overall interpersonal distress was negatively related with outcomes at post-treatment ( $\gamma = 0.11$ ,  $CI_{95}[0.06, 0.16]$ ,  $r = 0.11$ ), 12-month follow-up ( $\gamma = 0.17$ ,  $CI_{95}[0.08, 0.25]$ ,  $r = 0.17$ ), and 24-month follow-up ( $\gamma = 0.16$ ,  $CI_{95}[0.05, 0.26]$ ,  $r = 0.16$ ), indicative of smaller effect sizes. The agency and communion dimensions were not significantly related to outcome. Treatment type did not significantly moderate interpersonal distress-outcome associations.

**Discussion:** Results show a small association between patient baseline overall interpersonal distress and subsequent depression treatment outcome in brief treatments for depression. Further studies might require to account for therapist effects.

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## 1. Introduction

Recent (Constantino et al., 2012; Hames et al., 2013; Horowitz, 2004; Lemma et al., 2024; McCullough, 2000; Segrin, 2001) and classical (Coyne, 1976; Horowitz & Vitkus, 1986; Sullivan, 1953) theoretical models have suggested that maladaptive interpersonal traits and processes are at the core of depressive etiopathogenesis, explaining the onset and maintenance of depressive symptoms. Empirical studies have provided supportive evidence, showing that the onset of depression is predicted by overall interpersonal dysfunction (Hammen et al., 2008), relational stress (Vrshek-Schallhorn et al., 2015), interpersonal inhibition (Karevold et al., 2009; Murberg, 2009), dependency (Mazure et al., 2000; Sanathara et al., 2003), and interpersonal mistrust (Kim et al., 2012).

To assess the association between interpersonal problems and depressive symptomatology, many studies have drawn on the model developed by Len Horowitz (2004; see also Altenstein-Yamanaka et al., 2017; Anderson et al., 2018; Lemmens et al., 2017). This model postulates that there are eight types of interpersonal problems (i.e., [being too] domineering, intrusive, nurturant, exploitable, non-assertive, socially inhibited, cold, and vindictive) representing interpersonal excesses or inhibitions that produce distress. The aggregate levels of distress across the different types of problems define an overall level of self-reported or perceived interpersonal distress (that from here on we refer to as “overall interpersonal distress”). Furthermore, these eight interpersonal problems are distributed around a circumplex model defined by two orthogonal interpersonal dimensions of *communion*, defined as the needs for developing close relationships (with the negative pole of the dimension representing problems of being too detached/indifferent and the positive pole representing issues of being too dependent), and *agency*, defined as the needs for influencing others (with the negative pole representing problems of being too submissive and the positive pole representing issues of being too dominant).

Following Horowitz’ (2004) model, several studies have shown that higher overall interpersonal distress was associated with greater clinical severity in patients with depression (Altenstein-Yamanaka et al., 2017; Anderson et al., 2018; Grosse Holtforth et al., 2014; Lemmens et al., 2017; Vittengl et al., 2018). Furthermore, patients diagnosed with depressive disorders have consistently reported higher overall interpersonal distress when compared to non-depressed individuals (Klein et al., 2016; Stangier et al., 2007; Struck et al., 2021; te Wildt et al., 2007). Overall interpersonal distress in depressed patients has also been associated with other mental health outcomes and risk factors connected to the condition, such as lower levels of self-esteem (Adams, 2010; Bernholtz, 2013; Watson et al., 2020), quality of life (McEvoy et al., 2013) and well-being (Gómez Penedo et al., 2020), as well as dysfunctional attitudes (Watson et al., 2020) and coping strategies (Bernholtz, 2013). Summarizing the literature on this topic, a recent meta-analysis

reported significant medium-to-large cross-sectional associations between overall interpersonal distress and mental health indicators (e.g., clinical severity, quality of life, self-esteem, etc.) in depressive disorders ( $r = 0.41$ ;  $k = 30$ ; Gómez Penedo et al., 2024).

Both the robust association of overall interpersonal distress with depressive severity and the theories that postulate it as a key factor in depression onset and maintenance (see Horowitz, 2004), suggest that interpersonal problems at the beginning of a treatment for depression might play an important role in predicting how much a patient would benefit from an intervention. Consistently, empirical evidence had positioned overall interpersonal distress as a meaningful predictor of treatment outcome for depressive disorders. Greater overall interpersonal distress has been related to worse outcome in a variety of interventions for depression such as interpersonal psychotherapy (Ravitz et al., 2008), cognitive therapy (Vittengl et al., 2010), and cognitive-behavioral therapy (Fitzpatrick et al., 2020).

A recent meta-analysis has synthesized the effect of overall interpersonal distress as a predictor of outcome in depressive and anxiety disorders, finding a small but significant effect, with higher interpersonal distress associated with worse outcome (Gómez Penedo & Flückiger, 2023). Although this meta-analysis supports the relevance of overall interpersonal distress in the prediction of treatment outcome for depression, several limitations call for a cautious interpretation of the findings. This meta-analysis combined studies of depression and anxiety, whereas major differences have been found in the outcome of psychotherapy for these two conditions. Moreover, the results showed a moderate heterogeneity in the aggregate effect, with 39.69 % of the total variance explained by between-study variability. Further, there was large variability in the methods, analytic procedures, and types of coefficients (i.e., Pearson correlations, F-tests, Rsquared, gamma coefficients, standardized Betas, odd ratios, and Cohen’s  $d$ s) reported among studies, with the risk of biasing the aggregate estimation of the effect. Hence, empirical studies within a more consistent methodological framework might support a more precise estimation of the actual predictive capacity of overall interpersonal distress on treatment outcome for depression. Furthermore, a meta-analytic review exploring changes in interpersonal problems in the treatment of depression, had highlighted the absence of attention to reporting interpersonal problem effects in main outcome studies from depression trials, making that information not available for conventional meta-analyses (McFarquhar et al., 2018).

Individual participant data meta-analysis (IPD-MA) represents a methodological advance over conventional meta-analyses that might address the above-mentioned issues (Tierney et al., 2023). In an IPD-MA, raw data at the level of the individual participant are used for analyses instead of the results reported in publications, as is the case for conventional study-level meta-analyses (Burke et al., 2017). In IPD-MA, the same analytic procedure can be used across studies and therefore can

overcome the heterogeneity of analytic procedures and reporting strategies used in the individual studies (Tierney et al., 2023).

Some investigators have reported that treatment outcomes for depression were significantly predicted by only one of the Horowitz model's orthogonal interpersonal dimensions of interpersonal problems, namely either communion (Dinger et al., 2013) or agency (Sayegh et al., 2020; Zeeck et al., 2016). Others have failed to find such effects (Altenstein-Yamanaka et al., 2017; Dinger et al., 2013; Gómez Penedo et al., 2020; Renner et al., 2012), and many have not assessed them at all. An IPD-MA approach is a particularly suitable way to examine these questions as access to raw data provides an opportunity to analyze associations with these dimensions even when they were not reported in the original publications.

In the current study we conducted an IPD-MA of the association between patients' baseline interpersonal problems and treatment outcomes in studies analyzing effects of treatments for depression. By using this procedure, we sought to reduce potential biases due to the wide methodological and analytic variability observed in the literature. We aimed to further reduce heterogeneity by focusing on depressive disorders only (the only other such meta-analysis included both depressive and anxiety disorders; i.e., Gómez Penedo & Flückiger, 2023). In addition, we also focused on six empirically-supported depression treatments (cognitive behavioral therapy [CBT], interpersonal psychotherapy [IPT], short-term psychodynamic psychotherapy [STPP], psychodynamic-interpersonal therapy [PIT], behavioral activation [BA], and antidepressant medication [ADM]), which are all included in major practice guidelines for depression treatment and frequently used in clinical practice (American Psychological Association, 2019; Malhi et al., 2022; Norcross et al., 2023). Finally, we aimed to add to the existing literature on overall interpersonal distress by additionally examining the interpersonal dimensions of agency and communion as predictors of outcome. That is, we hypothesized that higher overall interpersonal distress (Hypothesis #1), higher negative communion (Hypothesis #2), and higher negative agency (Hypothesis #3) will predict worse treatment outcome in terms of depression severity.

## 2. Methods

### 2.1. Design

The current study was pre-registered ([doi:10.17605/OSF.IO/U46T7](https://doi.org/10.17605/OSF.IO/U46T7)) and is reported according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses – Individual Participant Data (PRISMA-IPD) guidelines (Stewart et al., 2015). This study drew on data collected for two IPD-MA projects with considerable similarity in methods. The first was aimed at examining different aspects of short-term psychodynamic psychotherapy (STPP) for depression efficacy and included studies using standardized outcome measures in depressed adult patients receiving STPP (Driessen et al., 2018, 2020; Driessen, Fokkema, et al., 2022; Wienicke et al., 2023). The second project was aimed at identifying factors associated with efficacy of six depression treatments (CBT, IPT, STPP, PIT, BA, and ADM) including randomized clinical trials comparing at least two of these treatments in the acute phase among depressed adults (Driessen et al., 2023).

### 2.2. Search strategy

Relevant studies for the first project were identified via systematic literature searches in the online databases PubMed, PsycINFO, Embase.com, Web of Science, and Cochrane's Central Register of Controlled Trials. Additionally, databases of grey literature (GLIN) and digital dissertations (ProQuest), and a clinical trial register (ISRCTNR) were searched. The search strings comprised index and free-text terms with synonyms for "Psychodynamic Psychotherapy" and "Depression." Additionally, relevant studies were identified via references of STPP efficacy reviews, consultations with psychodynamic researchers, and the

METAPSY database of randomized depression psychotherapy trials (<https://www.metapsy.org/>). These searches were performed on June 17th, 2017, while they were updated until January 1st, 2024.

To identify more recent STPP for depression studies and relevant studies for the second project, the METAPSY database was searched from inception to May 1st, 2024. This database was developed through comprehensive literature searches in PubMed, PsycINFO, Embase.com, and Cochrane Library. It has been used in a series of meta-analyses and is updated every four months. The search strings used a combination of index terms and free-text words indicative of depression and psychotherapies, with filters for randomized clinical trials. For the exact terms used in the search strings we refer to: <https://osf.io/nv3ea/>. To identify studies that might have been missed, we checked the references of prior reviews and meta-analyses and reference lists of included studies. Furthermore, we contacted psychotherapy listservs to request ongoing or unpublished studies, and studies that were missed (Driessen et al., 2021; Driessen, Cohen, et al., 2022).

Two raters independently screened all records and full-text papers. Disagreements were resolved through consensus in each phase.

### 2.3. Study eligibility criteria

Studies that met the inclusion criteria for one of the two IPD-MA projects and administered the Inventory of Interpersonal Problems (IIP) to patients before the start of treatment were included in the study. No restrictions were placed concerning the years when the study was conducted, or with regard to publication language, date, or status.

Psychotherapies in any delivery format (e.g., face-to-face, telephone, or video-conferencing), were included as long as a clinician delivered the therapy synchronously. Thus, unguided bibliotherapy or unguided internet interventions were excluded. Guided bibliotherapy, guided internet therapy, or other guided self-help formats were included if provided by a trained health care worker. Restrictions were not placed on the setting in which treatment was delivered (e.g., primary care, outpatient, and inpatient psychiatric care), the number of sessions, and the duration of follow-up. For a detailed definition of the included interventions, see Driessen et al. (2018, 2023).

### 2.4. Data extraction (selection and coding)

A multi-step protocol was applied to contact authors and invite them to share their studies' datasets. The following participant-level data items were requested: treatment condition, all outcome variables assessed before, during, and after treatment (with item-level data for depression outcome measures), and all potential moderator variables assessed in the study. The primary study's authors anonymized the participant-level dataset before transferring it.

We next checked whether the received IPD-MA matched the data reported in the publications and whether outcome and moderator variables had out-of-range, invalid, or inconsistent scores. Discrepancies were resolved with the original authors.

We extracted the following study-level characteristics from the publications: country in which the study took place, treatment types, number of treatment sessions, research design, IIP version used and language, and depressive outcome measure.

In this study, we did not include quality ratings in the coding process. In contrast with meta-analyses focusing on treatment efficacy, quality ratings are not common in meta-analyses of correlations. There are also no accepted procedures to conduct quality ratings in this context. Although correlational meta-analyses are prone to bias (see e.g., Stanley et al., 2024), working with IPD (instead of study-level data extracted from publications) mitigated some of the main sources of bias in correlation meta-analysis due to small sample sizes and the use of z-transformed data.

## 2.5. Targeted participants/population

Participants were required to meet specified diagnostic criteria (e.g., Diagnostic and Statistical Manual of Mental Disorders [DSM]) for major depressive disorder or another unipolar mood disorder assessed by means of a semi-structured interview or clinicians' assessment, or to present an elevated score above the 'no depression' cut-off on an evaluator-assessed, clinician-assessed, or self-reported measure of depression. Comorbid mental and somatic disorders were allowed. Participants were required to be at least 18 years old, and studies concerning older adult populations were included. Participant criteria were assessed at the study level (Driessen et al., 2018, 2023).

## 2.6. Measures

### 2.6.1. Interpersonal problems measure

Interpersonal problems were required to be assessed at baseline with the Inventory of Interpersonal Problems (IIP; Horowitz et al., 1988, Horowitz et al., 2000). This widely used self-report instrument measures interpersonal distress in terms of behavioral excesses (e.g., "I am too aggressive toward other people.") or inhibitions (e.g., "It is hard for me to feel close to other people"), following Horowitz' (Horowitz, 2004; Horowitz & Vitkus, 1986) model of interpersonal problems. The items are rated on a 5-point Likert-like scale ranging from 0 (*not at all*) to 4 (*extremely*) and describe to what degree the subject experiences distress due to these interpersonal excesses or inhibitions (Horowitz et al., 2000). The IIP has various formats (for a revision see e.g., Hughes & Barkham, 2005). The original IIP has 127 items distributed among six subscales (i.e., hard to be assertive, hard to sociable, hard to be intimate, hard to be submissive, too responsible, and too controlling) (Horowitz et al., 1988). The IIP-64 (Alden et al., 1990), integrated by 64 items derivative from the original IIP, proposed a circumplex structure that identifies eight different interpersonal problems subtypes (i.e., domineering, intrusive, overly nurturant, exploitable, non-assertive, socially inhibited, cold, and vindictive). Those subtypes of IIP-64 result from the combination of the main interpersonal dimensions of communion (i.e., needs to build close relationships) and agency (i.e., needs to influence in other). The IIP-32 is a briefer, 32-item version of the IIP grounded also on the circumplex model (Horowitz et al., 2000; Soldz et al., 1995). In all the versions of the IIP, the unweighted aggregation of all the interpersonal problem items provides a measure of overall interpersonal distress (Grosse Holtforth et al., 2006). The orthogonal interpersonal dimensions of agency and communion are computed by the following formulas based on different interpersonal subtypes (Ruiz et al., 2004): Communal =  $0.25 * [\text{overly nurturant} - \text{cold} + 0.71 * (\text{intrusive} - \text{vindictive} - \text{socially inhibited} + \text{exploitable})]$ ; Agency =  $0.25 * [\text{domineering} - \text{non-assertive} + 0.71 * (\text{intrusive} + \text{vindictive} - \text{socially inhibited} - \text{exploitable})]$ . The different versions of the IIP have shown good test-retest reliability, predictive validity, and internal consistency (IIP-127:  $\alpha = 0.82\text{--}0.94$ , IIP-64:  $\alpha = 0.72\text{--}0.85$ , IIP-32:  $\alpha = 0.72\text{--}0.88$ , IIP-SC:  $\alpha = 0.69\text{--}0.84$ ; Hughes & Barkham, 2005).

### 2.6.2. Outcome variables

Depressive symptom severity level at treatment completion and follow-up constituted the pre-specified outcomes for this study, as symptom reduction is considered to be the main aim of the acute-phase depression treatments. As an index of patient outcome, we included specific depressive symptom severity measures such as the Beck Depression Inventory (BDI; Beck et al., 1961), the Beck Depression Inventory-II (Beck et al., 1996), the Hamilton Depression Rating Scale (HAM—D; Hamilton, 1960), Patient Health Questionnaire-9 (PHQ-9; Kroenke et al., 2001) as well as depressive subscales from general psychopathology measures such as the Brief Symptom Inventory (BSI; Derogatis, 1993) and the Symptom Checklist (SCL-90-R; Derogatis, 1994). All the specific symptoms severity measures showed good psychometric properties (BDI-I:  $\alpha = 0.88$ , Beck & Steer, 1984; BDI-II:  $\alpha =$

$0.83\text{--}0.96$ , Wang & Gorenstein, 2013; HAM—D: inter-rater agreement  $r = 0.90$ , Hamilton, 1960; PHQ-9:  $\alpha = 0.89$ , Kroenke et al., 2001). Good psychometric properties were also observed in the depressive subscales of BSI ( $\alpha = 0.85$ , Derogatis, 1993) and SCL-90-R ( $\alpha = 0.90$ , Derogatis, 1994).

## 2.7. Measures of effect size

We reported standardized coefficients of the effect of each interpersonal problems index on patient outcome. To enhance interpretability, we transformed the standardized coefficients into  $r$  coefficients.

## 2.8. Statistical analyses

First, we calculated the correlations among the three interpersonal problems indices at baseline (i.e., overall interpersonal problems, communion dimension, and agency communion), as well as the correlations between these indices and baseline depression severity.

We then conducted one-stage IPD-MA (Burke et al., 2017) using mixed models with a three-level structure, with different measures (Level-1) nested within patients (Level-2) nested within studies (Level-3) (Raudenbush & Bryk, 2002). First, we conducted unconditional models with standardized depression severity as outcome and only adjusting for its baseline levels. By computing intraclass correlation coefficients, these models allowed us to estimate the variance of outcome explained by the patient (Level-2) and study level (Level-3). Separate unconditional models were conducted for depression severity at post-treatment, 12-month follow-up, and 24-month follow-up.

Then, we conducted separate conditional models for each of the three predictors (i.e., overall interpersonal distress, communion dimension, and agency dimension) with depression severity as the dependent variable, adjusting for baseline depression severity. Cases with missing data on baseline IIP scores were excluded, while cases with outcome information in at least one of the outcome measures were included in the multilevel model. As studies varied on when the last follow-up outcome was assessed (i.e., 3-month, 6-month, 12-month, etc.), in cases of lack of information at 12-month follow-up we carried forward the last follow-up information assessed before 12-months. No post-treatment scores were carried forward in the 12-month analyses. Likewise, in cases where 24-months outcome information was missing we carried forward the last follow-up information assessed after 12-months follow-up (i.e., and before 24-months follow-up).

To have a common scale across studies, all predictors and outcome variables were standardized using  $z$ -scores within-study before being introduced in the models. Due to the multiple models conducted we adjusted the probability level to 0.005 (i.e.,  $0.05/9$ ) using Bonferroni correction.

As pre-registered moderation analysis, we tested if treatment condition moderated the interpersonal problems-outcome association. As the most frequent interventions included within the trials were STPP, on a first model we compared interpersonal problems-outcome associations in STPP versus other type of treatments. In a second model we tested if psychotherapeutic interventions versus pharmacotherapeutic treatments differed in the association between interpersonal problems and outcome. Considering that outcome measures differed in their degree of specificity across trials, we also tested, as pre-registered moderation analysis, differential effects of specific depressive symptom measure versus depression subscales within general psychopathology measures.

Finally, as explorative (i.e., not pre-registered) sensitivity analyses, we tested if patients' interpersonal problems indices predicted the likelihood of measurement drop-out before treatment termination using two-level (i.e., patients nested within studies) generalized linear mixed models. Since (early) drop-out was not consistently assessed in the primary studies, we used measurement drop-out as a proxy of treatment drop-out. Although the correlation (Matthews, 1975) between treatment and measurement drop-out was high ( $\phi = 0.59$ ,  $\chi^2(1) = 291.86$ ,  $p <$



.001) with a large effect size (Cohen, 1988) in the four studies that assessed treatment drop-out ( $n = 844$ ; Barber et al., 2012; Joyce, 2002; McBride et al., 2006; Menchetti et al., 2014), it did not meet usual correlational thresholds for convergent validity ( $\sim 0.85$ ; Freiberg Hoffmann et al., 2014). Hence, the results from the (non-preregistered) exploratory analyses evaluating the association of interpersonal problems and measurement drop-out should be interpreted cautiously.

The model equations are provided in the supplemental material. All the multilevel analyses were performed in the R package *lme4* (Bates et al., 2015). Furthermore, for each conditional multilevel model conducted, we performed post-hoc power analyses with the R package *simr* (Green & MacLeod, 2016) using 1000 simulations to determine the minimum sample required to reach a power = 0.80 ( $\alpha = 0.05$ ).

### 3. Results

#### 3.1. Sample descriptives

A total of 10 datasets were included totaling  $n = 1349$  participants. However, 67 participants were excluded due to missing data in baseline IIP (i.e., final  $n = 1282$  participants). The post-hoc power analyses for the conditional models showed that the minimum sample required to reach a power = 0.80 ( $\alpha = 0.05$ ) when estimating interpersonal problems association with outcome was  $n = 500$  for post-treatment,  $n = 270$  for 12-month follow-up, and  $n = 240$  for 24-month follow-up. Descriptions of the included studies and their characteristics are presented in Table 1. The mean number of participants per study was 128.20, ranged from 27 to 261. The gender distribution was 61.1 % female (ranged from 34.3 % to 74.3 % female), and the mean participants' age was 40.91 ( $SD = 12.35$ ) years, ranged from 34.81 to 44.91 years. In addition, it was reported in 7 datasets ( $N = 871$ ) that 38.0 % of patients had reached a college or higher educational level. Treatment orientations included psychodynamic therapies (31.4 %), interpersonal therapies (20.7 %), cognitive-behavioral therapy (17.9 %), pharmacotherapy (17.9 %), other/various orientations (6.2 %), and psychodynamic-interpersonal psychotherapy (5.9 %). Eight datasets were gathered under randomized controlled trial conditions, while two datasets came from open/naturalistic studies. Studies were conducted in Canada ( $k = 4$ ), United Kingdom ( $k = 3$ ) Netherlands, United States, Italy (each  $k = 1$ ). Depression outcome was assessed by: BDI I or II ( $k = 7$ ); HAM-D ( $k = 5$ ) in its versions of 17, 21 and 29 items; BSI ( $k = 4$ ); SCL-90-R ( $k = 2$ ); PHQ-9 ( $k = 1$ ).

The duration of the treatments varied among the different datasets (see Table 1). Regarding follow-up, based on the ITT approach used (see Methods section), the mean time to the last follow-up at 12-months post-treatment was 10.50 months ( $SD = 2.77$ ,  $k = 7$ ) and between 13 and 24-months post-treatment was 19.43 months ( $SD = 5.20$ ,  $k = 4$ ). In addition, the percentage drop-out ranged from 0.0 % to 59.3 %, with an overall mean of 21.2 %.

The 127-item ( $k = 2$ ), 64-item ( $k = 5$ ) and 32-item ( $k = 3$ ) versions of the IIP were used, mainly in English ( $k = 8$ ). As the 127-item version of IIP is not structured within the circumplex model, the items from the 64-version were extracted in those cases to calculate overall interpersonal distress and interpersonal dimension indexes (Alden et al., 1990). The mean value of the IIP total overall interpersonal distress scale was 1.55 ( $SD = 0.54$ ) points with a distribution of 1.30 to 1.75 among the datasets. This is in line with the norms reported for clinical samples in the US ( $M = 1.45$ ;  $SD = 0.60$ ; Woodward et al., 2005). Furthermore, the mean values for the interpersonal dimension of communion were 0.13 ( $SD = 0.53$ ; the distribution ranged from  $-0.05$  to  $0.23$ ) and for the interpersonal dimension of agency were  $-0.54$  ( $SD = 0.52$ ; the distribution ranged from  $-0.98$  to  $-0.36$ ). Correlations among the targeted variables at measured at baseline are presented at Table 2.

#### 3.2. Unconditional models predicting outcome adjusting for baseline levels

Results of the three-level unconditional models (i.e., only with baseline levels as a covariate) are presented in Table 3. At post-treatment, the study level explained a small percentage of outcome variance (5.5 %), while most of the variance was explained by the patient level (67.6 %). At 12-months and 24-months follow-up, there was a lower percentage of variance explained by the study level variability (3.7 % and 4.2 %, respectively). Furthermore, 72.1 % of outcome variance at 12-month follow-up and 82.1 % at 24-month follow-up was explained by patients' variability.

#### 3.3. Conditional models with overall interpersonal distress as predictor of treatment outcome (Hypothesis #1)

Full results of the conditional models are presented in Table 4. Baseline overall interpersonal distress significantly predicted post-treatment depressive symptoms when adjusting for baseline outcome levels ( $\gamma_{010} = 0.11$ ,  $SE = 0.03$ ,  $CI_{95}[0.06, 0.16]$ ,  $t(1060.05) = 4.20$ ,  $p < .001$ ,  $r = 0.11$ ).<sup>1</sup> Baseline overall interpersonal distress also significantly predicted outcome at 12-month follow-up ( $\gamma_{010} = 0.17$ ,  $SE = 0.04$ ,  $CI_{95}[0.08, 0.25]$ ,  $t(478.89) = 3.71$ ,  $p < .001$ ,  $r = 0.17$ ) and 24-months follow-up ( $\gamma_{010} = 0.16$ ,  $SE = 0.05$ ,  $CI_{95}[0.05, 0.26]$ ,  $t(253.67) = 2.96$ ,  $p = .003$ ,  $r = 0.16$ ). In all the models, greater overall interpersonal distress was associated with worse post-treatment severity, supporting Hypothesis #1.

#### 3.4. Conditional models with interpersonal communion as predictor of treatment outcome (Hypothesis #2)

The results of the conditional models including baseline interpersonal communion as a predictor are fully presented at Table 5. The models showed non-significant predictive effects of baseline communion on depressive symptoms at post-treatment ( $\gamma_{010} = -0.002$ ,  $SE = 0.03$ ,  $CI_{95}[-0.05, 0.05]$ ,  $t(975.54) = -0.07$ ,  $p = .946$ ,  $r = -0.002$ ). Additionally, the models did not reveal an association of communion and long-term outcomes at 12-months follow-up ( $\gamma_{010} = -0.009$ ,  $SE = 0.05$ ,  $CI_{95}[-0.10, 0.08]$ ,  $t(435.09) = -0.19$ ,  $p = .852$ ,  $r = -0.009$ ) and 24-months follow-up ( $\gamma_{010} = -0.04$ ,  $SE = 0.05$ ,  $CI_{95}[-0.14, 0.06]$ ,  $t(235.58) = -0.78$ ,  $p = .437$ ,  $r = -0.04$ ). Results from these models did not support Hypothesis #2.

#### 3.5. Conditional models with interpersonal agency as predictor of treatment outcome (Hypothesis #3)

The models exploring the predictive effects of baseline agency on outcome are presented in Table 6. There were no significant effects of baseline agency on post-treatment depressive symptoms ( $\gamma_{010} = -0.03$ ,  $SE = 0.03$ ,  $CI_{95}[-0.08, 0.02]$ ,  $t(979.71) = -1.07$ ,  $p = .287$ ,  $r = -0.03$ ). Furthermore, interpersonal agency did not predict long-term outcome at 12-months ( $\gamma_{010} = -0.03$ ,  $SE = 0.05$ ,  $CI_{95}[-0.12, 0.06]$ ,  $t(446.88) = -0.63$ ,  $p = .531$ ,  $r = -0.03$ ) or at 24-months follow-up ( $\gamma_{010} = -0.05$ ,  $SE = 0.05$ ,  $CI_{95}[-0.16, 0.05]$ ,  $t(240.67) = -0.98$ ,  $p = .329$ ,  $r = -0.05$ ). Results from these models did not support Hypothesis #3.

<sup>1</sup> As an exploratory, not pre-registered, analysis, we tested if baseline depression severity predicted post-treatment interpersonal distress whilst adjusting for baseline interpersonal distress levels. Due to lack of variability in the outcome variable at the patient level and study levels, multilevel models did not converge. Hence, we ran an ordinary least squared regression that showed a non-significant association between baseline depression severity and post-treatment interpersonal distress ( $B = 0.07$ ,  $SE = 0.04$ ,  $CI_{95}[-0.01, 0.15]$ ,  $t(1006) = 1.79$ ,  $p = .07$ ).

**Table 1**  
Study characteristics of the included datasets.

| First-Author                    | N   | Females<br>rate | Age   | Type                | Duration  | Design       | Country     | IIP                |              |          | IIP            |                 |                 | Depression<br>Outcome    | TOT - DO    | AG - DO     | COM - DO    | Last<br>Follow-<br>up<br>0–12<br>month | Last<br>Follow-<br>up<br>13–24<br>month | Dropout<br>rate |
|---------------------------------|-----|-----------------|-------|---------------------|-----------|--------------|-------------|--------------------|--------------|----------|----------------|-----------------|-----------------|--------------------------|-------------|-------------|-------------|----------------------------------------|-----------------------------------------|-----------------|
|                                 |     |                 |       |                     |           |              |             | IIP                | IIP          | IIP      | TOT            | AG              | COM             |                          |             |             |             |                                        |                                         |                 |
| (Publication<br>year)           |     |                 |       |                     |           |              |             | Scale              | Version      | Language | M (SE)         | M (SE)          | M (SE)          | Measure                  | Correlation | Correlation | Correlation | M (SE)                                 | M (SE)                                  |                 |
| Barber et al.<br>(2012)         | 100 | 0.60            | 37.20 | ADM,<br>STPP        | 16 w      | RCT          | USA         | TOT                | 64<br>items  | English  | 1.55<br>(0.53) | −0.47<br>(0.53) | −0.05<br>(0.53) | HAMD-17,<br>BDI-I        | 0.15**      | −0.05       | −0.11       | 8.62<br>(2.92)                         | 20.24<br>(3.95)                         | 0.15            |
| Barkham, Rees,<br>et al. (1996) | 33  | 0.67            | 38.31 | CBT,<br>PIT         | 8 s, 16 s | RCT          | UK          | TOT,<br>COM,<br>AG | 127<br>items | English  | 1.63<br>(0.54) | −0.64<br>(0.52) | 0.03<br>(0.43)  | BDI-I, SCL-<br>90-R*     | 0.26**      | 0.05        | −0.03       | 10.84<br>(3.07)                        | –                                       | 0.15            |
| Fonagy et al.<br>(2020)         | 137 | 0.34            | 37.00 | CBT,<br>STPP,<br>OT | 6 m       | RCT          | UK          | TOT,<br>COM,<br>AG | 64<br>items  | English  | 1.75<br>(0.49) | −0.62<br>(0.53) | 0.08<br>(0.47)  | HAMD-17,<br>BDI-II, BSI* | 0.18**      | −0.10       | −0.03       | 12.00<br>(0.00)                        | –                                       | 0.34            |
| Johansson et al.<br>(2014)      | 231 | 0.59            | 41.72 | STPP                | 2–100 s   | Open trial   | Canada      | TOT                | 32<br>items  | English  | 1.62<br>(0.61) | −0.43<br>(0.60) | 0.12<br>(0.56)  | BSI*                     | 0.58**      | 0.05        | −0.06       | –                                      | –                                       | 0.59            |
| Joyce (2002)                    | 27  | 0.63            | 34.81 | STPP                | –         | Naturalistic | Canada      | TOT,<br>COM,<br>AG | 64<br>items  | English  | 1.30<br>(0.47) | −0.52<br>(0.47) | 0.10<br>(0.39)  | BDI-II, BSI*             | 0.53**      | 0.04        | 0.11        | –                                      | –                                       | 0.00            |
| Lemmens et al.<br>(2015)        | 150 | 0.67            | 41.10 | CBT,<br>IPT         | 12–20 s   | RCT          | Netherlands | TOT,<br>COM,<br>AG | 64<br>items  | Dutch    | 1.35<br>(0.46) | −0.56<br>(0.42) | 0.11<br>(0.40)  | BDI-II, BSI*             | 0.42**      | −0.20**     | 0.00        | 12.00<br>(0.00)                        | 24.00<br>(0.00)                         | 0.11            |
| McBride et al.<br>(2006)        | 167 | 0.64            | 40.73 | CBT,<br>ADM,<br>IPT | 16–20 w   | RCT          | Canada      | TOT,<br>COM,<br>AG | 32<br>items  | English  | 1.58<br>(0.51) | −0.70<br>(0.54) | 0.23<br>(0.64)  | HAMD-29,<br>BDI-II       | 0.08        | −0.03       | 0.09        | 7.99<br>(3.57)                         | 12.83<br>(0.68)                         | 0.10            |
| Menchetti et al.<br>(2014)      | 261 | 0.74            | 44.91 | ADM,<br>IPT         | 2 m       | RCT          | Italy       | TOT,<br>COM,<br>AG | 64<br>items  | Italian  | 1.45<br>(0.53) | −0.36<br>(0.38) | 0.18<br>(0.51)  | HAMD-21                  | 0.30**      | −0.14**     | −0.11       | –                                      | –                                       | 0.09            |
| Shapiro et al.<br>(1994)        | 116 | 0.53            | 40.52 | CBT,<br>PIT         | 8 s, 16 s | RCT          | UK          | TOT,<br>COM,<br>AG | 127<br>items | English  | 1.60<br>(0.44) | −0.61<br>(0.50) | 0.18<br>(0.49)  | BDI-I, SCL-<br>90-R      | 0.33**      | −0.20**     | 0.07        | 10.99<br>(2.85)                        | –                                       | 0.03            |
| Town et al.<br>(2017)           | 60  | 0.63            | 41.55 | STPP,<br>OT         | 1–20 s    | RCT          | Canada      | TOT,<br>COM,<br>AG | 32<br>items  | English  | 1.64<br>(0.53) | −0.98<br>(0.53) | 0.08<br>(0.63)  | HAMD-17,<br>PHQ-9        | 0.22**      | −0.07       | −0.02       | 7.47<br>(1.16)                         | 14.00<br>(0.00)                         | 0.13            |

Note. N = patient sample size of the session-by-session analyses, Last Follow-up = time of the last observation conducted in the follow-up, IIP = Inventory of Interpersonal Problems, TOT = total interpersonal distress, AG = interpersonal dimension of agency, COM = interpersonal dimension of communion, ADM = Antidepressant Medications, STPP = Short-Term Psychodynamic Psychotherapy, CBT = Cognitive Behavioral Therapy, IPT = Interpersonal Psychotherapy, PIT = Psychodynamic-Interpersonal Therapy, OT = Other Therapies, Duration: Prescriptive duration of a therapy; m = months, w = weeks, s = sessions, d = days, RCT = Randomized Clinical Trial, DO = Depression Outcome, HAMD-17 = Hamilton Depression Rating Scale - 17 (patient selfreport), HAMD-21 = Hamilton Depression Rating Scale - 21 (patient selfreport), HAMD-29 = Hamilton Depression Rating Scale - 29 (patient selfreport), BDI-I = Beck Depression Inventory I, BDI-II = Beck Depression Inventory II, BSI = Brief Symptom Inventory, SCL-90-R = Symptom Checklist - 90 - Revised, PHQ-9 = Patient Health Questionnaire - 9. \* only depression subscale, \*\*  $p < .05$ .

Table 2

Correlation among measures of initial depression and measures of interpersonal distress.

|         | BD       | IIP-TOT  | IIP-AG   |
|---------|----------|----------|----------|
|         | <i>r</i> | <i>r</i> | <i>r</i> |
| IIP-TOT | 0.29*    |          |          |
| IIP-AG  | −0.09*   | −.25*    |          |
| IIP-COM | −0.03    | −0.06    | −0.08*   |

Note. BD = Baseline Depression, IIP = Inventory of Interpersonal Problems, TOT = total interpersonal distress, AG = interpersonal dimension of agency, COM = interpersonal dimension of communion, *r* = Pearson correlation coefficient. \* *p* < .01.

Table 3

Results of the three-level unconditional models estimating outcome at post-treatment, 12-months follow-up and 24-months follow-up, adjusted for baseline severity.

| Parameters                       | $\gamma$ | SE   | 95 % CI        | <i>p</i> |
|----------------------------------|----------|------|----------------|----------|
| Post-treatment outcome model     |          |      |                |          |
| Intercept                        | −0.61    | 0.07 | [−0.76, −0.46] | <0.001*  |
| Baseline severity                | 0.35     | 0.03 | [0.30, 0.41]   | <0.001*  |
| 12-month follow-up outcome model |          |      |                |          |
| Intercept                        | −0.46    | 0.09 | [−0.66, −0.27] | 0.002*   |
| Baseline severity                | 0.16     | 0.04 | [0.08, 0.25]   | <0.001*  |
| 24-month follow-up outcome model |          |      |                |          |
| Intercept                        | −0.71    | 0.11 | [−0.95, −0.48] | 0.003*   |
| Baseline severity                | 0.11     | 0.05 | [0.02, 0.21]   | 0.020    |

Note. \* Effect of predictors is significant at  $\alpha = 0.005$  (Bonferroni correction: 0.05/9 = 0.005).

Table 4

Results of the conditional three-level models predicting outcome by interpersonal distress.

| Parameters             | $\gamma$ | SE   | 95 % CI        | <i>p</i> |
|------------------------|----------|------|----------------|----------|
| Posttreatment          |          |      |                |          |
| Intercept              | −0.59    | 0.07 | [−0.74, −0.44] | <0.001*  |
| Baseline severity      | 0.32     | 0.03 | [0.27, 0.38]   | <0.001*  |
| Interpersonal distress | 0.11     | 0.03 | [0.06, 0.16]   | <0.001*  |
| 12-month follow-up     |          |      |                |          |
| Intercept              | −0.44    | 0.10 | [−0.64, −0.23] | 0.004*   |
| Baseline severity      | 0.13     | 0.04 | [0.04, 0.22]   | 0.004*   |
| Interpersonal distress | 0.17     | 0.04 | [0.08, 0.25]   | <0.001*  |
| 24-month follow-up     |          |      |                |          |
| Intercept              | −0.70    | 0.12 | [−0.97, −0.45] | 0.006    |
| Baseline severity      | 0.08     | 0.05 | [−0.01, 0.18]  | 0.086    |
| Interpersonal distress | 0.16     | 0.05 | [0.05, 0.26]   | 0.003*   |

Note. \* Effect of predictors is significant at  $\alpha = 0.005$  (Bonferroni correction: 0.05/9 = 0.005).

3.6. Moderators of overall interpersonal distress and outcomes association

We did not find a significant interaction effect between the type of outcome measurement (i.e., specific depression measures versus depression subscales of generic measures) and overall interpersonal distress on post-treatment outcome ( $\gamma_{030} = 0.02$ ,  $SE = 0.03$ ,  $CI_{95}[-0.03, 0.08]$ ,  $t(848.73) = 0.83$ ,  $p = .410$ ,  $r = 0.02$ ), 12-month follow-up outcome ( $\gamma_{030} = 0.05$ ,  $SE = 0.04$ ,  $CI_{95}[-0.03, 0.12]$ ,  $t(438.90) = 1.20$ ,  $p = .232$ ,  $r = 0.05$ ), or 24-month follow-up outcome ( $\gamma_{030} = 0.02$ ,  $SE = 0.04$ ,  $CI_{95}[-0.05, 0.10]$ ,  $t(213.38) = 0.59$ ,  $p = .555$ ,  $r = 0.02$ ).

Furthermore, treatment with psychodynamic therapy versus other

Table 5

Results of the conditional three-level models predicting outcome by interpersonal communion.

| Parameters              | $\gamma$ | SE   | 95 % CI        | <i>p</i> |
|-------------------------|----------|------|----------------|----------|
| Posttreatment           |          |      |                |          |
| Intercept               | −0.61    | 0.07 | [−0.76, −0.46] | <0.001*  |
| Baseline severity       | 0.35     | 0.03 | [0.30, 0.41]   | <0.001*  |
| Interpersonal communion | −0.002   | 0.03 | [−0.05, 0.05]  | 0.946    |
| 12-month follow-up      |          |      |                |          |
| Intercept               | −0.46    | 0.09 | [−0.65, −0.27] | 0.002*   |
| Baseline severity       | 0.16     | 0.04 | [0.08, 0.25]   | <0.001*  |
| Interpersonal communion | −0.009   | 0.05 | [−0.10, 0.08]  | 0.852    |
| 24-month follow-up      |          |      |                |          |
| Intercept               | −0.71    | 0.11 | [−0.96, −0.48] | 0.003*   |
| Baseline severity       | 0.11     | 0.05 | [0.02, 0.21]   | 0.021    |
| Interpersonal communion | −0.04    | 0.05 | [−0.14, 0.06]  | 0.437    |

Note. \* Effect of predictors is significant at  $\alpha = 0.005$  (Bonferroni correction: 0.05/9 = 0.005).

Table 6

Results of the conditional three-level models predicting outcome by interpersonal agency.

| Parameters           | $\gamma$ | SE   | 95 % CI        | <i>p</i> |
|----------------------|----------|------|----------------|----------|
| Posttreatment        |          |      |                |          |
| Intercept            | −0.61    | 0.07 | [−0.76, −0.46] | <0.001*  |
| Baseline severity    | 0.35     | 0.03 | [0.29, 0.41]   | <0.001*  |
| Interpersonal agency | −0.03    | 0.03 | [−0.08, 0.02]  | 0.287    |
| 12-month follow-up   |          |      |                |          |
| Intercept            | −0.46    | 0.09 | [−0.66, −0.26] | 0.002*   |
| Baseline severity    | 0.16     | 0.04 | [0.07, 0.25]   | <0.001*  |
| Interpersonal agency | −0.03    | 0.04 | [−0.12, 0.06]  | 0.531    |
| 24-month follow-up   |          |      |                |          |
| Intercept            | −0.71    | 0.11 | [−0.96, −0.47] | 0.004*   |
| Baseline severity    | 0.11     | 0.05 | [0.01, 0.20]   | 0.027    |
| Interpersonal agency | −0.05    | 0.05 | [−0.16, 0.05]  | 0.329    |

Note. \* Effect of predictors is significant at  $\alpha = 0.005$  (Bonferroni correction: 0.05/9 = 0.005).

treatments did not moderate the relationship between overall interpersonal distress and post-treatment outcome ( $\gamma_{030} = -0.03$ ,  $SE = 0.06$ ,  $CI_{95}[-0.16, 0.09]$ ,  $t(996.48) = -0.55$ ,  $p = .581$ ,  $r = -0.03$ ), 12-month follow-up outcome ( $\gamma_{030} = -0.21$ ,  $SE = 0.12$ ,  $CI_{95}[-0.44, 0.02]$ ,  $t(456.49) = -1.82$ ,  $p = .070$ ,  $r = -0.21$ ), or 24-month follow-up outcome ( $\gamma_{030} = 0.14$ ,  $SE = 0.15$ ,  $CI_{95}[-0.16, 0.43]$ ,  $t(241.04) = 0.94$ ,  $p = .349$ ,  $r = 0.14$ ).

Finally, when comparing psychological versus pharmacological treatments, the differential overall interpersonal distress effects by these two types of treatments did not reach the Bonferroni corrected significance level at post-treatment outcome ( $\gamma_{210} = -0.07$ ,  $SE = 0.06$ ,  $CI_{95}[-0.20, 0.05]$ ,  $t(1066.14) = -1.11$ ,  $p = .266$ ,  $r = -0.07$ ), 12-month follow-up outcome ( $\gamma_{210} = -0.19$ ,  $SE = 0.17$ ,  $CI_{95}[-0.53, 0.15]$ ,  $t(511.88) = -1.10$ ,  $p = .272$ ,  $r = -0.19$ ), or 24-month follow-up outcome ( $\gamma_{210} = -0.42$ ,  $SE = 0.17$ ,  $CI_{95}[-0.75, -0.09]$ ,  $t(249.69) = -2.50$ ,  $p = .013$ ,  $r = -0.40$ ).

3.7. Exploratory analysis of interpersonal problems as predictors of measurement drop-out

The exploratory models suggested that overall interpersonal distress at baseline was significantly associated with the likelihood of measurement drop-out ( $\gamma_{10} = 0.16$ ,  $SE = 0.06$ ,  $CI_{95}[0.04, 0.28]$ ,  $z = 2.58$ ,  $p = .010$ ). Higher overall interpersonal distress was related to a higher

chance of measurement drop-out. When adjusting for baseline levels in the outcome variables the effect of overall interpersonal distress on measurement drop-out remained significant ( $\gamma_{10} = 0.13$ ,  $SE = 0.07$ ,  $CI_{95}[0.002, 0.26]$ ,  $z = 1.99$ ,  $p = .047$ ). Measurement drop-out was not related to patients' interpersonal agency ( $\gamma_{10} = -0.03$ ,  $SE = 0.06$ ,  $CI_{95}[-0.15, 0.09]$ ,  $z = -0.49$ ,  $p = .627$ ) or communion ( $\gamma_{10} = -0.05$ ,  $SE = 0.06$ ,  $CI_{95}[-0.17, 0.07]$ ,  $z = -0.86$ ,  $p = .389$ ).

#### 4. Discussion

The findings of this IPD-MA analysis supported the pre-registered hypotheses that overall interpersonal distress in depressive patients was a significant predictor of treatment outcome at post-treatment, 12-months follow-up, and 24-months follow-up. Greater overall interpersonal distress was associated with worse outcomes. However, contrary to some of our hypotheses, no significant effects of baseline interpersonal communion or agency on outcome were found. Moderation analyses did not find evidence of interactive effects of overall interpersonal distress by type of treatment or type of outcome measure used, although these moderator analyses need to be treated with caution given the relatively small number of studies and patients per treatment type.

The effect sizes observed for both posttreatment and longer-term outcomes ( $r = 0.11$ – $0.17$ ) represent small effects following the traditional rules-of-thumb proposed by Cohen (1988), or small-to-moderate effects following empirically-derived benchmarks (e.g., Brydges, 2019; Gignac & Szodorai, 2016). The significance and size of these effects are consistent (although slightly smaller) with a previous meta-analysis on anxiety and depressive disorders, estimating baseline overall interpersonal distress effects on outcome ( $r = 0.13$ ; Gómez Penedo & Flückiger, 2023). The current study restricted the analysis to patients with depression, and limited the effects of differential analytic strategies applied to estimate the targeted effects, by performing a one-stage IPD-MA. Thus, this study provides relatively sound support for the association between baseline overall interpersonal distress and outcome of the treatment of depression. Although the effect sizes observed were small, they might be clinically significant. At the population level and/or if incorporated within other evidence-based information for treatment personalization or precision in mental health, might represent a meaningful contribution to enhance mental health care (Barkham, 2023). Furthermore, the small effect sizes observed, could also imply that therapists within the studied treatments were able to spontaneously tailor their therapies to baseline patient differences in overall interpersonal distress.

Our results did not support the hypothesized association of interpersonal communion or agency with treatment outcomes. It is important to note that the overall interpersonal distress measure does not result from a linear combination of the interpersonal dimensions of agency and communion. Each dimension is calculated based on a weighted subset of interpersonal problem subtypes, some of which are used for both dimensions and others uniquely for each dimension (see formulas in the Methods section). This difference may explain why overall, unweighted interpersonal distress can be related to treatment outcome without the two interpersonal dimensions being associated with outcome.

Previous research concerning the association of these interpersonal dimensions with outcome was less consistent than for overall interpersonal distress. Whereas some studies found that the agency dimension significantly predicted treatment outcome (Sayegh et al., 2020; Zeeck et al., 2016), other studies did not (Altenstein-Yamanaka et al., 2017; Dinger et al., 2013; Gómez Penedo et al., 2020; Renner et al., 2012). Likewise, although one study found that baseline communion predicted treatment outcome (Dinger et al., 2013) other studies did not replicate that finding (Altenstein-Yamanaka et al., 2017; Renner et al., 2012).

The failure to find linear predictions of outcome by communion and agency does not mean that these interpersonal dimensions are irrelevant in the treatment of depression. For example, within each dimension extreme values (e.g., having extremely low or extremely high agentic

traits) might represent pathological interpersonal characteristics (e.g., being interpersonally too submissive or too dominant), that could cancel each other out in linear outcome prediction. Additionally, these dimensions could be predictors of differential treatment effects (Probst et al., 2020). In other words, patients' characteristic interpersonal functioning on the communion and/or agency dimensions could suggest which treatment would be more suitable for each individual patient. For example, in the treatment of depression, patients presenting problems of high agency (i.e., being too dominant) responded better to a mindfulness-based cognitive therapy, while patients presenting problems of low agency (i.e., being too submissive) responded better to a cognitive-behavioral analysis system of psychotherapy treatment (Probst et al., 2020). Differential treatment effects moderated by baseline interpersonal problem dimensions have been also observed in patients with generalized anxiety disorders (Gómez Penedo et al., 2017; Newman et al., 2017) and eating disorders (Gómez Penedo et al., 2019). In our view, these observations justify continuing research on interpersonal communion and agency as putative moderators of treatment effects on depression.

##### 4.1. Strengths and limitations of the study

This study addressed several limitations found in previous research on the association of interpersonal problems and treatment outcome. First, in this study we conducted an IPD-MA meta-analysis (Burke et al., 2017) rather than a conventional study-level meta-analysis. Conducting analysis grounded on raw individual participants data allowed us to apply the same data-analytic methods across studies and thus reduce potential biases due to heterogeneity of analytic and reporting strategies among the constituent studies (Tierney et al., 2023). This strength was empirically supported in this IPD-MA, when comparing the small percentage of variance observed at the study level in the mixed models performed in this study (between 3.7 %–5.5 %) with the high percentage of variance explained at the study level (39.69 %) in the conventional meta-analysis from Gómez Penedo and Flückiger (2023). Furthermore, by incorporating IPD from different studies, we were able to reach adequate levels of statistical power for our analyses.

Second, different from previous meta-analysis evaluating the association of interpersonal problems and outcome (e.g., Gómez Penedo & Flückiger, 2023) this study focused specifically on the treatment of depressive disorders, further limiting the heterogeneity of the estimates due to variability account for participants diagnoses. Finally, this study broadened the previous meta-analytic attempts at evaluating interpersonal problems and outcome association, by not only exploring the effects of baseline interpersonal distress, but also the interpersonal dimensions of agency and communion.

This study has also several limitations that will need to be addressed in future research. To operationalize interpersonal problems, we focused the study on one specific self-report instrument (i.e., Inventory of Interpersonal Problems; Horowitz et al., 2000). Although this inventory is one of the most widely used measures of interpersonal problems (e.g., Gómez Penedo & Flückiger, 2023; Iovoli et al., 2024; McFarquhar et al., 2018), is firmly based on a theoretical model (Horowitz, 2004), and has good psychometric properties (e.g., Hughes & Barkham, 2005), it is not the only one evaluating relational problems (e.g., Social Adjustment Scale; Weissman, 1999). While focusing on the IIP likely reduced heterogeneity, it also introduced the risk of study selection bias as it potentially resulted in an overrepresentation of studies from research groups or with certain theoretical orientations using this instrument more frequently than others. Future research would need to replicate these findings incorporating a broader set of measures of overall relational problems, including information from other sources such as therapists or significant others, and behavioral observations.

The pre-post design observed in most of the studies included did not allow us to estimate patients' trajectories in the outcome. Moreover, due to the lack of relevant information we were not able to incorporate



therapists effects within the multilevel models. Furthermore, the lack of a control group (i.e., depressive patients that were not exposed to treatment) limits the possibility of disaggregating predictor effects on outcome from other sources of variations besides treatment. This issue, which is common across most predictive studies, calls for a cautious interpretation of the results.

Concerning generalizability, we had data sampled from only five types of bona fide interventions (i.e., CBT, IPT, STPP, PIT, and ADM; none of the included studies had a BA condition). Hence, it is unclear to what extent findings generalize to other treatments, such as longer-term psychodynamic therapy or mindfulness-based interventions. Related, a relatively large proportion of the included studies incorporated STPP for depression treatment condition. Nevertheless, moderation analyses showed no significant differences in the interpersonal problems-outcome association between STPP and the other types of treatment included in the analyses.

#### 4.2. Conclusions and clinical implications

The findings of the current study suggest that it might be relevant to include a measure of interpersonal distress at baseline to improve prognosis inferences at the beginning of therapy. Patients presenting with higher interpersonal distress tend to have a worse treatment response, although the size of this effect was small. Thus, mental health professionals might have a modest benefit from incorporating an evaluation of patients' initial levels of interpersonal distress in both their conceptualization and treatment design. However, these results would need to be replicated with experimental designs to determine that the incorporation of this information would result in better outcome.

Although therapists might spontaneously tailor their treatments in patients presenting with more relational problems, there are no clear guidelines to adapt treatments for depressive patients with higher interpersonal distress. Hence, in order to enhance treatment personalization based on the findings of this paper, future studies would need to develop and test specific clinical strategies in order to best address the presenting conditions of these patients (Zavlis, 2023). Once developed and empirically-supported, these strategies could be incorporated at the early stages of bona fide treatments, as it has been proposed in treatments for other conditions, such as addressing high levels of ambivalence in generalized anxiety disorders (Westra et al., 2016). Furthermore, considering the worst response expected, depressed patients with higher overall interpersonal distress might be candidates for a combination of psychotherapeutic intervention and antidepressant medication, an option that has been shown to be more effective than psychotherapy alone (Cuijpers et al., 2020).

Despite limitations, this study provides sound empirical evidence supporting the association between baseline patients' overall interpersonal distress and subsequent successful treatment outcome, and thereby helping to enhance depression treatment outcome and reduce the large personal and societal costs of this condition.

#### CRediT authorship contribution statement

**Juan Martín Gómez Penedo:** Conceptualization, Methodology, Formal analysis, Writing – original draft, Writing – review & editing. **Manuel Meglio:** Formal analysis, Writing – original draft, Writing – review & editing. **Christoph Flückiger:** Conceptualization, Methodology, Formal analysis, Supervision, Writing – review & editing. **Frederik J. Wienicke:** Investigation, Writing – review & editing. **Jasmijn Breunese:** Investigation, Writing – review & editing. **Marco Menchetti:** Investigation, Writing – review & editing. **Paola Rucci:** Investigation, Writing – review & editing. **Robert Johansson:** Investigation, Writing – review & editing. **Joel M. Town:** Investigation, Writing – review & editing. **Allan A. Abbass:** Investigation, Writing – review & editing. **Peter Lilliengren:** Investigation, Writing – review & editing. **R. Michael Bagby:** Investigation, Writing – review & editing. **Lena C.**

**Quilty:** Investigation, Writing – review & editing. **Lotte H.J.M. Lemmens:** Investigation, Writing – review & editing. **Suzanne C. van Bronswijk:** Investigation, Writing – review & editing. **Michael Barkham:** Investigation, Writing – review & editing. **William B. Stiles:** Investigation, Writing – review & editing. **Gillian E. Hardy:** Investigation, Writing – review & editing. **Peter Fonagy:** Investigation, Writing – review & editing. **Patrick Luyten:** Investigation, Writing – review & editing. **Matthew P. Constantinou:** Investigation, Writing – review & editing. **Jacques P. Barber:** Investigation, Writing – review & editing. **Kevin S. McCarthy:** Investigation, Writing – review & editing. **Nili Solomonov:** Investigation, Writing – review & editing. **Anthony S. Joyce:** Investigation, Writing – review & editing. **Pim Cuijpers:** Conceptualization, Writing – review & editing, Funding acquisition. **Ellen Driessen:** Conceptualization, Methodology, Writing – review & editing, Supervision, Project administration, Funding acquisition.

#### Declaration of competing interest

Peter Fonagy is the Chief Executive of the Anna Freud Centre, which benefits from training professionals in Dynamic Interpersonal Therapy. Joel M. Town is the director of Dynamic Health Psychological Services, which benefits from training people in Intensive Short-Term Dynamic Psychotherapy. Patrick Luyten has been involved in the development, evaluation, and dissemination of psychotherapy for depression. The authors declare no other conflicts of interest.

#### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.cpr.2025.102570>.

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