Abstract

Identifying differences in the clinical response to specific interventions is an important challenge in the field of Clinical Psychology. This is especially true in the treatment of depression where many treatments appear to have comparable outcomes. In a controlled trial, we compared a positive psychology group intervention, the Integrative Positive Psychological Intervention for Depression (IPPI-D; n = 62) to a cognitive-behavioral therapy group intervention (CBT; n = 66) for depression. No statistically or clinically-significant differences between the treatments were found, but a slight advantage was observed, on average, for IPPI-D. The aim of the present study was to identify and combine moderators of the differential efficacy of these two psychological interventions for clinical depression. For this purpose, a secondary analysis using the Personalized Advantage Index (PAI) was performed to identify the intervention predicted to produce the better outcome for each patient. Six of the 21 potential moderators were found to predict differential efficacy between the treatments. IPPI-D was predicted to be the optimal treatment for 73% of the sample. Features that characterized these individuals were: mental and physical comorbidity, prior antidepressant medication, high levels of negative thoughts, and high personal growth. The 27% who were predicted to achieve better outcomes in CBT than in IPPI-D tended to have these features: no comorbidities, no prior antidepressant medication, low levels of negative thoughts, and low personal growth.

Keywords: Positive psychology; psychotherapy; cognitive-behavioral therapy; depression; Personalized Advantage Index; moderators; positive psychotherapy

Introduction

In 1967, Gordon Paul proposed that the appropriate question to be answered by psychotherapy outcome research was "What treatment, by whom, is most effective for this individual with that specific problem, and under which set of circumstances?" In the biomedical field, the precision medicine framework similarly aims at tailoring treatment strategies to individual's characteristics and circumstances. Following this framework, baseline characteristics of individuals have started to be used as predictive factors of differential response to intervention strategies (Cuijpers, Reynolds, Donker, Li, Andersson, & Beekman, 2012). This information can help to develop treatment selection tools to choose the optimal treatment for each individual. We explored and combined moderators of outcomes in a cognitive-behavioral therapy group intervention (CBT) vs. a positive psychology group intervention (the Integrative Positive Psychological Intervention for Depression; IPPI-D).

Treatment selection in mental health

Diverse types of psychotherapy have shown similar efficacy for major depression, including CBT, interpersonal therapy (IPT), and problem-solving therapy (PST; Cuijpers, Karyotak, Weitz, Andersson, Hollon, & van Straten, 2014). Despite the availability of multiple effective treatments, around 38% of patients continue to meet criteria for major depression disorder (MDD) after psychotherapy. One avenue towards attempting to improve outcomes in depression is the development of new psychotherapeutic interventions as positive psychology interventions (PPI). Meta-analyses focused on the efficacy of PPI, in both clinical and nonclinical samples, have shown it is efficacious in reducing symptoms of depression and increasing well-being (Bolier et al., 2013;

Chakhssi, Kraiss, Sommers-Spijkerman, & Bohlmeijer, 2018; Sin & Lyubomirsky, 2009). However, there is no evidence that PPI are superior to existing treatments (Chaves, Lopez-Gomez, Hervas, & Vazquez, 2017; Lopez-Gomez, Chaves, Hervas, & Vazquez, 2017), which is consistent with the general observation that when new treatments for depression are developed they are generally not more efficacious than existing alternatives (Cuijpers, 2017). This fact, along with the heterogeneity of symptoms and causes of depression (Lorenzo-Luaces, 2015), explains why personalizing treatments of depression is one of the major challenges for mental health research (Cuijpers et al., 2016). It is believed that the lack of differences between treatments, on average, may obscure different patterns of efficacy between different types of individuals (Barlow, Bullis, Comer, & Ametaj, 2013).

Treatment prognostic factors, also known as predictors, are variables that predict response to any treatment, whereas treatment prescriptive factors, or moderators, predict a differential response to different treatments (Cohen & DeRubeis, 2018). There is a growing interest in this topic, although there is still limited knowledge of outcome predictors and moderators in the mental health field (Simon & Perlis, 2010). The identification of reliable moderators has been particularly difficult. At least two meta-analyses and two reviews (Cuijpers et al., 2012; 2016; Kessler et al., 2016; Zhang et al., 2018) have provided evidence of the potential for baseline variables to moderate outcomes, including demographics (e.g., age, employment status), features of depression (e.g., overall symptom severity, particular symptoms like psychomotor activation) comorbid mental disorders (e.g., anxiety) or personality style, as well as other features (e.g., childhood trauma).

Research on moderators of depression treatment efficacy has focused mainly on CBT, IPT, supportive interventions, antidepressant medication or combinations of the latter with some of these types of psychotherapy (Cuijpers et al., 2016). Although the PPI approach can help to broaden the treatment options for depression, little is known about moderators of positive interventions (Boehm & Lyubomirsky, 2009; Schueller, 2011). To our knowledge, none of the studies that have directly compared CBT and PPI in depression (e.g., Asgharipoor et al., 2012; Carr et al., 2016; Fava et al., 1998a,b; Moeenizadeh & Salagame, 2010; Seligman et al., 2006) have analyzed moderators that are associated to better therapeutic outcomes for each modality. The goal of personalizing interventions, based on research of moderators has been clearly articulated in the positive-activity fit model (Lyubomirsky & Layous, 2013) that proposes that features of positive activities (e.g., timing, variety), persons and, ultimately, person-activity fit may moderate the effect of positive interventions on well-being. In this line, there have been recent attempts to find moderators of different modalities of PPI, such as personality characteristics, personal preferences and baseline level of the feature for which the intervention is designed (Proyer, Gander, Wellenzohn, & Ruch, 2015; Schueller, 2011, 2012).

Combined indexes of moderation

One issue with the existing literature on moderators is that it has mainly focused on the effect of individual moderators (Cohen & DeRubeis, 2018). However, moderators tend to have small effects and evidence suggest that response to treatments for depression is not singly determined (Cuijpers et al., 2012; Kraemer, 2013). In other words, there are probably multiple moderators that need to be accounted for. Accordingly, combined

moderator indexes have recently been developed (DeRubeis et al., 2014; Kraemer, 2013). One such example, the Personalized Advantage Index (PAI) proposed by DeRubeis et al. (2014), is based on algorithms that identify the treatment predicted to produce the better outcome for a given patient. They provide, for each patient, a quantitative estimate of the magnitude by which one treatment is predicted to outperform the other (Cohen, & DeRubeis, 2018; DeRubeis et al., 2014). In randomized clinical trials, one way of testing the utility of the approach is by comparing the outcomes of those who had been randomly assigned to their indicated treatment versus those assigned to the "non-indicated" treatment. In previous studies, the PAI approach has shown promise as a means of predicting differential outcomes to interventions, particularly for patients who are predicted to have larger differences between treatments (e.g., Huibers et al., 2015; DeRubeis et al., 2014) as well as differential probability of dropout (Keefe et al., 2018).

The present study

The aim of this study was to identify moderators of the differential efficacy of two psychological group interventions for clinical depression and to create a combined index of predictors and moderators to predict the optimal treatment for each individual patient. For this purpose, the treatment selection method developed by DeRubeis et al. (2014) was applied as a post-hoc analysis of data from a recently published trial comparing the efficacy of a CBT group intervention and a positive psychology group intervention (IPPI-D) for clinical depression (Chaves, Lopez-Gomez, Hervas, & Vazquez, 2017; Lopez-Gomez et al., 2017; Vazquez et al., 2018). Results showed that both intervention programs were statistically and clinically effective as well as highly acceptable for clinically depressed participants, with no significant differences either in the main (i.e.,

severity of depressive symptoms and clinical diagnosis) or secondary (e.g., emotional functioning, well-being) outcomes.

Despite lack of differences between treatments, there may be important differential effects for some groups of patients that could guide treatment assignment for patients. The PAI was calculated in this exploratory study to identify the intervention predicted to produce the better outcome for a given patient. The present study included a large number of potential moderators in the analyses. In addition to the traditional pool of variables, this study includes positive functioning variables that are often neglected but may be very relevant for clinical depression (Dunn & Roberts, 2016).

Methods

Participants and procedures

A comprehensive description of the participants and procedures can be found in previous publications (Chaves et al., 2017, 2019; Lopez-Gomez et al., 2017). Participants were 128 women between the ages of 27 and 83 (mean age: 52.02; SD: 10.58) who met criteria for a DSM-IV diagnosis of major depression or dysthymia, using the SCID structured interview (Structured Clinical Interview for the DSM-IV; First et al. 1996). They were blindly allocated to the Integrative Positive Psychological Intervention for Depression (IPPI-D; n = 62) or the CBT (n = 66) condition. Participants were recruited in a women's center, linked to the community health centers system, which periodically offers group interventions for depression. The women signed an informed consent to participate in the study and answered some demographic and clinical questions through a structured interview (e.g., previous psychological or pharmacological treatments, family history of mental problems). The University Ethics Committee approved the study

protocol. Exclusion criteria included: present substance abuse or dependence disorder, past or present manic or hypomanic episodes, past or present psychotic disorder, and a cognitive disorder (e.g., dementia or intellectual disability) that might prevent participants to follow the interventions.

Intervention conditions

CBT and IPPI-D were each delivered in 10 weekly, 2 hour sessions, of group intervention (five groups of each condition were conducted with 10–15 members each). CBT was adapted from the widely used Coping with Depression course (Cuijpers, Muñoz, Clarke, & Lewinsohn, 2009; Lewinsohn et al., 1984). IPPI-D was designed using positive empirically-validated interventions (for further details, see Chaves et al., 2017).

Measures

The Beck Depression Inventory II (BDI-II; Beck, Steer, & Brown, 1996; Sanz et al., 2003; $\alpha = .87$) assesses depressive symptomatology. In this analysis, baseline (0 months) and post-treatment (3 months) scores on the BDI-II were used. On average, participants were severely depressed (CBT: M = 37.42, SD = 10.68; IPPI-D: M = 34.66, SD = 10.13) and presented high comorbidity (Lopez-Gomez et al., 2017). Treatment condition was a binary variable and referred to either CBT or IPPI-D. Hypothesized predictors were measured at baseline and are displayed in Table 1.

Analytic Plan

Variables

Change in depressive symptoms was the dependent variable, operationalized as the residualized change in the BDI-II. It was calculated by regressing raw change scores

on baseline BDI-II symptoms. For each individual patient, the model-based residual (i.e., the amount of symptom change that is not accounted for by baseline depression) is added to the average group change. End-of-treatment scores were available for 101 participants (78.9% of total sample).

The candidate moderators were chosen from the available variables assessed in the study (Chaves et al., 2017). Only variables supported by the previous literature and with theoretical and clinical relevance were included (see Table S1 in the Supplementary materials for information supporting variables selected). A total of 21 variables were chosen following the criteria that are displayed in the Supplementary material. Missing data (<10%) were imputed using non-parametric missing value imputation method based on random forests (R package 'missForest'; Stekhoven & Bühlmann, 2012). The variables were then prepared to be entered in the prediction model (see Supplementary material).

Variable selection

Variable selection was a two-step process (Cohen & DeRubeis, 2018). First, to reduce the number of variables under consideration, we submitted them to a bootstrap-aggregated model-based recursive partitioning via random forests using the R package 'mobForest' (Garge et al., 2013). In model-based recursive partitioning by random forests, model-based trees are constructed based on bootstraps of the original sample. The first parameter in the model is the regression of residualized change on the treatment condition, as reported in the main outcome paper (Chaves et al., 2017). The analysis searches for splits in the sample that alter the first parameter (i.e., that suggest differential efficacy of the treatments in a subgroup of patients). Second, the variables that were

indicated by this procedure to be robust moderators of treatment differences were then entered in penalized regression equations using elastic net regularization (ENR), with 10-fold cross-validation. ENR penalizes the fit of linear regressions. This shrinks the size of regression coefficients which makes them less susceptible to overfitting. The penalization procedure also doubles as a means of excluding variables from the set that will be used in calculating patients' PAI scores. A variable is excluded when its coefficient is shrunk to zero. For further details, see the Supplementary materials.

Building a Personalized Advantage Index (PAI)

To build a PAI from this regression model, we followed the methods outlined by DeRubeis et al. (2014) once moderators had been identified. The PAI represents the expected difference between a patient's optimal treatment and his/her non-optimal treatment. For example, if a model, when applied to a set of values on the baseline variables given by a patient, predicts that the patient would improve 15 BDI points on PPI but 20 BDI points on CBT, the PAI for that patient is a +5.0, indicating a prediction that CBT was the optimal treatment. To quantify the potential effect of matching all patients to their indicated treatment, we compared the outcomes of patients assigned to their optimal treatment versus those assigned to their non-optimal treatment. A detailed description of the building of the PAI can be found in the Supplementary materials.

Results

Descriptive statistics are presented in Table 2. The treatment condition was not a significant predictor of residualized change on the BDI, though on average patients appeared to experience more change in IPPI-D than CBT (B = 2.99, SE = 1.68. t = 1.78, p =0.08, d =0.31).

The model-based recursive partitioning suggested that 6 of the 21 variables were moderators. In order of importance, the variables were: a) having an Axis III medical condition; b) a history of prior treatment with antidepressants; c) having an Axis I additional diagnosis; d) baseline ATQ scores, e) baseline personal growth-PWB scores, and f) the difference between the cognitive and non-cognitive subscales of the BDI[1] (BDI difference). The other variables did not moderate treatment outcome above and beyond what would be expected by chance. We stratified the sample by treatment to explore the effect of these variables on outcomes, as given by the elastic net. Four of them, Axis I co-morbidity, Axis III medical conditions, prior antidepressants treatment, and high baseline personal growth-PWB scores predicted less change in both treatment conditions. However, these variables were stronger predictors of change in the CBT than in the IPPI-D condition (see Table 3). Additionally, baseline ATQ and BDI difference scores predicted less improvement in the CBT, while, in the IPPI-D condition, higher scores actually predicted more overall improvement. The Figure 1 shows the moderation pattern of ATQ, which parallels the pattern of BDI difference moderator.

[1] *BDI Difference***:** this variable resulted of subtracting the scores on the non-cognitive items from the scores on the cognitive items of the BDI-II. To create the variable we followed the classification of Steer, Ball, Ranieri, & Beck (1999) of the BDI-II Cognitive subscale (i.e., pessimism, past failure, guilty feelings, punishment feelings, self-dislike, self- criticalness, suicidal thoughts or wishes, and worthlessness) and the BDI-II Non-cognitive subscale (i.e., sadness, loss of pleasure, loss of interest, indecisiveness, loss of energy, irritability, change in appetite, concentration difficulty, tiredness & fatigue, loss of interest in sex, crying, agitation, and changes in sleeping.). If the variable Difference between cognitive and non-cognitive depressive symptoms has a negative value means that the non-cognitive symptoms are more prominent in the specific patient.

Predicted outcomes and PAIs

Overall, the model-based predicted scores significantly predicted residualized change on the BDI (R^{2pred}= 0.12, $p < 0.001$). The "true" error of prediction (i.e., the average deviation from each patient's actual score) was 7.20 (SD = 5.32). Using the identified moderators, PAI scores were calculated for each individual patient, by subtracting the predicted outcomes in each of the two therapies for that patient, when they were apart in a 10-fold "held-out" sample. The average PAI score was 4.02 (SD = 2.69). The positive value was expected, as it reflects the (non-significant) advantage of IPPI-D observed in this sample.

The model identified that the assignment of participants allocated sixty five patients to their predicted optimal treatment (See Figure 2). These patients experienced superior outcomes (M = 15.59, SD = 10.03) to patients who, by chance, were assigned to the treatment that was predicted to be suboptimal (M = 13.29, SD = 9.04). However, this average difference was small (d = 0.27) and not statistically significant [$t(126)$ = -1.37, p = 0.18, d = 0.24].

IPPI-D was predicted to be the optimal treatment for a majority (73%) of the participants. Among these ninety three patients, IPPI-D (M = 14.94, SD = 9.43) produced significantly greater change than did CBT (M = 11.33, SD=9.65, t(91) = -1.82, p = 0.07, d = 0.37]. Among the thirty five patients (27% of the sample) for whom the model predicted that CBT would be the optimal treatment, outcomes did not differ between CBT (M = 17.18, SD = 8.08, and IPPI-D (M = 19.05, SD = 9.05, t(33) = 0.65, p = 0.52, d= 0.21).

Because many patients had PAI scores close to 0, which indicated that there is little to none difference in predicted outcomes between the treatments, we repeated the

analyses above focusing on patients with PAI scores ≥ 3 (i.e., clinically significant advantage). The results showed an overall benefit of being randomly assigned to one's "optimal" treatment (M = 16.64, SD = 9.32) vs. not (M = 10.41, SD = 9.40, t(71) = -2.77, p = .007, d = 0.65). Examining the outcomes by treatment condition again suggested that there was no effect of treatment selection (see Figure. 2) for the subsample for which CBT was the hypothetical optimal treatment. For the subsample for which IPPI-D was the hypothetical optimal treatment, patients had much better outcome if they were assigned to IPPI-D (M = 16.43, SD =10.28) than if they were assigned to CBT (M = 9.38, SD =9.06, t(58) = -2.80, p = 0.007, d = 0.72).

Discussion

This study aimed to identify moderators of the differential efficacy of CBT and IPPI-D for clinical depression and to predict the optimal treatment for each patient by combining information from the moderators. Prior treatment with antidepressants, as well as physical and/or psychological co-morbidity predicted less change in both treatments, but especially so in CBT. These variables had been identified as moderators in reviews of findings from comparative studies (Cuijpers et al., 2016; Kessler et al., 2016). Specifically, comorbidity variables have been selected in previous studies using the PAI method (i.e., comorbid personality disorder, paranoid symptoms, somatic complaints) as well as prior medication (DeRubeis et al., 2014; Huibers et al., 2015). As Barlow and colleagues (2013) pointed out, one of the main barriers of the current psychological treatments is that they are designed for treating a specific disorder whereas most patients present comorbid psychological or medical conditions. Personalizing treatments based on comorbidities and baseline characteristics such as those highlighted in this study may help

to improve their efficacy in each patient. In addition to these moderators, we found that a variable reflecting positive functioning at baseline (i.e., score on a scale of personal growth) was related to subsequent change. In particular, patients who reported having experienced more growth in the recent past evidenced more improvement in the PPI condition, relative to CBT. Perhaps PPI are better able to activate growth experiences in individuals irrespective of baseline of personal growth. Previous research has found that the higher the level of positive emotions, the higher the presence of posttraumatic growth (e.g., Vazquez & Hervas, 2010). Since IPPI-D includes several modules devoted to increase positive emotions, it is possible that participants overall found it more original and engaging. On the contrary, since growth has been found to be a key road to improvement in some CBT treatments for depression (e.g., Hart, Vella, & Mohr, 2008), it is possible that patients that actually have experienced growth before treatment cannot take full advantage of it.

Results also showed that patients characterized by a pattern of increased automatic negative thoughts, as well as those who presented a profile of predominant cognitive depressive symptoms, showed greater change in the positive intervention. It is possible that, for these individuals with high dysfunctional beliefs, the form of CBT implemented in this study may have focused primarily on an area – negative cognition – that patients experienced as a weakness. As a result, they may find it difficult to address negative cognitions directly, or that by facing them directly the result may be thought suppression or rumination rather than cognitive restructuring. In contrast, it is possible that positive interventions may overcome dysfunctional cognitions through direct changes in quality of life of patients and by increasing the focus on daily positive emotions. At least one

prior RCT found that focusing on individual's strengths, rather than attempting to overcome a weakness, was a more effective treatment for depression (Cheavens, Strunk, Lazarus, & Goldstein, 2012). Although the apparent advantage of a positive intervention over CBT in clinically depressed patients with frequent negative thoughts and dysfunctional cognitions seems to be counterintuitive, the NIMH Collaborative Study on Depression showed that higher levels of negative cognitive structures (i.e., dysfunctional beliefs) predicted a superior response to IPT, relative to either CBT or antidepressant medication coupled with clinical management (Sotsky et al., 1991). In this line, Huibers and colleagues (2015) applied the PAI method in a comparative study finding that depressed patients with more interpersonal problems and external triggers benefitted more from CBT intervention, whereas IPT intervention was superior for patients with cognitive dysfunction and low interpersonal problems and external triggers. Thus, CBT may be a relatively poor choice of treatment, relative to other evidence-based treatments, for a person with depression who experiences an especially high frequency and intensity of negative cognitions (see for a similar result, Shankman et al., 2013). Overall, this line of results supports further research efforts along the lines of treatment selection analyses, as data-driven approaches may be better suited than theory-based expectations for the purpose of finding the best fit of persons to treatments.

The PAI model yielded some additional interesting results. When predicting for each patient which treatment was more likely to lead to better outcomes, results showed an overall advantage of IPPI-D over CBT with substantial variability in the sample. The PAI model predicted that most patients (73%) would experience more improvement if assigned to IPPI-D than to CBT in this sample. Although marginally significant, the effect

size of 0.37 of this difference is substantially greater than most reported differences between types of psychotherapies (Cuijpers et al., 2008), suggesting it is a clinically important effect. Besides this overall advantage of being assigned to IPPI-D, there was an interesting difference between both therapeutic conditions. For patients whose optimal treatment was identified as CBT (27% of the sample), being assigned to the IPPI-D condition did not penalize their results. On the contrary, for patients whose optimal treatment was IPPI-D, being assigned to the CBT condition significantly penalized their improvement in terms of depression change. One explanation of this finding could be that the variables associated with a relatively better response to CBT in our study are the ones that are typically associated with a generally good prognosis (e.g., being treatment-naïve, no co-morbidities) (Kessler et al., 2016). Additionally, the characteristics of the study's sample, as older age and high comorbidity (see Lopez-Gomez et al., 2017), fit with the patient profile that seems to be more benefited from IPPI-D and, therefore, this fact may partially explain the small superiority of the IPPI-D found in the results.

This is the first study of which we are aware that analyzes moderators of differential efficacy of PPI vs CBT. In it, two specific intervention programs were compared, so the results are constrained to such comparison until more studies are conducted. Additionally, the format of interventions delivery, as a group intervention, and the number of session (10 weekly sessions) might have influenced the findings. Research based on personalization of treatment is in its infancy and it would be necessary to compare different interventions in diverse contexts, formats of delivery and different dosages. The characteristics of the study's sample (i.e., only women, mean age of 52 years old) also limit the conclusions of the study because the variables that resulted as

moderators in this specific sample (e.g., Axis III comorbidity and prior treatment with antidepressants) may have not been selected in other samples with different inclusion criteria. Furthermore, gender may be a moderator in itself and this study cannot account for its potential effect. Finally, the small sample size of this study constitute a limitation of its conclusions, although is similar to the samples generally used in treatment selection studies. Accordingly, the results of the study must be interpreted with caution as they might not be generalized to other samples that could differ on important variables (e.g. sex, age, motivation for treatment, chronicity, etc.). Since this is an exploratory study, other randomized trials, using larger and more heterogeneous samples, would be necessary to verify the validity of the present model (Kraemer, 2013).

Among the approaches for personalization of interventions, the one used in this study (i.e., using data of comparative trials of different treatments in an unselected sample to estimate individualized metrics to predict the optimal treatment for each patient) has been a recommended method (Cuijpers et al., 2016; Ng & Weisz, 2016). Clinical psychology of the future would be the one tailored to the patient in dosage, combination of components within and between psychological approaches, format of delivery (group or individual), specific context, needs and preferences from patients and therapists. New multivariable treatment selection approaches as the PAI can be useful tools to develop this kind of precision mental health (Cohen & DeRubeis, 2018).

Table 1. *Candidate variables per domain*

Domain 1: Depression
Type of depression (chronic or dysthymia; recurrent) (SCID-I)
Previous pharmacological treatment (0 = no, 1 = yes)
Previous psychological treatment (0 = no, 1 = yes)
Domain 2: Demographics
Age
Marital status (1 = no partner, 0 = partner)
Employment status (1 = no active employment, 0 = active employment)
Domain 3: General functioning
Comorbid Axis I Diagnosis (SCID-I; 0 = no, 1 = yes)
Comorbid Axis III Diagnosis (SCID-I; 0 = no, 1 = yes)
Current ADM treatment (0 = no, 1 = yes)
Axis IV Diagnosis of Psychosocial and Environmental problems (SCID-I; 0 = no, 1 = yes)
Domain 4: Clinical symptoms
Difference between cognitive and non-cognitive depressive symptoms (BDI-II)
Automatic thoughts (ATQ-30)
Negative affect (PANAS)
Anxiety (BAI)
Domain 5: Positive functioning
Positive affect (PANAS)
Optimism (LOT-R)
Satisfaction with Life (SWLS)
Personal growth (PWBS)
Positive relations (PWBS)
Behavioral activation system (BAS)

Note.

SCID = Structured Clinical Interview for the DSM-IV; BDI-II = Beck Depression Inventory; BAI = Beck Anxiety Inventory; ATQ-30 = The Automatic Thoughts Questionnaire; PANAS-NA = Positive and Negative Affect Schedule, Negative Affect subscale; PWBS = Psychological Well-Being Scales; SWLS = Satisfaction with Life Scale; PANAS-PA = Positive and Negative Affect Schedule, Positive Affect subscale; LOT-R = Life Orientation Test Revised; BAS = Behavioral Activation Scale..

Table 2. *Descriptive statistics for baseline variables.*

	IPPI-D (*n* = 62)		**CBT (*n*= 66)**	
Variable	**Mean or %**	**SD**	**Mean or %**	**SD**
Previous pharmacological treatment	54.8%	-	65.2%	-
Comorbid Axis I Diagnosis (SCID-I)	48.4%	-	65.2%	-
Comorbid Axis III Diagnosis (SCID-I)	37.5%	-	37.9%	-
Difference between cognitive and non-cognitive depressive symptoms (BDI-II)	-10.73	4.95	-11.,52	4.98
Automatic thoughts (ATQ-30)	84.88	27.46	87.96	27.86
Personal growth (PWBS)	13.56	4.83	13.01	4.82

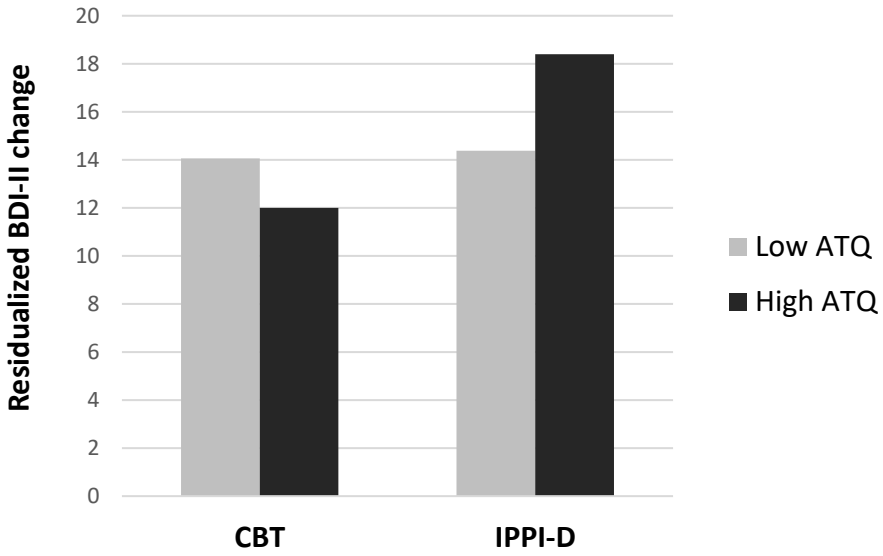
Note. None of the differences between groups in these variables were statistically significant. IPPI-D = Integrative Positive Psychological Intervention for Depression; CBT=Cognitive-Behavioral Therapy; SCID = Structured Clinical Interview for the DSM-IV; BDI-II = Beck Depression Inventory; ATQ-30 = Automatic Thoughts Questionnaire; PWBS = Psychological Well-Being Scales.

Table 3. *Moderators included in the model for the full sample and in 10-fold cross-validation splits*

CBT		**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Intercept	13.54	13.63	13.21	13.72	13.33	13.57	13.66	13.60	13.67	13.61	13.33
Axis III medical condition	-2.22	-2.28	-2.43	-2.10	-2.46	-2.51	-2.19	-1.55	-1.57	-2.43	-2.49
Prior treatment with antidepressants	-2.01	-2.12	-1.32	-2.09	-1.96	-1.94	-2.22	-2.52	-1.80	-2.24	-2.05
Axis I co-morbid diagnosis	-2.15	-2.12	-2.67	-1.80	-2.33	-2.01	-2.16	-1.77	-2.21	-2.46	-2.07
Baseline ATQ scores	-1.02	-1.09	-0.70	-1.09	-1.24	-0.64	-0.87	-1.53	-0.45	-1.26	-1.46
Baseline personal growth-PWB scores	-1.92	-1.87	-1.42	-1.96	-2.00	-1.51	-2.17	-1.76	-1.89	-1.92	-2.67
Baseline BDI-II difference scores	-0.56	-0.54	-0.48	-0.42	-0.59	-0.80	-0.32	0.21	-0.94	-0.84	-0.84
IPPI-D		**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Intercept	16.01	16.08	15.46	15.98	15.93	16.44	16.13	15.91	16.35	16.06	15.73
Axis III medical condition	-0.80	-1.05	-0.81	-0.29	-0.97	-0.70	-1.26	-0.70	-0.65	-0.85	-0.74
Prior treatment with antidepressants	-0.02	0.27	0.02	-0.25	-0.05	0.09	0.12	-0.32	-0.09	0.06	-0.06
Axis I co-morbid diagnosis	-0.40	-0.30	-0.70	-0.36	-0.36	-0.50	-0.25	-0.34	-0.21	-0.33	-0.61
Baseline ATQ scores	1.20	1.12	1.55	0.69	1.31	1.22	1.02	1.25	1.14	1.22	1.38
Baseline personal growth-PWB scores	-0.21	-0.42	0.05	-0.10	-0.14	-0.13	-0.57	-0.02	-0.23	-0.20	-0.23
Baseline BDI-II difference scores	0.62	0.52	0.57	0.24	0.71	0.97	0.71	0.75	0.60	0.68	0.55

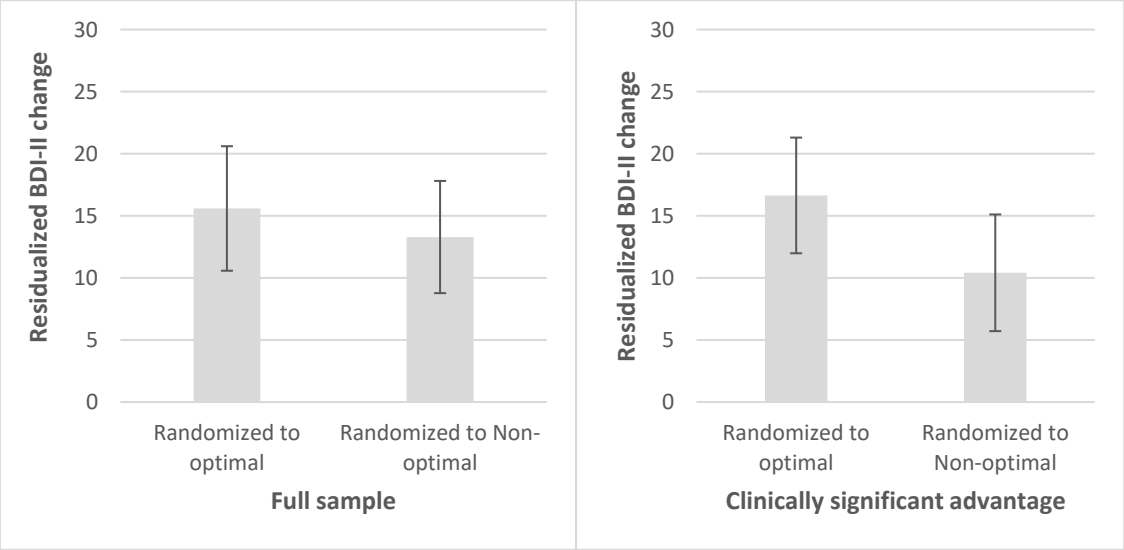
Note. IPPI-D: Integrative Positive Psychological Intervention for Depression; CBT=Cognitive-Behavioral Therapy; BDI-II = Beck Depression Inventory; ATQ = Automatic Thoughts Questionnaire; PWBS = Psychological Well-Being Scales.

Figure 1. BDI change by ATQ level and intervention condition.



Note. IPPI-D: Integrative Positive Psychological Intervention for Depression; CBT=Cognitive-Behavioral Therapy; BDI-II = Beck Depression Inventory; ATQ = Automatic Thoughts Questionnaire.

Figure 2. Observed advantage of treatment selection



Note. Comparison of mean residualized BDI-II change for patients randomly assigned to their optimal treatment versus those assigned to their non-optimal treatment. The left graph gives the results for the full sample. The right graph includes only patients for whom the algorithm predicted a clinically significant advantage on the PAI of ≥3. BDI-II = Beck Depression Inventory.

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