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Research report

The clinical effectiveness of evidence-based interventions for depression: A pragmatic trial in routine practice

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ABSTRACT

Background: Controversy persists about how effectively empirically-supported treatments for major depression work in actual clinical practice as well as how patients choose among them. We examined the acute phase effectiveness of cognitive therapy (CT), interpersonal psychotherapy (IPT), and combined psychotherapy–pharmacotherapy (PHT) in a naturalistic setting, allowing patients their choice of treatment.

Methods: The study compared CT ($n=63$), IPT ($n=56$), CT–PHT ($n=34$), and IPT-PHT ($n=21$) for 174 subjects with major depression in a secondary care mood disorders clinic. Patient preference, rather than randomization, determined treatment selection. The Beck Depression Inventory-II (BDI) was the primary outcome variable. Exclusion criteria were minimal.

Results: All treatments were associated with a reduction in depressive symptoms, with a 35% remission rate by week 26. Overall improvement was well within ranges reported in efficacy trials. On average, treatment effects of the different interventions straddled the same range, but moderation analyses revealed that BDI scores dropped faster in the first 16 weeks in patients who received CT alone than patients who received CT and pharmacotherapy, a pattern not found in patients who received IPT (with or without pharmacotherapy).

Limitations: Limitations consist of a modest sample size, choice of treatment was made by participants which may have been influenced by many sources, and the absence of a non-active control group.

Conclusions: This study supports the effectiveness of empirically-supported antidepressant treatments selected by patients in routine settings, and provides an indication that speed of therapeutic response may vary amongst treatments.

1. Introduction

Current treatment guidelines rely heavily on the results of randomized controlled trials (RCTs) of treatment efficacy. Based on the results of such trials, guidelines for major depressive disorder (MDD) call for first line application of pharmacotherapy (PHT) or time-limited psychotherapies like cognitive therapy (CT) or interpersonal psychotherapy (IPT), which possess the best documented efficacy for acute phase treatment of MDD in secondary care settings (APA, 2010; Lam et al., 2009; Parikh et al., 2009).

Yet for over a decade, concerns have been expressed about the utility of generalizing the results of such *efficacy* studies to daily clinical practice. This may partially explain the gap between science and daily practice in depression treatment (Gonzalez et al., 2010; Shafran et al., 2009; Young et al., 2001). Researchers and clinicians have questioned whether depressed patients fare as well in "real life" treatment outside a highly controlled study (*effectiveness*). Several considerations underlie this concern (Goldfried and Wolfe, 1998; Westen et al., 2004). First, real life patients participate in the process of choosing type of treatment,

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which may help empower them by counteracting demoralization and satisfying their treatment preference (Corrigan and Salzer, 2003; Seligman, 1995). The absence of choice may reduce external validity of RCTs, although recent evidence is equivocal about this claim (Hegerl et al., 2010; Kendrick et al., 2006; Kocsis et al., 2009; Leykin et al., 2007; Raue et al., 2009). Second, participants volunteering in RCTs may not be representative of the self-declared patients seeking treatment in routine daily practice because of differing clinical characteristics (e.g., severity and duration of current episode, comorbidity), many exclusion criteria, and willingness to be randomized (Stirman et al., 2005; Wisniewski et al., 2009; Zimmerman et al., 2005). Third, treatments within the context of a RCT are highly controlled in content, duration, number of sessions, therapist qualifications, and patient choice, complicating translation to real-world clinical practice (Cuijpers et al., 2010b; Shadish et al., 2000; Shadish et al., 1997). Finally, doubts have been expressed about reported efficacy of empirically-supported therapies (ESTs) in the light of evidence for publication bias; real efficacy figures may be lower than previously reported (Cuijpers et al., 2010a; Turner et al., 2008).

Consequently, there have been calls for research to address the effectiveness rather than efficacy of the ESTs for MDD in naturalistic treatment settings (March et al., 2005; Tunis et al., 2003). This translational research aims to convert the results from clinical studies into everyday clinical practice (Sullivan and Goldmann, 2011; Woolf, 2008).

Recently, some studies have examined the effectiveness of treatment-as-usual (TAU) in large clinical samples and compared them to the efficacy of the same treatments in clinical trials (Barkham et al., 2008; Cuffel et al., 2003; Minami et al., 2008; Shadish et al., 2000; Stiles et al., 2008; van der Lem et al., 2011). Although most of these studies seem to show that TAU overall retains the benefits of ESTs observed in clinical trials, methodological limitations hinder reliable interpretation of their results. Drawbacks of these studies include the largely unknown characteristics of the provided treatments, the large number of missing cases, and the use of unreliable diagnostic categories and outcome measures (Clark et al., 2008). Studies examining the effectiveness of ESTs in routine daily practice are scarce. Additionally, most of these studies suffers from methodological limitations like absence of well-validated diagnostic procedures, uncertainty about therapists' training and treatment integrity, or lack of control of the use of concurrent psychotropic medication. However, there are some indications that IPT may be effective outside RCT settings (Markowitz et al., 2009), and that the effectiveness of CT is almost comparable to its reported efficacy (Gibbons et al., 2011; Merrill et al., 2003; Persons et al., 1999; Schindler et al., 2011; Westbrook and Kirk, 2005). The effectiveness of community PHT in comparison to efficacy estimates varies widely among studies (Rush et al., 2004; Wisniewski et al., 2009).

To date, no studies have investigated the effectiveness of these ESTs, alone or in combination, delivered at one site by the same team of therapists in a secondary care, integrated mood disorders treatment setting in which formally diagnosed patients with MDD, who actively seek treatment, could freely choose among treatment options.

The present study examined the effectiveness of IPT and CT (each alone and combined with antidepressant medication) in patients with a well-classified of MDD episode actively seeking treatment in an outpatient treatment facility. From the outset, our purpose was to test the effectiveness of the treatments as administered in routine daily practice under clinically representative conditions (Shadish et al., 2000). As already stated, patient preference for a treatment may enhance outcome. As RCTs by definition prevent patients from choosing their preferred treatment, we did not randomize but followed the patients' preference in treatment allocation. We hypothesized that the effectiveness of treatments would be comparable to the outcome typically found in RCTs. Thus, this is, to our knowledge, the first study to examine the comparative effectiveness of freely chosen, empirically supported antidepressant treatments in a naturalistic setting.

2. Methods

2.1. Design

We conducted a controlled treatment study with a 26-week follow-up. Length of acute treatment depended on achieving remission and varied accordingly between 6 and 26 weeks. Some treatments lasted longer than 26 weeks due to treatment-resistance; these patients were included in the present analysis. In this naturalistic treatment setting, patient preference determined treatment allocation. This report closely follows the guideline for reporting pragmatic trials recently published by Zwarenstein et al. (2008).

2.2. Participants

Data were collected from depressed patients seeking treatment at the mood disorders treatment program of an outpatient mental health care center (RIAGG Maastricht) in Maastricht, the Netherlands. This secondary care facility treats individuals aged 18–65 years with varied psychiatric disorders referred by other health professionals (e.g., general practitioners and social workers). Health insurance companies cover the entire cost of treatments at the center. After initial screening, patients are assigned to specialized treatment programs for further diagnostic interviewing and treatment. In the mood disorders program, depressed individuals are preferentially being treated with CT, IPT, or a combination of CT–PHT or IPT–PHT.

The only inclusion criterion was a primary diagnosis of non-delusional major depressive disorder (MDD) determined with the Structured Clinical Interview for DSM-IV Axis I (SCID-I: First et al., 1995). Trained masters or doctoral-level psychologists, psychotherapists, psychiatrists, and senior psychiatric residents (supervised by psychiatrists with a minimum of 5 years clinical experience) administered the SCID-I, which compromises a routine part of the diagnostic procedure in the mood disorders program. Inter-rater reliability of the SCID-I was not assessed. The only exclusion criteria at entry were primary diagnoses other than MDD (e.g., bipolar disorder, psychotic disorder, or substance abuse), high acute suicide risk, and insufficient fluency in Dutch. Comorbid secondary Axis I diagnoses like anxiety disorders or substance abuse were permitted.

The Ethics Committee of Maastricht University approved the study. All participants provided written informed consent. Of all eligible individuals referred to the mood disorders treatment program, 65% agreed to participate in the study. No information about baseline characteristics of the non-participants is available, which prevents comparing them with study participants.

2.3. Treatments

2.3.1. Cognitive therapy

Licensed psychologists and psychotherapists provided CT. Their CT experience ranged from 1 to 12 years at study onset. Three therapists are faculty who teach post-graduate courses in CT. All therapists received appropriate training and followed the procedures outlined in

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standard texts of cognitive therapy for depression (Beck et al., 1979). Sessions typically lasted 50 min weekly, with the possibility of fortnightly booster sessions in later stages. CT therapists reviewed ongoing cases and addressed difficulties encountered during therapy in weekly 60 min sessions.

2.3.2. Interpersonal psychotherapy

Licensed psychologists, psychotherapists, and psychiatrists with IPT experience of between 1 and 10 years at the beginning of the study provided IPT, based on the manual by Klerman et al. (1984). Three therapists are faculty in post-graduate IPT courses. All therapists received appropriate training. As in CT, sessions were held for 50 min weekly with the possibility of maintenance sessions following the acute phase treatment. IPT therapists also convened for an hour weekly to review ongoing cases.

2.3.3. Pharmacotherapy

Participants in the combined treatment conditions received some additional PHT sessions. These sessions typically lasted 15 min and focused on medication management (biochemical rationale, discussion of adverse events, dosage adjustment), and management of the participants' functioning (assessing functioning in major life spheres). Application of techniques and strategies specific to CT or IPT was neither encouraged nor strictly prohibited. Participants generally received a serotonin reuptake inhibitor (SSRI) following national and international guidelines. In case of SSRI non-response in the current episode, participants were prescribed another SSRI, venlafaxine or a tricyclic agent augmented with lithium in case of subsequent non-response.

2.4. Procedures and outcomes

During the diagnostic work-up, consisting of an open interview and the SCID-I, patients received verbal and written information about treatment options in the mood disorders program. Patients were explicitly informed that CT and IPT are time-limited, empirically validated therapies lasting a maximum of 15–20 sessions. After this work-up, a multidisciplinary team meeting, briefly discussing clinical history and diagnosis, yielded a treatment recommendation. As is typical in Dutch treatment settings, the final choice of treatment was made by patient and therapist agreement, but predominantly guided by patient preference. Following the diagnostic work-up, staff provided comprehensive information on the study procedure, asked patients to participate, and obtained written informed consent.

2.5. Measures

Measures were administered prior to treatment and at 8, 16, and 26 weeks. The main outcome variable was the Beck Depression Inventory Second Edition BDI-II (Beck et al., 1996). The BDI measures depressive severity, with higher scores indicating more severe depression (range 0–63). Its construct validity and reliability have consistent support in varied samples (Beck et al., 1996). Using the guidelines of Jacobson and Truax (1991), response was defined a priori as a decrease of at least 10 points from baseline BDI-score, whereas remission was defined as an absolute BDI-score of 10 points or less. General psychopathology (i.e., overall emotional dysfunction) was measured at baseline with the Symptom Check-List 90 (SCL-90), with a score range from 90 (asymptomatic) to 450 (severe psychopathology). The SCL-90 has high reliability and research supports its validity (Derogatis et al., 1976). The SCID-I assessed Axis I diagnoses. Other baseline measures included sex, age, marital status, employment, and the duration of the current depressive episode.

2.6. Data analysis

Comparisons of demographic- and baseline-characteristics and differences between treatment groups were done with χ^2 tests for categorical data and ANOVAs for quantitative data. Effect sizes were calculated using Cohen's D (mean_0 weeks–mean_26 weeks/pooled SD), only with patients whose data were available at 26 weeks. The effectiveness of the different treatments was tested with mixed linear regression modeling, using maximum likelihood estimation in SPSS (version, 18.0). The mixed model had three levels: therapists, patients and measurements (time at 0, 8, 16, 26 weeks). The influence of the therapists' level was analyzed, but since there were too many therapists in this study, resulting in too small nested patient clusters per therapist, this level was omitted from further analyses. Patient effects were included by choosing an unstructured covariance matrix for the repeated measures, which is the most general structure.

The dependent variable in the analysis was the BDI (measured at 0, 8, 16, 26 weeks). Intervention was represented by two dummy variables: CT vs IPT (CT=1, IPT=0) and psychotherapy alone vs psychotherapy combined with PHT (PSY vs COM; psychotherapy alone=1, combination treatment=0).

First, we fitted the growth curve for time. It emerged that the best fit was not provided by a linear model (time), but by a polynomial model (time and time^2) instead. We then built a full-saturated model, with the main effects of time, time^2, CT vs IPT,

Table 1
Demographic and clinical characteristics of subjects entering treatment (n=174).

	CT (n=63)	CT–PHT (n=34)	IPT (n=56)	IPT-PHT (n=21)
Female, n (%)	38 (60)	19 (55)	32 (57)	16 (76)
Age in years, M (sd)**	42 (11)	36 (13)	41 (12)	45 (11)
Spouse (%)	32 (50)	16 (47)	28 (50)	11 (52)
At work, n (%)	23 (37)	14 (41)	17 (30)	7 (33)
BDI, M (SD)	25.5 (9.7)	24.8 (8.9)	22.1 (9.5)	27.1 (9.6)
SCL-90 total score, M (SD)	219 (56)	217 (61)	203 (49)	230 (63)
Axis I diagnosis, n (%)				
MDD, first episode	28 (44)	14 (41)	26 (46)	10 (47)
MDD, recurrent	35 (56)	20 (59)	30 (54)	11 (53)
Axis I comorbidity, n (%)	30 (46)	19 (55)	26 (46)	9 (43)
Duration current episode >24 months, n (%)	27 (44)	15 (44)	29 (52)	9 (41)

Note: CT=cognitive therapy, CT–PHT=cognitive therapy and pharmacotherapy, IPT=interpersonal psychotherapy, IPT–PHT=interpersonal psychotherapy and pharmacotherapy.

** $p<0.01$.

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PSY vs COM, and all two- and three-way interactions of these variables. Non-significant interaction effects were hierarchically excluded from the model until only significant terms remained (using $\alpha=0.05$, two-tailed). Treatment group differences were made 'visible' in plots of predicted values using SPSS Graphs. Initially we included a selection of potential confounders as covariates in the saturated model. Since adjustment for confounds did not affect the results, we excluded them from the present analysis for ease of interpretation.

3. Results

The study sample compromised 174 participants. Table 1 summarizes their demographic and clinical characteristics, grouped by treatment. There was a significant difference in age between the groups, with CT–PHT participants being somewhat younger, but adjustment for age did not affect the outcome results. Other baseline characteristics between the treatment groups were not significantly different. Of participants, 103 (59%) were female. Mean age in the total group was 42.4 (SD=11.1), mean baseline BDI was 24.5 (SD=9.6), mean SCL-90 score was 215.1 (SD=56.4), and mean duration of the current episode was 8.2 months (SD=13.3). Chronic depression (> 2 years) was diagnosed in 63 (36%) participants, and 92 (53%) suffered from at least one comorbid axis I diagnosis. Due to the extensive Dutch social welfare system, in which long-term sick leave does not have major financial consequences, many participants were not currently working.

3.1. Attrition, mean scores, response, and remission

The percentage of participants available for analyses (not lost to follow-up) at 8, 16, and 26 weeks were 91%, 83%, and 76% respectively, which is within an acceptable range of attrition. All available data from all 174 patients were included into the mixed regression without imputation of missing data and without dropping any patient.

The mean number of all sessions was 13.5 (S.D.=6.3) for CT, 17.6 (S.D.=7.7) for CT–PHT, 14.6 (S.D.=6.1) for IPT, and 20.1 (S.D.=8.4) for IPT–PHT. In the combined treatment conditions, most patients saw different therapists for PHT and psychotherapy, which may account for the greater number of sessions in these treatments. Observed mean BDI-scores, attrition and rates of participants achieving response and remission during follow-up in the different treatment groups appear in Table 2. No significant differences in attrition, response or remission emerged across treatments (although there appear to be some meaningful differences in attrition, especially in respect to the low rate of attrition in the IPT–PHT group).

Clinical improvement after the first 8 weeks of treatment was modest, yielding remission in 20% of participants. However, BDI scores decreased steadily thereafter, with an overall remission rate at 26 weeks in the sample of 35% (of the original 174 patients). Considerable clinical improvement could still be observed between weeks 16 and 26. Treatment effect sizes were large (Table 3). Effect sizes of ≥ 0.8 are generally considered large, effect sizes of 0.5 moderate, and effect sizes of 0.2 small (Cohen, 1988). Table 3 also compares the current remission rates with estimates based on literature review reported by Keitner et al. (2006). The remission rates achieved in our study lie well within the range of those reported in clinical efficacy trials.

3.2. Multilevel analysis of effectiveness

Table 4 summarizes results from the mixed regression analyses. The final model displays a moderating effect of the different treatment conditions and time. As these cannot be interpreted from the regression model only, we investigated the shape and direction of the moderation in subsequent subgroup analyses, depicted in Fig. 1a and b.

As Fig. 1a illustrates, the drop in BDI scores of those patients who received IPT only and IPT in combination with an antidepressant appeared to have a parallel development, although those who received combination treatment started out and ended up with higher BDI scores, a difference between the two groups that remained almost stable in the course of treatment. However, in the cognitive therapy group (Fig. 1B), BDI scores appeared to drop much faster in patients who received only CT compared to those receiving CT–PHT. Despite this difference, both groups (CT and CT–PHT) started out and ended up around the same BDI mean. This indicates that it is the differential rate of response of those receiving CT vs those receiving CT–PHT (and the absence of such a differential rate in the IPT group) that explains the moderation effect of CT vs IPT we found. Residuals were checked, but our results could not be explained by outliers or non-normality.

4. Discussion

This study examined the effectiveness of ESTs for MDD in a naturalistic setting. Participants were self-declared patients seeking treatment in a 'real world' mental health setting and suffering from moderately severe depression, considerable rates of chronicity and recurrence, and high rates of Axis I comorbidity. Treatment assignment was not random but, reflecting daily practice in the Netherlands, guided by patient preferences. With a paucity of exclusion criteria, our study included participants who would have been refused by many efficacy trials (Stirman et al., 2005; Wisniewski et al., 2009; Zimmerman et al., 2005), which should make its results more generalizable to routine clinical practice.

The overall remission (35%) rate after 26 weeks was considerable, within the range of reported within RCT efficacy contexts (Keitner et al., 2006), and comparable to most naturalistic studies (Barkham et al., 2008; Cuffel et al., 2003; Minami et al., 2008; Shadish et al., 2000; Stiles et al., 2008; Trivedi et al., 2006). The effect sizes in our study are somewhat larger than reported in recent meta-analyses (Cuijpers et al., 2008, 2011a, 2011b). All treatment groups also generated effect sizes reliably greater (d's ≥ 1.0, Table 3) than natural course benchmarks ($d=0.15$) for MDD (Minami et al., 2007).

We observed no difference in overall effectiveness among treatments either as monotherapies or in combination. This accords with what in psychotherapy has become known as the 'dodo-bird verdict': the persistent finding that psychotherapies for MDD exhibit similar efficacy (Cuijpers et al., 2008; Luborsky, 1995; Wampold et al., 1997). Moreover, it jibes with recent, but not all meta-analyses that reported no overall differences in efficacy between monotherapy and combination therapy in moderately severe, non-chronic MDD (Cuijpers et al., 2008, 2011a; de Maat et al., 2007; Friedman et al., 2004; Pampallona et al., 2004). Surprisingly, a moderation analysis showed that BDI-scores in patients receiving CT alone, although ending around the same mean, decreased faster than these scores in patients receiving CT combined with antidepressant medication. This moderation was not seen in IPT vs IPT–PHT. One can speculate that differences between CT and CT–PHT in (1) therapeutic alliance, (2) adherence to and engagement with therapeutic techniques by therapist and/or patient, and/or (3) unknown patient characteristics are associated with this difference in time path (DeRubeis et al., 2005).

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Table 2
Observed mean (S.D.) BDI-scores and number (%) of depressed patients lost to follow-up and achieving response and remission during treatment.

	Time point	CT	CT–PHT	IPT	IPT–PHT	Overall
BDI	8 weeks	18.2 (11.2)	20.4 (10.3)	17.2 (9.8)	21.8 (12.1)	18.7 (10.7)
	16 weeks	14.2 (9.9)	18.0 (11.6)	14.3 (9.8)	18.9 (10.6)	15.6 (10.4)
	26 weeks	12.9 (11.3)	14.7 (11.3)	9.9 (8.3)	16.3 (10.7)	12.9 (10.6)
Attrition	8 weeks	7 (11)	6 (17)	3 (5)	0 (0)	16 (9)
	16 weeks	15 (23)	6 (17)	7 (12)	3 (14)	31 (17)
	26 weeks	18 (28)	7 (20)	16 (28)	1 (4)	42 (24)
Response	8 weeks	19 (30)	7 (20)	14 (25)	5 (24)	45 (26)
	16 weeks	23 (36)	10 (29)	17 (30)	6 (28)	56 (32)
	26 weeks	26 (41)	12 (35)	22 (39)	7 (33)	67 (39)
Remission	8 weeks	13 (21)	5 (15)	13 (23)	3 (14)	34 (20)
	16 weeks	18 (29)	5 (15)	15 (27)	3 (14)	41 (24)
	26 weeks	23 (37)	10 (29)	20 (36)	7 (33)	60 (35)

Note: CT=cognitive therapy, CT–PHT=cognitive therapy and pharmacotherapy, IPT=interpersonal psychotherapy, IPT–PHT=interpersonal psychotherapy and pharmacotherapy. Attrition is the number (%) of participants lost to follow-up (BDI-scores). Response was defined as a decrease of at least 10 points from baseline BDI-score, remission was defined as an absolute BDI-score of 10 points or less. Remission and response rates were based on available data only, without imputation of missing data.

Table 3
Effect sizes of EST and remission rates in comparison to RCT evidence base (based on Keitner et al. (2006)).

	Effect size	Remission (%)	
		Current study	RCTs
CT	1.3	37	30–48
CT–PHT	1.0	29	16–40
IPT	1.5	36	30–48
IPT–PHT	1.0	33	16–40

Note: CT=cognitive therapy, CT–PHT=cognitive therapy and pharmacotherapy, IPT=interpersonal psychotherapy, IPT–PHT=interpersonal psychotherapy and pharmacotherapy.

Table 4
Effects of cognitive therapy vs interpersonal therapy and psychotherapy alone vs combination treatment of psychotherapy and antidepressant medication on depressive symptoms (BDI) in the course of 26 weeks.

Variable	ß	S.E.	p
Intercept	22.25	1.22	
Time	−4.61	1.26	<0.001
Time^2	0.31	0.39	0.440
CT vs IPT	3.33	1.69	0.052
PSY vs COM	4.84	2.37	0.043
CT vs IPT × Time	−4.00	1.76	0.024
CT vs IPT × Time^2	1.17	0.54	0.034
PSY vs COM × Time	−1.51	2.42	0.533
PSY vs COM × Time^2	0.61	0.74	0.406
CT vs IPT × PSY vs COM	−5.43	3.11	0.082
CT vs IPT × PSY vs COM × Time	**6.59**	**3.19**	**0.041**
CT vs IPT × PSY vs COM × Time^2	**−2.09**	**0.97**	**0.033**

Note: time=0, 8, 16, 26 week measurement (coded in the regression analyses as 0, 1, 2, 3, respectively).
CT vs IPT=Cognitive Therapy (1) vs Interpersonal Therapy (0).
PSY vs COM=Psychotherapy alone (1) vs Combination treatment of psychotherapy and Antidepressant medication (0).

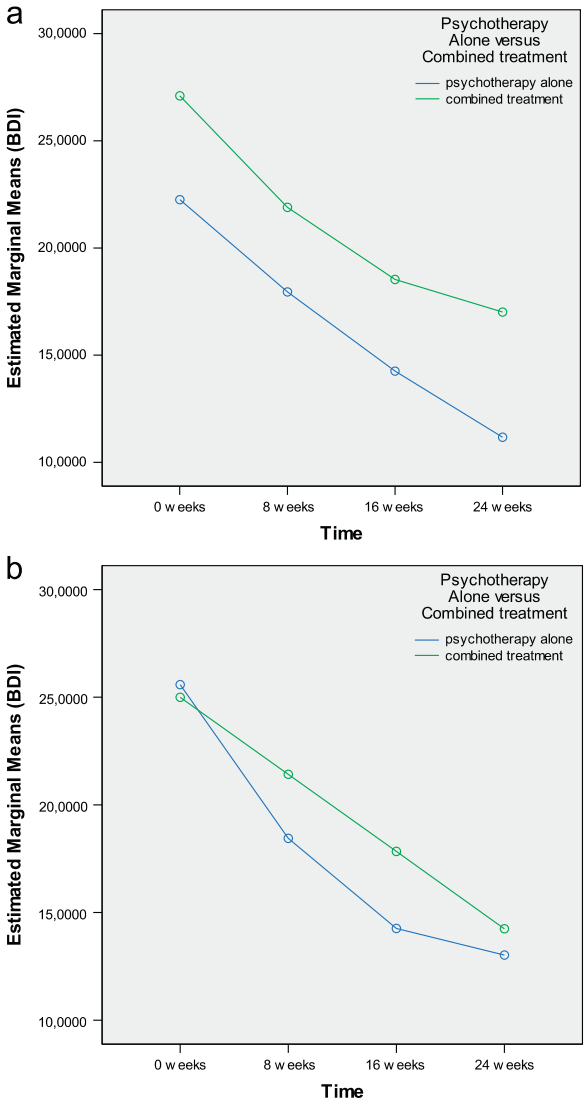

Fig. 1. (a) Effects of psychotherapy alone vs combination treatment in the IPT-group. (b) Effects of psychotherapy alone vs combination treatment in the CT-group.

Only a minority (20%) of patients remitted through 8 weeks of treatment; between weeks 8 and 26 many participants reported further improvement. As in the STAR*D study (Trivedi et al., 2006), which investigated serial treatment of MDD with the SSRI citalopram as the initial step, patients in the real clinical world seem to achieve significant clinical improvements more slowly than typically assessed in RCTs. These results seem to justify a longer treatment duration aimed at response and remission than most manuals, textbooks, and guidelines describe. We can only hypothesize possible reasons for this different treatment time frame. Possibilities include a lower treatment adherence by therapists or patients, the absence of the fixed time limit employed in RCTs that pressures patients and therapists to work fast, or unknown participant characteristics.

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As patient preference determined treatment choice, it should be noted that the vast majority of participants preferred psychotherapy alone, while a smaller group chose the combination of psychotherapy and PHT. This corroborates earlier reports on treatment preference by individuals seeking treatment for MDD (Kessing et al., 2005; Raue et al., 2009; van Schaik et al., 2004). Congruence between the treatment patients prefer and the treatment they actually receive is generally considered as a positive prognostic indicator of outcome (Raue et al., 2009). Given the low compliance rates in pharmacotherapy treatment of depression (Vergouwen et al., 2003) this suggests the need for wider availability of evidence-based psychotherapies for MDD in routine clinical practice. Although 'routine clinical practice' may differ considerably across settings, cultures and health care systems, our results may inform both clinicians and decision makers even in contexts that do not offer the array of available treatments available in our center. Doubts about generalizability of efficacy data, and cultural and socioeconomic factors appear to discourage implementation and availability of ESTs for MDD (Mojtabai, 2009). Despite patient treatment preference and current empirical data like that presented in this study, pharmacological treatment predominates (Marcus and Olfson, 2010; Olfson and Marcus, 2010) and many depressed patients remain undertreated (Gonzalez et al., 2010).

This study has both limitations and strengths. First, the somewhat modest sample size may have obscured significant differences in effectiveness between treatments. Second, 35% of eligible patients referred to the mood disorders treatment program chose not to participate in the study which may hamper generalization. Additionally, as in other naturalistic studies (Rush et al., 2006), a substantial number of participants were lost to follow-up. We addressed the latter problem by the use of mixed linear regression modeling. Third, inherent in our pragmatic design, participants were not randomized. Treatment choice depended on participants' preferences, which may have been influenced by many sources. Fourth, the absence of a non-active control group raises uncertainty about whether the observed improvement indicates ESTs in our setting were effective. Natural history might conceivably account for the sample's symptomatic improvement. We deem this unlikely, in as much as the mean duration of current episode in our sample was more than 8 months, and more than a third suffered from chronic MDD (>2 years). Rates of spontaneous improvement and remission decline considerably once an episode of MDD surpasses 6 months (Spijker et al., 2002). Additionally, the treatment effect sizes were substantially larger than natural history benchmarks for MDD. Fifth, treatments were delivered as usual in our treatment program. Although therapists were encouraged to adhere to published manuals (Beck et al., 1979; Klerman et al., 1984), we did not monitor treatment integrity, content, and quality beyond the weekly therapist meetings that reviewed ongoing cases. Thus differences in quality of therapy and therapists might have influenced results. However, we consider this unlikely, as therapies followed treatment manuals, therapists were adequately trained to deliver treatments, and inexperienced and experienced therapists were equally divided across the different ESTs.

The study's main strength is its realism: it examined the effectiveness of ESTs for MDD as they are delivered in daily practice to the people who actively seek psychiatric treatment. A structured diagnostic interview ensured accurate classification of patients' diagnoses, and well-defined, well-administered therapeutic approaches were assessed with a psychometrically robust outcome measure. Further, unlike RCTs, our study assessed patients assigned to an empirically supported treatment of their choice. To our knowledge, this is the first naturalistic study to examine the effectiveness of CT, IPT, and their combination with antidepressant medication in the treatment of MDD. No accepted standards exist for reporting the results of a pragmatic trial like ours. To maximize the applicability of our results, we followed recent guidelines to describe setting, interventions, therapists, participants, and outcomes (Zwarenstein et al., 2008).

Because of differences in key variables (e.g., setting, patients), no single naturalistic study of antidepressant treatments can definitively determine their effectiveness. More effectiveness studies, together with efficacy trials, are needed to fully explore the magnitude of our therapeutic abilities.

Role of funding source

None.

Conflict of interest

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