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Differential efficacy of cognitive behavioral therapy and psychodynamic therapy for major depression: a study of prescriptive factors

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Abstract

Context: Minimal efficacy differences have been found between cognitive behavioral therapy and psychodynamic therapies in the treatment of depression, but little is known about patient characteristics that might moderate differential treatment effects.

Objective: To generate hypotheses regarding potential prescriptive factors associated with differential post-treatment efficacy for these two psychotherapies.

Design: Post-hoc analyses alongside a randomized clinical trial (2006-2009).

Setting: Three non-academic routine outpatient mental health clinics in Amsterdam, the Netherlands.

Patients: A referred sample of 233 (out of 341) adults meeting DSM-IV criteria for a depressive episode and with Hamilton Depression Rating Scale scores ≥ 14 that completed post-treatment assessment.

Interventions: 16 sessions of individual manualized cognitive behavioral therapy or short psychodynamic supportive therapy within 22 weeks. Severely depressed patients received additional antidepressant medication according to protocol.

Main outcome measure: Hamilton Depression Rating Scale scores rated by observers not blind to patient grouping.

Results: While treatment differences were minimal in the total sample of patients completing post-treatment assessment (*d*=0.04), model-based recursive partitioning indicated differential treatment efficacy in certain subgroups of patients. Psychodynamic therapy was found more efficacious among moderately depressed patients receiving psychotherapy only that showed low baseline comorbid anxiety levels (d=-0.40) and among severely depressed patients receiving combined treatment that reported a duration of the depressive episode of one year or longer (*d*=-0.31), while cognitive behavioral therapy was found more efficacious for such patients reporting a duration shorter than one year (*d*=0.83).

Conclusions: Our findings are observational and need validation before they can be used to guide treatment selection, but suggest that knowledge of prescriptive factors can help improving the efficacy of psychotherapy for depression. Depressive episode duration and comorbid anxiety level should be included as stratification variables in future randomized clinical trials comparing cognitive behavioral therapy and psychodynamic therapy.

Trial registration: Current Controlled Trials ISRCTN31263312 (http://www.controlled-trials.com)

Introduction

Psychological treatments for depression have different theoretical backgrounds, but are generally found equally efficacious (Cuijpers, van Straten, Andersson, & van Oppen, 2008). Cognitive behavioral therapy (CBT), for example, aims at alleviating depressive symptoms by changing maladaptive thought schemata and errors in thinking in combination with engaging more in activities that affect mood positively, while psychodynamic therapies assume that gaining insight in (partly) unconscious emotions and relational functioning related to vulnerability for depression is curative. Notwithstanding these markedly different theoretical backgrounds, minimal differences have been found between CBT and psychodynamic therapies with regard to the reduction of depressive symptom during short-term treatment (Cuijpers et al., 2008; Leichsenring, 2001).

If minimal efficacy differences are found when CBT and psychodynamic therapies are compared across larger patient samples, the question can be raised whether smaller subgroups of patients can be identified that might benefit more from one of these treatments than the other and whether such patient characteristics can be used to guide treatment selection. A useful distinction in this regard can be made between prognostic and prescriptive factors. Prognostic factors (or non-specific predictors of treatment outcome; Kraemer, Wilson, Fairburn, & Agras, 2002), predict outcome to a given treatment (or to treatment in general) and can be used to determine which patients are more likely to respond to that given treatment relative to other patients. Van, Schoevers, and Dekker (2008), for instance, identified female gender, younger age, and duration of the depressive episode shorter than one year as prognostic factors associated with better response to psychodynamic therapy relative to patients of male gender, older age, and with longer episode duration. Although such prognostic factors can help shape expectations when starting treatment, they are of little use in deciding what treatment to select. On the other hand, prescriptive information (or moderators; Kraemer et al., 2002) relate to different patterns of outcomes between different treatments for different types of patients and provide a basis for choosing the best treatment for a given patient.

Little is known about prescriptive factors that are associated with differential efficacy to CBT and psychodynamic therapy for depression. We could retrieve only three studies in this regard. Two studies in the same sample found that comorbid cluster-C personality disorder and treatment credibility predicted differential response within psychodynamic-interpersonal psychotherapy, but not in CBT (prognostic; Hardy et al.,1995a, b). However, the investigators did not conduct the kinds of direct treatment comparisons within patient subgroups required to establish a prescriptive relationship (Driessen & Hollon, 2010). A third study found that clinically depressed family caregivers who had been caregivers for less than 44 months improved more in psychodynamic therapy than in CBT, while patients who had been caregivers longer improved more in CBT than in psychodynamic therapy (Gallagher & Steffen,1994). None of these studies examined demographic or illness characteristics as possible prescriptive factors.

Given the lack of research findings in this regard, the National Institute for Health and Clinical Excellence (NICE, 2009, p.46) called for the examination of moderators of response to CBT and psychodynamic therapy in the treatment of moderate and severe depression as a research recommendation in order to improve patient care. Considering the paucity of findings, we aimed to conduct a hypothesis-generating (rather than a hypothesis-testing [Kraemer et al., 2002]) study by means of conducting post-hoc analyses alongside a randomized clinical trial (RCT) comparing CBT and psychodynamic therapy in the outpatient treatment of depression (Driessen et al., 2007). Hypothesis-generating studies are often dismissed as "fishing expeditions", but as argued by Kraemer et al. (2002) such studies "are necessary to foster stronger hypotheses for the next generation of hypothesis-testing studies and to provide the background information necessary to design such powerful studies" (p. 882). Kraemer et al. (2002), therefore, state that "RCTs should routinely include and report such analyses" (p. 883).

Given the hypothesis-generating nature of our study, we chose to examine a large set of demographic, clinical and psychological patient characteristics as potential prescriptive variables. We expected to find patient characteristics moderating treatment efficacy, and formulated two preliminary hypotheses (Driessen et al., 2007). We hypothesized CBT being more efficacious than psychodynamic therapy for patients with comorbid anxiety symptoms of anxiety, because we found that a subgroup of depressed patients with such symptoms benefited less from psychodynamic therapy in a previous study (prognostic; Van et al., 2012) and CBT has resulted in large effects for patients with different anxiety disorders (Butler, Chapman, Forman, & Beck, 2006*)*. We also hypothesized CBT being more efficacious than psychodynamic therapy for patients showing relatively high levels of cognitive reactivity to sad mood, because CBT attends more specifically to this aspect than psychodynamic therapy and patients who recovered through CBT have shown less cognitive reactivity than patients recovered through other treatment (Segal et al., 2006). However, as mentioned above, the primary aim of this study is hypothesis-generating rather than hypothesis-testing.

Methods

Design

This paper draws from data collected in the context of a randomized clinical trial comparing the efficacy of cognitive behavioral therapy and psychodynamic therapy in the outpatient treatment of depression that included 341 patients. This intervention study was registered as ISRCTN31263312 with Current Controlled Trials (http://www.controlled-trials.com). The Dutch Union of Medical-Ethic Trial Committees for mental health organizations approved the study design and the study protocol was published (Driessen et al., 2007). Efficacy results of this study are reported elsewhere (Driessen et al., 2012a, b); here we report an effort to identify prescriptive factors associated with differential treatment efficacy. Although these

analyses are post-hoc, the decision to conduct them was made a priori (Driessen et al., 2007).

Patients

Participants were referred by their general practitioner to one of three non-academic routine outpatient mental health clinics in Amsterdam, The Netherlands. Inclusion criteria were: 1) presence of a depressive episode according to DSM-IV criteria as assessed with the *MINI-International Neuropsychiatric Interview – Plus* (Sheehan et al., 1998), 2) *Hamilton Depression Rating Scale* (HAM-D [Hamilton, 1960]) scores ≥ 14, 3) age between 18 and 65 years, and 4) written informed consent after complete description of the study. Exclusion criteria are described elsewhere (Driessen et al., 2007).

Interventions

Both psychotherapies encompassed 16 individual sessions within 22 weeks and were conducted according to published treatment manuals (de Jonghe, 2005; Molenaar, Don, van den Bout, Sterk, & Dekker, 2009). CBT was based on the principals of Beck (Beck, 1976) and included behavioral activation and cognitive restructuring. Short psychodynamic supportive psychotherapy (de Jonghe, 2005; de Jonghe et al, in press; de Jonghe, Kool, van Aalst, Dekker, & Peen, 2001; de Jonghe et al., 2004; Dekker et al., 2005; Dekker et al., 2008) constituted psychodynamic therapy in this study and addressed emotional, behavioral, and cognitive aspects of relational functioning, internalized relationships, and intrapersonal patterns related to the onset of depression using supportive and insight-facilitating techniques. Psychotherapists in both conditions were trained (resident) psychiatrists or psychologists. Without using specific measures, manual adherence was checked by means of bi-weekly (weekly for residents) supervision sessions chaired by a study supervisor in which audio-taped material was discussed.

Severely depressed patients (HAM-D>24 at baseline; *n*=129) and moderately depressed patients at baseline that developed severe symptoms during treatment (*n*=21) were offered additional antidepressant medication administrated by (resident) psychiatrists according to a protocol starting with extended-release venlafaxine 75 mg/day that could be raised to a maximum of 225 mg/day and switched to either citalopram or nortriptyline in case of intolerance or complete nonresponse. Pharmacotherapy consults addressed symptom evaluation, side-effects and adherence.

Instruments

Post-treatment remission rate (HAM-D≤7) constituted the RCT's primary outcome. However, as the rather low remission rates found (Driessen et al., 2012a) would likely result in empty cells when examining subgroups of patients, thereby compromising logistic analyses, we decided to use continuous post-treatment HAM-D scores as primary outcome measure in this study. HAM-D assessors were trained master-level clinical psychology students not blind to patient grouping, who assessed the HAM-D

Table 1: Baseline characteristics of the study sample

Variable	Total sample (*n*=233)		CBT (*n*=111)		Psychodynamic (*n*=122)		Test statistic (df)	*p*
Additional antidepressant medication? (n, %)							$\chi^2(1)=0.28$	.34
Psychotherapy only (HAM-D≤24)	151	64.8	68	61.3	83	68.0		
Combined treatment (HAM-D>24)	82	35.2	43	38.7	39	32.0		
Pretreatment HAM-D score (mean, SD)	23.03	5.20	23.17	5.04	22.90	5.35	*t*(231)=0.39	.69
Demographic characteristics								
Age (mean, SD)	39.98	10.33	39.46	10.16	40.46	10.50	*t*(231)=-0.74	.46
Gender (n, %)							$\chi^2(1)=0.04$	.89
Male	75	32.2	35	31.5	40	32.8		
Female	158	67.8	76	68.5	82	67.2		
Nationality (n, %)							$\chi^2(1)=0.05$	1.00
Dutch	208	91.2	99	91.7	109	90.8		
Non-Dutch	20	8.8	9	8.3	11	9.2		
Cultural background (n, %)							Fisher's exact=3.00	.95
North-west European	140	60.1	68	61.3	72	59.0		
South-European	2	0.9	1	0.9	1	0.8		
Caribbean	27	11.6	11	9.9	16	13.1		
North-African	1	0.4	1	0.9	0	0.0		
Moroccan	23	9.9	12	10.8	11	9.0		
Turkish	18	7.7	7	6.3	11	9.0		
Asian	5	2.1	3	2.7	2	1.6		
Other	17	7.3	8	7.2	9	7.4		
Marital status (n, %)							Fisher's exact=9.66	.02
Married	62	26.6	38	34.2	24	19.7		
Divorced	46	19.7	24	21.6	22	18.0		
Widowed	6	2.6	1	0.9	5	4.1		
Never married	119	51.1	48	43.2	71	58.2		
Living situation (n, %)							Fisher's exact=2.11	.38
Living with at least one other person	147	63.4	74	66.7	73	60.3		
Living alone	77	33.2	35	31.5	42	34.7		
Other	8	3.4	2	1.8	6	5.0		

Religion (n, %)							Fisher's exact=1.94	1.00
Christian	53	24.4	26	24.5	27	24.3		
Moslim	43	19.8	22	20.8	21	18.9		
Hindu/Buddhist	2	0.9	1	0.9	1	0.9		
Other	45	20.7	22	20.8	23	20.7		
Educational level (n, %)							$\chi^2(2)=2.04$	.38
Low	49	21.2	23	20.9	26	21.5		
Intermediate	102	44.2	44	40.0	58	47.9		
High	80	34.6	43	39.1	37	30.6		
Current profession (n, %)							Fisher's exact=6.50	.49
No profession	43	19.9	19	18.6	24	21.1		
Houseman/housewife	34	15.7	17	16.7	17	14.9		
Unskilled labor	23	10.6	9	8.8	14	12.3		
Skilled labor	61	28.2	26	25.5	35	30.7		
Low-level white collar work	6	2.8	4	3.9	2	1.8		
Small company entrepreneur	14	6.5	5	4.9	9	7.9		
Middle-level white collar executive/ high-level white collar non-executive	32	14.8	20	19.6	12	10.5		
Large company entrepreneur/high-level white collar executive	3	1.4	2	2.0	1	1.6		
Job status (n, %)							Fisher's exact=5.10	.41
Currently working	92	40.0	42	38.2	50	41.7		
Sickness benefits	41	17.8	25	22.7	16	13.3		
Social security benefits	41	17.8	17	15.5	24	20.0		
Disability benefits	25	10.9	12	10.9	13	10.8		
Student	10	4.3	3	2.7	7	5.2		
Other	21	9.1	11	10.0	10	8.3		
Family bread winner (n, %)							Fisher's exact=1.74	.83
Yes	153	69.5	70	67.3	83	71.6		
No: partner is bread winner	48	21.8	23	22.1	25	21.6		
No: parent is breadwinner	4	1.8	3	2.9	1	0.9		
No: two-earner household	11	5.0	6	5.8	5	4.3		
Other	4	1.8	2	1.9	2	1.7		
Breadwinner's main source of income (n, %)							Fisher's exact=5.20	.53
Salary	141	65.9	74	71.2	67	60.9		
Pension	2	0.9	1	1.0	1	0.9		
Welfare	26	12.1	13	12.5	13	11.8		

Variable	Total sample (*n*=233)		CBT (*n*=111)		Psychodynamic (*n*=122)		Test statistic (df)	*p*
Disability benefit	15	7.0	6	5.8	9	8.2		
Unemployment benefit	10	4.7	4	3.8	6	5.5		
Study subsidy	2	0.9	1	1.0	1	0.9		
Other	18	8.4	5	4.8	13	11.8		
Clinical characteristics								
Duration present episode (n, %)							Fisher's exact=8.25	.08
Less than 6 months	58	24.9	32	28.8	26	21.3		
6 months to 1 year	57	24.5	30	27.0	27	22.1		
1 to 2 years	32	13.7	18	16.2	14	11.5		
More than 2 years	78	33.5	27	24.3	51	41.8		
Unknown		3.4	4	3.6	4	3.3		
Prior treatment for current depressive episode (n, %)							$\chi^2(1)=1.49$	.27
No	150	64.4	67	60.4	83	68.0		
Yes	83	35.6	44	39.6	39	32.0		
Number of prior depressive episodes (n, %)							$\chi^2(2)=0.68$	.73
None	70	30.3	36	32.7	34	28.1		
One	41	17.7	18	16.4	23	19.0		
Two or more	120	51.9	56	50.9	64	52.9		
Medication use (n, %)							$\chi^2(1)=3.15$	.08
Yes	110	50.5	58	56.9	52	44.8		
No	108	49.5	44	43.1	64	55.2		
Comorbid anxiety (Beck Anxiety Inventory; mean, SD)	23.59	12.97	23.84	13.07	23.37	12.93	$t(218)=0.27$	.79
Comorbid psychopathology (Brief Symptom Inventory; mean, SD)	1.83	0.76	1.89	0.78	1.78	0.74	$t(193)=1.10$	.27
Consults with general practitioner in the last 4 weeks (mean, SD)	0.87	1.19	0.85	1.01	0.88	1.34	$t(221)=-0.20$	.85
Consults with mental health care in the last 4 weeks (mean, SD)	0.75	1.12	0.71	1.04	0.78	1.20	$t(221)=-0.43$	.67
Consults with industrial medical officer in the last 4 weeks (mean, SD)	0.39	0.72	0.48	0.78	0.31	0.65	$t(202)=1.75$	.08
Psychological characteristics								
Cognitive reactivity to sad mood (LEIDS; mean, SD)	54.55	16.62	54.26	15.94	54.80	17.26	$t(219)=0.03$	.98
Anxiety sensitivity (ASI; mean, SD)	36.83	13.58	36.86	13.09	36.81	14.07	$t(212)=-0.24$	.81

CBT = cognitive behavioral therapy, HAM-D = Hamilton Depression Rating Scale, SD = standard deviation.

according to the Dutch scoring manual (de Jonghe, 1994). Assessors engaged in one-hour peer supervision sessions bi-weekly, in which audio-taped interviews were discussed. The average intraclass correlation coefficient over 46 audio-taped assessments scored by multiple assessors was .97.

We aimed at examining a large set of potential prescriptive factors (see Driessen et al., 2007), but were faced with missing data on a number of these due to patients not returning questionnaire booklets. We decided to examine a variable as a potential prescriptive factor only if 10% or less of the cases were missing. All potential prescriptive demographic, clinical and psychological patient characteristics were assessed at baseline assessment. With regard to demographic characteristics, age and gender were extracted from the mental health clinic registration system, while a self-report demographic questionnaire designed by the investigators was used to assess nationality, cultural background, marital status, living situation, religion, educational level, current profession, job status, breadwinnership, and breadwinner's main source of income. The classification options for these variables are listed in Table 1. Cultural background was included in this study, because we considered it a potential prescriptive factor of differential treatment efficacy. Patients classified themselves with regard to cultural background, with options (see Table 1) being defined by the investigators.

With regard to clinical characteristics, we used the Beck Anxiety Inventory (Beck, Epstein, Brown, & Steer, 1998) total score to assess comorbid anxiety symptoms, the Brief Symptom Inventory (de Beurs & Zitman, 2006) total score to assess (comorbid) general psychopathology, and four items of the Trimbos/iMTA questionnaire for costs associated with psychiatric illness (Hakkaart-van Roijen, 2002) to assess health care use (medication use and number of consults with general practitioner, outpatient mental health care, and industrial medical officer in the last four weeks). Duration of the current depressive episode, previous treatment for the current depressive episode, and life-time number of depressive episodes were self-reported by the patient during a baseline clinical interview (see Table 1 for classification options).

Psychological characteristics included cognitive reactivity to sad mood (the relative ease with which maladaptive cognitions or cognitive styles are triggered by mild mood fluctuations) and anxiety sensitivity (a person's beliefs that anxiety experiences have negative somatic, psychological or social consequences), which were measured by total scores of, respectively, the Anxiety Sensitivity Index (Reiss, Peterson, Gursky, & McNally, 1986) and the Leiden Index of Depression Sensitivity (van der Does, 2002).

Statistical analysis

Rather than using the intention-to-treat sample and imputing missing post-treatment HAM-D scores, we examined potential prescriptive factors in the group of patients that completed post-treatment HAM-D assessment. We chose to do so because loss to HAM-D assessment was significantly associated with missing baseline data for a number of variables, such that for the patients who were lost to assessment and whose HAM-D value was to be imputed, data on which the imputation should be

based was missing as well and imputation would likely result in unreliable post-treatment HAM-D values.

In clinical trials, prescriptive factors are often examined by means of stepwise regression analysis, adding a main effect and a predictor-by-treatment interaction effect into the model for each potential prescriptive factor (Kraemer et al., 2002). However, the power of finding significant effects in such a model with a multitude of parameters may be low in a sample of modest size, the resulting model can be quite complex making it hard to interpret, and stepwise regression does not allow for modeling non-linear relationships. A new method that can also be used in this regard, but does not suffer from these issues is model-based recursive partitioning (MOB; Zeileis, Hothorn, & Hornik, 2008; Strobl, Malley, & Tutz, 2009; Zeileis, Hothorn, & Hornik, n.d.). MOB is a method for finding subgroups for which a specified basic model has different parameters. In the case of our study, this basic model is an ANOVA model including post-treatment HAM-D score as dependent variable and a dichotomous treatment factor (CBT or psychodynamic therapy) as independent variable. This ANOVA model has two parameters: an intercept (equaling the average post-treatment HAM-D score of all subjects) and a treatment parameter (equaling the average difference in post-treatment HAM-D score between the treatment conditions). This latter parameter is considered the most interesting as it reflects differential treatment efficacy.

MOB uses potential prescriptive variables (e.g., demographic characteristics) to identify groups of patients for which the ANOVA model parameters differ. If the treatment parameter differs between subgroups, this means that the average difference between the two treatments is different for these subgroups. Consequently, the predictor(s) defining these groups can be considered prescriptive factors. For example, if MOB would show a positive treatment parameter for males and a negative one for females, this would mean that, on average, the one treatment gives better outcomes for males, whereas the other treatment gives better outcomes for females and gender could be considered a prescriptive factor.

To identify these subgroups, a binary tree is used in MOB. In the first node of the tree, all observations are used to estimate the basic ANOVA model. Next, for each potential prescriptive variable, its values are ordered, and for each of these values, the appropriateness of the parameter estimate is quantified, and it is tested if a structural change occurs with increasing predictor, which results in a *p*-value. Next, it is checked if the lowest *p*-value is lower than some pre-specified α, and if so, the predictor associated with this minimal value is chosen to split up the observations into two subgroups (child nodes) using the cut-score which shows the highest structural change. Next, in the left child node, the data of the first subgroup are used to refit the ANOVA model, and again it is tested if there is a structural change for each predictor. Likewise, in the right child node the ANOVA model is refitted on the data of the second subgroup and again, a test for structural change is carried out for each predictor. This process of splitting nodes into child nodes is continued until the lowest *p*-value fails to be significant.

In this study, MOB was conducted in R (R Development Core Team, 2010) using the party library (Hothorn, Hornik, Strobl, & Zeileis, 2012). As described above, we chose an ANOVA model as the basic model. We decided not to include pre-treatment HAM-D score as a covariate in this basic model, because pre-treatment HAM-D score was used as a decision variable to add antidepressant medication to psychotherapy. Adding it as a covariate would be problematic, as this would result in a spurious relationship between the medication factor and the covariate's regression parameter in the basic model. We changed party's default value for minimal observations in the end nodes from 20 to 30 (about 15 of each therapy group), which we deemed the minimal for estimating the ANOVA. We used an α of 10%, because of the theory-generating nature of our study (Kraemer et al., 2002 pp.881-882; Stevens, 2002) and because sample size was reduced by the exclusion of patients not completing post-treatment HAM-D assessment and might be further decreased by missing values among the prescriptive variables.

In standard MOB, all predictors are entered in the model simultaneously, but we preferred a forward selection approach for two reasons. First, MOB as implemented in R's party library uses complete observations on all variables entered. Although the algorithm usually only selects a small subset of the potential predictors, observations with any missing value on the full set of variables are removed before the actual analysis. As missing value patterns varied over variables, entering all variables simultaneously would result in a large number of excluded cases, while this was not the case with the forward selection approach. Second, patients with a baseline HAM-D scores>24 received additional antidepressant medication. Because all other predictors should be nested under this design factor, it should be in the first node of the binary tree. The only way to incorporate this into the model is to force this factor as the first predictor in the forward approach, and then expand the model with additional predictors in each of the child nodes. Our data-analytic strategy bares a strong resemblance with a method reported by Dusseldorp and colleagues (Dusseldorp & Meulman, 2004; Dusseldorp, Spinhoven, Bakker, van Dyck, & van Balkom, 2007) in a study of prescriptive factors associated with differential efficacy of cognitive therapy or antidepressants for panic disorder patients, but the current method can be considered more advanced due to MOB improvements over the last couple of years.

Results

Patient sample

Of the 341 patients randomized, 233 (68.3%) completed post-treatment HAM-D assessment and no significant differences were found between treatment conditions with regard to the number of patients lost to post-treatment HAM-D assessment (CBT: 32.3%; psychodynamic: 31.1%; $\chi^2(1)=.06$, $p=.81$). The group of patients that completed post-treatment HAM-D assessment is described in Table 1 with regard to all potential prescriptive variables examined. With the exception of marital status, no significant differences between conditions were found. In Table 2, patients that completed post-

Table 2: Differences between patients completing post-treatment HAM-D assessment and patients not completing this assessment, which were excluded from the analyses

Variable	Total sample (*n*=341)		Completers (*n*=233)		Non-completers (*n*=108)		Test statistic (df)	*p*
Additional antidepressant medication? (n, %)								
Psychotherapy only (HAM-D≤24)	212	62.2	151	64.8	61	56.5	$\chi^2(1)=2.18$	.15
Combined treatment (HAM-D>24)	129	37.8	82	35.2	47	43.2		
Pretreatment HAM-D score (mean, SD)	23.40	5.35	23.03	5.20	24.19	5.59	$t(339)=-1.88$	.06
Demographic characteristics								
Age (mean, SD)	38.91	10.29	39.98	10.33	36.58	9.88	$t(339)=2.87$	<.01
Gender (n, %)							$\chi^2(1)=1.82$	.20
Male	102	29.9	75	32.2	27	25.0		
Female	239	70.1	158	67.8	81	75.0		
Nationality (n, %)							$\chi^2(1)=4.70$	.04
Dutch	291	88.7	208	91.2	83	83.0		
Non-Dutch	37	11.3	20	8.8	17	17.0		
Cultural background (n, %)							Fisher's exact=22.15	<.01
North-west European	186	55.0	140	60.1	46	43.8		
South-European	2	0.6	2	0.9	0	0.0		
Caribbean	46	13.6	27	11.6	19	18.1		
North-African	6	1.8	1	0.4	5	4.8		
Moroccan	46	13.6	23	9.9	23	21.9		
Turkish	22	6.5	18	7.7	4	3.8		
Asian	7	2.1	5	2.1	2	1.9		
Other	23	6.8	17	7.3	6	5.7		
Marital status (n, %)							Fisher's exact=9.23	.04
Married	80	23.7	62	26.6	18	17.1		
Divorced	69	20.4	46	19.7	23	21.9		
Widowed	10	3.0	6	2.6	4	3.8		
Never married	176	52.1	119	51.1	57	54.3		
Other	3	0.9	0	0.0	3	2.9		
Living situation (n, %)							Fisher's exact=1.17	.58
Living with at least one other person	220	65.3	147	63.4	73	69.5		
Living alone	106	31.5	77	33.2	29	27.6		

Other	11	3.3	8	3.4	3	2.9		
Religion (n, %)							Fisher's exact=12.34	.10
Christian	76	25.5	53	24.4	23	28.4		
Moslim	66	22.1	43	19.8	23	28.4		
Hindu/Buddhist	6	2.0	2	0.9	4	4.9		
Other	60	20.1	45	20.7	15	18.3		
Educational level (n, %)							$\chi^2(2)=6.01$	.05
Low	71	21.2	49	21.2	22	21.2		
Intermediate	161	48.1	102	44.2	59	56.7		
High	103	30.7	80	34.6	23	22.1		
Current profession (n, %)							Fisher's exact=16.10	.02
No profession	73	24.3	43	19.9	30	35.3		
Houseman/housewife	39	13.0	34	15.7	5	5.9		
Unskilled labor	35	11.6	23	10.6	12	14.1		
Skilled labor	87	28.9	61	28.2	26	30.6		
Low-level white collar work	7	2.3	6	2.8	1	1.2		
Small company entrepreneur	16	5.3	14	6.5	2	2.4		
Middle-level executive/high-level non-executive white collar work	39	13.0	32	14.8	7	8.2		
Large company entrepreneur/high-level white collar executive	5	1.7	3	1.4	2	2.4		
Job status (n, %)							Fisher's exact=8.16	.14
Currently working	130	38.8	92	40.0	38	36.2		
Sickness benefits	55	16.4	41	17.8	14	13.3		
Social security benefits	74	22.1	41	17.8	33	31.4		
Disability benefits	32	9.6	25	10.9	7	6.7		
Student	14	4.2	10	4.3	4	3.8		
Other	30	9.0	21	9.1	9	8.6		
Family bread winner (n, %)							Fisher's exact=14.99	<.01
Yes	210	69.8	153	69.5	57	70.4		
No: partner is bread winner	56	18.6	48	21.8	8	9.9		
No: parent is breadwinner	11	3.7	4	1.8	7	8.6		
No: two-earner household	15	5.0	11	5.0	4	4.9		
Other	9	3.0	4	1.8	5	6.2		
Breadwinner's main source of income (n, %)							Fisher's exact=26.25	<.01
Salary	177	60.6	141	65.9	36	46.2		
Pension	6	2.1	2	0.9	4	5.1		

Variable	Total sample (*n*=341)		Completers (*n*=233)		Non-completers (*n*=108)		Test statistic (df)	*p*
Welfare	37	12.7	26	12.1	11	14.1		
Disability benefit	19	6.5	15	7.0	4	5.1		
Unemployment benefit	27	9.2	10	4.7	17	21.8		
Study subsidy	4	1.4	2	0.9	2	2.6		
Other	22	7.5	18	8.4	4	5.1		
Clinical characteristics								
Duration present episode (n, %)							Fisher's exact=2.46	.66
Less than 6 months	84	25.1	58	24.9	26	25.7		
6 months to 1 year	89	26.6	57	24.5	32	31.7		
1 to 2 years	43	12.9	32	13.7	11	10.9		
More than 2 years	108	32.3	78	33.5	30	29.7		
Unknown	10	3.0	8	3.4	2	2.0		
Prior treatment for current depressive episode (n, %)							$\chi^2(1)=0.27$	.62
No	218	65.3	150	64.4	68	67.3		
Yes	116	34.7	83	35.6	33	32.7		
Number of prior depressive episodes (n, %)							$\chi^2(2)=6.12$	<.05
None	103	31.1	70	30.3	33	33.0		
One	69	20.8	41	17.7	28	28.0		
Two or more	159	48.0	120	51.9	39	39.0		
Medication use in the last 4 weeks (n, %)							$\chi^2(1)=0.03$	.89
Yes	145	50.2	110	50.5	35	49.3		
No	144	49.8	108	49.5	36	50.7		
Comorbid anxiety (Beck Anxiety Inventory; mean, SD)	24.46	13.16	23.59	12.97	27.13	13.47	*t*(290)=-1.99	.05
Comorbid psychopathology (Brief Symptom Inventory; mean, SD)	1.86	0.76	1.83	0.76	1.93	0.77	*t*(260)=-0.94	.35
Consults with general practitioner in the last 4 weeks (mean, SD)	0.85	1.21	0.87	1.19	0.80	1.26	*t*(303)=0.39	.70
Consults with mental health care in the last 4 weeks (mean, SD)	0.73	1.14	0.75	1.12	0.67	1.21	*t*(303)=0.53	.60
Consults with industrial medical officer in the last 4 weeks (mean, SD)	0.40	0.78	0.39	0.72	0.43	0.95	*t*(290)=-0.38	.71
Psychological characteristics								
Cognitive reactivity to sad mood (LEIDS; mean, SD)	55.09	16.88	54.55	16.62	56.84	17.72	*t*(287)=-1.03	.30
Anxiety sensitivity (ASI; mean, SD)	37.31	13.99	36.83	13.58	38.83	15.25	*t*(278)=-0.97	.34

CBT = cognitive behavioral therapy, HAM-D = Hamilton Depression Rating Scale, SD = standard deviation.

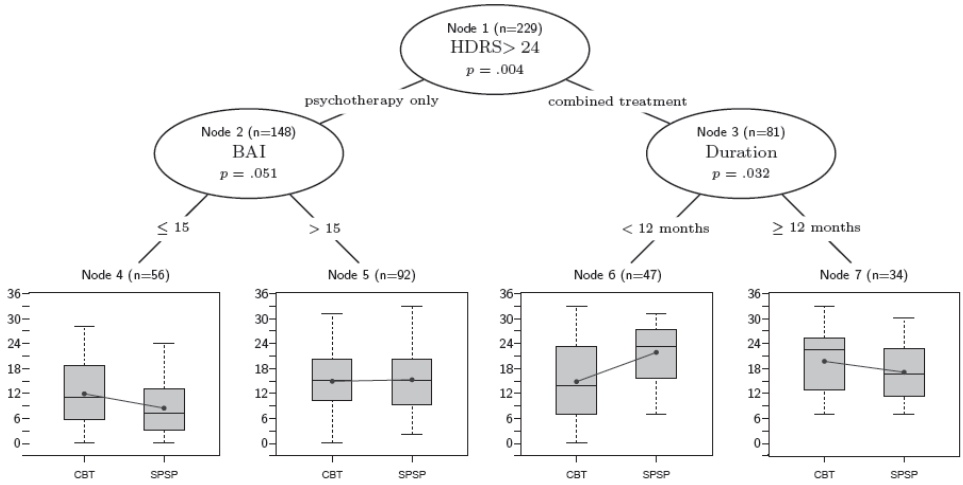
treatment HAM-D assessment are compared with patients that were lost to this assessment. It can be seen from this Table that significant differences were found between these two groups on a large number of baseline characteristics.

Model-based recursive partitioning analysis

The results of the model-based recursive partitioning analysis are represented in Figure 1 and treatment outcomes in each node of the tree are listed in Table 3. Node 1 includes all patients and treatment differences in this group were minimal (*d*=0.04; Table 2). Node 1's p-value (*p*=.004; Figure 1) indicates that the parameters of the basic model are significantly different for the two subgroups in which this Node is divided: left-hand Node 2 representing the subgroup of patients with baseline HAM-D scores ≤ 24 that received psychotherapy only and right-hand Node 3 representing the subgroup of patients with baseline HAM-D scores > 24 that received additional antidepressant medication. While minimal treatment differences (*d*=-0.07; Table 3) are found in the first group, larger treatment differences (*d*=0.36) are apparent in the latter group.

Left-hand Node 2 represents the low-severity patients receiving psychotherapy only and its p-value (*p*=.051; Figure 1) indicates that the parameters of the basic model are significantly different for the two subgroups in which this Node is divided: Node 4 including patients with baseline comorbid anxiety scores of 15 or lower and Node 5 including patients with comorbid anxiety scores above 15. In the first, post-treatment depression scores are lower in the psychodynamic therapy condition than in the CBT condition (*d*=-0.40; Table 3), while in the latter post-treatment depression scores differ minimally (*d*=0.04).

Figure 1: ANOVA-based tree



Note: The model predicts HDRS score at post-treatment using Factor Therapy (CBT vs SPSP). Boxplots represent scores for both groups under the ANOVA model; the dots connected by a line represent the averages in the two groups.

Table 3: Outcomes in each node of the model-based recursive partitioning tree

Node	CBT			Psychodynamic			Contrast	
	N	M	SD	N	M	SD	Cohen's *d*	*p*
1	111	14.91	8.80	122	15.25	8.72	0.04	0.77
2	68	13.43	8.08	83	12.82	8.20	-0.07	0.65
3	43	17.26	9.45	39	20.44	7.50	0.36	0.10
4	27	11.74	7.66	29	8.28	6.95	-0.40	0.08
5	39	14.77	8.28	53	15.13	7.84	0.04	0.83
6	25	15.12	9.80	22	22.41	7.20	0.83	0.01
7	18	20.22	8.32	16	17.50	7.36	-0.31	0.32

Note: pooled standard deviation is 8.754. CBT = cognitive behavioral therapy

Right-hand Node 3 represents the group of high-severity patients that received psychotherapy combined with antidepressant medication and its p-value (*p*=.032; Figure 1) indicates that the parameters of the basic model are significantly different for the two subgroups in which this Node is divided; Node 6 including patients with a duration of the current depressive episode shorter than 12 months and Node 7 including patients that report a duration of 12 months or longer. In the first, post-treatment depression scores are lower in the CBT condition (*d*=0.83; Table 3), while in the latter post-treatment depression scores are lower in the psychodynamic therapy condition (*d*=-0.31).

Sensitivity analyses

As pre-treatment HAM-D score was not included as a covariate in the basic model, one might argue that the post-treatment differences in HAM-D scores between conditions found in Nodes 4, 6, and 7 might be the consequence of chance differences in pre-treatment HAM-D scores between the treatment conditions within these Nodes. Such that, for instance, the moderately severe patients with low anxiety levels in the psychodynamic therapy condition in Node 4 coincidently had lower pre-treatment HAM-D scores than these patients in the CBT condition in this Node and that this chance finding resulted in the lower post-treatment HAM-D scores found in the psychodynamic therapy condition. We, therefore, checked for differences in pre-treatment HAM-D scores between treatment conditions within Nodes 4, 6, and 7, but found none, suggesting that chance differences in pre-treatment HAM-D scores within these Nodes do not provide an alternative explanation for our findings.

Discussion

We conducted a hypothesis-generating study of prescriptive factors associated with differential efficacy of CBT and psychodynamic therapy in a sample of patients seeking

treatment for a depressive episode in non-academic routine outpatient clinics. Minimal differences between treatments were found when examining the total sample of patients that completed post-treatment assessment, but model-based recursive partitioning analyses suggested differential efficacy among subgroups of patients that differed with regard to episode duration and comorbid anxiety level. These findings are in line with our expectation to find patient characteristics moderating treatment efficacy and with a previous study that found (another) specific factor associated with differential efficacy of CBT and psychodynamic therapy for depression (Gallagher & Steffen, 1994).

P-values within some of the Nodes, relating to treatment differences in the group of patient represented in that Node, were not significant at a α=0.05 level. Therefore, one might argue that no significant treatment differences are found in these subgroups and that, consequently, the factors that define these subgroups cannot be considered prescriptive factors. However, Kraemer et al. (2002) have argued that moderators of treatment should not be defined by p-values ("because moderator status … would then change with sample size" p. 881), but by population parameters in stead. Effect sizes within these Nodes did show relevant treatment differences, which can be considered large enough to be of importance.

Given the primary hypothesis-generating nature of our study, we only formulated two preliminary hypotheses, both of which were not supported. We expected CBT being more efficacious than psychodynamic therapy for patients with comorbid symptoms of anxiety and found comorbid anxiety level moderating differential treatment efficacy, but in the opposite way. No treatment differences were found among patients that presented higher comorbid anxiety levels and psychodynamic therapy was found to be more efficacious than CBT for patients with low anxiety levels. Our preliminary hypothesis was based on prognostic findings in a previous study, and appears not to be supported in this study of prescriptive factors. We speculate that patients with low anxiety levels might benefit from psychodynamic therapy, as they are not inhibited by anxiety to share and reflect upon their interpersonal problems and are capable of structuring their problems, but that these same patients might feel restricted by the more strictly protocolized CBT.

Duration of the current depressive episode was associated with differential treatment efficacy in severely depressed patients receiving combined treatment of psychotherapy with antidepressants. CBT was more efficacious than psychodynamic therapy for patients reporting duration of less than one year, while psychodynamic therapy was more efficacious than CBT for such patients reporting duration of one year or longer. We speculate that patients with longer episode durations have depressive symptoms that are more rooted in their personality structure resulting in more complex transference issues; psychodynamic therapists are trained to handle such symptoms and issues. At the same time, we think that it is harder for patients with longer episode duration to start doing homework and to change their lifestyle and activities, which is what CBT calls for. Similarly, patients with relative short episode durations, whose depressive symptoms might be less related to personality structure, might benefit less from psychodynamic therapy, while the combination of

antidepressant medication and behavioral activation resulting from completed homework assignments in the first part of CBT might lead to alleviation of depressive symptoms in this group.

This study has a number of strengths. First, it is one of few studies examining prescriptive factors associated with differential efficacy of CBT and psychodynamic therapy for depression, which refers to a clinically relevant but yet rather unexplored research topic related to a highly prevalent mental disorder. It also is the first study that considered demographic and illness characteristic as potential prescriptive factors and it is the first to apply model-based recursive partitioning in this regard, which provides the benefits of reducing the number of prescriptive factors and selecting the most important ones, resulting in models that are easily interpretable. Additional strengths of this study include its efforts to increase external validity, such as providing treatment in non-academic routine outpatient clinics by a large number of therapists with different experience levels and including patients with relatively low social-economic status (Driessen et al., 2012a).

However, this study also has a number of limitations. First, we examined prescriptive factors of CBT and psychodynamic therapy efficacy in a group of patients restricted to those that completed post-treatment assessment. Comparative analyses suggested that this group of patients differed from the group of patients lost to this assessment. Therefore, we need to be cautious in generalizing this study's results. Second, HAM-D assessors were not blind to patient grouping, therefore we cannot rule out observer bias. Third, treatment adherence was not assessed objectively. Instead, it was checked by means of intensive supervision by experienced supervisors. Fourth, research assistants enrolling participants were aware of the allocation sequence; although no significant differences were found between treatment conditions at baseline in the total study sample, we cannot rule out selection bias.

The most important limitation of our study is, however, its post-hoc nature. Our findings are observational and can be the consequence of chance findings in the sample studied. They should, therefore, be validated before being used to guide treatment selection. Validation should occur by including comorbid anxiety level and episode duration as stratification variables in a future randomized clinical trial comparing CBT and psychodynamic therapy in the treatment of depression and conduct a formal test of a moderator-by-treatment interaction (Kraemer et al.,2002). We also encourage replication of our study by means of applying model-based recursive partitioning in samples of other studies that compare CBT and psychodynamic therapy for depression in order to identify further potential prescriptive factors to test in such a study.

In sum, although generally similar efficacy is found for CBT and psychodynamic therapy across larger patient samples, efficacy differences can be apparent in specific subgroups of patients. We identified comorbid anxiety level and depressive episode duration as possible prescriptive factors associated with differential efficacy of CBT and PDT. If validated, these variables might be used to guide treatment selection, which might improve the efficacy of psychotherapy for depression.

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