Article

The Efficacy of Cognitive-Behavioral Therapy and Psychodynamic Therapy in the Outpatient Treatment of Major Depression: A Randomized Clinical Trial

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Objective: The efficacy of psychodynamic therapies for depression remains open to debate because of a paucity of high-quality studies. The authors compared the efficacy of psychodynamic therapy with that of cognitive-behavioral therapy (CBT), hypothesizing nonsignificant differences and the noninferiority of psychodynamic therapy relative to CBT.

Method: A total of 341 adults who met DSM-IV criteria for a major depressive episode and had Hamilton Depression Rating Scale (HAM-D) scores ≥14 were randomly assigned to 16 sessions of individual manualized CBT or short-term psychodynamic supportive therapy. Severely depressed patients (HAM-D score >24) also received antidepressant medication according to protocol. The primary outcome measure was posttreatment remission rate (HAM-D score ≤7). Secondary outcome measures included mean posttreatment HAM-D score and patient-rated depression score and 1-year follow-up outcomes. Data were analyzed with generalized estimating equations and mixed-model analyses using intent-to-treat samples. Noninferiority margins were prespecified as an odds ratio of 0.49 for remission rates and a Cohen's d value of 0.30 for continuous outcome measures.

Results: No statistically significant treatment differences were found for any of the outcome measures. The average posttreatment remission rate was 22.7%. Noninferiority was shown for posttreatment HAM-D and patient-rated depression scores but could not be demonstrated for posttreatment remission rates or any of the follow-up measures.

Conclusions: The findings extend the evidence base of psychodynamic therapy for depression but also indicate that time-limited treatment is insufficient for a substantial number of patients encountered in psychiatric outpatient clinics.

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Major depressive disorder is a highly prevalent mental disorder, substantially debilitating patients and imposing a tremendous financial burden on society (1, 2). Patients seeking treatment for depression typically are offered antidepressant medication or psychotherapy alone or in combination (3). Given that antidepressants may not be as specifically efficacious as was previously believed (4–6), treatment guidelines increasingly advocate the option of psychotherapy for mild to moderate depression (7, 8).

However, efficacy research with respect to psychotherapy for depression needs to be broadened for two reasons. First, the efficacy of psychodynamic therapy remains controversial because of a lack of adequately conducted trials (7–10). Second, while different psychotherapeutic approaches for depression are considered equally efficacious by many (11), high-quality studies directly comparing psychotherapies for depression are rare (12), and the literature is dominated by superiority trials designed to show significant differences between conditions, which cannot demonstrate equal efficacy (13).

We report the results of a randomized clinical trial comparing psychodynamic therapy with cognitive-behavioral therapy (CBT) in patients seeking treatment for a major depressive episode in psychiatric outpatient clinics (the study protocol was described previously [14]). We first examined whether treatment outcomes differed significantly, and in case of nonsignificant differences, we examined whether psychodynamic therapy was noninferior to CBT. We hypothesized that there would be 1) no significant differences between the modalities at the posttreatment assessment and 1-year follow-up and 2) noninferiority of psychodynamic therapy relative to CBT at the posttreatment assessment and 1-year follow-up.

Method

Design

This study was a randomized clinical trial with an allocation ratio of 1:1 for CBT and psychodynamic therapy. The study

This article is featured in this month's AJP Audio, is an article that provides Clinical Guidance (p. 1050), and is discussed in an Editorial by Dr. Thase (p. 953)

design was approved by the Dutch Union of Medical Ethics Trial Committees for mental health organizations.

Participants

Participants were referred by their general practitioner to one of three psychiatric outpatient clinics in Amsterdam. Inclusion criteria were presence of a major depressive episode according to DSM-IV criteria, as assessed with the Mini-International Neuropsychiatric Interview–Plus (15); a Hamilton Depression Rating Scale (HAM-D [16]) score ≥14; age 18–65 years; and written informed consent after receiving a complete description of the study.

Exclusion criteria included presence of psychotic symptoms or bipolar disorder, severe suicidality warranting immediate intensive treatment or hospitalization, substance misuse or abuse in the past 6 months, pregnancy, inability to meet trial demands, and use of psychotropic or other medications that might influence mental functions. Patients on an antidepressant regimen were included only if the medication they were currently taking was judged to be inefficacious by both the patient and the intake psychiatrist. If so, the medication was tapered off under medical supervision, and baseline assessment took place after a washout period of at least 1 week after the medication was completely stopped (16/25 of these patients subsequently restarted medication during the study).

Interventions

Both psychotherapies comprised 16 individual sessions within 22 weeks and were conducted according to published treatment manuals (17, 18). Additionally, both were suitable for application in a broad group of patients, including those of a non-Northwest European (immigrant) cultural background. CBT was based on the principles described by Beck (19) and included behavioral activation and cognitive restructuring according to a session-by-session protocol with homework assignments. Short-term psychodynamic supportive psychotherapy (18, 20–24) was used to represent the psychodynamic intervention. This modality involved an open patient-therapist dialogue that used supportive and insight-facilitating techniques to address the emotional background of the depressive symptoms by discussing current relationships, internalized past relationships, and intrapersonal patterns.

Psychotherapists in both treatment conditions were psychiatrists or psychologists with at least a master's degree who completed either a 3-day course in short-term psychodynamic supportive psychotherapy or a 100-hour basic CBT training course accredited by the Dutch Association for Behavioral and Cognitive Therapy. Moreover, all therapists adequately conducted at least one intensively supervised therapy case in accordance with the relevant treatment manual as judged by a study supervisor. Although no formal assessments were conducted, manual fidelity was checked by means of biweekly supervision sessions, chaired by a study supervisor, in which audiotaped material was discussed. All study supervisors were registered supervisors with either the Dutch Association of Psychoanalytic Psychotherapy (one supervisor was in training) or the Dutch Association for Behavioral and Cognitive Therapy. Differences in the mean number of years that the supervisors had been conducting their respective modalities were minimal (CBT, 10.9 years [SD=11.0]; psychodynamic therapy, 9.7 years [SD=2.9]) but somewhat larger with respect to mean years conducting supervision (CBT, 14.6 years [SD=10.3]; psychodynamic therapy, 6.3 years [SD=3.2]), although neither difference was significant.

Thirty-seven CBT therapists and 56 psychodynamic therapists treated, on average, 4.2 patients (range, 1–16) and 3.0 patients (range, 1–12), respectively. No differences between treatment conditions were found with regard to the average number of times a patient was discussed in supervision (CBT, 4.3; psychodynamic therapy, 4.6) or the mean number of therapy sessions patients received (CBT, 10.6; psychodynamic therapy, 10.9; mean numbers are lower than the maximum of 16 because of premature termination, dropout, and patients missing sessions). Regarding therapist protocol adherence, CBT therapists reported a mean score of 7.1 (scale range, 0–10) over 1,218 CBT sessions. Conditions did not differ regarding the mean number of years of clinical experience therapists had after completing their master's degree or medical degree (CBT, 7.5 years [SD=7.3]; psychodynamic therapy, 7.4 years [SD=6.7]), but CBT was more often conducted by psychologists, and psychodynamic therapy was more often conducted by psychiatrists (χ^2=109.80, df=1, $p<0.001$). Furthermore, CBT was conducted more often by a female therapist than was psychodynamic therapy (χ^2=15.91, df=1, $p<0.001$). We therefore conducted a sensitivity analysis controlling for therapist gender and profession (psychologist, psychiatrist).

Patients with severe depression (HAM-D score >24) at baseline (N=129) and those with moderate depression at baseline who developed severe symptoms during psychotherapy monotherapy (N=21) were offered additional antidepressant medication administrated by a psychiatrist (who was not the patient's psychotherapist) according to a protocol starting with extended-release venlafaxine at 75 mg/day, which could be increased to a maximum dosage of 225 mg/day. In case of intolerance or nonresponse, venlafaxine was switched to either citalopram or nortriptyline. Pharmacotherapy consultations addressed symptom evaluation, side effects, and adherence. Three research psychiatrists supervised pharmacotherapy.

Eight patients (6.2%) did not start the recommended pharmacotherapy, and 14 (10.8%) switched medication during treatment. The number of patients not starting pharmacotherapy, the pharmacotherapy dosages used, and patient-reported medication adherence did not differ significantly between treatment conditions.

Outcome Measures

The primary outcome measure was posttreatment remission rate (HAM-D score ≤7). Secondary outcome measures included 1-year follow-up remission rates and posttreatment and follow-up observer-rated (HAM-D) and patient-rated mean depression scores (Inventory of Depressive Symptomatology–Self-Report [IDS-SR] [25]).

Trained research assistants (master's-level graduate students in clinical psychology) assessed the HAM-D according to the Dutch scoring manual (26). Assessors participated in biweekly 1-hour peer supervision sessions, in which audiotaped interviews were discussed. The average intraclass correlation coefficient over 46 audiotaped assessments scored by multiple assessors was 0.97. Both observer- and patient-rated depression measures showed good reliability at baseline assessment (Cronbach's alpha: observer-rated, 0.75; patient-rated, 0.78). HAM-D assessors were not blind to treatment condition. We therefore requested the assessors' hypotheses regarding treatment effects at the posttreatment and follow-up assessments and conducted a sensitivity analysis controlling for these variables.

Randomization

Separate random allocation sequences were generated for each of the three clinics by one of the authors (J.P.) using the SPSS random number generator (SPSS, Chicago). Randomization was stratified by gender and age (<32.5 years and >32.5 years). Research assistants, aware of the allocation sequence, enrolled participants and assigned them to interventions.

Statistical Methods

Analyses were based on an intent-to-treat sample, including all patients randomly assigned. Patients were considered dropouts if they completed less than eight psychotherapy sessions.

Response was defined as a reduction in HAM-D scores ≥50% at posttreatment.

Given the hierarchical data structure, linear mixed-model analyses were used for continuous outcomes, and logistic generalized estimating equation analyses were used for dichotomous outcomes. These analyses were preferred over logistic mixed-model analyses because of the instability of the latter (27). In examining pre- to posttreatment outcomes, we excluded follow-up data (for which additional help-seeking could not be controlled) from the analyses. Mixed-model analyses were conducted according to a three-level structure (therapist, patient, and repeated measures). Location (clinic) was included as a covariate in a sensitivity analysis, rather than as a level because of the small number of categories (N=3). Mixed-model analyses were performed with MLwiN, version 2.22 (http://www.bristol.ac.uk/cmm/software/mlwin). All other analyses were performed with SPSS, version 16.0.

We started with a basic model including main effects for treatment and time and a time-by-treatment interaction. Time was treated as a categorical variable to assess treatment effects at the different time points. To control for possible confounders, we next added the following sets of covariates: 1) clinic and number of patients with a baseline HAM-D score >24; 2) demographic characteristics (as listed in Table 1); 3) depression characteristics (as listed in Table 1); 4) therapist gender and profession; 5) the HAM-D assessors' treatment outcome hypotheses; and 6) help-seeking during the follow-up period (as reported in Table S1 in the data supplement that accompanies the online edition of this article). The estimated main effects for treatment at different assessment points under these different models are reported as odds ratios with 95% confidence intervals for remission rates and differences in means for continuous outcomes. For the latter, we also calculated effect sizes (Cohen's d) and 95% confidence intervals using Comprehensive Meta-Analysis, version 2.2.046 (Biostat, Englewood, N.J.).

We then used a two-step strategy for the interpretation of outcomes. First, we examined whether treatment outcomes differed significantly. We considered treatment differences to be nonsignificant if the 95% confidence interval included 1.00 or 0.00 for odds ratios and effect sizes, respectively. This constituted our primary research question. Second, when differences were nonsignificant, we next examined whether psychodynamic therapy was noninferior to CBT by comparing outcomes to prespecified noninferiority margins. These margins were determined based on the expert opinion of 10 experienced depression research clinicians (unaware of preliminary trial results) who rated a difference of 10% for remission rates and 2.6 HAM-D points (equivalent to a Cohen's d value of 0.30) as the maximum difference allowable to conclude noninferiority. Based on a maximum difference of 10% (remission rates of 12% and 22%), noninferiority margins for remission were set at an odds ratio of 0.49. For all continuous outcome measures, noninferiority margins were prespecified at a Cohen's d value of 0.30. We compared the 95% confidence intervals of the effect sizes and odds ratios with the above-mentioned prespecified noninferiority margins and considered psychodynamic therapy noninferior to CBT on a given outcome measure if the 95% confidence interval limit did not exceed the prespecified noninferiority margin for that measure. This constituted our secondary research question. We repeated the main analyses in the subgroup of moderately depressed patients (HAM-D score ≤24) receiving psychotherapy only and in the subgroup of severely depressed patients (HAM-D score >24) receiving combined psychotherapy and pharmacotherapy in order to investigate whether pooling these subgroups may have obscured differential patterns of results.

Power Analysis

An a priori power analysis (14) indicated that 300 participants were required (alpha=0.05, 1−β=0.80) to answer our primary research question. To detect the 10% difference in remission rates between conditions that constituted the noninferiority margin (alpha=0.05, 1−β=0.80), 344 participants were needed (using SPSS SamplePower for equivalence studies, one-tailed). Power to detect an outcome difference of a Cohen's d value of 0.30 for continuous outcome measures was 0.87.

Results

Participants

The CONSORT diagram for the study is presented in Figure 1. From April 2006 to December 2009, 4,866 patients were assessed for eligibility during a standard intake procedure; 570 (11.7%) were found to be potentially eligible and invited for baseline assessment. Of these patients, 229 (40.2%) did not meet inclusion criteria or were not willing to participate. Therefore, 341 patients were randomly assigned to CBT (N=164) or psychodynamic therapy (N=177). Demographic and clinical characteristics of the sample are summarized in Table 1. No significant differences were found between the two treatment conditions.

No significant differences were found between treatment conditions regarding the proportion of patients who did not complete treatment (CBT, 31.1%; psychodynamic therapy, 25.9%). The majority of patients who dropped out were those who missed treatment appointments without specifying a reason (53.9%). Recruitment was discontinued when the intended number of participants was reached. One-year follow-up assessments were conducted from April 2007 to January 2011.

Posttreatment Outcomes

Based on observed data, 24.3% (N=27/111) of the patients in the CBT condition and 21.3% (N=26/122) in the psychodynamic therapy condition met the remission criterion at the posttreatment assessment. Observed response rates were 38.7% (N=43/111) for CBT and 36.9% (N=45/122) for psychodynamic therapy. Estimated odds ratios for remission at different assessment points are listed in Table 2. At the posttreatment assessment, the odds ratio was 0.82 (95% CI=0.45–1.50), indicating that remission rates did not differ significantly. The lower limit of the odds ratio's 95% confidence interval exceeded the prespecified noninferiority margin of 0.49. This pattern of results did not change when different sets of covariates were added (Table 2).

Mean observer- and patient-rated depression scores during treatment for both groups are presented in Figure 2; depressive symptom scores in both conditions improved over time. Estimated observer- and patient-rated mean differences at different assessment points are presented in Table 2, along with effect sizes of the posttreatment differences between conditions. At week 22, the estimated observer-rated difference between treatment conditions was 0.24 points (SE=0.90) on the HAM-D, corresponding with an effect size (Cohen's d) of 0.02 (95% CI=−0.24 to 0.27), indicating that treatment differences were nonsignificant.

TABLE 1. Baseline Demographic and Clinical Characteristics of Participants in a Study of the Efficacy of Psychodynamic Therapy Relative to Cognitive-Behavioral Therapy[a]

Characteristic	Total Sample (N=341)		CBT Group (N=164)		Psychodynamic Therapy Group (N=177)	
Demographic						
	Mean	SD	Mean	SD	Mean	SD
Age (years)	38.91	10.30	38.27	10.13	39.49	10.44
	N	%	N	%	N	%
Gender						
Male	102	29.9	51	31.1	51	28.8
Female	239	70.1	113	68.9	126	71.2
Cultural background						
Northwest European	186	55.0	92	56.1	94	54.0
Other	152	44.9	72	43.9	80	46.0
Marital status						
Married	80	23.7	45	27.4	35	20.1
Divorced	69	20.4	34	20.7	35	20.1
Widowed	10	3.0	4	2.4	6	3.4
Never married	176	52.1	80	48.8	96	55.2
Other	3	0.9	1	0.6	2	1.1
Living situation						
Living with at least one other person	220	65.3	110	67.1	110	63.6
Living alone	106	31.5	51	31.1	55	31.8
Other	11	3.3	3	1.8	8	4.6
Job status						
Currently working	130	38.8	61	37.4	69	40.1
Receiving sickness benefits	55	16.4	35	21.5	20	11.6
Receiving social security benefits	74	22.1	34	20.9	40	23.3
Receiving disability benefits	32	9.6	13	8.0	19	11.0
Student	14	4.2	5	3.1	9	5.2
Other	30	9.0	15	9.2	15	8.7
Education level						
Low	67	20.0	35	21.5	32	18.6
Intermediate	159	47.5	71	43.6	88	51.2
High	101	30.1	55	33.7	46	26.7
Other	8	2.4	2	1.2	6	3.5
Main income before taxes						
≤€1,273 a month	113	42.8	49	37.4	64	48.1
≥€1,274 a month	151	57.2	82	62.6	69	51.9
Symptom severity						
HAM-D score >24	129	37.8	66	40.2	63	35.6
	Mean	SD	Mean	SD	Mean	SD
HAM-D score	23.40	5.35	23.68	5.47	23.14	5.24
Patient-rated depression score	42.73	11.00	42.88	10.08	42.60	11.82
	N	%	N	%	N	%
Comorbid axis I disorder[b]						
No	204	59.8	98	59.8	106	59.9
Yes	137	40.2	66	40.2	71	40.1
Depression						
Duration present episode						
<6 months	84	25.1	48	29.8	36	20.8
6 months–1 year	88	26.3	43	26.7	45	26.0
1–2 years	43	12.9	22	13.7	21	12.1
>2 years	86	25.7	35	21.7	51	29.5
Unknown	33	9.9	13	8.1	20	11.6
Previous treatment for current depressive episode						
No	218	65.3	100	62.1	118	68.2
Yes	116	34.7	61	37.9	55	31.8

continued

TABLE 1. Baseline Demographic and Clinical Characteristics of Participants in a Study of the Efficacy of Psychodynamic Therapy Relative to Cognitive-Behavioral Therapy[a] (*continued*)

Characteristic	Total Sample (N=341)		CBT Group (N=164)		Psychodynamic Therapy Group (N=177)	
Number of previous depressive episodes						
None	103	31.1	55	34.6	48	27.9
One	69	20.8	29	18.2	40	23.3
Two or more	159	48.0	75	47.2	84	48.8
Comorbid dysthymia						
No	194	66.0	94	68.1	100	64.1
Yes	100	34.0	44	31.9	56	35.9

[a] CBT=cognitive-behavioral therapy; HAM-D=Hamilton Depression Rating Scale.
[b] Comorbid axis I disorders were assessed by the psychotherapists during treatment without the use of a structured interview, and comorbidity rates may therefore be underestimated.

The estimated patient-rated difference between treatment conditions was 1.94 points (SE=1.92) on the IDS-SR, corresponding with an effect size of −0.08 (95% CI=−0.38 to 0.22), also indicating that differences were not significant. The upper limits of the 95% confidence intervals for both effect sizes did not exceed the prespecified noninferiority margin of 0.30. This pattern of results did not change when controlling for different covariates, although the noninferiority margin was slightly exceeded when controlling for clinic and number of patients with baseline HAM-D scores >24 (HAM-D estimated mean difference=0.64 [SE=0.81]; Cohen's d=0.05, 95% CI=−0.21 to 0.31).

In the moderately depressed subgroup, observed remission rates for CBT and psychodynamic therapy were 26.5% (N=18/68) and 27.7% (N=23/83), respectively, with estimated odds ratios (1.02, 95% CI=0.50–2.06), observer ratings (Cohen's d=–0.05, 95% CI=–0.37 to 0.27), and patient ratings (Cohen's d=–0.24, 95% CI=–0.61 to 0.13) all indicating that psychodynamic therapy was noninferior to CBT. In the severely depressed subgroup receiving additional pharmacotherapy, observed remission rates for CBT and psychodynamic therapy were 20.9% (N=9/43) and 7.7% (N=3/39), respectively, with estimated odds ratios (0.31, 95% CI=0.08–1.26), observer ratings (Cohen's d=0.21, 95% CI=–0.23 to 0.64), and patient ratings (Cohen's d=0.17, 95% CI=–0.35 to 0.69) all indicating no significant differences, without demonstrating noninferiority of psychodynamic therapy relative to CBT.

Follow-Up Outcomes

Follow-up assessments were conducted with 192 (56.3%) participants (Figure 1). More patients reported having received additional treatment during the follow-up period in the CBT condition (N=41 [44.6%]) than in the psychodynamic therapy condition (N=32 [33.0%]), but this difference did not reach significance (χ^2=2.67, df=1, p=0.10) (see Table S1 in the online data supplement).

Based on observed data, 34.7% (N=33/95) of patients in the CBT condition and 26.8% (N=26/97) of those in the psychodynamic therapy condition met the remission criterion. The estimated odds ratio of remission rates at follow-up was 0.74 (95% CI=0.41–1.34) (Table 3), indicating that remission rates did not differ significantly. The lower limit of the odds ratio's 95% confidence interval exceeded the prespecified noninferiority margin of 0.49. This pattern of results did not change when different sets of covariates were added.

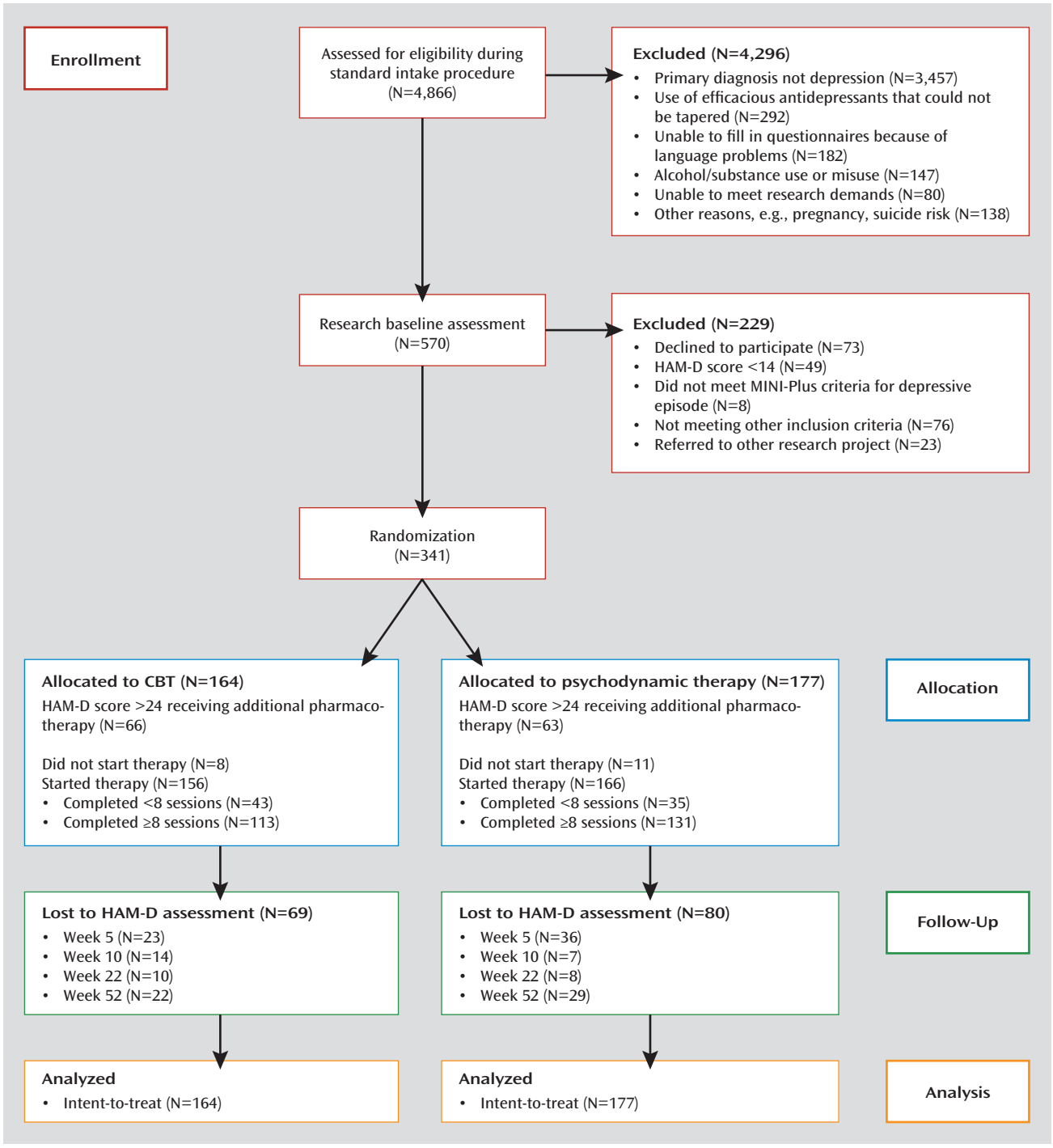
Estimated observer- and patient-rated mean differences at follow-up and corresponding effect sizes are presented in Table 3. The estimated observer-rated difference between treatment conditions was 1.94 points (SE=1.01) on the HAM-D (Cohen's d=0.14, 95% CI=−0.14 to 0.42), and the estimated patient-rated difference was 2.99 points (SE=2.22) on the IDS-SR (Cohen's d=0.12, 95% CI=−0.23 to 0.48), both indicating that treatment differences were not significant. The upper limits of the 95% confidence intervals for both effect sizes exceeded the prespecified noninferiority margin of 0.30. This pattern of results did not change when controlling for different covariates.

In the moderately depressed subgroup, observed remission rates were 40.0% (N=22/55) in the CBT condition and 35.4% (N=23/65) in the psychodynamic therapy condition (odds ratio=0.84, 95% CI=0.41–1.73; observer rated: Cohen's d=0.08, 95% CI=−0.28 to 0.44; patient rated: Cohen's d=0.02, 95% CI=−0.40 to 0.45). In the severely depressed subgroup receiving additional pharmacotherapy, observed remission rates were 27.5% (N=11/40) for CBT and 9.4% (N=3/32) for psychodynamic therapy (odds ratio=0.27, 95% CI=0.07–1.08; observer rated: Cohen's d=0.32, 95% CI=−0.15 to 0.79; patient rated: Cohen's d=0.40, 95% CI=−0.27 to 1.07). All these differences were nonsignificant, but noninferiority could not be demonstrated for any of them.

Adverse Events

Serious adverse events during treatment and follow-up were mostly increases in depressive symptoms or suicidality for which additional treatment was needed (see Table S2 in the online data supplement). No differences were found between the treatment conditions with regard to the proportion of patients reporting serious adverse events during treatment (CBT, 6.1%; psychodynamic therapy, 6.2%) or follow-up (CBT, 1.8%; psychodynamic therapy, 2.3%).

FIGURE 1. CONSORT Diagram of Participants in a Study of the Efficacy of Psychodynamic Therapy Relative to Cognitive-Behavioral Therapy[a]



[a] CBT=cognitive-behavioral therapy; HAM-D=Hamilton Depression Rating Scale; MINI-Plus=Mini-International Neuropsychiatric Interview–Plus.

Discussion

We used a randomized clinical design and noninferiority margins to compare the efficacy of CBT and psychodynamic therapy for major depression in a large sample of patients treated in psychiatric outpatient clinics. Primary analyses indicated no significant differences between treatment conditions at the posttreatment assessment. In secondary analyses, noninferiority could not be demonstrated for posttreatment remission rates but was demonstrated for posttreatment patient- and observer-rated depression scores. Follow-up findings again showed no significant differences between treatments, but noninferiority

TABLE 2. Treatment Effects at Different Assessment Points According to the Basic Model of Analysis and When Corrected for Different Sets of Covariates[a]

	Remission		HAM-D Score				IDS-SR Score			
			Estimated Mean Difference		Effect Size		Estimated Mean Difference		Effect Size	
Time and Model	Odds Ratio	95% CI	Difference	SE	Cohen's d	95% CI	Difference	SE	Cohen's d	95% CI
Week 0										
Model 1			–0.55	0.78			–0.31	1.62		
Model 2			–0.21	0.69			0.35	1.51		
Model 3			–0.65	0.77			–0.40	1.55		
Model 4			–0.42	0.80			0.05	1.63		
Model 5			–0.88	0.95			–1.33	1.98		
Model 6			–0.56	0.79			–0.29	1.64		
Week 5										
Model 1	0.61	0.19–1.98	0.46	0.88						
Model 2	0.58	0.18–1.87	0.79	0.79						
Model 3	0.52	0.17–1.65	0.30	0.87						
Model 4	0.44	0.13–1.55	0.68	0.89						
Model 5	0.65	0.19–2.25	0.11	1.03						
Model 6	0.62	0.19–2.03	0.58	0.89						
Week 10										
Model 1	1.26	0.58–2.77	1.00	0.89			1.34	1.85		
Model 2	1.22	0.56–2.66	1.34	0.81			1.74	1.74		
Model 3	1.13	0.50–2.59	0.92	0.88			1.32	1.79		
Model 4	1.11	0.49–2.50	1.22	0.91			1.95	1.85		
Model 5	1.35	0.56–3.22	0.64	1.05			0.25	2.19		
Model 6	1.31	0.60–2.85	0.83	0.91			1.04	1.87		
Week 22										
Model 1	0.82	0.45–1.50	0.24	0.90	0.02	–0.24 to 0.27	–1.94	1.92	–0.08	–0.38 to 0.22
Model 2	0.78	0.42–1.43	0.64	0.81	0.05	–0.21 to 0.31	–1.60	1.82	–0.07	–0.37 to 0.23
Model 3	0.70	0.36–1.38	0.14	0.89	0.01	–0.25 to 0.27	–1.92	1.88	–0.08	–0.38 to 0.22
Model 4	0.72	0.38–1.35	0.36	0.91	0.03	–0.23 to 0.28	–2.04	1.93	–0.08	–0.38 to 0.22
Model 5	0.89	0.41–1.93	–0.12	1.05	–0.01	–0.26 to 0.25	–2.99	2.26	–0.10	–0.40 to 0.20
Model 6	0.83	0.45–1.53	0.31	0.91	0.02	–0.24 to 0.28	–1.96	1.94	–0.08	–0.38 to 0.23

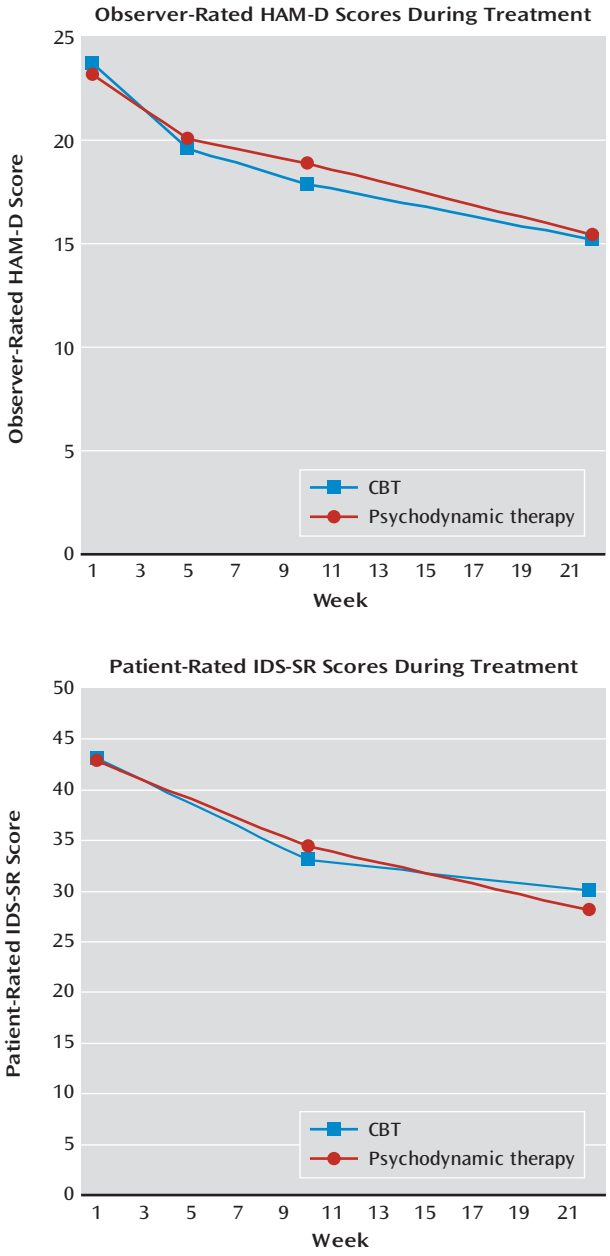
[a] HAM-D=Hamilton Depression Rating Scale; IDS-SR=Inventory of Depressive Symptomatology–Self Report. Model 1 is the basic model including a main effect for treatment and time and a time-by-treatment interaction; model 2 is the basic model with clinic and number of patients with baseline HAM-D scores >24 added as covariates; model 3 is the basic model with demographic characteristics (as listed in Table 1) added as covariates; model 4 is the basic model with depression characteristics (as listed in Table 1) added as covariates; model 5 is the basic model with therapist gender and profession added as covariates; and model 6 is the basic model with HAM-D assessors' hypotheses regarding treatment outcomes added as a covariate.

could not be demonstrated for any of the three outcome measures. However, the follow-up findings must be interpreted with caution because of a nonsignificant result suggesting that patients in the CBT condition received more additional treatment during the follow-up period. Our findings are in line with previous meta-analyses (9, 11, 28) that reported no significant differences between individual CBT and psychodynamic therapy at posttreatment assessments.

Post hoc analyses revealed no significant differences between treatment conditions in the subgroup of moderately depressed patients receiving psychotherapy only, and noninferiority of psychodynamic therapy relative to CBT was shown for all posttreatment outcome measures in this group of patients. These findings add to the evidence base of psychodynamic therapy for depression. No significant differences between treatments were found in the subgroup of severely depressed patients receiving combined treatment, but differences were large enough to be significant if replicated in a larger sample, and noninferiority could not be concluded in this group.

One notable finding was that only 22.7% of the patients achieved remission at posttreatment, with 40% seeking additional treatment afterward. These remission rates are lower than those found in previous trials examining either short-term psychodynamic supportive psychotherapy (22) or CBT (29, 30). This difference may be related to the relatively low socioeconomic status and income levels in our sample, which in naturalistic studies have been identified as predictors for less favorable treatment response (31, 32), or to the relatively high rate of comorbid axis I disorders. Our findings indicate that a substantial proportion of patients in specialized second-line outpatient clinics require more than time-limited treatment to achieve remission. These results are in line with findings

FIGURE 2. Observer-Rated and Patient-Rated Mean Depression Scores During Treatment[a]



[a] CBT=cognitive-behavioral therapy; HAM-D=Hamilton Depression Rating Scale; IDS-SR=Inventory of Depressive Symptomatology–Self Report.

regarding psychotherapy in real-world clinical practice (33) and show that depression as it is encountered in secondary care can be characterized as a difficult-to-treat disorder. Since residual depressive symptoms have been found to be the main predictor of future relapse (34), our findings also indicate that psychotherapeutic treatment needs to be improved. The findings suggest that clinicians and policymakers should be realistic about the expected outcome of time-limited depression treatments and should bear in mind that mandated limits on treatment duration may lead to undertreatment of depression.

Strengths and Limitations

This study has a number of strengths. First, several elements contribute to the generalizability of the study's findings. Treatment was provided in regular psychiatric outpatient clinics by a large number of therapists with different experience levels. Patients were not recruited by advertisement but instead were referred by general practitioners, and no selection criteria with regard to previous treatment or suitability for psychotherapy were applied. Patients with relatively low socioeconomic status were included, and almost one-half of the patient sample reported a non-Northwest European (immigrant) cultural background. Second, we included severely depressed patients who were additionally treated with pharmacotherapy prescribed according to a protocol. Third, this is, to our knowledge, the largest randomized controlled trial to date comparing CBT and psychodynamic therapy in the treatment of depression (N=341). By comparison, a meta-analysis of psychodynamic therapy for depression included a total of 421 patients across six CBT-psychodynamic randomized controlled trials (9). Finally, this was the first study to test whether psychodynamic therapy can be demonstrated to be noninferior to CBT in the treatment of depression.

This study also has a number of limitations. First, a substantial number of patients did not complete treatment or were lost to assessment. Second, treatment fidelity was not systematically assessed but was instead checked by means of intensive supervision by experienced supervisors and subjective therapist ratings. These ratings suggested adequate adherence to the CBT manual, but no such measure was available for psychodynamic treatment. Third, HAM-D assessors were not blind to treatment condition, and therefore we cannot rule out observer bias. However, controlling for assessor-rated treatment expectations did not alter the pattern of results, and results were similar for observer- and patient-rated outcomes. Fourth, research assistants enrolling participants were aware of the allocation sequence, which may have introduced selection bias. However, no significant differences were found with regard to any of the sample baseline characteristics. Fifth, although noninferiority margins were carefully thought through and based on clinical expert opinion, they were still set in an arbitrary fashion. Sixth, we could not prevent patients from seeking additional treatment during the follow-up period, and a nonsignificant finding suggested that patients in the CBT group may have returned to treatment more than those in the psychodynamic therapy group. However, controlling for additional treatment in the follow-up period did not change the general pattern of results. Finally, the study did not include a control condition.

Conclusions

No statistically significant differences were found between psychodynamic therapy and CBT in a large sample

TABLE 3. Follow-Up Outcomes According to the Basic Model of Analysis and When Corrected for Different Sets of Covariates[a]

	Remission		HAM-D Score				IDS-SR Score			
			Estimated Mean Difference		Effect Size		Estimated Mean Difference		Effect Size	
Model	Odds Ratio	95% CI	Difference	SE	Cohen's d	95% CI	Difference	SE	Cohen's d	95% CI
Model 1	0.74	0.41–1.34	1.94	1.01	0.14	–0.14 to 0.42	2.99	2.22	0.12	–0.23 to 0.48
Model 2	0.69	0.38–1.27	2.36	0.93	0.18	–0.10 to 0.47	3.49	2.14	0.15	–0.21 to 0.51
Model 3	0.64	0.33–1.26	1.82	1.00	0.13	–0.15 to 0.42	3.37	2.17	0.14	–0.22 to 0.50
Model 4	0.61	0.33–1.14	2.20	1.02	0.16	–0.13 to 0.44	3.16	2.23	0.13	–0.23 to 0.49
Model 5	0.72	0.35–1.47	1.62	1.15	0.10	–0.18 to 0.38	1.94	2.52	0.07	–0.29 to 0.43
Model 6	0.75	0.41–1.37	1.95	1.02	0.14	–0.15 to 0.43	3.16	2.26	0.13	–0.23 to 0.49
Model 7	0.68	0.35–1.33	1.74	1.09	0.12	–0.17 to 0.41	2.68	2.31	0.11	–0.26 to 0.47

[a] HAM-D=Hamilton Depression Rating Scale; IDS-SR=Inventory of Depressive Symptomatology–Self Report. Model 1 is the basic model including a treatment and time main effect and a time-by-treatment interaction; model 2 is the basic model with clinic and number of patients with baseline HAM-D scores >24 added as covariates; model 3 is the basic model with demographic characteristics (as listed in Table 1) added as covariates; model 4 is the basic model with depression characteristics (as listed in Table 1) added as covariates; model 5 is the basic model with therapist gender and profession added as covariates; model 6 is the basic model with HAM-D assessors' hypotheses regarding treatment outcomes added as a covariate; and model 7 is the basic model with patient-reported treatments in the follow-up period added as a covariate.

of patients treated for a major depressive episode, and less than one-fourth of the patients reached remission within 22 weeks of treatment. Noninferiority of psychodynamic therapy relative to CBT was demonstrated for posttreatment mean depression scores but could not be demonstrated for remission rates and follow-up measures. Our findings extend the evidence base of psychodynamic therapy for depression but also indicate that time-limited psychotherapy is not sufficient for a substantial number of patients encountered in psychiatric outpatient clinics.

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Clinical Guidance: Comparison of CBT and Psychodynamic Therapy for Depression

Cognitive-behavioral therapy (CBT) and short-term psychodynamic psychotherapy provide similar outcomes for patients with a major depressive episode, but remission rates at the end of treatment are low for both treatments. The rates in the trial by Driessen et al. were less than 25% for patients referred to psychiatric clinics, who may be more difficult to treat than most primary care depressed patients. However, emphasizes Thase in an editorial (p. 953), the similarity in outcomes adds to the evidence for using both psychodynamic psychotherapy and CBT with depressed outpatients.