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Dose–effect relations in time-limited combined psycho-pharmacological treatment for depression

J. DEKKER*, P. J. MOLENAAR, S. KOOL, G. VAN AALST, J. PEEN AND F. DE JONGHE

Depression Research Group of the Mentrum Institute for Mental Health, Amsterdam, The Netherlands; Department Clinical Psychology, Vrije Universiteit, Amsterdam; Universiteit van Amsterdam

ABSTRACT

Background. A limited number of psychotherapy sessions in combination with medication is preferable to pharmacotherapy only in the treatment of ambulatory patients with major depression. Whether there is a relation between the number of sessions and the efficacy of the treatment is uncertain.

Method. Randomized clinical trial comparing two treatment conditions in outpatients with major depression. All patients studied had a baseline score of at least 14 points on the 17-item Hamilton Depression Rating Scale. The two conditions consist of 8-session or 16-session Short Psychodynamic Supportive Psychotherapy, both in combination with pharmacotherapy. Efficacy was assessed using the 17-item HDRS, the CGI of Severity and of Improvement, the depression subscale of the SCL-90 and the Quality of Life Depression Scale.

Results. The rate of change would seem to indicate that eight sessions are preferable for both moderately and severely depressed patients, although the results converged again at the end. Furthermore, in terms of satisfaction with the number of sessions and drop-out percentages during treatment, no differences were found between the conditions.

Conclusion. In the light of the outcome analysis (faster remission after fewer sessions), a short version of the psychotherapy treatment in a combined course of treatment seems to be justified.

INTRODUCTION

In the sixties, seventies and eighties longer courses of psychotherapy appeared to be more effective for depression than shorter courses (Luborsky *et al*. 1971; Smith *et al*. 1980; Howard *et al*. 1986; Orlinsky *et al*. 1994). In the eighties however, there were also studies which arrived at different conclusions (Shapiro & Shapiro, 1982; Miller & Berman, 1983; Berman *et al*. 1985; Robinson *et al*. 1990; Mynors-Wallis *et al*. 1995; Scott *et al*. 1997). Frank & Kupfer (1985) were among the first to question explicitly the prevailing consensus that 'longer' also meant 'better'.

* Address for correspondence: Professor Dr J. Dekker, Vrije Universiteit, Amsterdam and Mentrum Mental Health Amsterdam, Klaprozenweg 111, Postbus 75848, 1070 AV Amsterdam, The Netherlands.
(Email: jack.dekker@mentrum.nl)

The nineties witnessed the emergence of a trend towards brief courses of treatment with detailed protocols. Studies of these forms of treatment are easier in practical terms. Treatment costs less and it may be more efficient than longer-term forms of psychotherapy. Several studies showed that certain forms of psychotherapy [i.e. cognitive behaviour therapy (CBT) or interpersonal psychotherapy (IPT)] could achieve a satisfactory reduction in symptoms in a short space of time (Hollon & Najavits, 1988; Dobson, 1989; Thase *et al*. 1997; DeRubeis *et al*. 1999; Jarrett *et al*. 1999; Keller *et al*. 2000).

Little systematic research has been conducted in recent decades into the ideal dosage of psychotherapy. One of the few studies conducted in this area is the Second Sheffield Psychotherapy Project of Shapiro *et al*. (SPP2; 1994). This study assigned patients randomly to 8 or 16

sessions of IPT or CBT. The study showed that, when the entire study population was considered, there was no difference between the results obtained by 8 or 16 sessions. For patients with severe depression, 16 sessions were more effective than 8 sessions. In mild depression the best result was achieved with 8 sessions rather than 16 sessions. This study has been criticized for the fact that it was not corrected for pharmacotherapy. Some patients were effectively given combined treatment, whereas others received psychotherapy only.

Results from a substudy of the SPP2 project (Barkham *et al.* 1996*a*) covering the 'dose–effect' relationship indicate that patients with 8 sessions achieve a clinically relevant change before patients with 16 sessions. However, at the end of the treatment, the outcomes of both conditions were the same.

In a replica study of the SPP2 project, the Collaborative Psychotherapy Project (CPP; Barkham *et al.* 1996*b*), it was found that 16 sessions produced more benefits than 8 sessions in the study population as a whole. Given the fact that more severely depressed patients participated in this CPP study than in the SPP2 project, this finding would appear to concur with the differential effect found in the SPP2 project. A limitation of the CPP study was the low number of trial subjects ($n=36$) – in contrast to the number in the SPP2 project ($n=117$) – and the lack of correction for pharmacotherapy.

The present study deals with this drawback of the SPP2 and CPP studies. We studied the effect of short-term *versus* longer-term psychotherapy in a group of 90 patients who were given pharmacotherapy alongside psychotherapy. The authors are not aware of any similar study. The patients [suffering from at least moderate depression according to DSM-IV criteria (APA, 1994)] were allocated at random to 8 or 16 sessions of psychotherapy supplemented by pharmacotherapy for a period of 6 months. We studied the extent to which the patients in both conditions recovered from the depressive disorder. We also looked at levels of satisfaction among the patients and therapists with a number of psychotherapy sessions. Finally, we analysed the levels of compliance for medication and psychotherapy and/or levels of drop out for the study.

Our *a priori* hypothesis for this study was that the 16-session condition would benefit more in terms of depression severity.

METHOD

Study group

The study sample consisted of all consecutive patients newly registered ($n=1467$) during a period of approximately 2 years at an outpatient clinic of Mentrum Mental Health in the inner city of Amsterdam. The diagnosis of major depression was made by psychiatrists on the basis of a semi-structured interview which covered depression characteristics, severity and duration. The inclusion criteria were: age between 18 and 60 years, DSM-IV (APA, 1994) defined major depression (with or without dysthymia), a 17-item Hamilton Depression Rating Scale (HDRS) (Hamilton, 1967; de Jonghe *et al.* 1994) baseline score of at least 14 points and written informed consent. Important exclusion criteria were, e.g. presentation of a psycho-organic disorder, drug abuse, a psychotic disorder and/or a dissociative disorder; patient considered to be too unreliable to participate in a clinical trial (e.g. 'shopping', which is a frequent change of institution); a serious communicative problem (e.g. language barrier) making participation in the trial impossible; participation in the trial being physically impossible (e.g. the patient will soon leave the country); a contraindication for one of the antidepressants prescribed by the pharmacotherapy protocol is in force. Additional exclusion criteria were of the usual kind in drug research: the patient is considered 'too ill' by the psychiatrist (e.g. antidepressants must be started immediately) and/or 'too suicidal' (e.g. hospitalization is unavoidable) to participate in a clinical trial. For the flow of participants see Fig. 1.

Procedure of randomization

The question of the relative 6-month efficacy of the two treatment methods was addressed in a randomized parallel group design. The patients were randomized using block-randomization. Four blocks were formed, defined by sex and age. The patients were randomly allocated to either the 8-session or 16-session psychotherapy condition. The sessions lasted 45 min. The first 8 sessions were weekly in both conditions.

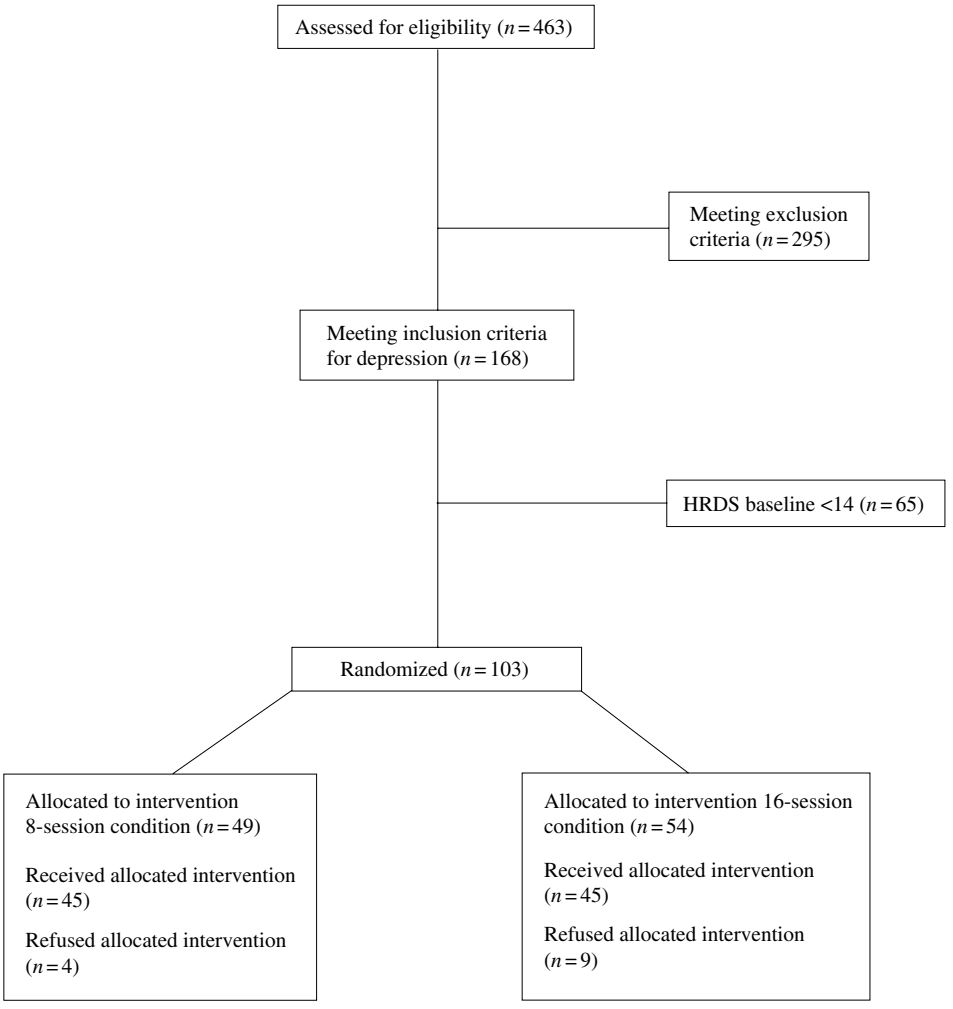

FIG. 1. Flow of participants through first stages of randomized trial.

Psychotherapy in the 8-session condition then stopped; in the 16-session condition, the last 8 sessions took place at intervals of 2 weeks. In both conditions, the patients were treated for a period of 6 months in accordance with a fixed antidepressant protocol.

Obviously, the patients and the treating physicians were not blind. The three research fellows who assessed the HDRS, however, were not informed about the treatment condition and were instructed to restrict themselves to the discussion of the HDRS items only. The trial was preceded by a 2-week period in which the diagnosis was assessed using a semi-structured interview (Huyser *et al.* 1996). During the same period, the inclusion and exclusion criteria were checked, and the baseline assessments were made. This period was used, if necessary, as a wash-out period (without placebo).

Pharmacotherapy

All patients in the two study groups were treated for a period of 6 months in accordance with a fixed antidepressant protocol. The medication contacts lasted for 15 min at intervals of 2 weeks during the first 2 months. Thereafter, contacts were monthly. When there was a change of medication, contacts were again scheduled every 2 weeks during the 2 months following the change. The task of the treating pharmacotherapist

was to provide adequate pharmacotherapy (motivation and monitoring of response and side-effects), psycho-education and limited supportive contact. This has been described in the literature as 'warm pharmacotherapy' (Hollon *et al.* 1991). The pharmacotherapy protocol consisted of three successive stages. Decisions about changes in medication were made on the basis of the clinical response (CGI-I) (see later for explanation) and the presence of side-effects (intolerance). Initially, patients were given fluoxetine in a fixed dose of 20 mg/day. In cases of intolerance or inefficacy, patients were switched to nortriptyline. The initial dose was 50 mg/day, rising to 150 mg/day and higher depending on the plasma concentration. If intolerance or inefficacy was found again, patients were switched to mirtazapine. The initial dose was 15 mg/day, rising to a maximum of 45 mg/day. If improvement was unsatisfactory after treatment with the three antidepressants listed here, patients were classified as therapy-resistant and given further treatment outside the study protocol as considered appropriate by the psychiatrist.

Psychotherapy: short psychodynamic supportive psychotherapy (SPSP)

In addition to the pharmacotherapy described above, the psychotherapy was given by seven fully trained psychotherapists (who were not the psychiatrists providing medication). They all had at least 5 years' experience in practising psychoanalytic supportive therapy. They met weekly for a 1-hour discussion of their audiotaped sessions in order to enhance their adherence to the psychotherapy manual [a draft of which is available (in Dutch) from the authors upon written request]. One of the authors (F.d.J.), who formulated the guidelines for SPSP, participated in most of these meetings, listened to several tapes of all psychotherapists, and was especially attentive to adherence to the manual. Psychotherapy started within 2 weeks after the initiation of pharmacotherapy. The psychotherapy provided was SPSP.

The supportive approach is not new in psychoanalysis. It has been described, for example, as supportive psychotherapy (Werman, 1984), psychoanalytic supportive psychotherapy (de Jonghe *et al.* 1994) and psychodynamically oriented supportive therapy (Rockland, 1989). It is generally seen as a segment of a supportive-exploratory continuum (Rockland, 1989). The short, brief, or time-limited approach in psychoanalysis is not new either. Typically, time-limited dynamic psychotherapy (Strupp & Binder, 1984), or brief dynamic psychotherapy, or short psychoanalytically oriented therapy, are situated towards the exploratory end of the supportive-exploratory continuum. The emphasis is on interpreting the transference (Strupp & Binder, 1984). SPSP, by contrast, is a brief approach situated towards the supportive end of that continuum.

Measurement of outcome

Efficacy assessment was based on data from three sources: the patients, the treating psychiatrists, and independent observers. The independent observers, three research fellows who were not informed of the treatment condition, collected their data using the 17-item HDRS in a semi-structured interview (de Jonghe, 1994), at weeks 4, 8, 12, 16 and 24. The reliability of their assessments was established prior to their participation in the study. During the study, in order to avoid slippage, they discussed their audiotaped assessments monthly with one of this paper's authors (F.d.J.). The treating psychiatrists obtained their data using the Clinical Global Impression of Severity (CGI-S) and of Improvement (CGI-I) (Guy, 1976) at weeks 4, 8, 12, 16 and 24. The patients provided data using two self-rating scales: the depression subscale of the Ninety Symptom Checklist (SCL-90) (Derogatis *et al.* 1973; Arrindell & Ettema, 1986), and the Quality of Life Depression Scale (QLDS) (Tuynman-Qua & de Jonghe, 1992), at weeks 8, 16 and 24 (logistics precluded the collection of information for every measurement scale at all the eight measurement moments).

In the analyses of the efficacy of the treatments, success is defined as HDRS remission (HDRS end score of 7 points or less), as a CGI success (CGI-S or CGI-I score of 1–2), and as SCL or QLDS success (an effect size of at least 1 S.D. from base rate on the SCL-90 depression subscale or QLDS).

Satisfaction with the number of psychotherapy sessions

Both patients and psychotherapists were instructed to complete the Luborsky inventory (Luborsky *et al.* 1985) after the final

psychotherapy session. The scale consists of twelve items. Eleven items were scored on a 6-point scale (ranging from 1 to 6, respectively dissatisfied and very satisfied). Examples of items include: degree of insight of the patient, degree of trust in the therapist, satisfaction of the working alliance, degree to which the target in therapy is achieved. One of the items is related to their assessment of the number of psychotherapy sessions. For this item response categories were: too few, enough and too much.

Drop out

In order to determine the drop-out rates, three different measures were used. Patients who stopped taking medication or attending psychotherapy sessions were considered to be *pharmacotherapy drop-outs* or *psychotherapy drop-outs* respectively. This does not necessarily mean that these patients are study drop-outs. Patients became *study drop-outs* if, for whatever reason, they no longer appeared for the assessments or refused to continue participating in the study. Drop out from the study may also have been a consequence of a decision taken by the psychiatrist (not by the psychotherapist) if exclusion criteria had been overlooked initially (e.g. alcohol abuse) or had emerged after the start of treatment (e.g. the wish to become pregnant), or if it was impossible or undesirable to continue with treatment based on the protocol (e.g. deterioration of clinical condition). Finally, all protocol violations resulted in study drop-out.

Statistical methods

For the analyses of the outcome, we used the following statistical analysis techniques.

(1) At weeks 4, 8, 12, 16 and 24, the mean scores [SCL-90 and QLDS (not at weeks 4 and 16), see 'measurement of outcome'] of each assessment were in the conditions separately compared with the scores of the last assessment. Besides that, the between-group comparisons of the continuous measures were analysed with ANCOVA. In this analysis, we compared the conditions at each assessment in terms of the mean scores for the HDRS, SCL-90, QLDS and CGI-S, including the initial measures as covariants. At the end we conducted analyses of the continuous measures with MANOVA.

(2) At weeks 4, 8, 12, 16 and 24, the remission and succession rates of the two treatment conditions were compared using 2-sided Pearson χ^2 (level of significance 0·05).

(3) For the HDRS remissions, we also used survival analysis. The Kaplan–Meier survival estimates were calculated for weeks 4, 8, 12, 16 and 24, and the curves obtained were compared using the log-rank test to take into account both the rate of remission and the time needed to achieve remission.

For the analyses of the satisfaction percentages and the drop-out rates for the two treatment conditions, we used 2-sided Pearson χ^2 (level of significance 0·05).

These data analysis methods for outcome and drop-out rates were conducted on three samples of patients. The first was the per protocol (PP) sample. This sample consisted of all patients who started the treatment to which they were allocated. In other words, the patients who refused after allocation were not taken into consideration. Here also, an initial measure was required for each patient. Secondary results were calculated in an intention-to-treat (ITT) sample, which consists of all randomized patients. In both these samples last observation carried forward was applied. Secondary results were also calculated in an observed cases (OC) sample, which consisted of all patients who did not drop out after the start of the treatment. In this article, we only present the results of the analyses with the PP sample, because these results were almost the same as those of the ITT and OC samples.

A limitation of the study is the statistical power. At the start of the study, the idea was to achieve an average recovery rate of 50% of the patients in the 16-session condition and an average recovery of 30% in the 8-session condition. Assuming power of approximately 75%, the intention was to involve approximately 130 patients in the study (65 in each condition). There were fewer intakes than planned and eventually 102 patients were included in the study. Statistical power, therefore, failed to live up to our initial assumption.

RESULTS

Patients

A total of 103 patients were randomized (8 psychotherapy sessions, $n=49$; 16 psychotherapy sessions, $n=54$). Of the randomized

Table 1. *Characteristics of the per protocol study sample*

		Condition		
		8 sessions ($n=45$) %	16 sessions ($n=45$) %	Total ($n=90$) %
Sex	Male	40·0	31·1	35·6
	Female	60·0	68·9	64·4
Age (years)	19–29	28·9	35·6	32·2
	30–39	28·9	28·9	28·9
	40–49	26·7	22·2	24·4
	50–59	15·6	13·3	14·4
Marital status	Married	42·2	20·5	31·5
	Divorced	11·1	20·5	15·7
	Widowed	2·2	0·0	1·1
	Never married	44·4	59·1	51·7
Educational level	Low	17·8	18·2	18·0
	Intermediate	44·4	36·4	40·4
	High	37·8	45·5	41·6
Living situation	Living with at least one person	66·7	56·8	61·8
	Living alone	33·3	43·2	38·2
Job status	Job	42·2	31·8	37·1
	On sickness benefit	28·9	36·4	32·6
	Social security benefit	17·8	6·8	12·4
	Disabled	2·2	6·8	4·5
	Student	4·4	6·8	5·6
	Other	4·4	11·4	7·9
Duration of present episode	<1 year	61·4	56·8	59·1
	1–2 years	15·9	31·8	23·9
	>2 years	22·7	11·4	17·0
Psychiatric treatment during present episode	Not treated	88·6	77·3	83·0
	Treated	11·4	22·7	17·0
Medication 3 months before study	No medication	79·5	79·5	79·5
	Medication	20·5	20·5	20·5
Depressed episodes within previous 5 years	0	75·0	65·1	70·1
	1 or 2	22·7	30·2	26·4
	$\geqslant 3$	2·3	4·7	3·4
HDRS*	Mean (S.D.)	19·4 (3·8)	20·3 (4·4)	19·9 (4·1)
	Median	19·0	20·0	19·0
CGI-Severity*	Mean (S.D.)	3·5 (0·7)	3·6 (0·6)	3·5 (0·7)
	Median	3·0	4·0	4·0
SCL-90 Depression subscale*	Mean (S.D.)	49·3 (8·7)	52·0 (10·1)	50·6 (9·5)
	Median	49·0	53·0	50·5
QLDS*	Mean (S.D.)	16·1 (6·4)	14·8 (7·0)	15·4 (6·7)
	Median	15·0	17·0	15·0

* The numbers presented are not percentages but means and standard deviations.

patients, 13 patients (12·6%) refused the proposed treatment; nine in the 8-session condition and four in the 16-session condition. Those who refused the proposed treatment did not differ significantly in HDRS, CGI, SCL-90 or QLDS base rates from those who accepted it. In both treatment conditions, 45 subjects actually started the treatment.

No selection bias for demographic background or psychiatric history was found in our sample. The characteristics of the study groups (based on the PP sample) are presented in Table 1.

As can be seen in Table 1, two thirds of the study group were women. More than half of the subjects were unmarried and well educated.

In 59% of the cases, the duration of the present episode was less than 1 year and less than 2 years in 83% of the cases. Most patients (83%) had not been treated during the present episode or taken any antidepressant medication during the 3 months before participation in this study (80%). The mean baseline scores in the study population were 19·9 on the 17-item HDRS, 3·5 on the CGI-S, 50·6 on the SCL-90 depression subscale and 15·4 on the QLDS.

No statistically significant differences were found between the two treatment groups in terms of the baseline scores on the measurement

Table 2. *Outcome scores for five outcome measures (per protocol sample)*

	Treatment								ANCOVA		
	8 sessions				16 sessions				Significance level		
	Mean	S.D.	*n*	Significance paired *t* test	Mean	S.D.	*n*	Significance paired *t* test	*F*	df	*p*
HDRS											
Pre-treatment	19·4	3·8	45		20·3	4·4	45		1·10	1	0·30
Week 4	16·0	6·5	45	***0·00***	16·9	5·7	45	***0·00***	0·15	1	0·70
Week 8	12·6	6·9	45	***0·00***	15·3	6·6	45	***0·05***	2·77	1	***0·10***
Week 12	12·1	7·2	45	N.S.	13·7	6·8	45	***0·04***	0·61	1	0·44
Week 16	11·3	7·6	45	N.S.	12·0	6·9	45	***0·04***	0·23	1	0·88
Week 24	11·1	6·8	45	N.S.	12·1	7·6	45	N.S.	0·12	1	0·73
CGI-Severity											
Pre-treatment	4·5	0·7	42		4·6	0·6	44		0·40	1	0·53
Week 4	3·7	1·0	45	***0·00***	4·0	0·9	45	***0·01***	1·18	1	0·28
Week 8	3·1	1·1	45	***0·00***	3·4	1·1	45	***0·01***	2·08	1	0·15
Week 12	2·8	1·3	45	*0·06*	3·1	1·1	45	***0·03***	1·35	1	0·25
Week 16	2·7	1·3	45	N.S.	2·8	1·1	45	***0·03***	0·66	1	0·42
Week 24	2·6	1·2	45	N.S.	2·7	1·3	45	N.S.	0·02	1	0·89
CGI-Improvement											
Week 4	3·1	0·9	43	***0·01***	3·2	0·8	43	***0·01***	0·02	1	0·89
Week 8	2·7	1·0	44	N.S.	2·9	0·9	44	***0·08***	0·91	1	0·34
Week 12	2·5	1·1	44	N.S.	2·6	0·8	44	***0·03***	0·16	1	0·69
Week 16	2·4	1·2	44	N.S.	2·4	0·8	44	***0·03***	0·09	1	0·77
Week 24	2·3	1·0	44	N.S.	2·3	0·9	44	N.S.	0·19	1	0·67
SCL-Depression											
Pre-treatment	49·3	8·7	45		52·0	10·1	45		1·85	1	0·18
Week 8	35·6	13·4	45	***0·00***	43·1	12·9	45	***0·00***	5·30	1	***0·02***
Week 16	34·6	13·6	45	N.S.	38·1	13·5	45	***0·00***	0·40	1	0·53
Week 24	35·2	12·8	45	N.S.	36·4	14·2	45	N.S.	0·04	1	0·85
QLDS											
Pre-treatment	16·1	6·4	44		14·8	7·0	43		0·75	1	0·39
Week 8	21·8	8·9	45	***0·00***	19·1	8·0	45	***0·00***	1·34	1	0·25
Week 16	22·9	8·8	45	N.S.	21·8	8·1	45	***0·02***	0·09	1	0·77
Week 24	22·6	8·6	45	N.S.	22·8	8·3	45	N.S.	0·28	1	0·60

instruments. Randomization was, therefore, successful.

Outcome

In Table 2, we present means and standard deviations of the four outcome measures in the PP sample. In the fourth and eight columns of this table we present the significance scores of the paired *t* tests. Each time we compared the scores of that assessment with the scores of the last assessment. In the last three columns we present the results of the ANCOVAs of the four outcome measures in the PP sample. We used baseline pre-treatment measurement as the covariate before comparing the means at week 24.

Obviously, the treatment of depression in both therapy conditions was successful. With the paired *t* tests we observed significant changes in all outcome measures in the first 8 weeks. After week 8, there were only significant further falls in the scores in the 16-session condition (up to week 16).

With the ANCOVA we see few differences between the conditions at the various measurement points. The few differences there are, indicate that remission levels are higher at around week 8 of the 8-session condition compared to the 16-session condition. After 6 months, there are no more differences between the 8- and 16-session conditions. In case of a Bonferroni adjustment of the *p* value, the minor differences which there are in favour of the 8-session condition are negligible.

When we used a MANOVA with repeated measurements, there was a significant main effect of the treatment factor on the HDRS ($F=44, 8$; $p=0{\cdot}00$), CGI-S ($F=60, 1$; $p=0{\cdot}00$), CGI-I ($F=23, 18$; $p=0{\cdot}00$) and QLDS ($F=39, 75$; $p=0{\cdot}00$), but there was not a main effect for the condition and also not an interaction

Table 3. *Success percentages and remission rates for five outcome measures (per protocol sample)*

	Treatment				Pearson χ^2 (2-sided) significance level		
	8 sessions		16 sessions				
	n	%	*n*	%	χ^2	df	*p*
HDRS remission							
Week 4	7	15·6	3	6·7	1·80	1	0·18
Week 8	14	31·1	8	17·8	2·17	1	0·14
Week 12	13	28·9	11	24·4	0·23	1	0·63
Week 16	18	40·0	13	28·9	1·23	1	0·27
Week 24	15	33·3	13	28·9	0·21	1	0·65
HDRS reduction >50%							
Week 4	8	17·8	5	11·1	0·81	1	0·37
Week 8	19	42·2	12	26·7	2·41	1	0·12
Week 12	17	37·8	16	35·6	0·05	1	0·83
Week 16	21	46·7	21	46·7	0·00	1	1·00
Week 24	19	42·2	19	42·2	0·00	1	1·00
CGI-Severity success							
Week 4	4	8·9	2	4·4	0·71	1	0·40
Week 8	12	26·7	8	17·8	1·03	1	0·31
Week 12	19	42·2	12	26·7	2·41	1	0·12
Week 16	21	46·7	15	33·3	1·67	1	0·20
Week 24	22	48·9	21	46·7	0·05	1	0·83
CGI-Improvement success							
Week 4	8	17·8	6	13·3	0·34	1	0·56
Week 8	20	44·4	16	35·6	0·74	1	0·39
Week 12	24	53·3	18	40·0	1·61	1	0·21
Week 16	27	60·0	26	57·8	0·05	1	0·83
Week 24	31	68·9	24	53·3	2·29	1	0·13
SCL-Depression success							
Week 8	25	55·6	25	55·6	0·00	1	1·00
Week 16	29	64·4	30	66·7	0·05	1	0·82
Week 24	30	66·7	27	60·0	0·43	1	0·51
QLDS success							
Week 8	18	40·9	14	32·6	0·65	1	0·42
Week 16	21	47·7	21	48·8	0·01	1	0·92
Week 24	20	45·5	26	60·5	1·97	1	0·16

effect between treatment and condition. Concerning the SCL scores, as well as the main effect of treatment ($F=69, 98$; $p=0{\cdot}00$) there is also a trend to an interaction effect between treatment and condition ($F=2, 59$; $p=0{\cdot}06$), but not a main effect for condition.

Remission and success rates for the outcome measures are presented in Table 3.

Again, there are virtually no differences between the conditions. The few trends that there are indicate higher remission levels in the 8-session condition around week 8. These differences in success percentages between the treatment groups gradually disappeared at 16 and 24 weeks.

In terms of HDRS remission, the Kaplan–Meier survival curves for the two treatment groups in all of the three samples generate much the same information. Fig. 2 plots the proportion of patients against the number of weeks until remission for the PP sample.

The 8-session treatment condition curve is below that of the 16-session condition, meaning that remission is reached earlier. The two curves coincide after 24 weeks.

The mean time to achieve remission – defined as an HDRS score below 8 – is 16 weeks in the 8-session condition and 18 weeks in the 16-session condition. With the Kaplan–Meier survival analysis, we find no significant difference in time to remission between the two treatment groups at 24 weeks. During the first 8 weeks, however, there is a significant difference in remission rates (log rank $=3{\cdot}90$; df $=2$; $p=0{\cdot}048$). At 8 weeks, 31% of the 8-session patients had already reached remission, while remission had

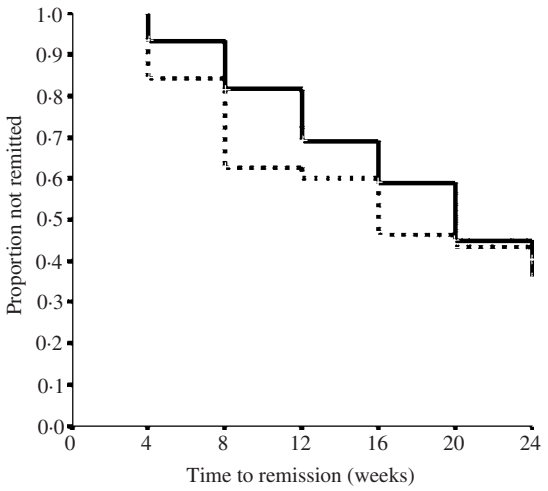

FIG. 2. The survival curves or the HDRS remission in the per protocol sample. Treatment: —, 16 sessions; ----, 8 sessions.

only been achieved in 18% of the 16-session patients. The same analysis was made for both SCL-90 and QLDS. There was also no significant difference for time to remission between the two treatment groups at 24 weeks (SCL-90: log rank = 1·27; df = 2; $p = 0{\cdot}261$ and QLDS: log rank = 0·19; df = 2; $p = 0{\cdot}665$), in the PP sample.

With regard to the distribution of antidepressants taken, no significant difference was found between the conditions at measurement times. The same applies to the mean dose per antidepressant (according to the protocol).

Logistical regression analysis was conducted to determine whether there was a link between severity of depression at the start of the treatment and remission. Here, HDRS remission was the dependent variable and condition, sex, age, severity of depression, marital status, educational level, and number of depressed episodes were the independent variables. This analysis showed that severity of depression at the start of the treatment, as well as the other independent variables, was not linked to remission during treatment.

Satisfaction with the number of psychotherapy sessions

Comparisons were made for the two conditions between the total scores for the patient version of the Luborsky and the scores for the therapist version. None of the versions indicated a significant difference between the conditions. We used a Pearson χ^2 (2-sided) test to determine whether there were any differences between the opinions of the patients and the therapists (on the Luborsky item) about the right number of psychotherapy sessions. Well over half (73% in the 8-session condition and 58% in the 16-session condition) of the therapists consider the number of sessions to be adequate, with only half of the patients being of the same opinion (54% and 50% respectively). There is no significant difference between the conditions ($p = 0{\cdot}13$; $\chi^2 = 4{\cdot}1$; df = 2). Approximately 43% of patients thought there were not enough therapy sessions. Again, this applies equally to both conditions ($p = 0{\cdot}23$; $\chi^2 = 2{\cdot}9$; df = 1). Only in the 16-session condition did 10% of both therapists and patients say there were 'too many sessions'. The others thought there were 'enough' sessions.

Therapy compliance

As we are looking at the effect of a combined therapy, reasons for drop out can be either discontinuation of pharmacotherapy or psychotherapy, or a violation of the study protocol. No explicit discontinuations of psychotherapy were registered. Based on the PP sample, we found no differences in drop-out percentages between the study conditions. In both conditions approximately 88% of the patients were still on medication 8 weeks after the start of the treatment. After 6 months, this percentage was, in both conditions, still approximately 76%. The dose of medication or the switching to other medication (according to the pharmacotherapy protocol) did not differ significantly between the conditions and could not have affected the drop-out rate.

DISCUSSION

Eight or 16 psychotherapy sessions in addition to 8 sessions of pharmacotherapy over a period of 6 months would appear to be equally effective in terms of dealing with symptoms. That is true for both moderately and severely depressed patients. The minor advantage of 16 compared to 8 sessions for severely depressed patients, which was found in previous studies (Shapiro *et al.* 1994; Barkham *et al.* 1996*a*) was, therefore, not confirmed by our study. Remission was faster in our study in the 8-session condition.

What are the possible explanations for our findings? With respect to faster remission in the 8-session psychotherapy condition, Reynolds *et al.* (1996) also found a trend of faster remission in the 8-session compared to the 16-session condition. Eckert (1993) suggests that there is an acceleration of therapeutic change when a limit is imposed on the number of sessions given to a client. He believes that it is, therefore, possible to achieve the same result with fewer sessions. If there is less time available, the therapeutic process can adapt and, in general, the work is done more efficiently (Howard *et al.* 1986). It is conceivable that patients in the 8-session condition adopt a more active attitude because they only have 8 sessions in which to bring about an improvement. This pressure may be less intense in the 16-session condition.

After 6 months, the results of 8 or 16 psychotherapy sessions (accompanied by pharmacotherapy) converged again. The 8-session condition shows a relatively rapid decrease on most of the outcome measures. Much of the improvement occurred during the first 8 weeks, which runs parallel with the psychotherapy sessions. A more gradual picture is seen in the 16-session condition, in which the outcome scores at the end of treatment reach the same values as in the 8-session condition. In terms of dealing with symptoms, then, a longer course of psychotherapy in a combined treatment context does not lead to better results than brief psychotherapy.

We found effect sizes that corresponded to the studies of Shapiro *et al.* (1994) and Barkham *et al.* (1996*b*). They report effect sizes of 1·77 and 1·60 respectively. In our study, we found an effect size of 2·18 for the 8-session condition and of 1·86 for the 16-session condition. In a meta-analysis, Thase *et al.* (1997) found recovery rates of 43% in more severely depressed patients and 48% in patients with less severe symptoms. These results are in accordance with our remission rate of 42·2% in both conditions. Compared to Keller *et al.* (2000), our results are not impressive. The effect size they found in their study was 3·69. This is much higher than reported in other studies. An explanation for this result could be the relatively large number of psychotherapy sessions in a short amount of time.

An assessment of the level of satisfaction among patients and therapists with the number of psychotherapy sessions indicates that there are no differences between the two conditions. However, there are differences between therapists and patients. Well over half (73% in the 8- session condition and 58% in the 16-session condition) of the therapists consider the number of sessions to be adequate, with only half of patients being of the same opinion (54% and 50% respectively). The average percentage of patients that thought that there were 'too few' sessions, was 43%. Despite improvements in depression, a sizable percentage of the patients, and to a lesser degree the therapists, therefore considered the number of psychotherapy sessions to be inadequate.

When the number of drop-outs is taken into consideration, there is once again no difference between the conditions. Although neither the distribution nor the mean dose of the antidepressants taken played a role in the outcome scores, the main reason for drop-out was associated with pharmacotherapy. In this study, none of the patients dropped out because of the psychotherapy. It has been claimed that the addition of psychotherapy actually improves compliance (Paykel, 1995; de Jonghe *et al.* 2001). It would appear to be the case that 8 sessions of psychotherapy generate the same level of medication compliance as 16 sessions of psychotherapy.

Several limitations of the study should be mentioned. First, there is the selection bias in the study population. The four inclusion criteria and the nine exclusion criteria meant that a specific group of depressed patients participated in this study. The selection criteria took suitability for pharmacotherapeutic research into account and not suitability for psychotherapeutic treatment, such as ego strength, introspective ability, psychological aptitude or verbal skills. Second, is the use of the CGI scores in the outcome data. Because the treating psychiatrist used this instrument to monitor the clinical progress, it is not a totally independent measure. This is overcome by using the HDRS and the SCL-90 (both assessed by an independent research fellow). Third, the study was limited in terms of statistical power, although the data does not give the impression that a larger number of patients would have tilted the

findings towards either condition. Furthermore, the lack of a control group obstructs the assessment of the effectiveness of the two study conditions.

It can be concluded that the rate of change would seem to be in favour of the condition with 8 sessions, and that the results of both conditions at the end converged again. In terms of satisfaction about the number of sessions and drop-out percentages during treatment, no differences were found between the conditions. Based on these results, one would appear to be justified in concluding provisionally that a short version of psychotherapy in a combined course of treatment should be the treatment of choice. However, this position would appear to be premature. It is possible that the longer course of psychotherapy, in the short term, will result in improved functioning levels in the areas of coping and social functioning. In the longer term, this could result in the improvements being maintained and in the postponement of any possible relapse. We hope to clarify these issues in later publications.

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DECLARATION OF INTEREST

None.

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