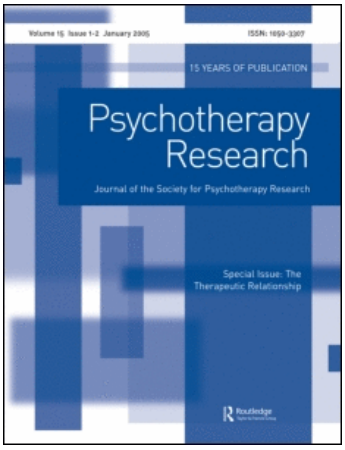
Patient preference compared with random allocation in short-term psychodynamic supportive psychotherapy with indicated addition of pharmacotherapy for depression.

Van, H.L.; Dekker, J.J.M.; Koelen, J.; Kool, S.; van Aalst, G.; Hendriksen, I.J.M.; Peen, J.; Schoevers, R.A.

published in
Psychotherapy Research
2009

DOI (link to publisher)
10.1080/10503300802702097

document version
Publisher's PDF, also known as Version of record



Psychotherapy Research
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713663589

Patient preference compared with random allocation in short-term psychodynamic supportive psychotherapy with indicated addition of pharmacotherapy for depression

Henricus L. Van[a]; Jack Dekker[a]; Jurrijn Koelen[a]; Simone Kool[a]; Gerda van Aalst[a]; Marielle Hendriksen[a]; Jaap Peen[a]; Robert Schoevers[a]
[a] Mentrum Depression Research Group, Mentrum Mental Health Care, Mentrum Mental Health Hospital, Amsterdam, The Netherlands

To cite this Article Van, Henricus L. , Dekker, Jack , Koelen, Jurrijn , Kool, Simone , van Aalst, Gerda , Hendriksen, Marielle , Peen, Jaap and Schoevers, Robert(2009) 'Patient preference compared with random allocation in short-term psychodynamic supportive psychotherapy with indicated addition of pharmacotherapy for depression', Psychotherapy Research, 19: 2, 205 — 212
To link to this Article: DOI: 10.1080/10503300802702097
URL: http://dx.doi.org/10.1080/10503300802702097

Psychotherapy Research, March 2009; 19(2): 205–212

Patient preference compared with random allocation in short-term psychodynamic supportive psychotherapy with indicated addition of pharmacotherapy for depression

HENRICUS L. VAN, JACK DEKKER, JURRIJN KOELEN, SIMONE KOOL, GERDA VAN AALST, MARIELLE HENDRIKSEN, JAAP PEEN, & ROBERT SCHOEVERS

Mentrum Depression Research Group, Mentrum Mental Health Care, Mentrum Mental Health Hospital, Amsterdam, The Netherlands

(Received 17 September 2007; revised 13 December 2008; accepted 17 December 2008)

Abstract
Depressed patients randomized to psychotherapy were compared with those who had been chosen for psychotherapy in a treatment algorithm, including addition of an antidepressant in case of early nonresponse. There were no differences between randomized and by-preference patients at baseline in adherence and outcome. About half of the early nonresponders refused the additional medication. However, no clear effect of medication addition on ultimate outcome could be demonstrated. In total, 37% of the patients achieved remission. The study suggested that randomization of patients does not induce a great influence on outcome. It might be warranted to continue an initially ineffective psychotherapy for depression, because a considerable number of patients do have a pattern of delayed response.

Keywords: brief psychotherapy; depression; long-term psychotherapy; outcome research; personality disorders; psychoanalytic/psychodynamic therapy; psychotherapist training/supervision/development; psychoses/severe mental illness

Two meta-analyses indicate that psychotherapy and pharmacotherapy are equally efficacious for the acute treatment of mild to moderate depression (Casacalenda, Perry, & Looper, 2002; De Maat, Dekker, Schoevers, & de Jonghe, 2006). Relatively little is known about the efficacy of psychodynamic psychotherapy in the treatment of depression, because most studies comparing pharmacotherapy and psychotherapy involve cognitive–behavioural therapy (e.g., DeRubeis et al., 2005). Over the past few years, we have sought to fill this gap in psychotherapy research by directly comparing short-term psychodynamic supportive psychotherapy (SPSP), pharmacotherapy, and their combination in various randomized controlled trials (RCTs; de Maat et al., 2008).

However, several criticisms have been raised against the designs of RCTs. It is argued that results from RCTs are artificial and cannot be generalized to real-world psychiatric settings (Westen, Novotny, & Thompson-Brenner, 2004; Rothwell, 2005). Among other things, the procedure of randomization fails to match patient with treatment (Brewin & Bradley, 1989; Parker, 2005). It may exclude highly motivated patients with a strong preference for a particular treatment, whereas patients unsuited to receive a particular treatment are more likely to be included in a randomization procedure. Therefore, it is assumed that this selection process may lead to an underestimation of effectiveness (Bedi et al., 2000; Howard & Thornicroft, 2006). To remedy this complication, in our current RCT comparing SPSP with pharmacotherapy, we opted to add a by-preference (BP) condition (Brewin & Bradley, 1989). This means that patients refusing to be randomized were given the treatment of choice.

Another point is that most research data concern monotreatments, whereas in clinical practice the addition of medication to psychotherapy is very common, especially in the case of (early) nonresponse. Indeed, in a previous study, we found that early nonresponse to psychotherapy for depression

Correspondence concerning this article should be addressed to Henricus L. Van, Mentrum Mental Health Hospital, PO Box 75848, 1070 AV, Amsterdam, The Netherlands. E-mail: rien.van@mentrum.nl

ISSN 1050-3307 print/ISSN 1468-4381 online
DOI: 10.1080/10503300802702097

carries the risk of ultimate treatment failure, although at the same time a considerable number of early nonresponsive patients appear to achieve remission at the end of treatment as well (Van et al., 2008). There is some evidence that in interpersonal therapy (IPT) for depression a sequential strategy with the later addition of medication is slightly more effective than combined therapy from the outset (Frank et al., 2000), but research on this issue is rare. In view of this state of affairs, we opted for a sequential treatment strategy. It started with monotherapy (psychotherapy or antidepressants) and proceeded to combined therapy in the case of early nonresponse, which was defined as less than 30% improvement of depressive symptoms after 8 weeks of treatment.

Thus, the principal aim of the present study was to investigate the influence of preference on outcome of psychotherapy for depression by comparing random allocation with BP psychotherapy. The effects are investigated for early response, dropout, and general efficacy. The second aim was to determine in both groups the acceptability and surplus value of additional medication in the case of early nonresponse.

Method

Patients

The study sample consists of consecutively referred outpatients of Mentrum Mental Health Care, a large psychiatric teaching hospital in Amsterdam. Inclusion criteria were age between 18 and 65 years, depressive episode with or without dysthymia (using the Composite International Diagnostic Interview) based on *Diagnostic and Statistical Manual of Mental Disorders* (fourth edition [American Psychiatric Association, 1994) criteria, a 17-item Hamilton Depression Rating Scale (HAM-D; Hamilton, 1967) baseline score between 14 and 25 points, and written informed consent. Exclusion criteria were drug abuse, psychotic symptoms, participation impossible as a result of a serious communicative problem (e.g., language barrier), pregnancy, hospitalization or day treatment is unavoidable. Patients who were still using antidepressants during intake and who met inclusion criteria were advised to stop the medication. If they agreed, they were included in the trial; if not, they were excluded. In addition, all patients who had used venlafaxine earlier in the present episode were excluded because this was the first drug to be administered according to the medication protocol.

Study Design and Procedure

The study compares the efficacy of pharmacotherapy to SPSP. After intake, the psychiatrist explained to the patients that both treatments were available and that the efficacy of both treatments had been demonstrated and then briefly discussed some basic characteristics of the treatments. Patients willing to participate in a study were referred to a research assistant, who administered the pretreatment measurements and explained the rationale of a randomization procedure using a standardized information form. If patients agreed to select their treatment by randomization, they were allocated to either pharmacotherapy or SPSP using block randomization stratified for age and gender. The RCT comparing psychotherapy and antidepressants directly has been published elsewhere (Dekker, Koelen, et al., 2008; Dekker, Van, et al., 2008). Patients who refused randomization but were nevertheless willing to participate in a study provided they were given their treatment of choice were entered in the BP condition. Measurements and treatments were identical in the randomized and by-preference groups. At the start of the study, 59 patients were allotted to the RCT psychotherapy and 60 chose BP psychotherapy. Because only three patients chose to start with pharmacotherapy, we are not able to report on the treatment algorithm that started with BP antidepressants.

Patients with less than 30% reduction on the HAM-D after 8 weeks were offered venlafaxine, 75 mg/day, which could be titrated up to a maximum of 225 mg/day. For patients who responded to treatment at Week 8, psychotherapy alone was continued as scheduled.

Treatment

SPSP consisted of 16 sessions, the first eight sessions weekly, the last every 2 weeks. SPSP is a manual-based approach (de Jonghe, 2005) focusing on the affective, behavioural, and cognitive aspects of relationships. By discerning levels, which depends on the phase of the therapy and the capacities of the patient, the therapists may choose more supportive interventions, such as encouraging adaptive coping mechanisms, guilt-reducing thoughts, or giving praise, or interventions to enhance insight, such as confrontation or interpretation. This means that the therapy can be placed on a variable point on the expressive–supportive continuum (Gabbard, 2005). Therapists were trained psychiatrists or psychotherapists. They met regularly to discuss audiotaped sessions and to ensure adherence to the psychotherapy manual.

Outcome Measures

The primary measurement was the 17-item HAM-D. The HAM-D was assessed by independent observers. Raters were trained by de Jonghe, the psychiatrist

who developed the manual for the Dutch version of the HAM-D (de Jonghe, 1994) and who has extensive experience in its training and application. Before being judged competent to assess the HAM-D, raters needed to score five interviews sufficiently reliably. During the study the assessors met monthly to discus videotaped interviews with the supervising psychiatrist to prevent slippage, but the interrater reliability was not formally assessed. Secondary outcome measures were the Clinical Global Impression of severity (CGI-S) and improvement (CGI-I; Guy, 1976) provided by the treating clinicians and the Symptom Checklist-90-Revised (SCL-90) Depression subscale (Arrindell & Ettema, 1986).

Assessments took place at baseline and Weeks 8, 16, and 24. On the primary outcome measure, efficacy was expressed both in terms of mean differences in HAM-D scores and in success rates. The latter was defined as response rate (50% reduction on the HAM-D) and remission rate (HAM-D ≤ 7). On the secondary measurements, only success rates are given. They are defined as a CGI-S and a CGI-I score of 1 (*very much improved*) or 2 (*much improved*) and SCL-90-R improvement of at least 1 *SD*. Patients who, regardless of the reason, completed fewer than five sessions in the first 8 weeks or terminated treatment between Week 8 and Week 24 were considered dropouts, with the exception of those who terminated after Week 20 (i.e., after 14 of the 16 psychotherapy sessions) if they had achieved a HAM-D score of ≤ 12.

Statistical Analysis

To test for the overall effectiveness of the treatments, within-group effects of time were calculated between Weeks 0 and 24 using paired *t* tests. Analyses of covariance (ANCOVAS) were used to test between-group differences in terms of means, including baseline measures as covariants. Pearson chi-square calculations (two-sided, level of significance = .05) were used to compare refusal rates, dropout rates, and success rates between therapy conditions. A per protocol analysis was performed for outcome measures. This means that the outcome data of all patients allocated to a treatment option were used and the last observation carried forward procedure applied in the case of missing data. The study was divided into two parts—the first phase from start to 8 weeks and the second phase from Weeks 8 to 24—to specifically examine the BP and sequential aspects of the design. Between-group analyses were performed on the whole sample of Week 0 and on the per protocol sample of Week 8 separately, thus excluding patients who dropped out before Week 8 and never were offered to combine SPSP with an antidepressant. A general linear model repeated measures analysis (GLM procedure in SPSS) using all data was performed. HAM-D outcomes of all assessments were entered as dependent variables and treatment condition (randomisation or BP) as independent variable. Use of antidepressants (yes–no) and dropout (yes–no) were entered as covariates. Finally, a separate logistic regression analysis was conducted to test the efficacy of addition in all early nonresponding patients.

Results

Baseline Characteristics

There were no baseline differences between randomized and BP patients in demographic and clinical characteristics (Table I). The mean age was 35.9 years ($SD = 10.4$), 79.8% of the sample were women. About half of patients had been treated earlier in the present episode, indicating refractory depression.

Phase 1: Weeks 0–8

Of the 59 patients in the RCT condition, 19 (32.2%) were considered study dropouts (i.e., attended fewer than five sessions SPSP) compared with 15 (25%) of 60 in the BP group, $\chi^2(1, N = 119) = 1.46$, $p = .23$. Subsequently, 40 originally randomized patients and 45 BP patients proceeded to the second phase of the study.

After the first 8 weeks, 11 of 40 (27.5%) randomized patients were responsive ($>30\%$ reduction on the HAM-D) in the RCT condition compared with 17 of 45 (37.8%) in the BP group. The difference was not statistically significant. Also, none of the secondary outcome measures differed between RCT and BP patients with the exception of the CGI-S, which was in favor of the BP patients, $\chi^2(1, N = 85) = 4.83$, $p = .03$.

Phase 2: Weeks 8–24

The distribution of patients at 8 weeks is shown in Figure 1.

Early responsive patients. All early responders continued treatment of SPSP without being offered medication. The results of mean HAM-D scores are shown in Figure 2. For RCT patients, the mean HAM-D score in responders had decreased from 20.4 ($SD = 3.8$) at baseline to 9.3 ($SD = 4.1$) at Week 8 and for BP patients from 19.6 ($SD = 3.9$) to 8.6 ($SD = 8.6$). The mean HAM-D scores declined only slightly further in the second phase: for RCT

Table I. Baseline Characteristics of Randomized and By-Preference Patient Sample

Variable	RCT ($n=59$)	BP ($n=60$)	Total ($n=119$)
Gender (%)			
Male	25.4	15.0	20.2
Female	74.6	85.0	79.8
Age (%)			
20–29 years	32.2	45.0	38.7
30–39 years	35.6	25.0	30.3
≥40 years	32.8	30.0	31.3
Marital status (%)			
Married	24.1	23.7	23.9
Divorced	12.1	8.5	10.3
Widowed	3.4	3.4	3.4
Never married	60.3	64.4	62.4
Educational level (%)			
Low	24.1	22.0	23.0
Intermediate	50.0	44.1	46.9
High	25.9	33.9	30.1
Duration of present episode (%)			
<1 year	48.2	50.9	49.5
>1 year	51.8	49.1	50.5
Any earlier treatment in present episode (%)			
Yes	48.6	50.9	47.3
No	56.4	49.1	52.7
Earlier antidepressant use in present episode (%)			
Yes	30.4	36.8	33.6
No	69.6	63.2	66.4
Recurrence (%)			
0	48.2	54.2	51.3
≥1	51.8	45.8	44.7
HAM-D ($M \pm SD$)	20.4 (3.8)	19.6 (3.9)	20.0 (3.8)
CGI-S ($M \pm SD$)	4.4 (0.7)	4.2 (0.8)	4.3 (0.8)
SCL-D ($M \pm SD$)	51.8 (10.0)	49.8 (12.0)	50.8 (11.0)

Note. RCT = randomized controlled trial; BP = by preference; HAM-D = Hamilton Rating Scale for Depression; CGI-S = Clinical Global Impression of severity; SCL-D = Symptom Checklist-90-R–Depression.

patients to 7.6 ($SD=5.1$) and for BP patients to 7.8 ($SD=7.9$).

Table II shows the success rates on the HAM-D, CGI, and SCL-90-R Depression scale for early responders. In total, 71.4% of all early responding patients achieved response and 57.1% achieved

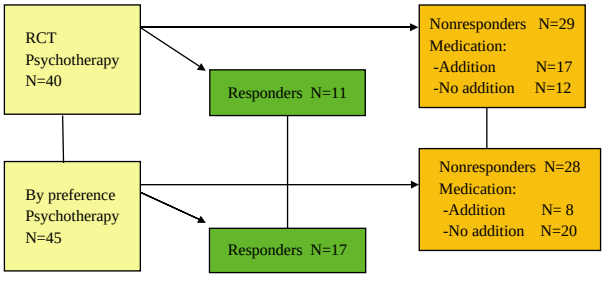


Figure 1. Flow diagram of the treatment algorithm from Week 8. (RCT = randomized controlled trials.)

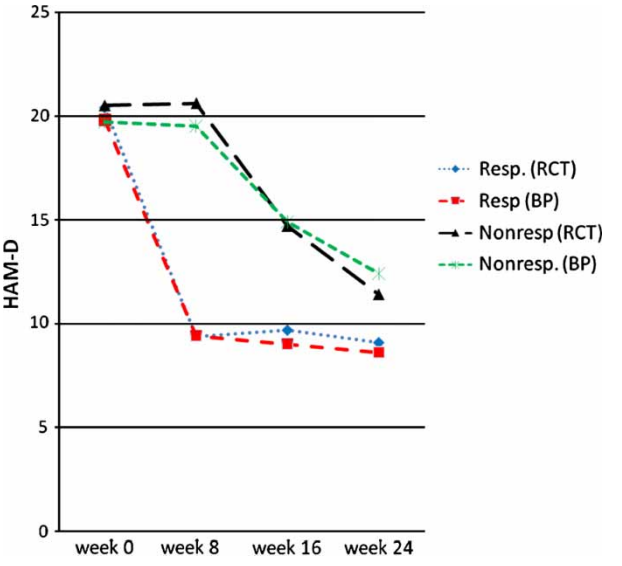


Figure 2. Mean scores of Hamilton Depression Rating Scale in time for patient with and without early response.

remission. No statistically significant differences were found between RCT and BP patients.

Early nonresponsive patients. All early nonresponders were offered to combine psychotherapy with venlafaxine. Of the 29 RCT patients who were nonresponsive, 17 (58.6%) started venlafaxine, and in the BP condition only 8 of 28 patients (28.6%) did so, $\chi^2(1, N=57)=5.22$, $p=.02$.

The following results concern the whole group, regardless of acceptance of medication. At Week 8, the mean HAM-D scores of nonresponders was still 20.6 ($SD=4.6$) for the RCT patients and 19.6 ($SD=4.1$) for the BP patients. As shown in Figure II, at the end of treatment the mean HAM-D score in RCT patients had improved to 11.4 ($SD=6.7$) and in BP patients to 12.5 ($SD=6.8$).

Of all early nonresponders, 43.9% achieved response and 26.7% achieved remission (see Table II). At the end of treatment, no difference was found between RCT and BP patients on any of the outcome measures. During treatment, no difference was found either with the exception of the therapist rated CGI-S score at Weeks 8 and 16.

Relative Efficacy at the End of Treatment for the Total Sample

Dropout rate in the second phase was relatively low: six in the RCT group (15%) and four (9%) in the BP group, $\chi^2(1, N=85)=0.76$, $p=.38$. The mean HAM-D score at the end of treatment, including both early responsive and nonresponsive patients, was 10.3 ($SD=6.5$) for RCT patients and 10.7 ($SD=7.5$) for BP patients. Table II shows also the

Table II. Success Rates (%) of Early Responders, Early Nonresponders, and Total Sample in RCT and BP Patients

	Early responders			Early nonresponders			Total sample		
Measurement	RCT ($n=11$)	BP ($n=17$)	Total ($n=28$)	RCT ($n=29$)	BP ($n=28$)	Total ($n=57$)	RCT ($n=40$)	BP ($n=45$)	Total ($n=85$)
HAM-D									
Response ($>50\%\downarrow$)									
Week 8	45.5	58.8	53.6	NA	NA	NA	12.5	22.2	17.6
Week 16	36.4	70.6	57.1	24.1	21.4	22.8	27.5	40.0	34.1
Week 24	63.6	76.5	71.4	55.6	43.9	43.9	57.5	48.9	52.9
HAM-D									
Remission (≤ 7)									
Week 8	36.4	41.2	39.6	NA	NA	NA	10.0	15.6	12.9
Week 16	36.5	52.9	46.4	18.8	14.3	14.0	20.0	28.9	24.7
Week 24	54.5	58.8	57.1	27.6	26.3	26.7	35.0	37.8	36.5
CGI-Severity									
Week 8	36.4	58.8	39.3	0.0*	17.9*	8.8	10.0*	33.3*	22.9
Week 16	54.5	82.4	46.4	37.9*	14.3*	26.3	42.5	40.0	41.2
Week 24	81.8	76.5	57.1	55.2	46.4	50.9	62.5	57.8	60.0
CGI–Improvement									
Week 8	36.4	52.9	50.0	10.3	14.3	12.3	17.5	28.9	23.5
Week 16	45.5	76.5	71.4	34.5	17.9	26.3	37.5	40.0	38.8
Week 24	72.7	76.5	78.6	55.2	53.6	54.4	60.0	62.2	61.2
SCL-D (>1 *SD* $\downarrow$)									
Week 8	40.0	58.8	51.9	21.4	11.1	16.4	26.3	29.5	28.0
Week 16	80.0	64.7	70.4	57.1	37.0	47.3	63.2	47.7	54.9
Week 24	80.0	64.7	70.4	64.3	48.1	56.4	68.4	54.5	61.0

Note. RCT = randomized controlled trial; BP = by preference; HAM-D = Hamilton Rating Scale for Depression; CGI = Clinical Global Impression; SCL-D = Symptom Checklist–Depression; NA = not applicable because of definition of nonresponse.
*$p<.05$.

aggregated success rates of the treatment algorithm. In total, 52.9% of the patients achieved response and 36.5% achieved remission. The only statistical difference appeared at Week 8 for the CGI-S favouring BP patients. This difference disappeared in the continuation phase of therapy. No other differences were found throughout the entire treatment. In addition, a repeated measures analysis using all available data was performed and did not yield a statistically significant association of treatment condition and outcome ($F=0.997$, $p=.41$).

Efficacy of Addition of Medication

In a logistic regression analysis, we explored the contribution of the addition of medication to treatment efficacy in all early nonresponding patients. HAM-D scores, treatment group, addition status, and the Treatment Group × Addition Status interaction were entered as variables in the analysis. No main effect for addition was found. Similarly, no Treatment Group × Addition Status was found, implying that the extent to which patients benefited from additional medication was similar for the randomized and BP conditions.

Discussion

This article reported on a partially randomized preference trial with a sequential strategy for the treatment of depression. Because few patients chose to start with an antidepressant, it is only possible to report on the comparison between randomized and BP psychotherapy patients.

Patients' Preference

Patients allocated to psychotherapy by chance and those choosing psychotherapy did not differ on baseline characteristics, thus indicating that the process of randomisation did not create a specifically selected group of depressed patients not willing to accept random allocation. These results appear to be in line with a comparable preference trial conducted in primary care, in which no clear selection bias was found, not even with regard to personality factors (Bedi et al., 2000).

Almost all patients in the BP modality chose to start with psychotherapy and not with an antidepressant. In a systematic review, a preference for psychotherapy was found in all available studies (van Schaik et al., 2004), but such a strong preference has

not been reported before. However, unlike other studies, it should be taken into account that in our treatment algorithm patients knew from the start that they would be offered augmentation of an antidepressant if the therapy was not working after 2 months, which might have influenced their choice.

Remarkably, at present, the situation in the United States appears to have changed. Despite the growing evidence of the efficacy of antidepressant psychotherapies, the recently emerging STAR*D data suggest that psychotherapy is no longer the treatment of choice for American patients (Wisniewski et al., 2007). This may reflect cultural variation but also points to a limited accessibility of psychotherapy for depression in the current American health care systems (Weissman, 2007).

In the current study, many patients declined an additional antidepressant after 8 weeks, not surprisingly within the BP group more so than within the RCT group. Apparently, they preferred to continue with psychotherapy alone in spite of early nonresponse. Obviously, we do not know to what extent this is typical for the patient population that has been studied. Again, in the United States, patients seem to choose rather differently. In a study on IPT, almost every patient with poor response accepted the addition of an antidepressant (Frank et al., 2000). We cannot rule out that, compared with SPSP, the IPT model is more to amenable to the integration of medication, which might have contributed to this difference. However, in SPSP also, depression is primarily considered as a medical condition that, if necessary, should be treated with medication. This is illustrated by an earlier finding showing that patients in combined therapy were more compliant with the medication regimen than patients using antidepressants alone (de Jonghe, Kool, Dekker, & Peen, 2001), suggesting a good acceptance of pharmacotherapy during SPSP. We, therefore, hypothesise that the difference in acceptability of antidepressants may reflect a more general positive attitude to medication in U.S. patients. It raises questions about the cross-cultural feasibility of sequential treatment strategies consisting of both psychotherapy and antidepressants, which need to be taken into account in guidelines and the application of treatment algorithms in clinical practice.

About one third of the patients did not complete the psychotherapy as planned. In earlier studies, both in our settings and those of others, comparable dropout rates were found (see, e.g., Blom, 2007; de Jonghe et al., 2004). Therefore, we assume it could be interpreted as a general characteristic of secondary care depressed patients. In contrast to what might be expected, choosing treatment did not enhance adherence to psychotherapy because dropout rates did not differ between RCT and BP patients, not even in the initial phase of treatment, shortly after they had made their choice. Clearly, a better understanding of the background of this phenomenon is important. It may indicate a need to try other strategies. Possibly, techniques derived from motivational interviewing (Cheng, 2007) are useful to improve adherence, particularly in the initial phase where most dropouts occurred.

In terms of general efficacy, patients in both conditions improved equally well on all instruments throughout the treatment period. Having a preference for psychotherapy did not convey a benefit in response. A similar absence of a profound influence of preference on outcome has been reported in two earlier trials (van Schaik et al., 2004). It refutes the assumption that randomisation may lead to an underestimation of efficacy as a result of unjustly neglecting patients' preference or the possibility of including less motivated patients in treatment (Thornett, 2001).

Sequential Strategy

If we look at the pattern of HAM-D response during treatment (see Figure II), two groups of patients can be identified: early responders (i.e., patients who improved rapidly) and delayed responders (i.e., those who started to improve in the second phase of treatment). This confirms a pattern of response we found in an earlier trial with SPSP (Van et al., 2008).

It suggests that it may be worthwhile to continue an ongoing psychotherapeutic strategy despite apparent absence of early symptom improvement. After all, a considerable number of patients do respond later on. In our study, the second phase consisted of eight sessions over a 4-month period. Unfortunately, we were not able to answer the question whether, after this second phase, again a group of nonresponding patient could be identified that might benefit from a further continuation of treatment. Future studies, preferably including ongoing response-monitoring procedures during psychotherapy (Percevic, Lambert, & Kordy, 2006), are required to shed more light on this issue.

It could be questioned whether it would have been necessary for early responders to continue therapy after Week 8. Because the mean HAM-D had already diminished to 9.0 by that time, there is little room for further symptom improvement. However, in SPSP the therapeutic process is structured in discourse levels (de Jonghe, 2005). This means that, in the initial phase, the therapy focuses on coping with symptoms and on (life) circumstances or problems directly related to the depression. If improvement at

this level has been achieved, the therapist may proceed to work on intrapersonal vulnerabilities in the middle and late stages of therapy, related to the onset of depression.

Preliminary data suggest that a change in personality pathology indeed could be achieved after SPSP (Kool et al., 2003). In future research, it would, therefore, be of interest to explore whether this in particular occurs in early symptom responders, because in these patients the therapist is better able to focus on underlying personality vulnerabilities. If so, this would legitimize a (time-limited) continuation of psychotherapy.

Strengths

We adopted a by-preference sequential strategy. This relatively rare design can illuminate what occurs in regular clinical practice because many patients prefer to choose their treatment, if possible. Furthermore, sequential treatment strategies appear to be widely advocated and used in clinical settings (Schatzberg et al., 2005) but rarely investigated. Therefore, using this strategy, we intended to increase the external validity of our study. A further strength is that outcome data came from three different sources: independent observers, patients, and therapists. Finally, many patients had been treated before in the present depressive episode, indicating they suffered from refractory depressions. Also, patients were not specifically selected for psychotherapy. Therefore, they may be representative of the broad sample of difficult-to-treat depressed patients commonly referred to outpatient psychiatric facilities.

Limitations

Our study involves outpatients with moderately severe depression; thus, the findings may not generalize to more or less severely depressed patients. Also, we did not take into account the influence of personality factors or attitude toward treatment, which might be associated with both the acceptability and efficacy of psychotherapeutic strategies (Iacoviello et al., 2007). Although additional medication could not explain subsequent outcome, it should be noted that the nonresponding patients were not randomized at Week 8. Therefore, it remains possible that they would have done poorer without medication addition.

Patients were only offered two options (randomization vs. by-preference SPSP or medication). Other antidepressant treatments such as different forms of psychotherapy, combined therapy from the outset, psychosocial support, and long-term psychotherapy could not be chosen, thereby limiting the generalizability to settings in which these treatments are offered. Finally, although a clear influence of choosing treatment could not be demonstrated in any of the statistical analyses, it needs to be taken into account that the groups were relatively small for the amount of measurements. Therefore, the occurrence of Type II errors cannot be ruled out.

Conclusion

This study indicated that patients who actively choose had outcomes similar to those who were randomly allocated to psychotherapy. In addition, no clear surplus value for a sequential strategy of adding medication after early nonresponse could be demonstrated. In contrast, a (time limited) and monitored continuation of the same psychotherapeutic strategy may be warranted in these patients because a considerable number do have a delayed response.

References

American Psychiatric Association. (1994). *Diagnostic and statistical manual of mental disorders* (4th ed.). Washington, DC: Author.

Arrindell, W. A., & Ettema, J. M. M. (1986). *Handleiding bij een multidimensionele psychopathologie-indicator* [Manual of measuring multidimensional psychopathology]. Lisse, The Netherlands: Swets & Zeitlinger.

Bedi, N., Chilvers, C., Churchill, R., Dewey, M., Duggan, C., Fielding, K., et al. (2000). Assessing effectiveness of treatment of depression in primary care: Partially randomized preference trial. *British Journal of Psychiatry*, *177*, 312–318.

Blom, M. B. J. (2007). *Combination treatment for depressed outpatients: Efficacy and prediction of outcome*. Amsterdam: Vrije University.

Brewin, C. R., & Bradley, C. (1989). Patient preferences and randomized clinical trials. *British Medical Journal*, *299*, 313–315.

Casacalenda, N., Perry, J. C., & Looper, K. (2002). Remission in major depressive disorder: A comparison of pharmacotherapy, psychotherapy and control conditions. *American Journal of Psychiatry*, *159*, 1354–1360.

Cheng, M. (2007). New approaches for creating the therapeutic alliance: Solution-focused interviewing, motivational interviewing, and the medication interest model. *Psychiatric Clinics of North America*, *30*, 157–166.

de Jonghe, F. (1994). *Leidraad voor het scoren van de Hamilton Depression Rating Scale*. Amsterdam: Benecke Consultants.

de Jonghe, F. (2005). *Kort en Krachtig* [Brief and potent]. Amsterdam: Benecke N.I.

de Jonghe, F., Hendriksen, M., van Aalst, G., Kool, S., Peen, J., Van, R., et al. (2004). Psychotherapy and combined therapy (pharmacotherapy plus psychotherapy) in the treatment of depression. *British Journal of Psychiatry*, *185*, 37–45.

de Jonghe, F., Kool, S., van Aalst, G., Dekker, J., & Peen, J. (2001). Combining psychotherapy and antidepressants in the treatment of depression. *Journal of Affective Disorders*, *64*, 217–229.

de Maat, S., Dekker, J., Schoevers, R., van Aalst, G., Hendriksen, M., Kool, S., et al. (2008). Short psychodynamic supportive psychotherapy, antidepressants, and their combination in the treatment of major depression: A mega-analysis based on three randomized clinical trials. *Depression and Anxiety*, *25*, 565–574.

de Maat, S., Dekker, J., Schoevers, R., & de Jonghe, F. (2006). Relative efficacy of psychotherapy and pharmacotherapy in the treatment of depression: A meta-analysis. *Psychotherapy Research*, *16*, 562–572.

Dekker, J., Koelen, J. A., Van, H. L., Schoevers, R. A., Peen, J., Hendriksen, M., et al. (2008). Speed of action: The efficacy of short-term psychodynamic supportive psychotherapy versus pharmacotherapy in the treatment of depression: Part I. The first 8 weeks of treatment. *Journal of Affective Disorders*, *109*, 183–188.

Dekker, J., Van, H. L., Schoevers, R. A., Koelen, J. A., van Aalst, G., Peen, J., et al. (2008). *Efficacy of short-term psychodynamic supportive psychotherapy and pharmacotherapy in a treatment algorithm for depression.* Manuscript submitted for publication.

DeRubeis, R. J., Hollon, S. D., Amsterdam, J. D., Shelton, R. C., Young, P. R., Salomon, R. M., et al. (2005). Cognitive therapy versus medications in the treatment of moderate to severe depression. *Archives of General Psychiatry*, *62*, 409–416.

Frank, E., Grochocinski, V. J., Spanier, C. A., Buysse, D. J., Cherry, C. R., Houck, P. R., et al. (2000). Interpersonal psychotherapy and antidepressant medication: Evaluation of a sequential treatment strategy in women with recurrent major depression. *Journal of Clinical Psychiatry*, *61*, 51–57.

Gabbard, G. (2005). *Psychodynamic psychiatry in clinical practice*. Arlington, VA: American Psychiatric Publishing, Inc.

Guy, W. (1976). *ECDEU assessment manual for psychopharmacology (revised)* (U.S. Department of Health, Education and Welfare Pub. ADM 76-338, 218-222). Rockville, MD: National Institute of Mental Health.

Hamilton, M. (1967). Development of a rating scale for primary depressive illness. *British Journal of Social and Clinical Psychology*, *6*, 278–296.

Howard, L., & Thornicroft, G. (2006). Patient preference randomised controlled trials in mental health research. *British Journal of Psychiatry*, *188*, 303–304.

Iacoviello, B. M., McCarthy, K. S., Barrett, M. S., Rynn, M., Gallop, R., & Barber, J. P. (2007). Treatment preferences affect the therapeutic alliance: Implications for randomized controlled trials. *Journal of Consulting and Clinical Psychology*, *75*, 194–198.

Kool, S., Dekker, J., Duijsens, I. J., de Jonghe, F. & Puite, B. (2003). Changes in personality pathology in depressed patients with pharmacotherapy and combined therapy. *Journal of Personality Disorders*, *17*, 60–72.

Parker, G. (2005). Beyond major depression. *Psychological Medicine*, *35*, 467–474.

Percevic, R., Lambert, J., & Kordy, H. (2006). What is the predictive value of response to psychotherapy for its future course? Empirical explorations and consequences for outcome. *Psychotherapy Research*, *16*, 364–373.

Rothwell, P. M. (2005). External validity of randomised controlled trials: "To whom do the results of this trial apply?" *The Lancet*, *365*, 82–93.

Schatzberg, A. F., Rush, A. J., Arnow, B. A., Banks, P. L. C., Blalock, J., Boriam, F., et al. (2005). Chronic depression. *Archives of General Psychiatry*, *62*, 513–520.

Thornett, A. (2001). Assessing the effect of patient and prescriber preference in trials of treatment of depression in general practice. *Medical Science Monitoring*, *7*, 1086–1091.

Van, H. L., Schoevers, R., Peen, J., Kool, S., Hendriksen, M., & Dekker, J. (2008). Does early response predict outcome in psychotherapy and combined therapy for major depression? *Journal of Affective Disorders*, *105*, 261–265.

van Schaik, D., Klijn, A., van Hout, H., Marwijk, H. W. J., de Haan, M., & van Dyck, R. (2004). Patients' preference in the treatment of depressive disorder in primary care. *General Hospital Psychiatry*, *26*, 184–189.

Weissman, M. M. (2007). Cognitive therapy and interpersonal psychotherapy: 30 years later. *American Journal of Psychiatry*, *164*, 693–696.

Westen, D., Novotny, C. M., & Thompson-Brenner, H. (2004). The empirical status of empirically supported psychotherapies: Assumptions, findings, and reporting in controlled clinical trials. *Psychological Bulletin*, *130*, 631–663.

Wisniewski, S. R., Fava, M., Trivedi, M. H., Thase, M. E., Warden, D., Niedere, G., et al. (2007). Acceptability of second-step treatments to depressed outpatients: A STAR*D report. *American Journal of Psychiatry*, *164*, 753–760.