

A Cognitive Behavioural Illness Management Program for Severe Depression: Predictors of Treatment Response

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Abstract

Background: Although combined pharmacotherapy and teaching illness management are the standard in the treatment of depressed inpatients, few studies have been reported of the effects of these programs. The purpose of this study was to determine the applicability and preliminary effectiveness of a brief, group-based cognitive-behavioural illness management program for depression, and to explore whether patient socio demographic and clinical characteristics predicted differential treatment response.

Methods: 97 inpatients with a major depression participated in a 6-week treatment program providing psycho education and skills to cope with the illness. Psychopathology, global functioning, knowledge about depression, self-esteem covering areas of problem solving, assertiveness and social competence were assessed as dependent variables.

Results: Overall, patients improved over the treatment period on most dimensions of psychopathology, knowledge about depression, and self-esteem. There was little evidence of differential treatment response as a function of either socio demographic or clinical variables. However, level of education was related to changes in psychopathology from pre- to post-treatment with higher educated patients benefiting most. Patients who were rapidly discharged from the hospital benefited more than inpatients in symptoms and problem solving skills. At two- and six year follow-ups, characteristics such as age and duration of illness were the only significant predictors for relapses.

Limitations: The absence of a control group limits the conclusions that can be drawn from this study.

Conclusion: These results suggest that this illness management program may be a useful approach to treating patients with severe depression, and that it warrants further investigation in a controlled study.

Keywords: Severe depression; Inpatient treatment; Illness management; Cognitive-behaviour therapy; Psycho education; Predictors; Psychopathology

Introduction

Pharmacological treatment is the mainstay in the management of recurrent depression, but accumulating evidence supports the role of cognitive behavioural therapy (CBT) as an important ingredient in comprehensive treatment programs for acute treatment and relapse prevention [1-7]. Cognitive Beck et al. [8] and interpersonal therapy Klerman et al. [9] are the most rapidly growing approaches for improving knowledge about the illness, symptoms, interpersonal competence as well as relapse prevention skills of patients with depression. New approaches mainly developed for the treatment of partially remitted or chronic forms of depression include the cognitive behavioural-analysis system of psychotherapy McCullough et al. [10], mindfulness based cognitive therapy Segal et al. [11] and cognitive-psycho educational interventions [12]. They are all based on cognitive techniques. The first additionally draws on behavioural Lewinsohn et al. [13] and interpersonal strategies Klerman et al. [9], the second on

stress reduction Kabat Zinn [14] and the latter on acquiring knowledge about the illness including its psychological and pharmacological treatment options [13,15].

Over the past two decades a range of different illness self-management programs have been developed based on Anderson's "psycho educational" multifamily workshops for schizophrenia Anderson et al. [16] and later depression Anderson et al. [15] providing information and skills about the illness and its treatment. Psycho educational programs are to train persons with a psychiatric disorder in subject areas that serve the goals of treatment and rehabilitation such as enhancing the person's acceptance of his illness, promoting active cooperation with treatment and rehabilitation, strengthening coping skills to deal with common aspects of the illness (e.g., stigma) and to compensate for deficiencies by the disorder Bäuml and Pitschel-Walz [17,18]. Pharmacotherapy and psychotherapy are not seen as conflicting but closely related to each other.

Up to now illness self-management group-based programs are offered to patients with schizophrenia and bipolar disorder, however, to a lesser extent to major depression [19]. Whereas former approaches merely focused on psychological or biological mono theories, such as

loss of positive reinforcement Lewinsohn et al. [13], dysfunctional core beliefs Beck et al. [8], serotonin-reuptake hypothesis or kindling Post [20], current programs refer to comprehensive vulnerability-stress-coping models integrating both aspects. These models highlight the interaction between vulnerability, stressors, deterioration in well-being up to relapse and provide the basis for illness-related cognitions that enable the patient to understand his illness and to realise how he can possibly influence its manifestations. Information about pharmacological (e.g., antidepressants), biological (e.g., sleep deprivation, electric convulsive shock treatment) and psychological treatment strategies are provided.

Although the data in reviews are mixed whether combining pharmacotherapy and psychotherapy leads to better outcome than mere pharmacotherapy Friedman et al., Pampallona et al., and Segal et al. [21-23] studies with depressive outpatients suggest that cognitive therapy is effective at teaching new skills in identifying and coping with early warning signs of relapse Paykel et al. [5] as well as in problem solving their maladaptive communication skills [3]. Furthermore, cognitive therapy has been found to lower depressive symptoms (DeRubeis et al. and Keller et al. [1,3] and vulnerability to relapse in some studies Hollon et al., Klein et al., Paykel et al., and Teasdale et al. [2-7] showing that it is clinically beneficial. Field testing of psycho educational programs indicates that they can be implemented in a variety of different facilities [24,25]. One controlled study shows no superior treatment effect in favour of psycho education compared to another treatment program Dowrick et al. [26]; however, there are striking effects of integrated treatment programs compared to standard treatment [27-30].

Up to now there are only few studies on inpatients available. Participating in interpersonal Schramm et al. [30], cognitive Stuart and Bowers [31] or cognitive-psycho educational programs Schaub et al. [12,32] led to high satisfaction with treatment and knowledge of depression as well as symptom reductions which were even maintained at six-month follow-up Backenstrass et al. [33]. Only two controlled studies showed no or only little short-term benefits of combining pharmacotherapy with cognitive therapy compared to each condition only Hautzinger et al. [34] or to the combination with supportive therapy De Jong-Meyer et al. [35], however, there was some evidence for long-term effects.

There is still an urgent need for further evaluation as combining pharmacotherapy with psychotherapy seems to be the standard in treating inpatients Depression Guideline Panel and Wolfersdorf [36,37] and patient pre-treatment predictors of outcome Hamilton and Dobson [38] have been scarcely investigated up to now. Even though cognitive behavioural therapy is an effective treatment for depression studies provide little guidance about whether it is best provided to inpatients while they are receiving inpatient services or after discharge [39]. Reasons for the inpatient setting are to use the time to provide empirically validated psychological treatments and to address difficulties with treatment adherence (e.g., homework assignment) more easily. Reasons to prefer the provision of CBT once an inpatient had been discharged include smaller costs, more opportunities to practice and to emphasize generalisation of skills beyond the therapeutic setting.

This paper focuses on the implementation and evaluation of a cognitive psycho educational treatment program with psychiatric inpatients suffering from depression [12]. Providing information about the illness and its treatment options, training patients in building up rewarding activities and in modifying negative, dysfunctional beliefs as

well as relapse prevention skills are the main ingredients of the program. The study investigates whether inpatients were able to acquire the information and targeted skills. Furthermore, the question was addressed whether socio demographic or clinical variables predicted treatment response to this illness management program and whether there were different effects of completing the program as inpatient or as outpatient.

Methods

Patients meeting the following criteria were consecutively recruited into the study from January 1999 to October 2000 at the University of the Ludwig Maximilian's University in Munich, Germany, Department of Psychiatry and Psychotherapy: diagnosis of major depression according to DSM IV, post-acute phase of the illness (i.e., remission of acute symptoms), sufficiently stable to become involved in a cognitive psycho educational group program twice a week, adequate intellectual and cognitive capacity and fluent in the German language. Exclusion criteria were comorbidity on axis I with organic brain syndrome, bipolar disorder, primary drug or alcohol dependency, schizophrenia and on axis II with borderline or antisocial personality disorder. As this study was to show whether this program could be implemented in the standard setting there was no age limit and simultaneous treatment with electroconvulsive shocks, trans cranial magnetic stimulation or sleep deprivation were no exclusion criteria. The study had been accepted by the ethical commission of the medical faculty in September 1998. It was supported by the German Ministry for Education and Research within the promotional emphasis "German Research Network on Depression" (1999-2000) as a pilot study.

Ninety-seven patients were recruited to participate in the study. 40 patients were diagnosed as having a single episode and 57 patients as having a recurrent type of major depression. About 50% of the patients suffered from a severe form of depression. Table 1 lists the patients' diagnoses.

DSM-IV	Diagnoses	Number (N)	Proportion (%)
296.2x	Major Depressive Disorder, Single Episode	40	41,2
296.21	MDD, Single Episode, Mild	3	3,1
296.22	MDD, Single Episode, Moderate	17	17,5
296.23	MDD, Single Episode, Severe, Without Psychotic Features	15	15,5
296.24	MDD, Single Episode, Severe With Psychotic Features	5	5,2
296.3x	Major Depressive Disorder, Recurrent	57	58,8
296.31	MDD, Recurrent, Mild	1	1,0
296.32	MDD, Recurrent, Moderate	24	24,7
296.33	MDD, Recurrent, Severe, Without Psychotic Features	24	24,7
296.34	MDD, Recurrent, Severe With Psychotic Features	8	8,2

Table 1: Distribution of diagnoses of the study sample (n = 97).

The patients had been stabilized for 3.9 weeks (SD =3.4) on average before they started the program. 63% of the sample was female, 26% were single, and 62% married, 14% divorced or separated. 17 patients (18.1%) were defined as drop-outs as they attended less than 2/3 of the training sessions because of acceleration of symptoms or discharge;

drop-outs did not differ from the treatment takers with regard to socio demographic or clinical variables. Table 2 summarizes the demographic and clinical data of 97 patients who participated in the study.

Characteristic		n	M	SD	Range
Diagnosis (ICD 10)	Depressive Episode	40			
	Recurrent depression	57			
Education	Elementary School without qualification	18			
	Elementary School With qualification	24			
	High School	18			
	College	29			
Work qualification	Unskilled, semi-skilled	11			
	Skilled worker	54			
	Academic career	27			
Employment status	Employed	36			
	Unemployed	57			
Age			50.2	12.1	24-77
Duration of illness (years)			11.1	11.5	0-50
Number of prior hospitalizations			2.8	2.5	1-15
Length of hospitalizations at the current stay before attending the group (weeks)			3.9	3.4	1-27

Table 2: Demographic and clinical characteristics of the study sample (n = 97).

Patients were treated with individualized pharmacotherapy and the cognitive psycho educational treatment program designed to help participants learn how to prevent serious mental illness from interfering with a functional life style. The treatment program provides information about the illness and its treatment based on a vulnerability-stress-coping model of the illness [40]. Building up rewarding activities and cognitive restructuring are both interventions that proved their effectiveness in depressive disorders [8,13,40]. The

program teaches strategies to cope with the illness and stressors as well as to prevent relapse such as identifying and managing early warning signs of relapse and cooperating with health-care providers. Psycho educational groups for relatives (6-8 sessions) are also important Anderson et al. [16] as engaging both patients and relatives might be most effective [25]. Table 3 gives an overview of the treatment program covering 12 sessions scheduled twice a week for 90 minutes including a 10 minutes' break.

Session	Topic
Psycho-education	
1	• Getting to know each other and explaining issues of organisation
	• Outlining the contents of the treatment program and its procedure (specific topic, working sheets, repetitions)
	• Focus on patients' expectations and explaining the rules of this group
	• Symptoms of depression and helpful strategies to cope with it
2	• Causes and treatment options
	• Developing the vulnerability-stress-coping-model
3	• Explaining the chemical processes in the brain
	• Biochemical modes of action in antipsychotics and other psychopharmacological agents

	<ul style="list-style-type: none"> • Side effects and strategies to cope with them
	<ul style="list-style-type: none"> • Other biological and psychotherapeutical approaches
Building up rewarding activities	
4	<ul style="list-style-type: none"> • The vicious circle of depression and how to get out of it
	<ul style="list-style-type: none"> • Mood record and list of activities
5	<ul style="list-style-type: none"> • Criteria for planning positive activities
	<ul style="list-style-type: none"> • Plan for the week
6	<ul style="list-style-type: none"> • Importance of establishing a balance between positive activities and requests (plans to reward oneself)
	<ul style="list-style-type: none"> • Planning partial goals and rewards
Cognitive therapy	
7	<ul style="list-style-type: none"> • Introduction of cognitive therapy
	<ul style="list-style-type: none"> • Recognizing the connection between thoughts, feelings, behavior: A-B-C- pattern
	<ul style="list-style-type: none"> • Identifying automatic thoughts
8	<ul style="list-style-type: none"> • Typical thought distortions and their modification
	<ul style="list-style-type: none"> • Split technique for modifying automatic depressive thoughts
	<ul style="list-style-type: none"> • Stopping rumination
9	<ul style="list-style-type: none"> • Recognizing the connection between automatic depressive thoughts and dysfunctional core beliefs (model of the iceberg)
	<ul style="list-style-type: none"> • Typical dysfunctional core beliefs
	<ul style="list-style-type: none"> • Record of automatic thoughts and realistic alternatives
10	<ul style="list-style-type: none"> • Identifying and modifying dysfunctional core beliefs
	<ul style="list-style-type: none"> • Summary of the inputs of cognitive therapy
Relapse prevention	
11	<ul style="list-style-type: none"> • Identifying early warning signs of relapse
	<ul style="list-style-type: none"> • Crisis worksheet and pharmacological relapse prevention
	<ul style="list-style-type: none"> • Individual relapse prevention
12	<ul style="list-style-type: none"> • Coping with the illness in social situations (eg., meeting co-workers)
	<ul style="list-style-type: none"> • Resource list (literature, addresses), end of the group treatment

Table 3: Description to the treatment program Schaub et al. [12].

16 training groups for patients took place in the inpatient setting. Patients were encouraged to continue the group treatment as outpatients if they were discharged. A psychologist was the main therapist with another psychologist or medical doctor as co-therapist. Seven psychologists, on average aged 35.1 years (SD=4.7) old, and in an advanced stage of their education as cognitive behavioural therapist ran the groups. Every week there was video based supervision to guarantee treatment fidelity.

Pharmacotherapy at the beginning of the group mainly covered SSRI (30%), tricyclic antidepressants (26%), mirtazapine (20%), at post-treatment tricyclic antidepressants (32%), mirtazapine (30%), SSRI (19%) and at discharge tricyclic antidepressants (30%), mirtazapine (31%), SSRI (21%). There was a significant decrease of

benzodiazepine from 50% to 7% and a significant increase of augmentation with lithium from 12% to 38%. Combined treatment was possible and only pharmacological agents above 20% are listed. 15.5% of the patients were treated with TMS and 7.2% with ECT.

The major goals of this cognitive psycho educational group intervention are to improve patients' understanding of the illness and its symptoms through teaching information about the nature of depression and strategies to cope with it. The patients are seen as experts of their illness and their self-awareness, coping strategies and self-efficacy are to be enhanced. The program should be up to their needs and satisfying in order to lay the basis for a good cooperation with health care providers at present and in the future. At pre- and post0training, psychopathology was assessed with semi-structured

interviews using the Hamilton Depression Scale (HAMD) Hamilton [41,42], Montgomery Asberg Depression Rating Scale (MADRS) Montgomery and Asberg [43] and the Global Assessment Functioning Scale (GAF; APA, 1987). Self-assessments included the Beck Depression Inventory (BDI) Beck and Steer [44] and parts of the Frankfurt Self-Concept Scale (FSCS) Deusinger [45], covering relevant aspects of the self-esteem such as problem solving (e.g., “I can cope with my personal problems quite well”), self-assertiveness (e.g., “I think I am all right”) and self-competence (e.g., “I am not afraid to meet with strangers”). A multiple choice knowledge test about depression Schaub [46], consisting of 17 questions was to assess changes in knowledge about depression. At post-training the patients were asked to fill out a self-developed questionnaire Schaub [47], including fourteen different areas on well-being and satisfaction with the treatment program.

Results

Data analyses were conducted to address the questions of whether inpatients who participate in the program were satisfied with it and showed improvements in psychopathology, psychosocial functioning, and knowledge about their illness and in self-esteem. Subsequent analyses evaluated whether patient variables could be identified that predicted differential response to treatment.

First, to evaluate whether the program covered the inpatients’ needs and expectations t-tests were performed on the feedback questionnaire. Figure 1 illustrates the results. All patients thought the program to be recommended to other patients, 95% felt much better informed about their illness and about 90% each appreciated it as helpful and its contents to be implemented in daily living. The patients were most interested in information about treatment options, aetiology and course of the illness, coping with the illness, relapse prevention and information about symptoms. Cognitive-behavioural strategies such as identifying depressive thoughts and excessive demands as well as building up rewarding activities were evaluated as effective in increasing coping enhancement. Concerning their well-being during the groups the patients assessed nine subscales and the majority rated the group as interesting and not too demanding.

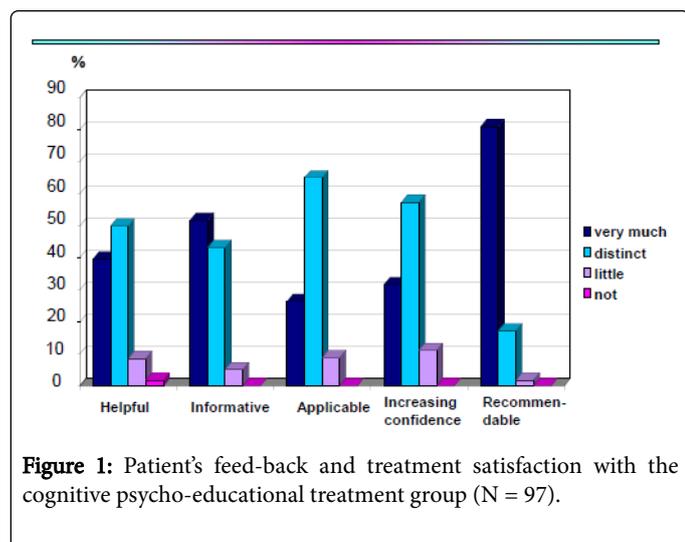


Figure 1: Patient’s feed-back and treatment satisfaction with the cognitive psycho-educational treatment group (N = 97).

Second, to determine whether changes occurred over treatment in the clinical variables, repeated measures analyses of variances (ANOVAs) were performed on each outcome measure. As can be seen

from Table 4, patients who participated in the cognitive-psycho educational treatment program were seriously impaired at pre-assessment. Both HAMD and MADRS pre-scores indicate moderate and even severe depression (HAMD > 20) in 43 patients (44% of the sample). GAF pre-scores of the sample indicate very low psychosocial functioning and the Knowledge Test about Depression pre-scores shows a moderate level of knowledge (80% of the right answers). BDI and FSCS pre-scores indicate high subjective impairment and deficits in line with depressed patients [45]. They show low problem solving abilities and self-esteem, however, adequate social competence.

Patients improved highly significant on dimensions of psychopathology, overall functioning, and knowledge about the illness as well as self-assessed depression and assertiveness from pre to post treatment, however, only few scales reached results within the normal range. After having completed the treatment program lasting for six weeks there were 40% treatment responders with regard to the HAMD (at least improvement of 50%; c.f., Frank et al. [48] and 36% of treatment responders with regard to the BDI. The detailed data include HAMD≤ 6: 22.4% (remitted according to Elkin et al. [49], Hollon et al. [50]), HAMD>20: 11.8%; BDI≤ 9: 27.8%, BDI> 20: 29.2%, BDI< 10 und HAMD< 10: 33%. These results are comparable to data on treatment programs with inpatients (such as Schramm et al. [30]), n=28, treatment responders according to HAMD: 68% and to the BDI: 36%, HAMD≤ 6: 35%, HAMD> 20: 8%; BDI≤ 9: 28%, BDI> 20: 11%, BDI< 10 und HAMD< 10: 48%.

Other significant time effects were on the subscale problem solving of the Frankfurt Self Concept Scale, however, not yet reaching the normal range of positive self-concepts. There were no changes in social competence. Data analyses showed that patients with older age (n=27, ≥60 years old) who were sufficiently stable to attend the groups were as capable as younger patients (n = 70) to participate at this program. Older patients showed as much decrease in depressive symptoms (HAMD; M≥60 years= 6.7, M<60 years =7.7; t=-0.554, p =0.581) as well as increase in knowledge about depression (M≥60 years= 7.0, M<60 years =4.6; t=-.873, p=0.387) as their counterparts (Table 4).

Outcome variable	Pretreatment		Posttreatment		Time effect	
	Mean	SD	Mean	SD	F-statistic	P
BDI N=69	25.2	9.7	16.3	10.6	47.69	< 0.001
MADRS N=69	22.6	8.1	15.3	8.8	39.976	< 0.001
HAMD N=69	19.1	6.2	12.5	6.6	63.146	< 0.001
Knowledge test about depression N=56	92.8	12.7	97.9	13.4	22.564	< 0.001
FSCS/ Problem-solving N=53	32.8	7.8	35.4	7.7	6.043	0.017
FSCS/ Self-assertiveness N=53	34.7	12	38.5	11.4	9.04	0.004
FSCS/ Social Competence N=53	23.9	5.4	24	4.9	0.05	n.s.

Table 4: Time effects on outcome variables for Repeated Measures ANOVAs (n = 69*).

To determine whether patient variables predicted a differential response to treatment a series of repeated measures ANOVAs was

computed. For these ANOVAs, dimensions of psychopathology, psychosocial functioning, knowledge about psychosis and self-esteem at pre- and post-treatment were the dependent variable, with the predictor variables (e.g., gender) as the independent variable. For each analysis, the main Group x Time interaction is a test of whether the patient groups changed differentially over time. There were no significant group differences for age, gender, employment status or marital status. Levels of education and work qualification as well as sub diagnosis were the only variables for which statistically significant interaction effects emerged. Table 5 summarizes the Group x Time interactions for significant repeated measures ANOVAs.

Outcome variable	Level of education	Level of work qualification	Sub diagnosis	Status of treatment
	Low (n=42) vs. medium to high (n=47)	Low (n=58) vs. medium to high (n=34)	First episode (n=40) vs. recurrent depression (n=57)	Outpatients (n = 44) vs. inpatients (n=53)
BDI	4.862*	1.199	(n= 57)	
MADRS	1.747	0.247	0	3.612
HAMD	0.638	0.318	0.036	0.583
GAF	0.524	0.01	4.208*	3.338
Knowledge test	3.349	3.31	2.93	2.215
FSCS/Problemsolving	6.689*	8.429**	0.007	4.190*
FSCS/Self-assertiveness	3.113	1.18	0.089	0.086
FSCS/ Social competence	5.197*	2.554	0.425	1.117

Note: *p < .05; **p < .01; ***p < .001

Table 5: Repeated Measures ANOVAs on patient predictors and clinical parameters of Out-come Measures: Group x Time Interaction F Statistics (n=97, degree of freedom=1)

The predictor variables of level of education and work qualification showed the most significant group differences in outcome variables at both assessments. Patients with a higher education showed larger decreases in self-assessed depressive symptoms (pre-treatment BDI (t1) = 24.5; post-treatment (t2) = 12.9) compared to less educated patients (t1 = 25.2, t2 =19.3). They also showed larger increases in self-concept scales such as problem solving (pre-treatment (t1) = 32.8; post-treatment (t2) = 37.9) compared to their counterparts who were stagnant at the previous level (t1 = 34.5, t2 = 34.4). The same was found with social competence (means for higher educated patients: t1 = 24.3, t2 = 25.8) compared to less educated patients (t1 = 24.3, t2 = 23.0), but there was only a trend in self-assertiveness. The status of work qualification showed even higher scores on problem solving than the level of education at both assessments. Patients with a higher work qualification also showed larger gains in problem solving (t1 = 32.5, t2 = 38.8) than less qualified patients (t1 = 33.7, t2 = 34.4). Patients suffering from a first episode improved more in overall functioning (GAF: t1 = 49.1, t2 = 66.6) than those with multiple episodes (t1 = 49.5, t2 = 59.7). There was also a trend in the knowledge test about depression with higher educated and higher qualified patients as well as patients with first episodes benefiting more than their counterparts.

Looking at neuropsychological functioning in a subgroup of 27 patients having assessed the verbal learning memory test Helmstedter and Durven [52], there was a significant effect between delayed recognition of words and higher level of education (Chi²-Test; Chi=4.636, p=0.031), however, there was no relationship between neuropsychological functioning and the knowledge test about depression.

Looking at differences between inpatients and outpatients the following results were found. 25 patients (25,8%) were discharged before the end of group treatment and participated as outpatients. 19 patients (19,6%) were discharged at the end of group treatment. 53 patients (54,6%) continued their inpatient stay at the end of group treatment for one more month (n=29; 54,7%), for three months (n=16; 30,2%) or more than three but less than seven months (n=8; 15,1%). There were no differences at the beginning of the group treatment in terms of depression (HAMD), psychosocial functioning (GAF) and self-assessments (e.g., BDI).

The drop-out rate in the sample of inpatients (7.5%; N=53) shows a significant difference to the rate of outpatients (29,5%; N=44). Outpatients significantly improved in all variables assessed except for Social Competence whereas inpatients did not improve in the latter and in problem-solving. Group x Time interactions for significant repeated measures ANOVAs emerged with outpatients performing better than inpatients in the BDI (pre- and post-treatment mean scores t1=24.3, t2=11.8; t1=25.7, t2=18.6) and problem-solving (pre- and post-treatment mean scores t1=33.4, t2 = 38.8; t1=33.1, t2=34.4).

For each analysis, the main group effect is an indication of whether the patient characteristic is related to the given variable at the baseline and follow-up assessments. These results are in line with Table 2 as there were treatment gains in all variables except social competence.

70 patients (72% of the sample) were followed up for two and six years. At two year follow-up of 15 patients (four males and eleven females) and at six-year follow-up 29 patients (nine males and twenty females) had a relapse. 48.6% of the patients were remitted, 22.9% partially remitted, 14.3% were treatment refractory and 7.1% had died (two patients committed suicide and three died of cancer). When the same variables were used to predict relapse in the preceding analysis, age (p =0.002 respectively p=0.010) and duration of illness (p=0.034, resp. p=0.046) were the only significant predictors of relapse (R2=0.351, resp. R2=0.197): Patients with younger age and longer duration of illness were more likely to relapse.

Discussion

Increasing evidence supported the effectiveness of cognitive therapy (CT) for depression in major clinical trials Beck et al. and Rush et al. [8,52] in the 80ies, however, patients unsuitable for, or with a history of poor response to antidepressants medication were excluded in these trials. Thus there was no evidence whether these encouraging results could be generalized to chronic, drug-refractory patients, yet the group that might be most in need of effective psychological treatment. At the beginning of the 21 century and based on complex vulnerability-stress models integrating biological and psychological aspects there is some evidence that chronic forms of depression can be effectively treated combining pharmacotherapy with cognitive treatment strategies, however, the treatment of non-responsive patients remains a challenge that needs to be faced.

This pilot study focused on severely ill depressed inpatients suffering mainly from recurrent depression that had been pre-treated with several antidepressants and psychotherapeutically interventions for a long time. The inclusion criteria covered a broad range of comorbidities on axis I and II as well as combined treatment options so that these data can be generalized to the population of severely depressed inpatients. Great age was no exclusion criteria as other studies already proved that patients with older age who were capable to attend the individual or group interventions can also benefit [3,53-55]. In all, the first results of combining cognitive psycho educational interventions with pharmacotherapy are very encouraging: the patients showed reductions in depressive symptoms rated by physicians and patients themselves, improvements in psychosocial functioning, gains in knowledge about the illness as well as in self-assertiveness and problem solving. Educating depressive inpatients about their illness and how to manage their symptoms and their medication can be a valuable component of a comprehensive treatment program. The intervention was set up as a group program because of time effectiveness and mediating effects such as sharing information with others and role modelling. The low drop-out rate as well as the high satisfaction with the treatment program demonstrates that inpatients are eager to learn how to improve coping with their illness. The absence of a control group limits the conclusions that can be drawn from this study.

However, these results are in line with other studies including severely depressed inpatients Backenstrass et al., De Jong-Meyer et al., Hautzinger et al., and Schramm et al., [30,32-34] or outpatients with severe acute, partially remitted or chronic forms of depression (e.g., Keller et al. and Teasdale et al. [3,6] indicating that the combination of pharmacotherapy with psychotherapeutically interventions has a beneficial effect. It is associated with higher improvement, satisfaction with treatment and treatment adherence with pharmacotherapy than drug treatment alone [21,22,56]. The remission rate (HAMD: 40%, BDI: 36%) during the inpatient group treatment is not as high as in other studies covering more comprehensive treatment programs including individual and group interpersonal therapy, however, these studies excluded treatment non-responders treated with ECT (e.g., HAMD: 68%, BDI: 36%) [30]. 55% of our patients continued inpatient treatment to optimize treatment outcome as residual symptoms may lead to relapses. Hollon et al. [50] treated outpatients with acute depression with imipramine and cognitive therapy for 12 weeks attaining a remission rate of 52%. Thase et al. [57] found a remission rate of 48% in their mega analysis including 595 outpatients on imipramine and interpersonal therapy. In the studies of Hautzinger et al. [34] and de Jong-Meyer et al. [35] with depressive inpatients the remission rate after eight weeks was 39%.

The major question of interest in this study was: "who gets better from illness management programs in an inpatient setting?" Up to now limited attention has been given to the identification of variables that are predictive of response to therapy with inpatients. Such information may enable clinicians to make differential treatment recommendations. Two different approaches to this question were taken here: a series of repeated measures ANOVAs was computed on patient predictors (independent variable) of outcome measures (e.g., HAMD total score at the pre- and post-treatment) focusing on Main Effects F Statistics and Group x Time Interaction F Statistics. Overall, there was some evidence of differential treatment response as a function of socio demographic and clinical variables. Level of education and work qualification as well as sub diagnosis were predictive of outcome in some analyses, with level of education most

consistently predicting differential outcome. This result suggests that better educated might be more knowledgeable about their illness. To the extent that these criteria reflect cognitive functioning, these results suggest that cognitive functioning may be an important factor for the acquisition of illness management skills. However, the lack of differences in the rate of learning information in this program suggests that this program is equally appropriate for patients with either high and low education or intelligence. There were no significant gender differences in response to treatment. This result is in line with Thase et al. [58] concluding from their study that men and women respond comparably to cognitive therapy of depression. Patients who rapidly changed to the outpatient setting - on average even at the same psychopathological level of impairment as the remaining patients - showed higher gains in well-being and problem solving compared to their counterparts remaining in the clinic. Other studies Page and Hooke [59], showed no differences in completing CBT as a patient in the inpatient setting or in the day clinic.

Studies on rate limiting factors examine the correlation between psychopathology or information processing variables and an outcome measure like psychosocial functioning. Some studies show a relationship of depressive symptoms to neuropsychological functioning, however, the direction of this relationship is not clear yet [60]. Up to now there are no studies available focusing on neuropsychological functioning (e.g., memory, attention), psychosocial interventions and treatment outcome. More pronounced memory impairments might be predictive of less improvement of treatment progress. The maintenance of illness management skills might be related to symptomatology with persistent severely depressive symptoms being a limiting factor, however, in this study even patient with severe symptoms could benefit from the program.

Major depression is a recurrent disease and brief cognitive therapy added to either regular care or medication is helpful in preventing relapse/recurrence. The two and six year cumulative relapse rate for the 70 patients followed-up was 15% and 30% respectively. Since residual symptoms are highly associated with future relapses Paykel et al. [61] the low prevalence of complete remission (48.6%) at follow-up in this naturalistic study is an important finding. Fava [56,62] showed that cognitive behaviour treatment resulted in a significant lower relapse rate at two and six year follow-up (15%/40%) than clinical management (35/90%). However, at six year follow-up antidepressants were tapered and discontinued whereas in our sample 61.5% of the patients were still treated with pharmacotherapy.

With regard to variables predicting relapse after two respectively six years patient age and duration of illness were predictive for outcome. With regard to CT outcome Sotsky et al. [63] found that briefer duration of the current episode of depression was associated with increased responsiveness to CT whereas Agosti et al. [64] showed no significant relationship. The number of previous episodes is a well-known predictor of recurrence in natural cohorts Geddes et al. [65] whereas this is not the case in preventive CT groups [6,66].

Conclusion

The adequate timing of psychosocial interventions is still a question to be answered and efficacy of combined, sequential and crossover psychotherapy and pharmacotherapy are being discussed Segal et al. [67]. When focusing on the economical perspective some authors vote that patients should be first stabilised by pharmacological treatment in the inpatient setting and then psychotherapeutically interventions

should be added in the outpatient setting [56]. Stabilised depressed patients living in the community seem to be the best candidates for psychosocial rehabilitation strategies as these patients are expected to most readily learn the knowledge about depression and targeted skills. These patients, however, are more difficult to motivate for this treatment if they did not participate at a short cognitive psycho educational inpatient program. From our point of view most inpatients if sufficiently stabilised to be able to attend the groups are very interested in sharing their experiences with others as well as to learn more about possible treatment options. Cognitive psycho educational treatment programs should therefore be initiated with severely depressed inpatients and then continued on an outpatient basis.

Future research needs to be conducted exploring the potential role illness cognition models play to patients' experiences with combined treatment. It is possible that there are challenges unique to combined treatment conditions, such as lack of coherence between psychotherapeutic and pharmacological models of depressions' causes, timeline and controllability, that should be addressed in future research [22]. Illness concepts already proved to be a powerful predictor of adherence to prophylactic treatment in bipolar disorder [68]. Studies are needed to investigate whether the improvement in response attributable to the combination of drug treatment and psychotherapy are achieved by specific treatment effects or mainly by improving treatment adherence with psycho pharmacotherapy. To assess cognitive deficits instruments should be used that are more sensitive for cognitive functioning. Research on a larger sample including these assessments in a randomised controlled design with long term follow-up has been conducted with support of the German federal ministry of education and research to address this issue [12].

In summary, the results of this study suggest that educating inpatients about their illness and how to cope with symptoms can be a valuable component of a comprehensive approach to the treatment of depression. We found that relatively few patient characteristics were predictive of benefit from participation in the cognitive psycho educational treatment program. Although level of education, work qualification and sub diagnosis were related to functioning in some areas, a consistent pattern of differential benefit was not evident, with most patients improving over time on most measures, despite their clinical status at baseline. Although limited by the lack of a no-treatment control group, this pattern of results suggests that this cognitive-psycho educational program may be beneficial to a wide variety of depressive patients, and that differential treatment recommendations cannot be made at this time. To determine the effects of the cognitive-psycho educational treatment program, further research is needed.

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References

1. DeRubeis RJ, Hollon SD, Amsterdam JD, Shelton RC, Young PR, et al. (2005) Cognitive therapy vs medications in the treatment of moderate to severe depression. *Arch Gen Psychiatry* 62: 409-416.
2. Hollon SD, DeRubeis RJ, Shelton RC, Amsterdam JD, Salomon RM, et al. (2005) Prevention of relapse following cognitive therapy vs medications in moderate to severe depression. *Arch Gen Psychiatry* 62: 417-422.
3. Keller MB, McCullough JP, Klein DN, Arnow B, Dunner DL, et al. (2000) A comparison of nefazodone the cognitive behavioural-analysis system of psychotherapy and their combination for the treatment of chronic depression. *New England Journal of Medicine*. 342: 1462-1470.
4. Klein DF, Santiago NJ, Vivian D, Blalock JA, Kocsis JH, et al. (2004) Cognitive behavioural analysis system of psychotherapy as maintenance treatment for chronic depression. *J Consult Clin Psychol* 72: 681-688.
5. Paykel ES, Scott J, Teasdale JD, Johnson AL, Garland A, et al. (1999) Prevention of relapse in residual depression by cognitive therapy. A controlled trial. *Arch Gen Psychiatry* 56: 829-835.
6. Teasdale JD, Segal ZV, Williams JMG, Ridgeway VA, Soulsby JM, et al. (2000) Prevention of relapse/ recurrence in major depression by mindfulness based cognitive therapy. *J Consult Clin Psychol* 68: 615-623.
7. Teasdale JD, Moore RG, Hayhurst H, Pope M, Williams S, et al. (2002) Metacognitive awareness and prevention of relapse in depression: Empirical evidences. *J Consult Clin Psychol* 70: 275-287.
8. Beck AT, Rush AJ, Shaw BF, Emery G (1979) *Cognitive Therapy of Depression*. Guilford, New York.
9. Klerman GL, Weissman MM, Rounsaville BJ, Chevron ES (1984) *Interpersonal Psychotherapy of Depression*. Basic Books Inc Publishers, New York.
10. McCullough JP (2000) *Treatment for chronic depression: Cognitive behavioural analysis system of psychotherapy*. Guilford, New York.
11. Segal ZV, Williams JMG, Teasdale JD, (2001) *Mindfulness-Based Cognitive Therapy for Depression: A new approach and preventing relapse*. Guilford Publications, New York.
12. Schaub A, Roth E, Goldmann U (2013) *Kognitiv-psychoedukative Therapie zur Bewältigung von Depressionen. Ein Therapiemanual*. 2nd Edition, Hogrefe, Göttingen.
13. Lewinsohn PM, Antonuccio DO, Steinmetz JL, Teri L, (1984) The coping with depression course. A psycho educational intervention for unipolar depression. *PEC* 8: 425-426.
14. Kabat-Zinn J (1990) *Full catastrophe living*. Delta, New York.
15. Anderson CM, Griffin S, Rossi A, Pagonis I, Holder DP, et al. (1986) A comparison study of the impact of education vs process groups for families of patients with affective disorder. *Fam Process* 25: 185-205.
16. Anderson CM, Hogarty G, Reiss DJ (1980) Family treatment of adult schizophrenic patients: a psycho educational approach. *Schizophr Bull* 6: 490-505.
17. Bäuml J, Pitschl Walz G (2008) (Eds.) *Psychoedukation bei schizophrenen Erkrankungen*. 2nd Edition, Schattauer, Stuttgart.
18. Goldman CR (1988) Toward a definition of psycho education. *Hosp Community Psychiatry*. 39: 666-668.
19. Mueser KT, Corrigan PW, Hilton DW, Tanzman B, Schaub A, et al. (2002) Illness management and recovery: A review of the research. *Psychiatr Serv* 53: 1272-1284.
20. Post RM (2002) Do the epilepsies, pain syndromes, and affective disorders share common kindling like mechanisms? *Epilepsy Research*. 50: 203-219.
21. Friedman MA, Detweiler-Bedell JB, Leventhal HW, Horne R, Keitner GI, et al. (2004) Combined psychotherapy and pharmacotherapy for the treatment of major depression disorder. *Clinical Psychology: Science and Practice*. 11: 47-68.
22. Pampallona S, Bollini P, Tibaldi G, Kupelnick B, Munizza C (2004) Combined pharmacotherapy and psychosocial treatment for depression. *Arch Gen Psychiatry* 61: 714-719.

23. Segal ZV, Kennedy SH, Cohen NL, CANMAT Depression work group, 2001a. Clinical guidelines for the treatment of depressive disorders. V. Combining psychotherapy and pharmacotherapy. *Can J Psychiatry* 46: 59-62.
24. Schaub A (2002) Illness Self-management Programs in Schizophrenia and Severe Affective Disorders. In: Schaub A (Ed), *New Family Interventions and Associated Research in Psychiatric Disorders. Gedenkschrift in Honor of Michael J. Goldstein*. Springer, Wien, New York, pp: 229-247.
25. Schaub A (2006) Angehörigenarbeit und psychoedukative Patientengruppen in der Therapie affektiver Störungen. In: Möller HJ (Ed) *Handbuch der Therapie psychiatrischer Erkrankungen*. Thieme, Stuttgart, New York, (3rd edn) pp: 462-473.
26. Dowrick C, Dunn G, Ayoso-Mateos JL, Dalgard OS, Page H, et al. (2000) Problem solving treatment and group psycho education for depression: multi centre randomised controlled trial. *BMJ* 9: 1450-1454.
27. Araya R, Rojas G, Fritsch R, Gaete J, Rojas M, et al. (2003) Treating depression in primary care in low income women in Santiago Chile: A randomised controlled trial. *Lancet*. 361: 995-999.
28. Katon W, Robinson P, Korff M, Lin E, et al. (1996) A multifaceted intervention to improve treatment of depression in primary care. *Arch Gen Psychiatry* 53: 924-932.
29. Katon W, Rutter C, Ludman E, Korff M, Lin E, et al. (2001) A randomized trial of relapse prevention of depression in primary care. *Arch Gen Psychiatry* 58: 241-247.
30. Schramm E, van Calker D, Berger M (2004) Efficacy and therapeutic factors of interpersonal psychotherapy for depressed inpatients results of a pilot study. *PsychotherPsychosomMed Psychol* 54: 65-72.
31. Stuart S, Bowers WA (1995) Cognitive therapy with inpatients. Review and meta-analysis. *Journal of Cognitive Psychotherapy*. 9: 85-92.
32. Schaub A, Kopinke J, Neusser A, Charypar M, (2007) Kognitiv-psychoedukative Gruppenintervention bei stationären Patienten mit depressiven Erkrankungen – Ergebnisse einer prospektiven Pilotstudie. *Verhaltenstherapie*, 17: 167-173.
33. Backenstrass M, Kronmüller KT, Schwarz T, Reck C, Karr M, et al. (2001) Kognitive Verhaltenstherapie in und mit Gruppen Ein Behandlungsprogramm für depressive Patienten in stationärer Behandlung. *Verhaltenstherapie*. 11: 305-311.
34. Hautzinger M, De Jong-Meyer R, Treiber R, Rudolf GAE, Thien U (1996) Wirksamkeit Kognitiver Verhaltenstherapie, Pharmakotherapie und deren Kombination bei nicht-endogen, unipolaren Depressionen. *Zeitschrift für Klinische Psychologie*. 25: 130-145.
35. De Jong-Meyer R, Hautzinger M, Rudolf GAE, Strauss W, Frick U, (1996) Die Überprüfung der Wirksamkeit einer Kombination von Antidepressiva- und Verhaltenstherapie bei endogen depressiven Patienten: Varianzanalytische Ergebnisse zu den Haupt- und Nebenkriterien des Therapieerfolgs. *Zeitschrift für Klinische Psychologie*. 25: 93-109.
36. Depression Guideline Panel (1993) In: *Clinical practice guideline. Depression in primary care: detection and diagnosis*. Rockville, MD. US Department of Health and Human Services. Agency for Health Care Policy and Research; Agency for Health Care Policy Research publication 93-0550.
37. Wolfersdorf M (1997) *Depressions stationen. Konzepte, Erfahrungen, Möglichkeiten heutiger Depressionsbehandlung*. Springer, Berlin.
38. Hamilton KE and Dobson KS (2002) Cognitive therapy of depression: Pre-treatment patient predictors and outcome. *Clinical Psychology Review*. 22: 875-893.
39. Page AC, Hooke GR (2003) Outcomes for depressed and anxious inpatients discharged before at after group cognitive behaviour therapy-A naturalistic follow-up. *J Nerv Ment Dis* 19: 653-659.
40. Berger M, van Calker D (2003) *Affektive Störungen*. In: Berger M (Ed) *Psychische Erkrankungen. Klinik und Therapie*. München, Urban & Fischer pp: 541-636.
41. Hautzinger M (2003) *Kognitive Verhaltenstherapie bei Depressionen* (edn). Psychologie Verlags Union Weinheim.
42. Hamilton M (1986) A rating scale for depression. *J Neurol Neurosurg Psychiatry* 23: 56-62.
43. Montgomery SA, Asberg M (1979) A new depression rating scale designed to be sensitive to change. *Br J Psychiatry* 134: 382-389.
44. Beck AT, Steer RA (1987) *Beck Depression Inventory (BDI)*. The Psychological Corporation Inc San Antonio.
45. Deusinger I (1986) *Die Frankfurter Selbstkonzeptskalen (FSKN)*. Hogrefe, Göttingen.
46. Schaub A (1998) Knowledge tests about depression. Unpublished manuscript. Department of Psychiatry and Psychotherapy. Ludwig Maximilian University of Munich.
47. Schaub A (2003) Feedback Fragebogen. In: Bäuml J, Pitschl-Walz G, *Psychoedukation bei schizophrenen Erkrankungen*. Schattauer Stuttgart pp: 330-333.
48. Frank E, Kupfer DJ, Wagner EF, McEachran AB, Cornes C (1991) Efficacy of interpersonal psychotherapy as a maintenance treatment of recurrent depression: contributing factors. *Arch Gen Psychiatry* 48: 1053-1059.
49. Elkin I, Shea MT, Watkins JT, Imber SD, Sotsky SM, et al. (1989) NIMH treatment of depression collaborative research program: General effectiveness of treatments. *Arch Gen Psychiatry* 46: 971-982.
50. Hollon SD, DeRubeis RJ, Evans DM, Wiener MJ, Garvey MJ, et al. (1992) Cognitive therapy and pharmacotherapy for depression. *Arch Gen Psychiatry* 47: 774-781.
51. Helmstedter C, Durwen HF (1990) VLMT: Verbaler Lern- und Merkfähigkeitstest. *Schweizer Archiv für Neurologie und Psychiatrie*. Bd. 141: 21-30.
52. Rush AJ, Beck AT, Kovacs M, Hollon SD (1977) Comparative efficacy of cognitive therapy and pharmacotherapy in the treatment of depressed outpatients. *Cognitive Therapy and Research* 1: 17-37.
53. Hautzinger M (2000) *Depressionen im Alter. Ein kognitiv-verhaltenstherapeutisches Gruppenprogramm*. PVU Beltz, Weinheim.
54. Reynolds CF, Frank E, Perel JM, Imber SD, Cornes C, et al. (1999) Nortriptyline and interpersonal psychotherapy as maintenance therapies for recurrent major depression. *JAMA* 281: 39-45.
55. Schaub A, Plattner A, Ehrhardt T, Kaschel R (2001) Kognitiv-verhaltenstherapeutische Interventionen bei kognitiven Defiziten und Depressionen im höheren Lebensalter. In: Hegerl U, Zaudig M, Möller HJ *Depression und Demenz im Alter*. Springer Wien pp: 125-150.
56. Fava GA, Ruini C, Rafanelli C, Finos L, Conti S, et al. (2004) Six year outcome of cognitive behavior therapy for prevention of recurrent depression. *Am J Psychiatry* 161: 1872-1876.
57. Thase ME, Greenhouse JB, Frank E, Reynolds CF, et al. (1997) Treatment of major depression with psychotherapy of psychotherapy-pharmacotherapy combinations. *Arch Gen Psychiatry* 54: 1009-1015.
58. Thase ME, Reynolds CF, Frank E, Simons AD, McGeary J, et al. (1994) Do Depressed women and men respond similarly to cognitive behavior therapy? *Am J Psychiatry* 151: 500-505.
59. Page AC, Hooke GR (2003) Outcomes for depressed and anxious inpatients discharged before at after group cognitive behavior therapy-A naturalistic follow-up. *J Nerv Ment Dis*. 19: 653-659.
60. Beblo T, Hermann M (2000) Neuropsychologische Defizite bei depressiven Störungen. *Fortschritte der Neurologie Psychiatrie* 68: 1-11.
61. Paykel ES, Ramana R, Cooper Z, Hayhurst H, Kerr J, et al. (1995) Residual symptoms after partial remission: an important outcome in depression. *Psychol Med* 25: 1171-1180.
62. Fava GA, Grandi S, Zieleszny M, Canestrari R, Morphy MA (1994) Cognitive behavioural treatment of residual symptoms in primary major depressive disorder. *Am J Psychiatry* 151: 1295-1299.
63. Sotsky SM, Glass DR, Shea MT, Pilkonis PA, Collins JF, et al. (1991) Patient predictors of response to psychotherapy and pharmacotherapy: findings in the NIMH Treatment of Depression Collaborative Research Program. *Am J Psychiatry* 148: 997-1008.
64. Agosti V, Ocepek-Welikson K (1997) The efficacy of imipramine and psychotherapy in early onset chronic depression: a reanalysis of the

-
- National Institute of Mental health Treatment of Depression Collaborative Research Program. *J Affect Disord* 43: 181-186.
65. Geddes JR, Carney SM, Davies C, Furukawa TA, Kupfer DJ, et al. (2003) Relapse prevention with antidepressant drug treatment in depressive disorders: a systematic review. *Lancet* 361: 653-661.
66. Bockting CLH, Spinhoven P, Koeter MWJ, Wouters LF, Visser I, et al. (2006) Differential Predictors of Response to Preventive Cognitive Therapy in Recurrent Depression: A 2-Year Prospective Study. *Psychother Psychosom* 75: 229-236.
67. Segal ZV, Vincent P, Levitt A (2002) Efficacy of combined sequential and crossover psychotherapy and pharmacotherapy in improving outcome in depression. *J Psychiatry Neurosci* 27: 281-290.
68. Kleindienst N, Greil E (2004) Are illness concepts a powerful predictor of adherence to prophylactic treatment in bipolar disorder? *J Clin Psychiatry* 65: 566-74.