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ORIGINAL ARTICLE

Effectiveness of cognitive behaviour therapy for treatment-resistant depression with psychiatric comorbidity: comparison of individual versus group CBT in an interdisciplinary rehabilitation setting

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ABSTRACT

Background: Cognitive behaviour therapy (CBT) has been shown to be effective, yet there is a paucity of research on the differential effectiveness of individual and group CBT for adults with treatment-resistant depression with psychiatric comorbidity.

Aims: To investigate the effectiveness of individual and group CBT for inpatients, in an interdisciplinary rehabilitation setting; the extent of psychiatric comorbidity; and who benefits the most from group CBT.

Methods: All patients ($n = 181$) received 6 weeks of rehabilitation (treatment as usual, TAU). In addition, they were randomly allocated to group CBT ($n = 86$) or individual CBT ($n = 59$) combined with TAU, or TAU only ($n = 36$). All CBT therapists were part of an interdisciplinary team, had at least 1-year CBT training, and attended weekly supervision. The same CBT manual was used for individual and group therapy, providing 12 sessions, two per week. Groups had 12–15 participants and two therapists in each session.

Results: Individual CBT was superior in efficacy to group CBT and TAU, with a large within-subject effect size (ES = 2.10). Group CBT was not superior to TAU. The benefits of treatment decreased over time, but remained large at 18-month follow-up for individual CBT (ES = 1.02), and medium for group CBT (ES = 0.46) and TAU (ES = 0.60).

Conclusions: Individual CBT was an effective addition to TAU and showed significant improvements in symptom severity post-treatment and at 18-month follow-up. Disorder severity and comorbidity may have decreased effectiveness of group therapy primarily aimed at depression.

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Cognitive behaviour therapy; group therapy; interdisciplinary rehabilitation; treatment-resistant depression; psychiatric comorbidity; efficacy; follow-up

Background

About 50–60% of depressed patients do not respond satisfactorily to treatment with antidepressant medications (1,2). Patients who fail to respond to at least two antidepressant trials of adequate doses and duration meet proposed criteria for treatment-resistant depression (TRD) (1,3,4). Several treatment approaches have been suggested. One is to progress from simpler (i.e. an alternate monotherapy) to more complex strategies (i.e. combination or augmentation regimens), with the non-selective monoamine oxidase inhibitors (± lithium salts) and electroconvulsive therapy typically reserved for treatment of the most difficult cases (5). Mindfulness-based cognitive therapy (MBCT) and a structurally equivalent active comparison condition have also been compared as adjuncts to treatment-as-usual (TAU) pharmacotherapy in TRD, with good results (6,7).

Cognitive behaviour therapy (CBT) for major depressive disorder has been shown to be an effective treatment for adult depression (8). A recent meta-analysis by Cuijpers et al. (9) indicates that combined treatment of CBT and pharmacotherapy is significantly more effective than pharmacotherapy alone, and studies suggest long-lasting effects and cost-effectiveness of CBT (10,11). CBT can be as effective as medication for the initial treatment of moderate-to-severe major depression, and is longer lasting (9,12). Apparently, CBT can be as effective as medication, even among more severely depressed outpatients, at least when provided by experienced therapists (13). However, there are obstacles to the use of CBT, like the interest or appropriateness of CBT to patient populations (14).

Studies have shown that adding CBT to medication for TRD can be beneficial in reducing depressive symptoms, in improving psychosocial functioning, and in decreasing hopelessness (15,16). In one study patients were randomly assigned to either cognitive therapy or alternative pharmacologic therapy after an unsatisfactory response to one antidepressant (citalopram). Switching to cognitive therapy was better tolerated than switching to a different antidepressant, although pharmacologic augmentation was more rapidly effective (15).

Wiles et al. (17) point out that very few studies on patients with TRD have a randomized controlled group

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design, due to difficulties in conducting such research. In a meta-analysis of 16 studies with 852 adult participants with depression, randomized controlled trials comparing the combination of psychotherapy and pharmacotherapy with the combination of psychotherapy and placebo showed that active medication has a small but significant contribution to the overall efficacy of combined treatments (18).

According to a recent metaregression analysis by Cuijpers et al. (19), including 70 studies with 5403 participants comparing individual psychotherapy with a control group, the number of treatment sessions per week, rather than a higher total number of treatment sessions, determined therapeutic effectiveness. When two instead of one treatment sessions were given per week, without increasing the total number of sessions, the effect size increased by 0.45.

The most common psychiatric comorbidities with major depressive disorder, according to DSM-5, are substance-related disorder, panic disorder, obsessive-compulsive disorder (OCD), anorexia nervosa, bulimia nervosa, and borderline personality disorder. Research has repeatedly reported high comorbidity of depression and anxiety; ~50% both in primary and psychiatric care settings (20). This has led to the development of transdiagnostic CBT groups with the strongest support for combinations of panic disorder, social anxiety disorder, and generalized anxiety disorder (21).

A study of 287 adult patients in primary care with diagnoses of depression and/or anxiety disorders indicated the feasibility of brief transdiagnostic group therapy for a wide range of mood and anxiety disorders (22).

Cognitive behavioural group therapy (CBGT) is a logical extension of successful individual CBT (21), and could help make evidence-based therapy more available for people with mental health problems (23). CBGT has been found to be effective, and is a cost-effective form of therapy, including for people with mixed diagnoses (22,24,25), but has mostly been used in the earlier stages of 'stepped care' and in diagnostically homogenous samples (26). One limitation of CBGT is the relative absence of individualized treatment plans. Strengths include a potential sense of belonging, validation, support, and connection to other group members (21). The group climate, such as participants' engagement, can affect the outcome of the group therapy, indicating higher engagement to be more effective in reducing depressive symptoms (27).

There is a paucity of research both on the benefits of CBT for adults with depression in routine clinical practice and on the differential effectiveness of individual and group CBT (28). However, meta-analysis suggests that individual psychotherapy (mainly CBT) may be somewhat more effective than group psychotherapy (29). However, the quality of this research is insufficient and, according to Cuijpers' (30) review on recent development in psychotherapies for adult depression, it is not clear if this difference is clinically meaningful. Furthermore, the effectiveness of CBGT compared to individual CBT for depression is similar according to other reviews and meta-analyses (21).

The efficacy of CBT is well established for depression, but less is known about its efficacy for chronic or treatment-resistant depression, or its efficacy for depression with psychiatric comorbidity. Studies of individual or group CBT for TRD have been sparse. In a series of meta-analyses, Cuijpers et al. (31) found no evidence showing that psychotherapy was less efficacious in severe depression (e.g. with mean BDI-II scores up to 36.5), but found smaller effects in chronic depression.

Several variations of CBT have been applied to inpatients (32). Studies suggest that patients who receive CBT in addition to TAU during inpatient stay have better long-term outcome than those who only receive TAU. Outcome is improved with additional CBT sessions after discharge (33). The aim of inpatient treatment should be to improve coping after discharge (34).

Patients with severe depression or chronic depression can benefit from CBT, including those who discontinue antidepressant medication (35) and patients with chronic depression who continue medication (36). CBT results in better treatment compliance and reduces symptom severity in patients with serious depression and in patients with schizophrenia (37).

Aims

The aim of this study was to evaluate, in an inpatient setting: (1) the efficacy of CBT, when added, to intensive interdisciplinary rehabilitation treatment as usual, for decreasing the symptoms of depression in treatment-resistant patients; (2) the relative efficacy of group CBT and individual CBT in this setting; (3) the extent of psychiatric comorbidity; and (4) who benefits the most from group CBT.

Materials and methods

This study received Institutional Review Board approval from the Icelandic National Bioethics Committee (VSNa2003050015/BH/-). Participation was voluntary. After detailed description of the study to the patients, written informed consent was sought. Treatment was provided at no cost to patients, and they received no remuneration for participation.

Participants

Participants were inpatients at an open psychiatric unit of an interdisciplinary rehabilitation institution in Iceland, Reykjalundur Rehabilitation Centre. All the unit's patients are voluntary.

One hundred and eighty-one participants who met the criteria for Major Depressive Disorder or Dysthymia, using the Mini International Neuropsychiatric Interview (MINI) (38) (see Measures, below), and had failed to respond to at least two antidepressant trials of adequate doses and duration (corresponding to the equivalent of at least 20 mg of fluoxetine for at least 2 months), and thus met criteria for TRD, were enrolled in the study. Exclusion criteria were current alcohol or drug abuse, or psychotic symptoms.

Most participants received high doses of antidepressants on arrival and had been receiving such medication for long

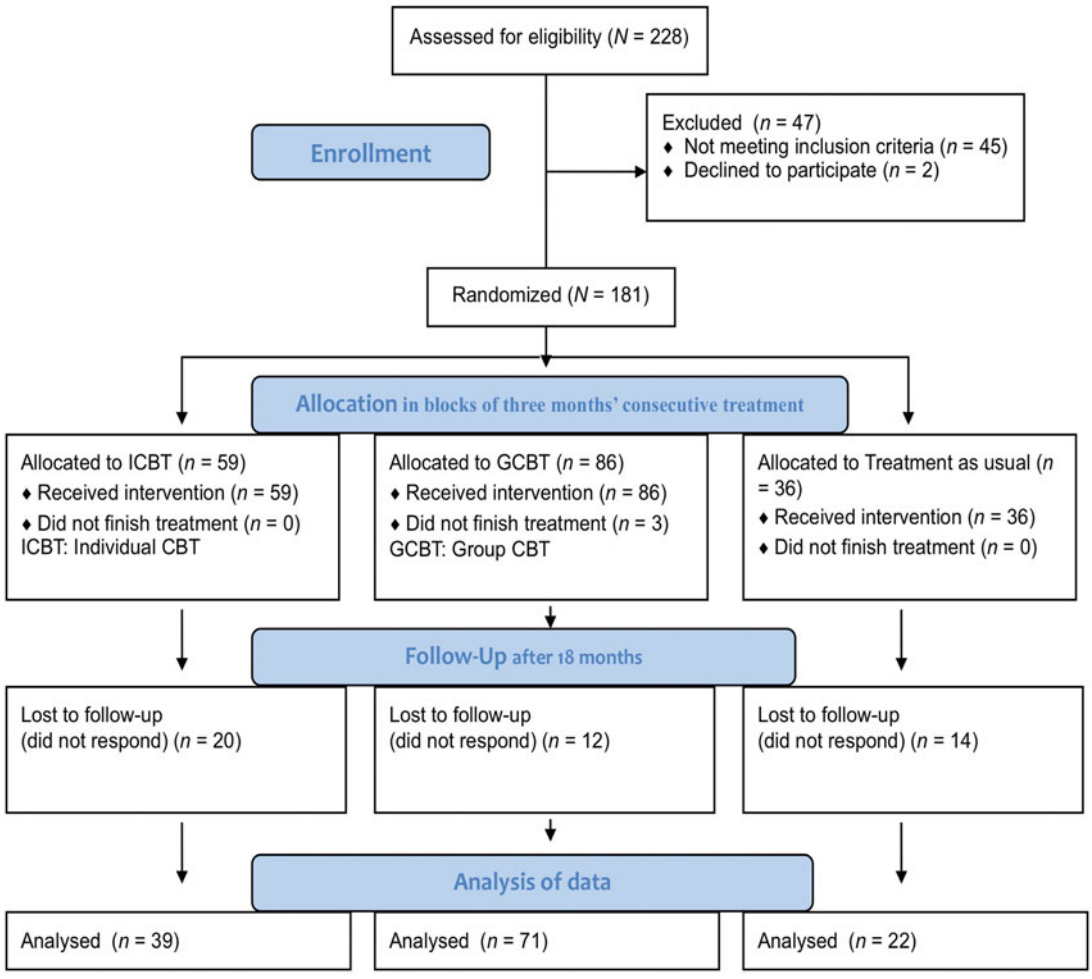

Figure 1. Study flow chart.

periods and still met the above admission criteria. Medication was continued during the study treatment.

Three participants did not attend the last session, so intention-to-treat analyses were based on their last scores. At 18 months' follow-up, data were analysed from a total of 132 (73%) participants responding to the follow-up questionnaires (Figure 1).

Randomization

In addition to inpatient interdisciplinary rehabilitation treatment as usual, the participants were randomly allocated to group CBT ($n = 86$), individual CBT ($n = 59$), or treatment as usual without CBT ($n = 36$). Randomization was ensured by providing only one of the three treatment modes at a time at the psychiatric unit, i.e. each treatment mode was conducted in blocks of 3 months' consecutive treatment periods. Admissions were consecutive, from a waiting list, thus unaffected by treatment modes being provided, further contributing to randomization. Inclusion criteria for randomization was current depression diagnoses and a score ≥ 14 on the Beck Depression Inventory. The participants admitted during a 3 months consecutive treatment period received treatment as usual and group CBT, those admitted during another 3-month period received treatment as usual only (i.e. no CBT was offered at the unit during those 3 months), and finally the participants in the third time period received treatment as usual and individual CBT (Figure 1).

Intervention

All participants received 6 weeks of rehabilitation treatment (TAU) conducted by an interdisciplinary psychiatric team at Reykjalundur Rehabilitation Centre (39), which included psychoeducation, counselling as needed by a psychiatrist, psychologist, nurse, or social worker, individual and/or group occupational and physical therapy and training, and medication as needed. Healthy lifestyle and self-care were emphasized, with a focus on encouragement of physical activity, healthy nutrition, improved sleep hygiene, and relaxation. All patients thus participated participated in an inpatient treatment programme from early morning to late afternoon, consisting of the above, configured individually for each patient, as needed. Individual or group CBT did not interfere with the TAU, provided to all. Treatment as usual did not include CBT for depression, but could include individual counselling.

The same CBT manual (40) was used for individual and group therapy. CBT included 12 sessions, two per week. Group sessions had a duration of 90 minutes, and individual

sessions were 50 minutes. Each session had a specific theme and appropriate homework assignments.

The CBT manual was mainly based on material from Fennell (41) and Greenberger and Padesky (42). Treatment included: (1) education about depression and anxiety, (2) identification of relationships between thoughts, moods, physiology, and behaviour, (3) identification of and challenging of maladaptive thought patterns and behaviour, and (4) relapse prevention. The treatment manual is available on-line (in Icelandic, text and audio) at http://ham.reykjalundur.is/ (43).

Groups had 12–15 participants and two therapists in each session. Sessions started with a presentation, after which the group was split into two smaller groups for discussion of the session's topics and homework. The format for the individual therapy was the same, only with one therapist and one patient in each session.

Therapist training

All the CBT therapists; including a psychiatrist, a psychologist, psychiatric nurses, occupational therapists and a social worker, had at least 1 year training in CBT and were a part of the unit's interdisciplinary clinical team. The training included education in CBT theory and case formulation, and covered topics such as Socratic questioning, teaching of basic cognitive and behavioural methods, relapse prevention, symptoms and treatment of depression and anxiety disorders, chronic pain, and chronic illness. The same therapists delivered both individual and group treatments. Ingibergsdóttir (44) compared outcome in this study between therapists of different professions. The conclusion was that there were no between-therapist differences in outcome. The therapists received 1-hour weekly group supervision from a specialist in CBT to ensure treatment fidelity and to provide guidance in individual cases.

Measures

Outcome measures included self-report inventories, with good psychometric properties, commonly used in depression research. Inventories were administered weekly during treatment sessions, using an intent to treat analysis. An 18-month follow-up was conducted by mailing the questionnaires to the participants, and re-mailing them to non-responders.

The MINI (38), a short structured diagnostic interview of mental disorders, was administered in the intake interview. The English version of the MINI has shown excellent reliability, and a preliminary study of the Icelandic version gives support to its validity (45).

The Icelandic translations of the Beck scales have good internal consistency; the coefficient alpha of the Beck Depression Inventory-II (BDI-II) was 0.93 in a patient population and 0.91 in a student population (46), 0.92 for the Beck Anxiety Inventory (BAI) (47), and 0.90–0.91 for the Beck Hopelessness Scale (BHS) (16,48). The Automatic Thoughts Questionnaire (ATQ) has good psychometric properties, and the internal consistency was 0.94–0.97 from three different samples (49).

Statistical analyses

Data were analysed using the statistics program SPSS, version 19 for Windows. Pre- and post-test design was adopted, using the BDI-II, BAI, BHS, and ATQ questionnaires. One-way ANOVA followed by a Bonferroni-corrected *post hoc* test was used to test for significant mean differences between groups at each assessment point for all outcomes.

APA has encouraged researchers to report the effect size in all outcome studies (50). Both between-group and within-group effect sizes can be used, but the latter captures improvement better. Within-group effect sizes indicate the difference between the depression score at baseline and the score at post-test in different groups (51).

The within-group effect size was computed using Cohen's d values for all pre-, post-and follow-up measures with the formula: $d = (M_{pre} - M_{post})/\sigma_{pooled}$. For Cohen's d, values of 0.2, 0.5, and 0.8 represent small, medium, and large effects (52). However, the limitation of pooled standard deviation is that it provides a slight under-estimate of the desired standard deviation, and, therefore, reduces the effect size obtained.

Potential attrition bias was evaluated by modelling response propensities to the follow-up measures using a logistic regression model. Response propensities were categorized in three groups, and One-way ANOVA was used to indicate if the difference between the propensity groups was sufficient to determine them as significantly different.

The effects of comorbidity in group CPT was examined by multiple regression and polyserial correlation coefficient.

Results

Clinical characteristics and baseline demographics

Of the 181 patients enrolled in the study, 138 (76%) were women, reflecting the gender ratio of the unit's patient group. The age range was 17–80 years, with the mean age of 45 years; 51% were married or cohabiting, 19% divorced, 4% widowed, and 26% were single; 58% were living in the capital area and 42% lived outside the capital area. Only 35% of patients were employed, 2% were enrolled in school, but 63% were unemployed, homemakers, or receiving disability pension.

There were no statistically significant differences at the start of treatment between the groups on the measures, except that the control group was significantly lower on ATQ than the group CBT. Baseline demographic and clinical characteristics are presented in Table 1.

Psychiatric comorbidity

The psychiatric comorbidity of depression was high. In addition to TRD, most of the participants had other psychiatric diagnoses. The diagnoses (DSM-IV, Axis I) were established by MINI. The mean number of psychiatric diagnoses for all the participants was 5.87 (SD = 2.43), for those receiving individual CBT it was 5.21 (SD = 1.92), for group CBT it was 6.55 (SD= 2.60), and for those not receiving CBT it was

Table 1. Baseline demographic and clinical characteristics among patients with treatment-resistant depression randomly assigned to receive individual CBT, group CBT, or rehabilitation treatment as usual.

Treatment								
	Participants ($n = 181$)		Individual CBT ($n = 59$)		Group CBT ($n = 86$)		Treatment as usual ($n = 36$)	
Characteristic	*n*	%	*n*	%	*n*	%	*n*	%
Gender								
Male	43	23.8	20	33.9	14	16.3	9	25.0
Female	138	76.2	39	66.1	72	83.7	27	75.0
Marital status								
Married[a]	93	51.4	29	49.2	49	57.0	15	41.7
Divorced	35	19.3	8	13.6	16	18.6	11	30.6
Widowed	7	3.9	3	5.1	3	3.5	1	2.8
Single	46	25.4	19	32.2	18	20.9	9	25.0
Residence								
Capital area	106	58.6	41	69.5	44	51.2	21	58.3
Rural	75	41.4	18	30.5	42	48.8	15	41.7
Employment								
Yes	64	35.4	25	42.4	29	33.7	10	27.8
No	113	62.4	32	54.2	56	65.1	25	69.4
In school	4	2.2	2	3.4	1	1.2	1	2.8
DSM-IV Mental Disorders								
MDE[b]	130	83.3	47	88.7	62	82.7	21	75.0
GAD[c]	113	72.4	42	79.2	54	72.0	17	60.7
SP[d]	94	60.3	33	62.3	43	57.3	18	64.3
AP[d]	80	51.3	25	47.2	42	56.0	13	46.4
Dysthymia[e]	57	36.5	13	24.5	35	46.7	9	32.1
PD[d]	75	48.1	24	45.3	38	50.7	13	46.4
PTSD[d]	51	32.7	13	24.5	33	44.0	5	17.9
Suicidality[d]	101	64.7	29	54.7	60	80	12	42.8
Alcohol DA[f]	27	17.3	6	11.3	11	14.7	10	35.7
HE[g]	33	21.2	12	22.6	12	16.0	9	32.1
OCD[d]	25	16.0	8	15.1	11	14.7	6	21.4
Substance[f]	18	11.5	6	11.3	7	9.3	5	17.9
Psychotic[g]	6	3.8	1	1.9	5	6.7	0	0.0
Bulimia[h]	12	7.7	4	7.5	7	9.5	1	3.6
Anorexia[h]	2	1.3	0	0.0	1	1.3	1	3.6
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Age (years)	44.57	12.34	45.39	13.94	43.36	11.75	46.14	10.87
Number PD	5.87	2.43	5.21	1.92	6.55	2.60	5.32	2.44

[a]or living together.
[b]Current (last 2 weeks).
[c]Current (past 6 months).
[d]Current (past month).
[e]Current (past 2 years),
[f]Past 12 months,
[g]Lifetime.
[h]Current (past 3 months).
MDE: Major Depressive Episode; GAD: Generalized Anxiety Disorder; SP: Social Phobia; AP: Agoraphobia; PD: Panic Disorder; PTSD: Posttraumatic Stress Disorder; DA: Dependence/Abuse; HE: Hypomanic Episode; OCD: Obsessive-Compulsive Disorder; Substance: Substance Dependence/Abuse;Psychotic: Psychotic Disorder; Number PD: Number of psychiatric diagnosis.

5.32 (SD = 2.44) (Table 1). Most of the patients had one or more anxiety diagnoses. The number of psychiatric diagnoses varied from one to 12, but most of the patients had three to seven psychiatric diagnoses. Only one had one diagnosis, but 36 had eight or more diagnoses (Figure 2).

Efficacy analyses

Efficacy analyses of individual and group CBT compared with the control group are presented in Table 2. All improvements pre–post were statistically significant using one-way analysis of variance. Individual CBT was superior to both group CBT and control treatment (treatment as usual) in lowering BDI-II, BAI, ATQ, and BHS scores. Group CBT was not statistically superior to control treatment (treatment as usual) in lowering BDI-II, BAI, ATQ, or BHS. Benefits of treatment decreased over time during the follow-up period.

Effect sizes

The findings show that the effect size (Cohen's d) represents large within-group effects for depression in pre–post treatment for all three groups (Individual CBT: ES = 2.10; Group CBT: ES = 1.46; and Treatment as usual: ES = 1.16). The effect size was still large at 18-months follow-up for individual CBT (ES = 1.02), but only medium for the follow-up in group CBT (ES = 0.46) and the treatment as usual (ES = 0.60) (Table 2).

Attrition bias

Attrition analysis was conducted by modelling response propensities to the follow-up measures using a logistic regression model where gender, age, marital status, residence, and occupational status were used as independent model variables. Response propensities were categorized in to three groups; where response likelihood was between 0.34–0.49; where the likelihood was between 0.50–0.64; and where the response likelihood was between 0.65–0.79. An analysis of this kind assumes that respondents with low response propensities are similar to the non-responding respondents or, in this case, respondents that did not participate due to attrition. The effects of attrition were examined by calculating

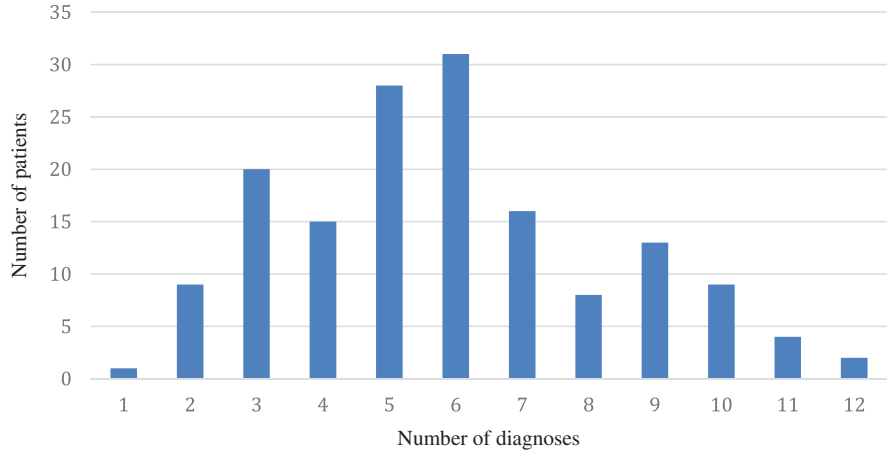

Figure 2. Number of patients per number of DSM-IV Axis 1 diagnoses.

Table 2. Efficacy results of individual CBT, group CBT, and rehabilitation treatment as usual in patients with treatment-resistant depression ($n = 181$).

	Individual CBT ($n = 59$)			Group CBT ($n = 86$)			Treatment as usual ($n = 36$)		
Measure	Pre ($n = 59$) Mean (SD)	Post ($n = 59$) Mean (SD)	Follow-up ($n = 39$) Mean (SD)	Pre ($n = 86$) Mean (SD)	Post ($n = 83$) Mean (SD)	Follow-up ($n = 71$) Mean (SD)	Pre ($n = 36$) Mean (SD)	Post ($n = 36$) Mean (SD)	Follow-up ($n = 22$) Mean (SD)
BDI-II	33.08 (9.86)	12.64a (9.59)	20.32 (15.12)	29.96 (8.88)	16.77[a] (9.21)	24.42 (14.99)	30.03 (9.98)	17.75a (11.15)	22.45 (15.20)
Cohen's d	2.10		1.02	1.46		0.46	1.16		0.60
BAI	26.21 (10.38)	13.57[b] (9.35)	17.45 (13.70)	27.32 (10.56)	19.10[b] (11.44)	23.37 (13.32)	25.06 (12.11)	15.19 (9.50)	19.13 (12.08)
Cohen's d	1.28		0.73	0.75		0.33	0.91		0.49
BHS	11.09 (5.82)	5.60b (4.79)	7.54 (6.03)	12.18 (4.62)	8.71[b] (5.28)	10.38 (5.69)	11.33 (4.99)	8.17 (4.88)	9.72 (6.11)
Cohen's d	1.04		0.60	0.70		0.35	0.64		0.29
ATQ	98.84 (28.05)	57.09[b] (23.82)	70.10 (33.41)	99.21[c] (25.46)	76.10[b] (27.10)	81.87 (33.48)	84.57c (25.84)	64.91 (27.41)	71.18 (33.70)
Cohen's d	1.61		0.94	0.88		0.59	0.74		0.45

BDI-II: Beck Depression Inventory; BAI: Beck Anxiety Inventory; BHS: Beck Hopelessness Scale; ATQ: Automatic Thoughts Questionnaire.
[a]Significant difference between the groups; Individual CBT is significantly lower than both Group CBT and Treatment as usual.
[b]Significant difference between the groups; Individual CBT is significantly lower than Group CBT.
[c]Significant difference between the groups; Treatment as usual is significantly lower than Group CBT.
Analysis of Variance–ANOVA–One Way: Main effect on time was significant ($p < 0.001$) at all measures, and interaction was significant ($p < 0.001$) at the end of the treatment and at follow-up ($p < 0.05$).
Cohen's d (Effect Size) was calculated within-group for the treatment period of pre–post and for the follow-up period of pre–follow-up.

Table 3. Attrition analysis conducted by modelling response propensities to follow-up measures.

	Measures at follow-up			
Response propensity	BDI-II Mean	BAI Mean	BHS Mean	ATQ Mean
Low	23.74	22.57	10.47	75.23
Medium	22.17	19.43	9.38	76.78
High	24.41	22.37	10.81	79.74

BDI-II: Beck Depression Inventory; BAI: Beck Anxiety Inventory; BHS: Beck Hopelessness Scale; ATQ: Automatic Thoughts Questionnaire.
Differences between response propensity groups were in all cases insignificant ($p > 0.05$).

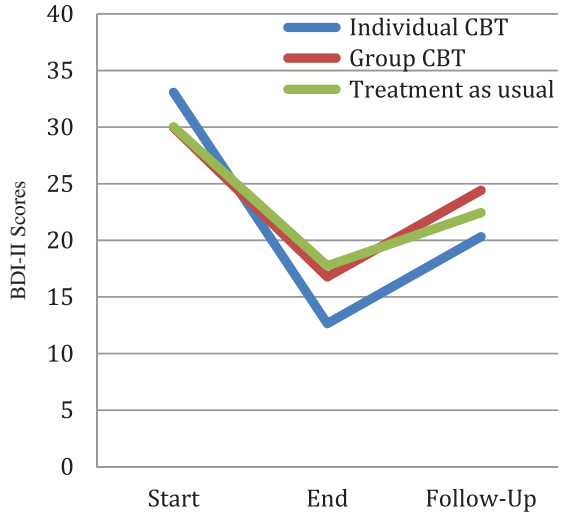

Figure 3. BDI-II scores of patients with treatment-resistant depression receiving individual CBT, group CBT, or rehabilitation treatment as usual at the start of treatment, at the end, and at follow-up at 18 months.

the mean of four target variables of the study, grouped by the response propensity groups (Table 3). One-way ANOVA was used to indicate if the difference between the propensity groups was sufficient to determine them significantly different. Differences between response propensity groups were in all cases insignificant ($p > 0.05$).

These results indicate that the attrition in the study was not selective, i.e. that respondents who scored higher on BDI-II, BAI, BHS, or ATQ were not more likely than other respondents to stop participating in the study.

Who benefits the most from group CBT?

Group therapy is more cost-effective than individual therapy. Accordingly, it is of interest to know who benefitted the most from group CBT and who benefitted least. Most of the patients who received group CBT met criteria for Major Depressive Disorder or 82.7%. As presented in Table 1, 72.0% had Generalized Anxiety Disorder, over half of the patients met criteria for Social Phobia (57.3%) and Agoraphobia (56.0%), 50.7% had Panic Disorder, 46.7% Dysthymia, and 44.0% had Posttraumatic Stress Disorder. Only one met the criteria for Anorexia or Bulimia.

The effects of comorbidity in group CBT were examined by multiple regression analysis. Another analysis was also done using polyserial correlation coefficient. Results of the two analyses were similar. The predictors of the regression were each psychiatric diagnosis based on the MINI, while the dependent variable was the difference in scores on the BDI-II at the beginning and at the end of treatment. Only one predictor was significant, Major Depressive Disorder ($b = -7.86$; $p = 0.03$), which was related to a significantly lower BDI-II measure at the end of treatment. Social Phobia ($b = 4.32$, $p = 0.14$) and Substance Dependence ($b = 9.32$, $p = 0.14$) were marginally significant, both related to a higher score of BDI-II at the end of treatment, compared to a baseline measure at the start of treatment. This indicates that patients with Major Depressive Disorder benefitted the most from this group CBT, but patients with comorbid Social Phobia or Substance Dependence benefitted the least.

Discussion

The findings show that adding 6 weeks of CBT, twice a week, to an intensive inpatient rehabilitation programme was effective in decreasing the symptoms of depression in patients with treatment-resistant depression. Individual CBT was superior to both the group CBT and the control group in lowering the scores of BDI-II, as Figure 3 reveals. The benefits of the treatment seemed to decrease over time, but

remained significant, at 18-month follow-up for all the groups.

Effect sizes were large for all the treatment groups; the individual CBT (2.10), group CBT (1.46), and treatment as usual (1.16), showing an effective 6-week treatment. Comorbid Social Phobia or Substance Dependence decreased the effects of group CBT.

The present results are promising for persons with treatment-resistant depression with psychiatric comorbidity. The results also support findings from other studies showing that adding CBT to medication for TRD may be beneficial in reducing depressive symptoms (15).

The therapeutic relationship formed in individual CBT and the possibility of adapting the treatment to individual needs may to some degree explain superior outcome for individual CBT over group CBT in this study.

The symptom severity and psychiatric comorbidity of the study's participants may also have been too great for group therapy primarily aimed at depression to show significant improvements over and above the intensive 6-week inpatient treatment as usual.

The findings also suggest that an interdisciplinary team of trained CBT therapists receiving regular supervision can be effective in conducting CBT for patients with TRD and psychiatric comorbidity in a rehabilitation setting. Results from the present study (not reported here) have also shown the relative reduction of hopelessness, and the equal efficacy of CBT provided by nurses and other healthcare professionals (44,48).

Limitations of the present study are that only self-report measures were used to examine outcomes, the large and diverse group-CBT groups, and the relatively small size of the control group. Future research might attempt to demonstrate the relative efficacy of group CBT for smaller and more homogeneous groups. Another limitation was the drop-out rate by the 18-month follow-up assessment point. However, complete data were available for 73% of the sample, and attrition analysis indicated that the attrition in the study was not selective. Longer follow-up may be needed to demonstrate the beneficial effects of CBT appearing later, as turned out to be the case for CBT for patients with chronic pain at Reykjalundur Rehabilitation Centre, where the difference in outcome was not significant after 1 year, but was significant after 3 years (53).

Conclusions

The main conclusion from this study is that inpatient interdisciplinary rehabilitation with cognitive behaviour therapy for depression is effective for treatment-resistant depression with psychiatric comorbidity, in decreasing symptoms of depression, anxiety, hopelessness, and automatic negative thoughts. However, group CBT seems less effective than individual CBT, at least for patients who have comorbid diagnoses of social phobia or substance dependence. Further research is needed to address the efficacy and effect endurance of CBT, individually tailored or in small homogeneous groups, for people with treatment-resistant depression, *inter alia* with psychiatric comorbidity.

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