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Cognitive behavior therapy in early psychosis with a focus on depression and low self-esteem: A randomized controlled trial

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ABSTRACT

Background: Patients in early phases of psychosis often struggle with depressive symptoms and low self-esteem. The main aims of the present study were to examine whether cognitive behavior therapy (CBT) compared to treatment as usual (TAU) would reduce depressive symptoms (primary outcome) and increase self-esteem (secondary outcome). Furthermore, we wanted to examine whether CBT reduces symptoms measured with the PANSS (positive, negative, cognitive, or excited symptoms) or increases general functioning compared to TAU.
Methods: A total of 63 early psychosis patients were included and randomly assigned to receive either CBT (maximum 26 sessions) or TAU for a period of up to six months. A linear mixed model was used for longitudinal analysis, with a focus on whether patients in the CBT group or the TAU group changed differently to one another between the baseline and 15-month follow-up.
Results: There were no differences between the CBT group and TAU group regarding improvements in depressive symptoms measured with the Calgary Depression Scale for Schizophrenia ($P = 0.188$) or self-esteem measured with the Rosenberg Self-Esteem Scale ($P = 0.580$). However, patients in the CBT group improved significantly more on negative symptoms ($P = 0.002$) and social functioning ($P = 0.001$).
Conclusions: We did not find CBT to be more effective than TAU in reducing depressive symptoms or increasing self-esteem in patients with early psychosis. However, CBT seems to improve negative symptoms and functioning. These results still need to be replicated in further studies as the present one was merely an exploratory analysis.
ClinicalTrials.gov Identifier: NCT01511406.

1. Introduction

Cognitive behavior therapy (CBT) for psychosis is an established psychotherapeutic intervention recommended by several international guidelines [1,2]. More than 60 randomized controlled trials (RCTs) have examined the efficacy of CBT for patients with schizophrenia and other psychotic disorders. However, systematic reviews and meta-analyses have reported decreasing effects in a wide range of symptoms between the first published meta-analyses in 2001 [3] and meta-analyses published in recent years [4–6]. The average effect sizes reported in the latter studies are small, and they are even smaller in methodologically rigorous studies [7]. Additionally, a recent Cochrane review has concluded that there is no clear evidence for favoring CBT over other, less sophisticated therapies for patients with psychosis [8]. These systematic reviews and meta-analyses have mostly included patients with a long-established diagnosis of schizophrenia and other psychotic disorders.

The effect of CBT for patients in early phases of psychosis is less examined in RCTs. This is of major importance because patients in early phases of psychosis may have quite different treatment needs compared to patients with multiple episodes and a longer history of illness. In addition to experiencing psychotic symptoms such as hallucinations and delusions, patients in early phases of psychosis often suffer from other conditions such as depression or low self-esteem, which can be just as challenging for the patients as the psychotic symptoms [9].

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Approximately 50% of patients who experience first-episode psychosis have a depressive disorder at the start of treatment, and approximately 80% of patients with schizophrenia experience a clinically significant depressive episode once or more than once during the early course of treatment [10–12]. For these patients, depressive symptoms are related to poorer clinical outcome, lower functioning, and reduced subjective quality of life [13].

In addition, patients with a psychotic disorder often experience low self-esteem. This has been related to the development and duration of psychotic symptoms [14,15] and a poorer clinical outcome [16–18]. The potential benefit of enhancing self-confidence has been examined in a study which included 30 patients who received six sessions of CBT [19]. A significant improvement in positive beliefs about the self and self-esteem were reported.

Depressive symptoms, low self-esteem, and negative schematic beliefs can contribute to the development of symptoms of psychosis [20,21]. Consequently, emotional processes may be important targets for treatment interventions in the early phases of psychotic disorders [22,23].

In randomized controlled trials aiming to reduce general psychotic symptoms among patients during the early phases of the disorder, CBT shows marginal advantages compared to other types of treatment [24–28]. However, in studies targeting specific symptoms, the picture becomes more heterogenous. For example, Jackson et al. aimed to reduce trauma symptoms attributable to the onset of psychosis [29], and their study showed significant improvement over six months for those receiving CBT compared with treatment as usual (TAU). Power et al. [30] examined whether a CBT intervention reduced the risk of suicidality in early psychosis patients. Patients in the CBT group reported less suicidal ideation than the control group, although the difference was not very significant. For their part, Fowler et al. designed a CBT intervention to improve social recovery among young people with early psychosis [31]. They found that subgroups of patients, to a larger extent, participated in structured daily activities. Furthermore, a randomized controlled trial compared patients with cannabis use undergoing a cannabis-focused CBT intervention for early psychosis and those attending a psycho-educative group [32]. The study revealed no differences between the groups in cannabis use, functioning, or psychopathology.

In a review focusing on CBT for early psychosis [9], Morrison concludes that there is little support for the effectiveness of CBT for this patient group. Most importantly, there were severe flaws in the study design, and the treatment approach was not meeting the concerns of patients in early phases of psychosis [9]. Studies examining the effect of CBT for patients in first-episode psychosis should target specific difficulties for this group of patients, such as depression, anxiety, and low self-esteem, and should aim to reduce the distress and problematic behavior associated with positive psychotic symptoms.

To our knowledge, no previous studies have specifically examined whether CBT can ameliorate symptoms of depression and low self-esteem in patients in an early psychotic phase and to what extent such amelioration could improve other symptoms or functioning. The main aims of the present study were therefore to test whether CBT, compared to TAU, would (1) reduce depressive symptoms (primary outcome) and increase self-esteem (secondary outcome); and (2) reduce symptoms measured with the PANSS (positive, negative, cognitive, or excited symptoms) and increase general functioning.

2. Material and method

2.1. Participants

Participants were recruited through the ongoing multi-center Thematically Organized Psychosis (TOP) Study at NORMENT KG Jebsen Centre for Psychosis Research between February 2010 and August 2013. All participants had a primary diagnosis of psychosis spectrum disorder according to the Diagnostic and Structural Manual of Mental Disorders, fourth edition (DSM-IV), were aged 18–65, and had a maximum of two illness episodes or two years of adequate treatment for psychosis (not five years as registered in ClinicalTrials.gov). Furthermore, the patients must have had a diagnosable depressive episode within the past year or have a score of five or higher on the Calgary Depression Scale for Schizophrenia (CDSS). Exclusion criteria were a history of severe head injury or of neurological or developmental disorders. All participants gave written informed consent before entering the study. The study was approved by the Regional Committee for Medical Research Ethics and the Norwegian Data Inspectorate and was completed in accordance with the Helsinki Declaration. ClinicalTrials.gov Identifier: NCT01511406. The trial was registered in ClinicalTrials.gov after the first patients were included in the study.

2.2. Measurements

Diagnosis was set according to the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID I) [33].

Symptom level was measured by the Structured Clinical Interview for the Positive and Negative Syndrome Scale Score (SCI-PANSS) [34]. Items on the scale are clinician rated from 1 (*not present*) to 7 (*severe impairment*), based on the patient's experience over the previous seven days. The study used the five-factor consensus structure suggested by Wallwork et al. [35], which has been found to have the most optimal fit in early psychosis [36]. It produces subscales for positive, negative, disorganized/concrete, excited, and depressive symptoms. This study reports the sum of item scores for all subscales except depression, with the following ranges: Positive (4–28), negative (6–42), disorganized/concrete (3−21), excited (4–28), and depression (3–21).

Depression was assessed with the CDSS [37]. The nine items on this scale are clinician rated on a 4-point Likert scale from 0 (*absent*) to 3 (*severe*). There is no definitive cut-off score, and studies have used different values to define the presence of depressive symptoms [12,38–41]. This study used a cut-off score of five or higher (≥5) as an indication that inclusion in the study was applicable, which is in line with the majority of previous studies [41–43].

Depression was also rated using the Beck Depression Inventory (BDI-II) [44], which is a self-report measure with 21 items on a 4-point Likert scale.

Self-esteem was measured by the Rosenberg Self-Esteem Scale (RSES) [45], which is a self-report measure with 10 items rated on a 4-point Likert scale ranging from 0 (*strongly disagree*) to 3 (*strongly agree*). Higher scores indicate better self-esteem (range 0–30).

Premorbid adjustment was assessed using the Premorbid Assessment Scale (PAS), whereby clinicians rate social and academic impairment on a 6-point Likert scale ranging from 0 (*no impairment*) to 6 (*severe impairment*). The premorbid phase is defined as time from birth until six months before onset of the psychotic disorder and assessed for childhood (age 0–11), early adolescence (age 12–15), adolescence (16–18), and adulthood (age 19+) [46].

Global functioning was measured by the clinician rated Global Assessment of Functioning (GAF) scale [47], split version [48]. Symptoms and function are assessed separately, with scores between 0 (poorest) and 100 (best).

Duration of untreated psychosis (DUP) was defined in line with the criteria described by Larsen et al. [49], namely, number of weeks with symptoms qualifying for a score of four or more on PANSS items *P1 Delusions*, *P3 Hallucinatory behavior*, *P5 Grandiosity*, *P6 Suspiciousness*, or *G9 Unusual thought content* before adequate treatment for psychosis.

Alcohol and drug use were self-reported by the Alcohol Use Disorder Identification Test (AUDIT) [50], and the Drug Use Disorders Identification Test (DUDIT) [51].

The primary (CDSS to measure depression) and secondary (RSES to measure self-esteem) outcome measures were registered in clinical trials. The other outcome measures reported in this study (BDI-II, PANSS, and GAF) were not preregistered.

Other outcome measures (not preregistered) were also included in this trial and will be reported in subsequent papers. These include metacognitive beliefs, social functioning, insight, and subjective quality of life.

2.3. Procedures

All aspects of recruitment, informed consent, screening, and baseline and outcome assessments were organized by a clinical assessment team. The clinical assessment team was independent of the research team, and included clinical psychologists or medical doctors in psychiatric training who had completed general training and a reliability program for the TOP Study protocol, using the UCLA program [52]. For DSM-IV diagnostics, mean overall kappa was 0.77 for both training videos and a randomly drawn subset of actual study patients ($CI_{95\%}$ 0.60–0.94). Inter-rater reliability, measured by the intra-class correlation coefficient (ICC 1.1) was 0.82 ($CI_{95\%}$ 0.66–0.94) for the PANSS positive subscale, 0.76 ($CI_{95\%}$ 0.58–0.93) for the PANSS negative subscale, and 0.73 ($CI_{95\%}$ 0.54–0.90) for the PANSS general subscale.

Consenting patients were randomly assigned to receive CBT plus TAU, or TAU alone, for a period of up to six months (maximum 26 sessions of CBT). Randomization of treatment groups was accomplished through a computerized random number generator and administered by staff at Oslo University Hospital independently of the research team.

Participants were invited to complete full assessments at baseline (inclusion in study), six months after baseline (after the end of therapy), and 15 months after baseline (follow-up). The clinical assessment team was blinded for group allocation, and therapists/clients were requested not to discuss group allocation with the clinical assessors to maintain blindness. In addition, CBT therapists facilitated self-reports of symptom levels at eight and 16 weeks after baseline.

2.4. Treatment procedures and intervention groups

2.4.1. Cognitive behavior therapy

The present study applied a CBT manual based on Kingdon and Turkington's CBT for psychosis [53], and Fennel's CBT approach to overcoming low self-esteem [54]. The CBT intervention was designed with weekly individual sessions of 45–60 min, delivered over a six-month period (maximum 26 sessions). The CBT treatment protocol was divided into three treatment stages. Stage 1 (sessions 1–5) focused on engagement and aimed to prepare the patient for CBT. During this stage the therapist informed the patient about the basic principles of CBT and explained how psychotic symptoms often develop based on the stress-vulnerability model [55]. Early sessions emphasized the importance of active participation and collaboration and the significance of homework and developing a list of problems and goals for the forthcoming sessions. A particular effort was made to clarify patients' expectations regarding therapy. Stage 2 (sessions 6–20) targeted depressive symptoms and low self-esteem, which were the study's main focus. However, a problem list was prepared for each patient to address the patient's everyday psychological challenges and tailor therapy to patients' individual needs. The case formulation developed by Morrison [56] was applied for each patient at this stage, developed in collaboration with the patients. The case formulation was updated and modified throughout the therapy period. Stage 3 (sessions 20–26) was dedicated to the termination of the therapy and relapse prevention. Specific attention was given to summarize the therapy and ensure that the patient had become "their own cognitive therapist."

2.4.2. Cognitive behavior therapists

Cognitive behavior therapy was delivered by a dedicated CBT treatment team consisting of clinical psychologists (one female and one male), psychiatrists (one female and one male), and an occupational therapist (female). All therapists had completed a two-year educational program in CBT provided by The Norwegian Association of Cognitive Therapy. In addition, all therapists attended monthly meetings starting two years prior to the study baseline in order to learn the specific CBT manual for the study and put it into practice. The RCT was preceded by a pilot period during which therapists recruited early psychosis patients from a first-episode psychosis unit. Video recordings of CBT sessions from this pilot were used for group supervision.

2.4.3. Treatment adherence

Fidelity to the treatment protocol was ensured by regular group supervision and was assessed by rating the video records of the CBT therapy sessions with the Cognitive Therapy Adherence and Competence Scale (CTACS) [57,58].

The CTACS contains 25 items in five sections: CT structure (items 1–9), development of a collaborative therapeutic relationship (items 10–15), development and application of the case conceptualization (items 16–21), cognitive and behavioral techniques (items 22–24), and overall performance (item 25). Items are rated from 0 (*poor*) to 6 (*excellent*) in regard to adherence and competence. The adherence rating reflects the degree to which the therapist engaged in the process or intervention. The competence ratings reflect how well the intervention was performed. The mean of the therapists' common coding of eight video records was 4.3 for adherence and 4.1 for competence, which indicates a mean rating of "competent" or above.

2.4.4. Treatment as usual

All patients continued to receive their ongoing usual treatment from their therapists/case managers in various psychiatric units in Oslo, Norway. The core components of TAU entailed ongoing medication, regular psychiatric review, and regular follow-ups by their case managers. Some of these patients had access to wider multidisciplinary community mental health services. The TAU patients most often received regular psychotherapy pertaining to different treatment methods, including some options of cognitive therapy. Treatment as usual specifications in terms of specific therapeutic interventions or number of sessions were not available to the research team. The CBT therapist team cooperated with the TAU patients' case managers to collect data for the primary outcome measures eight and 16 weeks into the study.

2.5. Dropouts

In total, seven patients (11%) dropped out between the baseline and six-month follow-up (CBT = 3; TAU = 4). The CBT dropouts attended zero, six, or eight sessions, respectively. Treatment as usual dropouts withdrew immediately after randomization (N = 2), due to a long hospitalization (N = 1), or just before the six-month assessment (N = 1). Eight more patients (14%) dropped out between the six- and 15-month assessments (CBT = 1; TAU = 7). The CBT dropout refused to be interviewed at the 15-month follow-up. Treatment as usual dropouts either refused to be interviewed (N = 3) or did not answer our request to participate in the final follow-up (N = 4).

2.6. Data analysis

Statistical analyses were performed with SPSS for Windows (version 25.0). Completing participants and dropouts were compared on demographic and clinical variables at baseline and at six months using chi-square analyses and independent samples *t*-tests. Differences between the completing participants in the CBT and TAU groups in regard to primary (CDSS) and secondary (RSES) outcome measures were also assessed with independent sample *t*-tests at all available time points.

Cohen's d was calculated with the mean difference between the two groups divided by the pooled standard deviation. Cohen's $d = (M_2 - M_1) / SD_{pooled}$, where $SD_{pooled} = \sqrt{((SD_1^2 + SD_2^2) / 2)}$.

Linear mixed model procedures in SPSS were used to analyze the longitudinal data of the primary outcome measures (BDI II, RSES) at baseline, eight, and 16 weeks into therapy, and at six- and 15-month

Table 1
Clinical and demographic characteristics of the cognitive behavior therapy (CBT) and treatment as usual (TAU) group.

	CBT group (N = 32)	TAU group (N = 31)	
Age, mean (range)	28.6 (19–51)	27.1 (18–43)	ns
	N (%)	**N (%)**	
Female	15 (46.9)	11 (35.5)	ns
Caucasian ethnicity	28 (87.5)	25 (80.6)	ns
Married or cohabiting	8 (25)	4 (13)	ns
Currently able to work/study	10 (31)	12 (38.7)	ns
Schizophrenia disorder	14 (44)	16 (51)	ns
Schizoaffective disorder	7 (22)	3 (10)	ns
Delusional disorder	2 (6)	3 (10)	ns
Other psychosis	9 (28)	9 (29)	ns
Currently using antipsychotics (%)[a]	27 (84.4)	28 (90.3)	ns
Duration of untreated psychosis (DUP) median in weeks[b]	17	20	ns
	Mean (SD)	**Mean (SD)**	***P***
GAF symptom	45.0 (12.5)	42.0 (9.5)	*0.293*
GAF function	47.3 (11.1)	46.1 (10.1)	*0.663*
PAS	0.24 (0.14)	0.26 (0.12)	*0.563*
PANSS positive component	9.4 (3.6)	9.5 (3.2)	*0.928*
PANSS negative component	12.4 (4.7)	13.2 (4.7)	*0.472*
PANSS depressive component	9.1 (2.5)	9.2 (2.9)	*0.839*
PANSS disorganized component	4.3 (1.5)	5.2 (2.4)	***0.049***
PANSS excitative component	4.8 (1.2)	5.9 (2.4)	***0.027***
AUDIT	6.39 (5.61)	5.48 (6.74)	*0.587*
DUDIT	4.29 (7.59)	3.25 (7.19)	*0.602*

Significance level was set to $P < 0.05$.
[a] Missing data for eight patients (CBT N = 27; TAU N = 28).
[b] Missing data for four patients (CBT N = 29; TAU N = 30).

follow-up. The same procedures were used to analyze the longitudinal data of all five PANSS subscales and GAF subscales at baseline and six- and 15-month follow-up. The linear mixed model was used to account for missing data and confounding variables. For the linear model, the best fit was for the model with random intercept.

This equation describes the model:

$$Y_{ij} = (\beta + b_{1j}) + \beta_2 * \text{group} + \beta_3 * \text{time} + \beta_4 * \text{time} * \text{group} + e_{ij},$$

where Y_{ij} is the outcome for patient $i = 1, \ldots, 63$ at time point $J = 1, \ldots 5$ (or 1, … 3 *eij* is the error). $\beta_1 \ldots \beta_4$ are the fixed effects (population averages) and b_{1j} is the individual specific random intercept and slopes.

To reduce the risk of type I errors, we multiplied the given *P*-values by the number of comparisons (nine comparisons for the *t*-tests and eight comparisons for the linear mixed model calculations).

3. Results

A total of 63 patients were included in the study and randomized to CBT (N = 32) or TAU (N = 31). Table 1 displays clinical and demographic characteristics for each treatment group.

As shown in Fig. 1, a total of 56 patients completed the six-month assessments and 48 patients the 15-month assessments.

Dropouts from the CBT and TAU groups did not differ significantly on demographic or clinical variables at baseline or six-month follow-up. On average, the CBT group received a mean number of 19.5 CBT sessions (median = 22 sessions).

Table 2 shows the BDI-II and RSES scores from baseline to 15-month follow-up. There were no significant differences between the two groups on any of the five assessment points.

Table 3 shows CDSS, PANSS, and GAF subscale scores from baseline to 15-month follow-up. The CBT group had significantly lower levels on the PANSS excited and disorganized subscales at baseline. The CBT group showed significantly lower levels of negative symptoms at the end of treatment (six months) and at 15-month follow-up. The CBT group also showed significantly higher GAF functioning at 15-month follow-up. The differences in PANSS negative symptoms at the end of treatment (six months) became non-significant after Bonferroni correction for multiple testing. The significant findings for PANSS negative symptoms and GAF functioning at 15-month follow-up remained significant after Bonferroni adjustments.

Fig. 2 shows the development of the primary and secondary outcome measures (CDSS and RSES). Fig. 3 shows the significant other outcome measure (PANSS negative symptoms and GAF functioning) from baseline to 15-month follow-up.

The linear mixed model analysis did not show any significant differences between the CBT and TAU groups over time in regard to the primary outcome measure, depressive symptoms, and secondary outcome, self-esteem (Table 4). However, both groups improved significantly from baseline to 15-month follow-up.

As shown in Table 4, patients who received CBT improved significantly more than patients who received TAU only in regard to negative symptoms ($P = 0.002$) and functioning ($P = 0.001$). These results remained significant after Bonferroni adjustment.

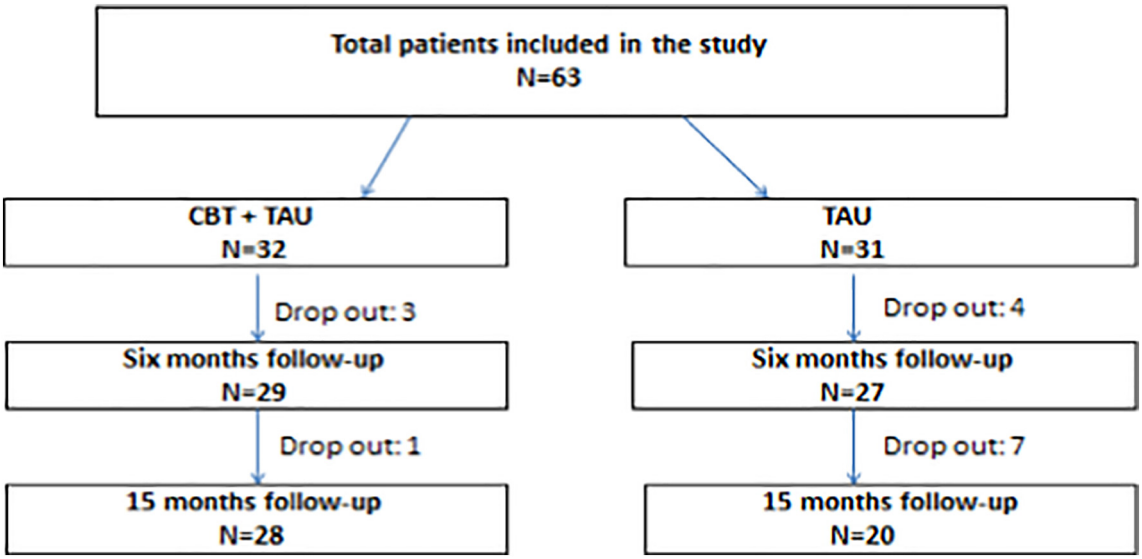

Fig. 1. Flow chart of included patients in the study.

Table 2
Means and standard deviations (SD) on the Beck Depression Index (BDI II) and Rosenberg Self-Esteem Scale (RSES) at baseline and follow-up (assessments for five time points).

	Baseline		8 weeks		16 weeks		6-Month follow-up		15-Month follow-up		Cohen's d	
	CBT mean (SD)	TAU mean (SD)	CBT mean (SD)	TAU mean (SD)	CBT mean (SD)	TAU mean (SD)	CBT mean (SD)	TAU mean (SD)	CBT mean (SD)	TAU mean (SD)	CBT	TAU
Rosenberg Self-Esteem Scale	24.5 (3.8) $P = 0.064$	26.1 (3.0)	25.2 (4.8) $P = 0.686$	24.8 (1.8)	24.7 (5.7) $P = 0.520$	25.6 (7.6)	27.1 (5.9) $P = 0.869$	26.8 (7.6)	26.8 (6.3) $P = 0.884$	26.5 (7.4)	0.442 Between groups 0.04	0.070
Beck Depression Inventory (BDI II)	22.2 (12.2) $P = 0.809$	21.5 (9.9)	15.3 (10.3) $P = 0.296$	18.6 (12.2)	12.0 (8.5) $P = 0.365$	14.5 (10.3)	12.6 (9.5) $P = 0.561$	14.3 (11.7)	12.5 (7.9) $P = 0.302$	15.5 (12.0)	0.944 Between groups 0.30	0.545

Patients in both groups improved significantly on PANSS positive, negative, and disorganized symptoms, as well as GAF functioning and symptoms, from baseline to 15-month follow-up. PANSS excited scores did not improve.

4. Discussion

To our knowledge, this is the first RCT examining whether CBT focusing on depressive symptoms and low self-esteem could be superior to TAU for patients in early phases of psychosis. Both groups showed significant improvements in depressive symptoms and self-esteem, as well as in most other symptom and function domains, during treatment and follow-up. Cognitive behavior therapy did not show additional benefits over TAU either with regards to the primary outcome (depressive symptoms) or the secondary outcome (self-esteem) measures. Cognitive behavior therapy did, however, demonstrate additional benefits in regard to improving negative symptoms and functioning.

4.1. Primary outcomes: depressive symptoms

Depressive symptoms decreased during treatment for all patients, but this was not accelerated by CBT as delivered in the present study. Our findings are in line with those of Jackson et al. [29], who found that CBT reduced post-psychotic trauma symptoms in early psychosis but did not provide additional benefits in regard to depressive symptoms or self-esteem.

Findings from meta-analyses and reviews of CBT for psychosis, regardless of stage of illness, have been mixed. Wykes et al. [59] report a small to moderate effect of CBT for psychosis on depressive symptoms, but depression was not a primary outcome in any of the studies they identified and included. A recent review [60] notes the same: Of 17 studies identified, none directly addressed depressive symptoms or recorded changes in depressive symptoms as a primary outcome. Only 6 of the 17 studies showed additional improvements in depressive symptoms from CBT, including three studies targeting psychotic symptoms, two targeting social anxiety, and one targeting self-esteem. In two of the studies, the effects of CBT on depression were significant only at follow-up. The authors concluded that CBT can have a positive effect on depressive symptoms comorbid to psychotic disorders, but given the sound effect of CBT for depression alone and the overlap in methodology in CBT for both disorders, it is difficult to interpret the lack of consistent effect on depressive symptoms.

4.2. Secondary outcomes: self-esteem

Self-esteem displayed the same change pattern as depression during the follow-up period. Patients in both groups reported improvements in self-esteem, but there were no differences between the groups. Few studies have focused on the effect of CBT in improving self-esteem in

Table 3
Means and standard deviations (SD) on PANNS symptom component scales, CDSS, and GAF symptoms and functioning (assessments for three time points).

	Baseline		6 months		15-Month follow-up		Cohen's d	
	CBT mean (SD)	TAU mean (SD)	CBT mean (SD)	TAU mean (SD)	CBT mean (SD)	TAU mean (SD)	CBT	TAU
PANSS positive symptoms	9.4 (3.6) $P = 0.928$	9.5 (3.2)	7.7 (4.3) $P = 0.720$	7.4 (2.9)	7.9 (3.9) $P = 0.693$	7.5 (2.8)	0.400 Between groups 0.12	0.655
PANSS negative symptoms	12.4 (4.7) $P = 0.472$	13.2 (4.7)	8.6 (2.7) $\mathbf{P = 0.043}$	10.7 (5.0)	8.6 (3.0) $\mathbf{P = 0.001}$	13.0 (5.1)	0.964 Between groups 1.05	0.038
PANSS excitative symptoms	4.8 (1.2) $\mathbf{P = 0.027}$	5.9 (2.4)	4.9 (1.1) $P = 0.454$	5.2 (1.4)	4.8 (1.4) $P = 0.539$	5.1 (1.5)	0.000 Between groups 0.21	0.400
PANSS disorganized symptoms	4.3 (1.5) $\mathbf{P = 0.049}$	5.2 (2.4)	4.1 (1.3) $P = 0.233$	4.7 (2.1)	3.9 (1.4) $P = 0.171$	4.5 (1.8)	0.276 Between groups 0.37	0.331
CDSS	7.84 (5.35) $P = 0.646$	8.43 (4.70)	4.69 (4.41) $P = 0.070$	2.74 (3.44)	4.29 (3.54) $P = 0.383$	3.30 (3.99)	0.783 Between groups 0.26	1.176
GAF symptoms	45.0 (12.5) $P = 0.293$	42.0 (9.5)	57.1 (12.7) $P = 0.529$	54.8 (14.1)	58.6 (16.5) $P = 0.102$	51.4 (11.8)	0.929 Between groups 0.62	0.878
GAF functioning	47.3 (11.1) $P = 0.660$	46.1 (10.1)	59.6 (12.3) $P = 0.070$	53.3 (13.2)	61.1 (11.8) $\mathbf{P = 0.004}$	48.8 (12.0)	1.205 Between groups 1.04	0.243

Significance level was set to $P < 0.05$.

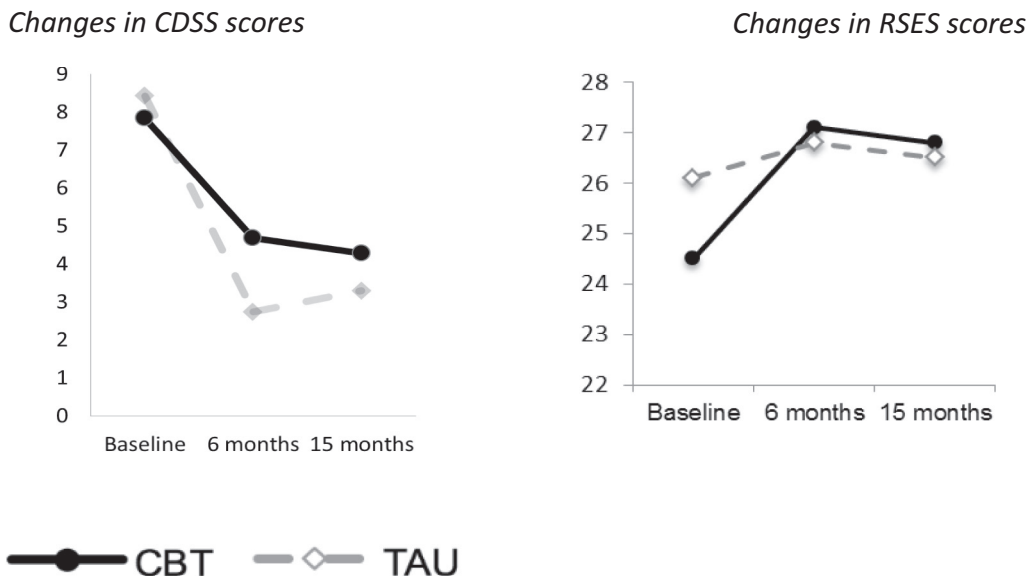

Fig. 2. Group differences (CBT vs. TAU) on primary and secondary outcomes.

psychotic patients. Hall and Tarrier [61], in a pilot study including 25 patients, aimed to evaluate the efficacy of a simple CBT intervention in improving self-esteem in psychotic patients who reported low self-esteem. They found significantly greater improvements in the CBT treatment group at post-treatment and three-month follow-up. In contrast to our study, they included chronic psychotic inpatients, and the CBT interventions were specifically targeted at improving self-esteem. For their part, Gumley et al. [62] tested whether CBT targeting early signs of relapse could reduce negative beliefs about psychosis and improve self-esteem. The CBT group showed greater improvements in negative appraisal of loss arising from psychosis as well as in self-esteem at 12-month follow-up. As in the study by Hall and Tarrier [61], mostly patients with chronic psychosis were included, and self-esteem was specifically targeted. Freeman et al. [19] examined whether 30 patients with persecutory delusions achieved a reduction in negative cognitions about the self after receiving six sessions of CBT. The study patients in the CBT group improved with regard to positive beliefs about the self and self-esteem. As in the other studies, the included patients had been struggling with psychosis for a long period. However, it is possible that the current study would reveal improvement in self-esteem if we focused more specifically on self-esteem or included only patients who specifically chose this as a treatment goal.

We also enforced a threshold of five or higher on the CDSS as an inclusion criterion for the study to ensure that depression was a relevant issue for all participants. While our therapy manual outlined depressive symptoms as a key target, it was also stressed that the problem list should be individually tailored for each patient, in line with the suggestions by Morrison [9]. It is therefore possible that other symptoms, such as hallucinations, delusions, or low functioning, were equal targets in the CBT sessions.

As we did not assess to what extent, or in how many sessions, depressive symptoms or low self-esteem were actively targeted, it is difficult to determine whether this may have impacted on the outcomes of the CBT group. Self-esteem, in particular, is a complex phenomenon that

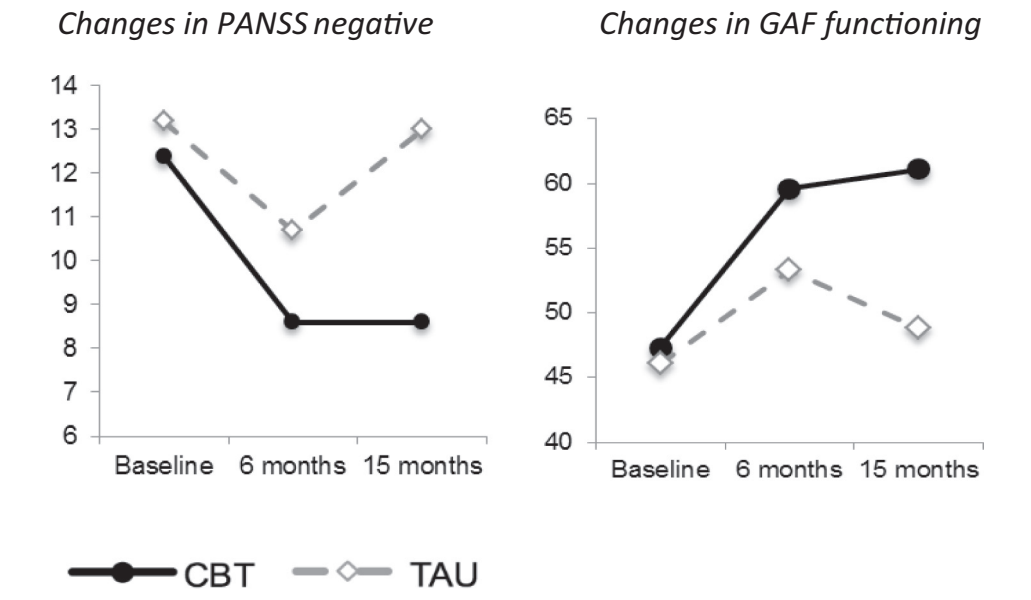

Fig. 3. Group differences (CBT vs. TAU) on other significant outcomes.

Table 4
Results from linear mixed model analysis of primary (depression) and secondary (self-esteem) outcomes and other symptoms and functioning.

Outcome	Fixed effect	Estimate	SE	CI (95%)		*P* value
	CBT			Lower	Upper	
CDSS	Main effect x time	−2.49	0.55	−3.36	−1.62	0.000
	Interaction group x time	0.50	0.37	−0.24	1.24	0.188
Rosenberg	Main effect x time	0.52	0.21	0.11	0.94	0.014
	Interaction group x time	−0.14	0.25	−0.62	0.35	0.580
PANSS positive symptoms	Main effect x time	−0.80	0.26	−1.32	−0.29	0.003
	Interaction group x time	−0.19	0.30	−0.79	0.41	0.539
PANSS negative symptoms	Main effect x time	−1.83	0.39	−2.60	−1.06	<0.001
	Interaction group x time	1.21	0.37	0.47	1.94	**0.002**
PANSS excitative symptoms	Main effect x time	−0.28	0.15	−0.57	0.02	0.069
	Interaction group x time	0.17	0.13	−0.08	0.41	0.187
PANSS disorganized symptoms	Main effect x time	−0.38	0.13	−0.64	−0.12	0.005
	Interaction group x time	0.19	0.14	−0.10	0.47	0.198
GAF symptoms	Main effect x time	6.96	1.16	4.67	9.24	0.000
	Interaction group x time	−1.60	1.15	−3.88	0.68	0.167
GAF functioning	Main effect x time	6.13	1.06	4.04	8.22	0.000
	Interaction group x time	−3.68	1.10	−5.85	−1.51	**0.001**

Significance level was set to $P < 0.05$.

may require a more elaborate focus and a longer duration of treatment [63] as CBT may fail to improve self-esteem if this issue is not specifically targeted [64].

4.3. PANSS symptoms and functioning

The present study found that CBT accelerated improvements in negative symptoms and functioning compared to TAU, even though this was not the primary or secondary outcome of the study. This is in line with a study by Grant et al. [65], who investigated the effect of recovery-oriented CBT on functioning and negative symptoms in a randomized controlled trial with schizophrenia patients who had low function and neurocognitive impairments. They found that targeted CBT accelerated improvements in functioning and positive symptoms as well as reduced avolition-apathy compared to standard therapy. In contrast, in a recent meta-analysis Velthorst et al. conclude that the beneficial effect of conventional CBT on negative symptoms found in older studies is not generally supported by more recent studies in which negative symptoms are not typically a primary target [66]. Furthermore, in a recently published meta-analysis, Laws et al., [5] found only a small effect of CBT on functioning at the end of treatment. This small effect was not evident at follow-up. Consequently, the findings must be regarded as preliminary, and further studies should replicate similar findings before firm conclusions can be drawn.

5. Limitations

Prior to this study, we performed a power calculation suggesting that a total of at least 100 patients (not 60 as incorrectly stated in ClinicalTrials.gov) are required to detect statistically significant differences between the two treatments. However, due to difficulties with recruitment, the final study had only 63 enrolled patients. Analyses by Jackson et al. [29] have shown that our original estimates were likely too optimistic and that our study would need a minimum of 320 patients to achieve the statistical power needed to draw firm conclusions about group differences. It is therefore clear that the current study is severely underpowered, and hence both the negative and positive findings should be interpreted with caution. The large number needed to reliably detect group differences suggests a likely low effect size. Considering similar difficulties in 11 out of 17 studies included in the recent review by Taalman et al. [60], the current literature lends little support to pursuing further CBT trials focusing on depressive symptoms in psychosis.

The study uses TAU as the control group. However, details of treatment approaches in the TAU group were not available to the research team, and thus we cannot specify what kind of treatment CBT has been compared to. It is reasonable to believe that TAU includes problem-oriented supportive therapy, but we cannot rule out that some therapists included CBT techniques as part of the treatment they offered. It is, however, unlikely that TAU included CBT in a systematic manner similar to the CBT group.

It should also be noted that the assessment team that provided the six- and 15-month follow-up measurements were assumed to be blinded to whether the patients received CBT or TAU and were conscious of this issue. The team reported that any loss of blinding resulted in transferring the relevant assessment to another assessor at the next follow-up. However, we did not ask them to provide ratings of which group they thought the patients tested belonged to, and as such have no formal measurement on whether blinding was successful.

6. Conclusions

Cognitive behavior therapy as an approach to reduce depressive symptoms or increase self-esteem among patients with early psychosis provided equal outcomes to TAU in this study. However, we found that CBT provided additional benefits in regard to improving negative symptoms and functioning. As these were assessed as additional outcomes and were not preregistered in the study, the results should be replicated. It should also be noted that the study is likely underpowered, and as a result both the negative and positive findings should be interpreted with caution.

Declaration of competing interest

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