Cognitive-Behavioural Therapy for Patients with Schizophrenia: A Multicenter Randomised Controlled Trial in Beijing, China

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Abstract

Background: Meta-analyses support the efficacy of cognitive-behavioural therapy (CBT) for schizophrenia in western cultures.

Aims: To compare the efficacy of CBT and Supportive Therapy (ST) for patients with schizophrenia in China.

Method: A multicenter randomized controlled, single-blinded, parallel group trial enrolled a sample of 192 patients with schizophrenia. All patients were offered 15 sessions of either CBT or ST over 24 weeks and followed up for additional 60 weeks.

Results: Effect size analysis showed that patients who had received CBT showed rapid improvements in all symptoms as measured by PANSS, insight and social functioning in the first 12 week and 24 weeks and maintained the improvement over the course of the study to week 84. Patients in the CBT group also showed significantly greater and more durable improvement in the total score of PANSS (P= 0.045; between group d=0.48), **positive symptoms (P = 0.018; between group d=0.42),** insight, and social functioning (P= 0.037; between group d=0.64).

Conclusions: CBT was superior to ST in improving the total score of PANSS, positive symptoms, insight and social functioning of patients with schizophrenia in China.

Declaration of interest: None.

Key words: cognitive behavioural therapy, supportive therapy, schizophrenia, Randomised Controlled Trial, China.

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Introduction

Schizophrenia is a chronic, severe and disabling mental disorder. However, the potential for recovery is increasingly being recognised. Schizophrenia affects approximately 0.7% of people at some point in their lives in China.[1] This translates to approximately five million people suffering from schizophrenia in China, representing over 20% of the total 24 million people suffering from the disorder worldwide.[1]

The primary treatment for schizophrenia continues to be pharmacological (National Institute for Clinical Excellence 2003.). However, long-term therapy using pharmacology is associated with a range of adverse effects, including a high rate of poor medication adherence (Velligan et al. 2006). Pharmacological treatment is limited in improving clinical, personal and social functioning and patients often have a high risk of relapse (Freeman et al. 1998; A. K. Morrison 2009; A. P. Morrison et al. 2011; Rathod et al. 2008; Tarrier et al. 2004). Certain psychosocial treatments, such as cognitive behaviour therapy (CBT) , have been shown to have a beneficial effect on positive and negative symptoms, mood, social functioning and social anxiety and is effective in reducing readmissions to hospital, duration of admission and symptom severity (Lysaker et al. 2010), (Wykes et al. 2008). CBT therefore addresses the limitations of medication-based treatment.

CBT is a well-established standard psychotherapy used in western clinical practice as an adjunct treatment for schizophrenia (National Institute for Clinical Excellence 2003.). CBT has been recommended as standard treatment for people with schizophrenia in Western countries. The guidelines for its use have been provided by the National Institute for Health and Clinical Excellence(NICE 2009) and the Schizophrenia Patient Outcomes Research Team (Kreyenbuhl et al. 2010).

When using CBT as a treatment for schizophrenia, studies focused on addressing positive and negative symptoms, mood, social functioning and social anxiety (Wykes et al. 2008). For example, Drury et al. showed that CBT reduced positive symptoms at a faster rate during the first 12 weeks following hospital admission(Drury et al. 2000). Positive symptoms were reduced during this time compared to those patients who did not receive the CBT treatment. Drury et al. (Drury et al. 2000) also found more rapid improvement in clinical recovery as indicated by increased insight, less dysphoria and ‘low level’ psychotic thinking and less disinhibition.

Emerging evidence indicates deficits in social functioning are prominent in patients with schizophrenia; their symptoms and cognitive functioning are predictive of their level of social functioning (Apiquian et al. 2009; Brissos et al. 2012). DSM-IV-TR acknowledges that assessing social function-

ing is important in the antipsychotic treatment of schizophrenia(American Psychiatric Association DSM-IV-TR 2000). Consequently, social functioning is an important measure of the effectiveness of psycho social treatment for schizophrenia (Burns and Patrick 2007).

Insight is another important outcome indicator that needs to be considered. Insight is defined as ‘a patient’s recognition of having a psychiatric disorder, of the social consequences of that disorder and of the need for treatment’(Wang et al. 2011). It is therefore critical for compliant behaviour and engaging patients in a treatment process (Rathod et al. 2008). Insight has recently become a major consideration in pharmacotherapy and psychosocial intervention in schizophrenia. Therefore, when examining the effectiveness of CBT treatment it is important to assess insight and its improvement.

CBT employs a number of strategies, such as a therapeutic alliance marked by collaboration on a problem list, normalisation of the psychotic experience and modification of dysfunctional cognitions and behaviours(Warman and Beck 2003). CBT also teaches and enhances personal coping strategies that allow patients to manage their symptoms and daily difficulties. The CBT approach may become the standard approach to schizophrenia, leading to multiple improved outcomes—not only does it reduce positive and negative symptoms, it also improves cognitive insight about the illness and the personal and social functioning of patients.

However, most published studies contain a lack of methodological rigour, either in their small sample sizes or in the short term of interventions. No studies comprehensively assess the effectiveness of using the CBT approach on the negative symptoms, positive symptoms, disorganization symptoms, excitement and emotional distres as well as insight and social functioning. Most importantly, there is no robust evidence indicating that using CBT to treat schizophrenia is effective for Chinese patients suffering from schizophrenia. To fill in these research gaps, this study sought to examine the efficacy of CBT over and above the effects of other psychosocial approaches by using a multicentre based randomised controlled trial in a large clinical sample. This study aimed to comprehensively assess the effectiveness of the CBT approach in improving not only negative symptoms, positive symptoms, disorganization symptoms, excitement and emotional distress, but also insight and social functioning, which are the important functioning areas of schizophrenia. The hypothesis asserts that the CBT approach is effective and has a beneficial effect on positive and negative symptoms, disorganization symptoms, excitement and emotional distress, as well as insight and social functioning in Chinese schizophrenia patients.

Methods

Participants

This study was conducted at three specialised psychiatric hospitals in Beijing, China. Patients were recruited from inpatient units or outpatient departments. Eligible participants met the following inclusion criteria:

aged between 18–60 years; diagnosed with schizophrenia through a Structured Clinical Interview for DSM-IV Axis I Disorders-Clinician Version[17] by raters who were well-trained research psychiatrists (intra-class correlation >0.80); had a total score of 60 or above on the Positive and Negative Syndrome Scale (PANSS) which indicated severe symptom burden; on an adequate dose of an antipsychotic for at least the past four weeks of treatment; capable of providing informed consent.

An adequate dose of antipsychotic medication was defined as regular use of antipsychotic medication with good adherence, at or above the equivalent of 300 mg daily of chlorpromazine, including a minimum period of at least two weeks of treatment with the equivalent of 600 mg of chlorpromazine. Participants were excluded if they met the following exclusion criteria: a comorbid diagnosis of mental retardation or primary substance dependence; a score of five or more of conceptual disorganisation according to PANSS, which included those who could not communicate, had poor rapport, or lack of spontaneity and flow of conversation; had received electroconvulsive therapy (ECT) within the past six months prior to entry into the study; currently receiving other types of systematic psychotherapy. Fig. 1 is the CONSORT diagram for the trial.

Sample size calculation

The sample size calculation was based on a previous randomised controlled trial of a similar design in the UK, which resulted in a recovery rate of 63% in the CBT group compared to 39% in the befriending group (recovery was defined as having a 50% or greater reduction in total scores of the Comprehensive Psychopathological Rating Scale by the end of treatment) (Sensky et al. 2000). Based on the difference between the two treatment groups of this trial, 80 patients across the two groups were required to achieve an alpha-value of 0.05 and a power of 80%. Assuming a 20% drop-out rate, a minimum sample of 96 patients was required for each group.

Procedures

Participants deemed eligible for the trial were randomly allocated to the CBT group and the ST group (1:1 randomisation). Block randomisation was conducted by computer-generated, random numbers to allocate the eligible participants to either of the two groups, stratified according to study site and performed at a geographically remote and independent location. The trial lasted for 84 weeks, with patients receiving 15 sessions of either CBT or ST over a 24-week period followed by 60 weeks of follow-up.

Interventions

Medications

Medication prescription was not affected or influenced by the trial protocol. The patients in both groups remained under their usual psychiatric care. The types or dose of medications were decided or adjusted by their primary treating teams based on clinical needs. The doses of antipsychotic medication were recorded and converted into equivalent doses of chlorpromazine dose

(Sim et al. 2004).

Cognitive-behavioural therapy

CBT is a manual-based treatment. In this study, it was delivered by therapists to patients who were allocated to the CBT group. There were 12 sessions in the first 12 weeks followed by three consolidated sessions in the subsequent 12 weeks. Each session lasted for about 50 minutes but flexibility on time was permitted depending on the attention, tolerance level and mental state of the participants.

The trial protocol for using CBT to treat schizophrenia was compiled in Chinese and based on the principles and practice developed by Kingdon and Turkington (Kingdon and Turkington 2004). This training manual was written in Chinese and translated to English before it was used as the training material for review by Kingdon and Turkington, and three CBT specialists in Hong Kong, Beijing and Changsha of China. Its cultural relevance and acceptability was tested on ten patients with schizophrenia.

The first four sessions were delivered twice a week and focused on the introduction of the treatment, building a therapeutic alliance based on collaboration on a problem list, psycho-education about the cognitive-behavioural model of psychosis and normalisation of the experience of psychosis. A cognitive formulation was developed to make sense of psychotic experiences. The next six sessions in the intermediate stage were offered once a week. These sessions involved teaching coping strategies and cognitive-behavioural work with delusions, hallucinations and negative symptoms. Homework was also assigned in a flexible manner after each session to consolidate what was learnt in the session. The two sessions in the final phase were delivered once every two weeks, including a discussion of attitudes to medication and relapse prevention work. Finally, three booster sessions were offered once monthly for reviewing progress and consolidating what patients had learnt of CBT strategies for coping with future problems related to the recurrence of psychotic symptoms.

Supportive therapy

Supportive therapy was also in the form of manual-based treatment and comprised 12 sessions in the first 12 weeks followed by three consolidated sessions in the subsequent 12 weeks. Each session lasted for about 50 minutes. This intervention was based on supportive models of psychotherapy and was the most widely practiced form of individual psychotherapy in psychiatric services (Winston et al. 2004). The primary goal of the ST in the first 12 sessions was to provide patients with emotional support, knowledge of mental disorders, and provide suggestions to patients on preventing a relapse of the disease. Similar to the CBT approach, ST also focused on developing and maintaining therapeutic alliance and providing psycho-education to patients. However, ST did nothave a problem list to work on, did not develop coping strategies, did not have a cognitive formulation or reality testing of paranoia and voices. For example, patients could select

session topics such as discussing interests, personal experiences, and expressing feelings. Therapists were nondirective but used reflective listening and summarising techniques to support patients in coping with current life events and in relapse prevention. No homework was given and no specific CBT techniques were used in ST.

Trial therapists

The eight therapists were experienced psychiatrists or psychologists with five to 20 years' experience using psychotherapy in hospitals on patients with a mental disorder. They had been trained and supervised in the application of cognitive therapy for psychosis by experienced cognitive behavioural therapists, and had special expertise in the application of CBT for psychosis using a translated Kingdon and Turkington manual (DK, DT and RN).[20] The on-site training courses of CBT for schizophrenia lasted more than 100 hours throughout the trial period, including didactic teaching, case presentation, in-vivo demonstration of skills and role-play. After the training courses, the eight therapists also participated in peer supervision using role-play and listening to other therapists' treatment tape recordings in biweekly consultation meetings. Their treatment sessions were monitored and reviewed by Kingdon via video conference once a week.

Supervision

Psychotherapy was supervised in three ways: peer supervision, expert supervision in CBT, and consultation on culturally-related issues.

During peer supervision, the therapist presented the case formulation, treatment plan and therapy progress for every CBT case during the first six sessions. The peer therapists also provided feedback and suggestions and selected sections of the individual case's session recordings for supervision. Supervision for ST also occurred for each participant focusing on the use of supportive methods and differentiating these from CBT.

In this study, expert supervision was provided for CBT only. Therapists submitted written case reports, case formulations, treatment plans, therapy processes and team members' questions about the cases arising from the peer supervision sessions to the second author. These submissions occurred once every two weeks throughout the intervention period. Supervision was delivered once every two weeks by an expert therapist in CBT for psychosis (DK) from the United Kingdom via phone, Skype or email. The principal investigator (ZJL), a consultant psychiatrist with specific knowledge of CBT techniques and culture related problems, also provided face-to-face supervision for all trial therapists on a monthly basis.

Ethical issues

The study protocol was approved by the Beijing Municipal Science & Technology Commission. The study was also approved by the IRB of participating hospitals, the Research & Ethics Committee of Beijing Anding Hospital, Beijing Huilongguan Hospital and The Sixth Hospital of Peking University. The protocol was explained

clearly and all the study participants signed informed consent forms before the baseline assessments were commenced. A participant could withdraw from the trial at any stage and this did not affect their clinical care.

Measures

Three outcomes—severity of psychopathology, insight and social functioning—were assessed by standardised measures through clinical interviews administered by the clinicians.

Severity of psychopathology

Severity of psychopathology was assessed according to the Chinese version of the Positive and Negative Syndrome Scale (PANSS) (Si et al. 2004). PANSS scores were calculated using five dimensions: positive symptoms, negative symptoms, disorganisation symptoms, excitement and emotional distress (van der Gaag et al. 2006). The PANSS includes 30 items, each of which is scored on a seven point Likert scale (1 = absence of psychopathology; 7 = very severe symptom). PANSS has demonstrated good psychometric properties with Cronbach's alphas of 0.73, 0.83 and 0.79 for positive, negative and GPS symptoms respectively (Kay et al. 1988). The reliability and validity of the scale for Chinese patients with schizophrenia was excellent. The internal consistency with Chrobach's alpha was 0.87 (Si et al. 2004). The reliability and validity for the present study was good: the scale explained 49% of the total variance. The reliability for the scale was also good with Chrobach's alphas of 0.72 for the total scale, and 0.67, 0.71, 0.65, 0.45, and 0.72 for positive symptoms, negative symptoms, disorganization symptoms, excitement and emotional distress respectively.

Insight

Insight was assessed using the Schedule for Assessing Insight (SAI) (David 1990). SAI comprises of questions to assess three dimensions of insight: awareness, relabeling of symptoms, and attitudes to treatment. SAI was translated into Chinese and back-translated into English to ensure the accuracy of the translation. The SAI includes seven items, each of which is scored on a three point Likert scale from 0 (no insight) to 2 (good insight). The range of total scores is from 0 to 14. For this study, the internal consistency of the scale was high, with Cronbach's alpha of 0.89 for the total scale, and 0.65, 0.80, and 0.53 for awareness, relabeling of symptoms and attitudes to treatment dimensions respectively. The test-retest reliability scores were 0.74, 0.44 and 0.79 for the three dimensions.

Social functioning

Social functioning was rated using the Personal and Social Performance Scale (PSP) (Morosini et al. 2000). PSP is reliable and well established, based on the most recent version of the DSM-IV Social and Occupational Functioning Assessment Scale (SOFAS). PSP assesses routine social functioning in schizophrenia(Tianmei et al. 2011). The Chinese version of PSP was used for this study (Si et al. 2011). The PSP is a

100-point single-item rating scale derived from four functioning areas of patients with schizophrenia: (1**)** participation in social activities; (2) personal and social relations; (3) self-care; (4) interruptive or aggressive behaviour. Each functioning area is rated on a six-point Likert scale based on the degree of difficulties ranging from 0 (absence of difficulty) to 6 (severe difficulty). The overall rating system of 100-points is calculated based on the degree of difficulty across the four functioning areas. The scoring ranges from 0 to 100 with a lower score indicating a lower level of social functioning. Trained mental health professionals interviewed patients and the family members or carers who lived with or cared for the patients.

The raters were trained in the use of the above assessment instruments and were responsible for conducting face-to-face interviews with the participants. The five independent trained raters were blind to the allocation status of the participants. The intra-class correlation coefficients of all of the PANSS, SAI, and PSP scales in this study were above 0.85 after training and before commencement of the study. All the raters were retrained in the use of the assessment scales bi-monthly to prevent rater's drift. Assessments were done at baseline, week 12, week 24 (post-therapy), week 36, week 60 and week 84.

Statistical analysis

Analysis of the outcome measures followed an intention to treat framework implementing linear mixed models. The six time periods were treated as a six-level repeated measure in the analysis. Age was found to be a confounding factor (Table 1) and was controlled in all mixed models. Mixed models produce a fitted mean (intercept) for the reference level of each factor in the analysis (for these analyses, the reference treatment group being CBT and the reference time point being the baseline measures). The mixed model analyses also calculated the estimates of the effect of each factor or a combination of factors on the intercept. Main effects of treatment group and time point and the interaction between treatment group and time point were also estimated. A significant treatment group by time interaction of 84 weeks supports the hypothesis that after 84 weeks, there is a significant difference in the observed outcome measures between the two treatment groups. Differences in demographic characteristics between the groups were determined by examining 95% Confidence Intervals for the difference in means or proportions according to the distribution of the dependent variable. All tests were two-tailed with alpha set at 0.05. A 25% or greater improvement in scores of PANSS, SAI and PSP between baseline and endpoint was identified and used to support a clinically significant change (CSC). Within groups, effect sizes are adjusted for correlation between means.

Results

Sample characteristics

Ninety six patients were recruited to each arm of the trial. Table 1 shows comparisons of the demographic characteristics of the two groups. The groups were evenly

matched in terms of demographics, with the exception of age. The ST group was significantly older (mean age – 33.44 years) than the CBT group (mean age – 29.27 years). Age was therefore treated as a confounding factor in subsequent analyses.

Eighty five participants (88.5%) in the CBT group and 82 participants (85.4%) in the ST group completed the 84-week study block. There was no significant difference between treatment groups in the proportion of participants failing to complete assessment at any individual time point. The majority of participants who dropped out of the study did so directly after their baseline assessment (n=22, 88%). Twelve (6 in each group) of these participants completed more than 6 treatment sessions before discontinuing treatment. The remaining 10 (4 in CBT group and 6 in ST group) participants failed to be engaged in treatment and completed a mean number of 3 CBT or ST sessions. There was no significant difference in demographic characteristics between the treatment groups among those participants who failed to complete the study. The reasons for missing or withdrawing included wanting "new type" CBT psychotherapy after being allocated to ST; reporting a significant improvement after therapy and therefore deciding to stop therapy; expressing a dislike of the idea of doing homework; showing discouragement about the lack of rapid improvement; being unwilling to self-disclose his or her problems; and having moved to other cities or going back to work or school.

[INSERT Table 1]

Outcome Measures

There were no differences in antipsychotic medication use at baseline to week 84, both in type and dosage of chlorpromazine equivalents. The CBT group took a 349 to 360 mg/day equivalent of chlorpromazine, and the control group took a 313 to 321 mg/day equivalent of chlorpromazine from baseline to 84 weeks (see Table 2). There was also no significant difference in the number of patients who changed medications or dosages during the trial period. On average, CBT group patients spent 40.43 (SD 1.95) minutes per session over the course of treatment, and each SP group patient spent 40.06 minutes (SD, 0.83) per session. The CBT and ST groups did not differ significantly in total psychotherapy time or number of sessions received. Reduction in scores over time was observed in both CBT and SP groups in all of the outcome measures, with the exception of SAI and PSP in which a score increase over time was observed in both treatment groups (Table 3). The significant effect measured by effect size occurred from 12 weeks and after for all measures of PANSS when a comparison was made between CBT and SP group from baseline to week 84; although, the statistical significance became apparent from 36 weeks to 84 weeks. CBT patients improved to a greater extent than the SP group over time, starting from week 36, and in all measures of PANSS, PSP and SAI (See Table 4).

The mean PANSS total scores decreased

significantly over time in both treatment groups [CBT mean change 25.86 points (36.01%, SD=17.26), within groups Cohen's d=1.51, ST mean change 19.04 points (26.71%, SD=14.89), Cohen's d= 1.30]. The mixed model interaction term for treatment groups was 24 weeks and the following times were significant (p=0.045, Table 3), showing that the CBT group had a significantly lower PANSS total score after 24 weeks compared to the ST group (adjusted CBT mean of 46.70, SD=12.33; adjusted ST mean of 52.91, SD=13.43, between groups Cohen's d=0.48). Fig. 2 shows the mean PANSS total scores by treatment groups at each time point.

A significant decrease in PANSS positive and negative symptoms was observed in both groups. For PANSS positive symptoms, the results were: CBT mean change 10.51 points (44.83%, SD=7.79), within groups Cohen's d=1.36, ST mean change 7.44 points (33.19%, SD=7.17), d=1.1. For PANSS negative symptoms, the results were: a CBT mean change of 5.85 points (29.92%, SD=6.71); within the groups, Cohen's d=0.83, and ST mean change was 4.57 points (21.92%, SD=6.15), d=0.74.

The interaction term of 84 weeks for the treatment group was significant for the positive symptoms (whereby p=0.018, Table 3). This demonstrates that the CBT group had significantly lower PANSS positive symptoms score after 84 weeks compared to the ST group (adjusted CBT mean of 13.18, SD=5.03; adjusted ST mean of 15.34, SD=5.26 , between groups Cohen's d=0.42). The interaction term of treatment group at 84 weeks was not significant for the negative symptoms subscale and therefore did not support a benefit of CBT over ST (Fig. 3 & 4).

There was also a significant decrease over time in PANSS disorganisation symptoms in both treatment groups: CBT mean change was 8.56 points (36.47%, SD=7.42), d=1.19; for ST the mean change was 5.96 points (25.43%, SD=6.32), d=0.92. There was no evidence of a benefit of CBT over ST at 84 weeks. The PANSS excitement subscale also showed a significant decrease over time in both treatment groups: for CBT the mean change was 4.53 points (29.98%, SD = 4.54), d=1.32; for ST the mean change was 3.45 points (20.73%, SD=4.8), d=0.69. However, there was no evidence at 84 weeks that CBT provided a benefit over ST. The PANSS emotional distress subscale decreased over time in both treatment groups: for CBT the mean change was 8.24 points (40.05%, SD=7.44), d=1.15; for ST the mean change was 6.06 points (29.65%, SD=5.64), d=1.40. The mixed model interaction term for treatment groups at 84 weeks was approaching significance (p=0.053, Table 3). The mean score of PANSS disorganisation symptoms, excitement and emotional distress decreased over time in both treatment groups (Fig. 5, 6, 7).

The mean SAI total score increased significantly over time by an average of 3.98 points (66.14%, SD=4.29) in the CBT group (within groups Cohen's d=-0.97) and by 2.37 points (40.38%, SD=4.86) in the ST group (d=-0.51). The interaction term of treatment group and time at 84 weeks was approaching statistical significance

(p=0.055, Table 3), indicating further improvement in the SAI total score after 84 weeks in the CBT group compared to the ST group. Mean SAI score by treatment group and time point is shown in Fig. 8.

Over the study period, the mean PSP total score increased significantly by an average of 22.27 points (45.96%, SD=15.86) in the CBT group (within groups Cohen's d=-1.45) and 15.89 points (32.01%, SD=16.31) in the ST group (d=-0.95). The mixed model interaction term of treatment group at 84 weeks was significant (p=0.037, Table 3). This showed that the CBT group had a significantly higher PSP total score after 84 weeks of treatment compared to the ST group. CBT group had am adjusted mean of 73.70, SD=13.73; the adjusted ST mean was 64.30, SD=15.16, between groups Cohen's d=0.64. Mean PSP score by treatment group and time point is shown in Fig. 9.

Over three quarters (65, 76.5%) of the CBT group made a significant clinical improvement, showing a 25% or more reduction in PANSS total score from the baseline, compared with 53.70% in the ST group (χ^2=9.35, P=0.002).

Discussion

This was the first randomised controlled trial using standardised cognitive-behavioural therapy for patients with schizophrenia in China. The study employed key cognitive and behavioural strategies that were adapted to suit this demographic of patients suffering from schizophrenia in China. Compared to ST, CBT showed a significantly greater and more durable effect on PANSS total score and PSP and SAI from week 36. Additionally, more participants in the CBT group achieved a more significant clinical improvement in PANSS total score, which indicated that receiving CBT increased the probability of meaningful symptom reduction.

The significant effect (as measured by the effect size shown in both CBT groups in most of the PANSS measures, SAI and PSP in 12 weeks) suggest that rapid change occurs in the first 12 weeks. This is consistent with Drury et al., who showed that CBT reduced positive symptoms and improved learnt insight at a faster rate during the first 12 weeks (Drury et al. 2000). Drury et al. also found more rapid improvement in clinical recovery, as measured by increased insight, less dysphoria and 'low level' psychotic thinking, and less disinhibition (Drury et al. 2000). This is consistent with the aim of CBT (but not supportive therapies) to develop new skills and enduring ways of coping with psychosis during the first 12 weeks. Cognitive and behavioural skills need at least 12 weeks to be learnt and put into practice; only then can the gains be consolidated. This was demonstrated in the follow-up stage that took place between weeks 24 to 84. Additionally, assigning and completing homework is a possible core mechanism to promote and sustain change gained during the first 12 weeks of CBT sessions (Kazantzis et al. 2010).

This study demonstrated the superiority of CBT over ST; the former had a durable effect on overall symptoms, and posi-

tive symptoms emerged after the completion of therapy in week 36. This is consistent with findings in similar studies in the UK, in which there were positive benefits of both ST and CBT but the CBT continued to show improvements whereas the ST began to lose effectiveness after it had been discontinued (Sensky et al. 2000). Our findings, showing an improvement in overall and positive symptoms during the course of treatment in the CBT group, are in line with Tarrier et al (Tarrier et al. 1998). These researchers found significant improvements in the severity and number of positive symptoms for patients treated with CBT(Tarrier et al. 1998). This was also in accordance with Zimmermann et al.'s meta-analysis (Zimmermann et al. 2005). This study concluded that CBT is a promising adjunctive treatment for positive symptoms in schizophrenia spectrum disorders. The positive effect of CBT in reducing positive symptoms may be due to both non-specific and specific factors of CBT, such as therapeutic alliance, normalisation, the psychotic experience, modification of dysfunctional cognitions and behaviours (Warman and Beck 2003) by examining the evidence, compensating for reasoning biases by using disconfirmation strategies, and developing rational explanations(Kuipers et al. 2006). Furthermore, building coping strategies is one of the most valuable CBT methods for helping people manage psychotic symptoms (Kingdon and Turkington 2008).

This study also showed that CBT could significantly improve social functioning in people with schizophrenia. CBT teaches or enhances personal coping strategies that allow patients to manage their symptoms and daily hassles more effectively. To support the contention that the above mechanisms lead to clinical improvement, Grant et al. proposed that these CBT techniques can trigger a cycle of functional recovery because dysfunctional 'self-defeating' beliefs or behaviours may inhibit a patient's active engagement in constructive activities (Grant et al. 2012).

Compared to ST, CBT failed to demonstrate statistical superiority in negative symptoms, disorganisation symptoms and excitement; however, it approached significance in reducing emotional distress. Alternative approaches may be required for these symptoms that may be influenced more by biological and cognitive dysfunctions.[36] Alternatively, research studies have compared the effectiveness of CBT with that of ST for psychosis and proposed that ST has important but non-trivial effects on a variety of clinical outcomes (Penn et al. 2004; Penn et al. 2009). Furthermore, psychotherapy might assist persons to recover by helping them develop more complex ideas about themselves and others and not just by correct discrete dysfunctional cognitions (Lysaker et al. 2010).

This study integrated Chinese cultural values and practices into the use of CBT. For example, the more hierarchical approach to the doctor-patient relationship could be geared to the therapist's advantage in the early phase of engagement in CBT. However, the emphasis then needed to shift to a more collaborative relationship, with encouragement of the patient contributing

to the therapy.[39] Higher levels of employment were seen in the patient group, as a whole, which was possibly due to financial pressures. In Chinese culture, family members play an important role in providing care, and offering support for returning to or maintaining employment. Therefore, expectations are raised (Naeem and Kingdon 2011). These cultural factors could have a mixed effect on a patient, but could also have enhanced social skills training and coping strategies enhancement in the CBT group. Family members were actively encouraged to participate in the therapy and help patients (although formal family work was not part of the intervention). This study also differed from patient presentation in Western studies, for example: the virtual absence of stimulant and cannabis misuse in the patient group.

The study had a number of limitations. Although peers or specialists supervised the therapists regularly, the competence of the CBT therapists was not assessed with taped sessions and objective scales. However, all trial therapists were experienced psychiatrists or psychologists who have received substantial amounts of training in CBT by recognised experts in the field and have passed the criterion level of competence before commencing the trial. Furthermore, the absence of a treatment-as-usual arm did not rule out the benefits of CBT and ST being attributed to spontaneous remission with time.[38] However, the specific benefit of CBT over ST in sustaining improvement in various outcome measures suggests a unique advantage of CBT over ST. Moreover, the findings of the current study are demonstrably more effective than TAU in both Western and native researches studies (Kumari et al. 2011; Rector and Beck 2012; Wykes et al. 2008; XU and Li 2007).

Conclusion

In comparison to the ST group, the CBT group showed a significant improvement in all measures of PANSS, PSP and insight. The CBT group had superior effects to SP in positive symptoms and total scores of the PANSS, as well as a significant improvement in social functioning as assessed by the PSP. CBT is a useful adjunct treatment to medication, with a durable effect at follow-up in people with schizophrenia in China.

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Table 1: Comparison of demographic data between treatment groups

Characteristics	CBT			ST			95% CI
	N	Mean	SD	N	Mean	SD	Diff in means
Age, y	96	29.27	8.36	96	33.44	9.51	1.62 to 6.72
Education, y	96	13.21	2.61	96	13.21	2.65	-0.75 to 0.75
Duration of schizophrenia, months	96	91.18	77.88	96	105.89	96.87	-39.73 to 10.31
No of hospital admissions	96	1.69	1.79	96	1.89	1.70	-0.70 to 0.30
Chlorpromazine equivalents at Baseline, mean, mg	96	340.23	185.29	96	344.87	160.22	-54.52 to 45.25
Psychotherapy duration, minutes	85	602.47	19.77	82	598.90	15.60	-1.89 to 9.02
	N	%		N	%		Diff in proportions
% Han ethnic group	93	96.9		93	96.9		-4.9% to 4.9%
% Male	32	33.3		40	41.7		-21.9% to 5.3%
% Single	70	72.9		58	60.4		-0.7% to 25.7%
% Unemployed	42	43.8		51	53.1		-23.5% to 4.7%
% Atypical antipsychotic medication	84	87.5		89	92.7		-0.4% to 1.7%

CI: Confidence interval.

Table 2
chlorpromazine dosage use

Variables	CBT	Control	t	p
Chlorpromazine use at baseline	360.60(186.07)	321.53(169.22)	1.542	.125
Chlorpromazine use at 12 weeks	349.80 (187.48)	313.37(158.23)	1.376	.171
Chlorpromazine use at 24 weeks	356.08 (188.31)	318.65(167.23)	1.369	.173
Chlorpromazine use at 36 weeks	351.88(188.3))	316.46(166/.85)	1.289	.199
Chlorpromazine use at 60 weeks	349.68(188.03)	316.46(166.85)	1.210	.228
Chlorpromazine use at 84 weeks	351.32 (188.14)	315.63 (168.34)	1.289	.199

Table 3 Assessment of CBT and ST groups (Mean, SD, 95% CI) during the intervention and follow-up period

Assessment	Mean, SD (95% CI)							Change 0-84 weeks Mean, SD, % change
	Baseline	Week 12	Effect size	Week 24	Week 36	Week 60	Week 84	
PANSS_ total								
CBT	73.00, 13.04 (70.36-75.64)	57.03, 13.08 (54.23-59.83)	**1.22**	51.32, 13.25 (48.44-54.20)	48.79, 12.52* (46.04-51.54)	48.99, 12.84** (46.19-51.79)	46.71, 13.12** (43.85-49.57)	25.86, 17.26, 36.01%
ST	72.19, 11.02 (69.96-74.42)	58.39, 11.92 (55.82-60.96)	**1.20**	52.23, 12.65 (49.45-55.01)	52.88, 13.64 (49.86-55.90)	54.71, 14.3 (51.57-57.85)	52.91, 14.45 (49.73-56.09)	19.04, 14.89, 26.71%
PANSS_positive								
CBT	23.89, 5.76 (22.72-25.06)	17.13, 5.52 (15.95-18.31)	**1.19**	15.23, 5.78 (13.98-16.48)	14.17, 5.76 (12.90-15.44)	13.55, 5.41 (12.37-14.73)	13.18, 5.35 (12.03-14.33)	10.51, 7.79, 44.83%
ST	22.96, 5.01 (21.94-23.98)	17.34, 4.82 (16.30-18.38)	**1.14**	15.04, 5.12 (13.92-16.16)	15.37, 5.32 (14.19-16.55)	15.67, 5.02 (14.57-16.77)	15.34, 5.67 (14.09-16.59)	7.44, 7.17, 33.19%
PANSS_negative								
CBT	19.99, 5.96 (18.78-21.20)	16.66, 5.44 (15.49-17.83)	**0.58**	15.51, 5.66 (14.28-16.74)	15.01, 5.58 (13.78-16.24)	15.67, 5.75 (14.41-16.93)	14.01, 5.18 (12.89-15.13)	5.85, 6.71, 29.91%
ST	20.80, 5.66 (19.65-21.95)	17.99, 5.35 (16.83-19.14)	**0.51**	16.45, 5.63 (15.21-17.69)	16.42, 5.80 (15.14-17.70)	17.21, 6.20 (15.85-18.57)	16.24, 6.45 (14.82-17.66)	4.57, 6.15, 21.92%
PANSS_Disorganization								
CBT	23.69, 6.23 (22.43-24.95)	18.81, 4.80 (17.78-19.84)	**0.88**	16.92, 4.55 (15.93-17.91)	16.27, 4.31 (15.32-17.22)	15.36, 3.95 (14.50-16.22)	15.05, 4.14 (14.16-15.94)	8.56, 7.42, 36.47%
ST	22.93, 5.62 (21.79-24.07)	18.95, 5.22 (17.82-20.08)	**0.73**	17.05, 4.47 (16.07-18.03)	17.04, 4.53 (16.03-18.04)	17.38, 4.48 (16.40-18.36)	17.10, 4.73 (16.06-18.14)	5.96, 6.32, 25.43%
PANSS_Excitement								
CBT	16.28, 3.72 (15.53-17.03)	12.93, 3.69 (12.14-13.72)	**0.90**	11.77, 3.72 (10.96-12.58)	11.45, 3.21 (10.83-12.25)	12.05, 3.66 (11.25-12.84)	11.40, 3.35 (10.68-12.12)	4.53, 4.54, 29.98%
ST	16.55, 3.82 (15.78-17.32)	13.49, 3.18 (12.114-13.72)	**0.87**	12.51, 3.59 (11.72-13.30)	12.81, 4.04 (11.92-13.70)	13.24, 4.62 (12.22-14.26)	13.12, 4.24 (12.19-14.05)	3.45, 4.80, 20.73%
PANSS_Emotional								
CBT	20.90, 6.13 (19.66-22.14)	15.41, 4.90 (14.36-16.46)	**1.0**	13.44, 4.17 (12.54-14.34)	12.82, 4.21 (11.89-13.74)	13.10, 4.18 (12.19-14.01)	12.53, 4.18 (11.62-13.43)	8.24, 7.44, 40.05%
ST	20.20, 4.74 (19.24-21.16)	15.71, 4.40 (14.76-16.66)	**0.98**	13.70, 4.12 (12.79-14.61)	14.09, 4.73 (13.04-15.14)	14.61, 4.31 (13.66-15.56)	14.21, 4.52 (13.22-15.20)	6.06, 5.64, 29.65%
SAI								
CBT	6.22, 3.85 (5.44-7.00)	8.80, 3.74 (8.00-9.60)	**0.68**	9.82, 3.67 (9.02-10.62)	10.05, 3.65 (9.25-10.85)	10.17, 3.65 (9.37-10.97)	10.38, 3.67 (9.58-11.17)	3.98, 4.29, 66.14%
ST	6.29, 4.25	8.22, 3.90	**0.47**	8.91, 4.03	8.78, 4.02	8.71, 3.99	8.83, 4.08	2.37, 4.86, 40.38%

	(5.43-7.15)	(7.38-9.06)		(8.02-9.80)	(7.89-9.67)	(7.83-9.59)	(7.93-9.73)	
PSP								
CBT	50.48, 12.85 (47.88-53.08)	61.99, 12.91 (59.22-64.76)	**0.89**	66.96, 11.04 (64.56-69.36)	70.35, 13.6 (67.34-73.36)	71.54, 13.97 (68.49-74.59)	73.68, 14.6 (70.53-76.83)	22.27, 15.86, 45.96%
ST	48.73, 13.42 (46.13-51.33)	58.33, 13.24 (55.47-61.19)	**0.72**	63.68, 13.56 (60.70-66.66)	63.63, 15.77 (60.14-67.12)	62.39, 15.87 (58.90-65.88)	64.33, 16.36 (60.74-67.92)	15.89, 16.31, 32.01%

PANSS: Positive and Negative Syndrome Scale; SAI: Schedule for Assessing Insight; PSP: Personal and Social Performance Scale; NS: non significant; CI: Confidence interval.

Table 4
Difference between CBT and SP group in PANSS, insight and PSP scores from baseline to 84 weeks assessment

Variables	**Control (n=90)**	**CBT (n-87)**	***T***	***p***	**Effect size**
PANSS baseline	72.77(10.90)	72.92(13.03)	-0.072	0.943	0.01
PANSS 12 weeks	58.84(11.60)	57.01(13.15)	0.948	0.345	**0.15**
PANSS 24 weeks	52.53(12.79)	51.30(13.33)	0.6	0.549	**0.10**
PANSS 36 weeks	53.09(13.69)	48.75(12.60)	2.074	**0.04**	**0.33**
PANSS 60 weeks	54.86(14.46)	49.05(12.91)	2.684	**0.008**	**0.42**

PANSS 84 weeks	53.00(14.60)	46.75(13.19)	2.863	**0.005**	**0.45**
PSP baseline	47.40(13.11)	51.09(12.46)	-1.918	0.057	0.29
PSP 12 weeks	58.01(13.37)	62.06(12.97)	-1.979	**0.049**	0.31
PSP 24 weeks	63.51(13.87)	67.05(11.08)	-1.792	0.075	0.28
PSP 36 weeks	63.36(16.11)	70.48(13.73)	-3.004	**0.003**	**0.48**
PSP 60 weeks	62.17(16.22)	71.68(14.00)	-3.979	**<0.001**	**0.63**
PSP 84 weeks	64.12(16.72)	73.85(14.61)	-3.946	**<0.001**	**0.62**
Insight baseline	6.08(4.06)	6.36(3.83)	-0.464	0.643	0.07
Insight 12 weeks	8.18(3.90)	8.86(3.73)	-1.137	0.257	**0.18**
Insight 24 weeks	8.83(4.07)	9.89(3.64)	-1.741	0.084	**0.28**
Insight 36 weeks	8.77(4.03)	10.12(3.61)	-2.232	**0.027**	**0.35**
Insight 60 weeks	8.65(3.98)	10.24(3.61)	-2.653	**0.009**	**0.42**
Insight 84 weeks	8.78(4.07)	10.44(3.65)	-2.735	**0.007**	**0.43**

Notes. Statistical significance: $p < 0.05$; Effect size: 1.0-1.90 small effect size, 0.20 to 0.39 moderate level Effect size, 0.40 and more: big effect size.

Table 5: Mixed models analysis of outcome measures

Outcome Measure 84 weeks	PANSS total	PANSS positive	PANSS negative	PANSS disorganization	PANSS excitement	PANSS emotional	SAI	PSP
Parameter Estimate	-5.60	-2.80	-0.94	-2.02	-1.32	-2.07	1.63	6.57
95% CI	-11.09 to 0.11	-5.13 to -0.47	-1.54 to 3.42	-4.21 to 0.16	-2.94 to 0.30	-4.16 to 0.03	-0.04 to 3.30	0.41 to 12.73
t	$t_{325} = 2.01$	$t_{344} = 2.37$	-	-	-	$t_{350} = 1.94$	$t_{349} = -1.92$	$T_{324} = -2.10$
P	0.045	0.018	NS	NS	NS	0.053	0.055	0.037

PANSS: Positive and Negative Syndrome Scale; SAI: Schedule for Assessing Insight; PSP: Personal and Social Performance Scale; NS: non significant; CI: Confidence interval.

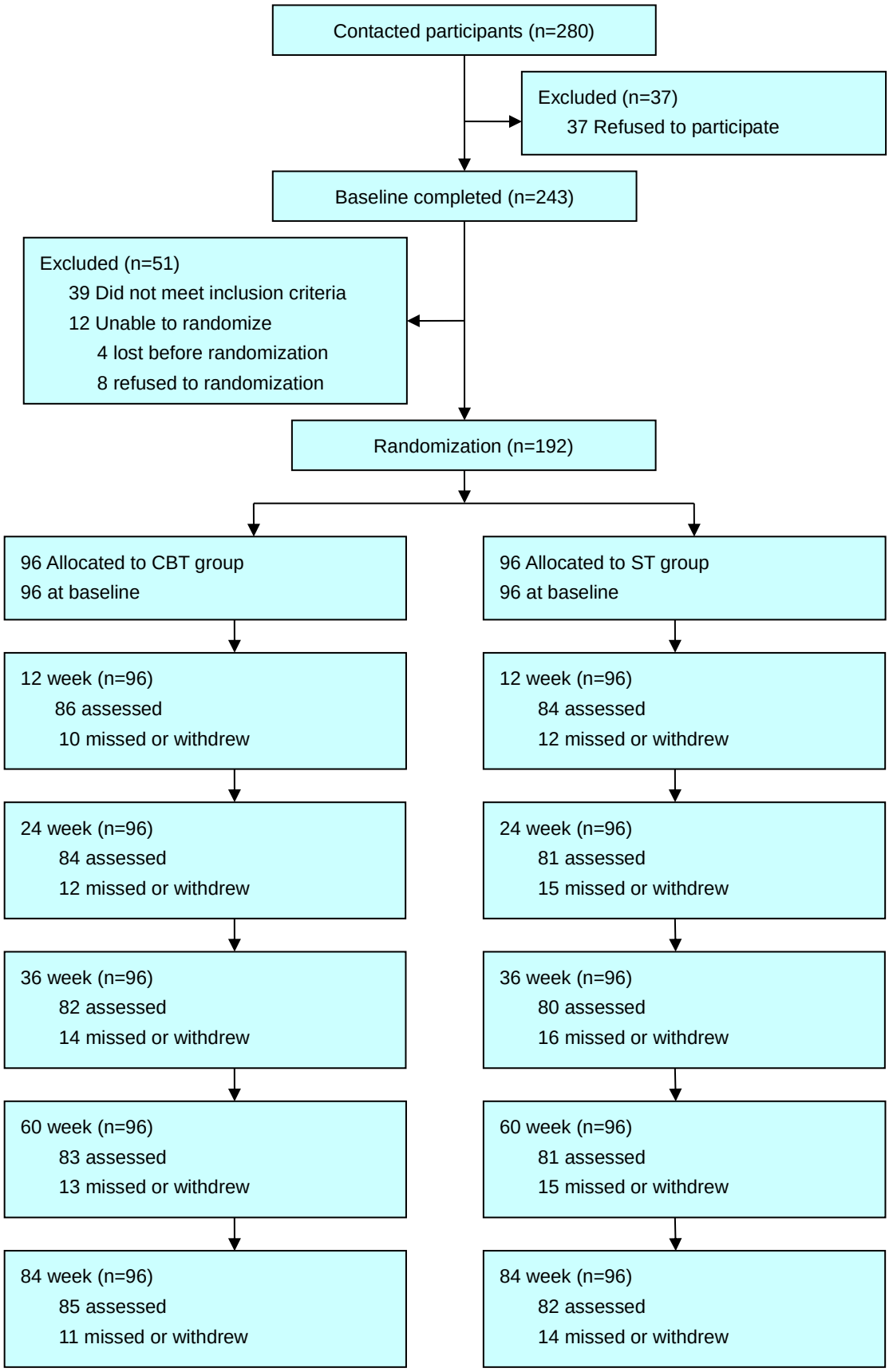

Figure 1. CONSORT diagram. CBT: Cognitive-Behavioural Therapy, ST: Supportive Therapy

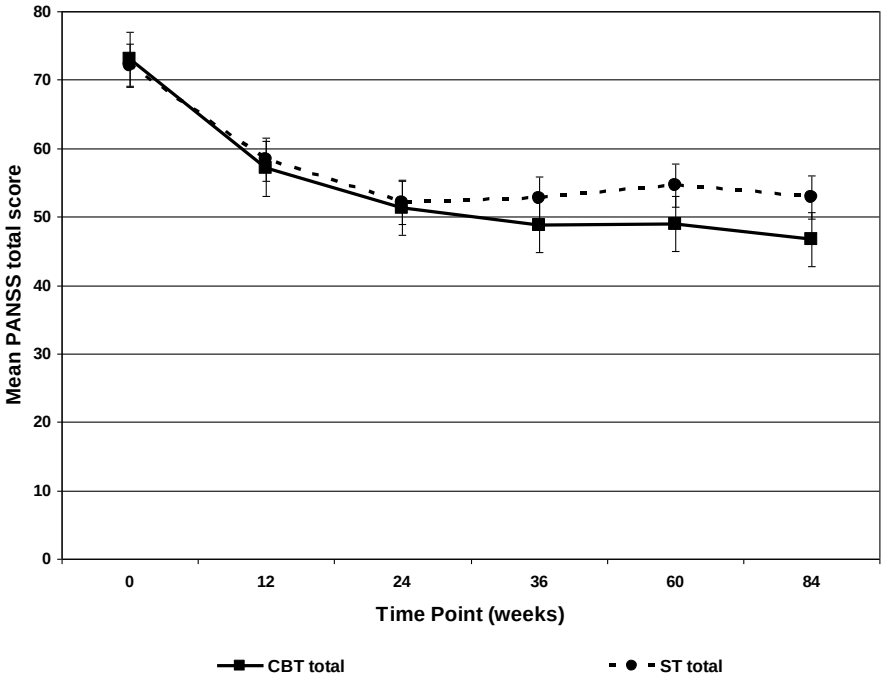

Figure 2: Mean (SE) PANSS total score by time point.

Baseline means are raw means, all other means are adjusted to include values from the mixed models

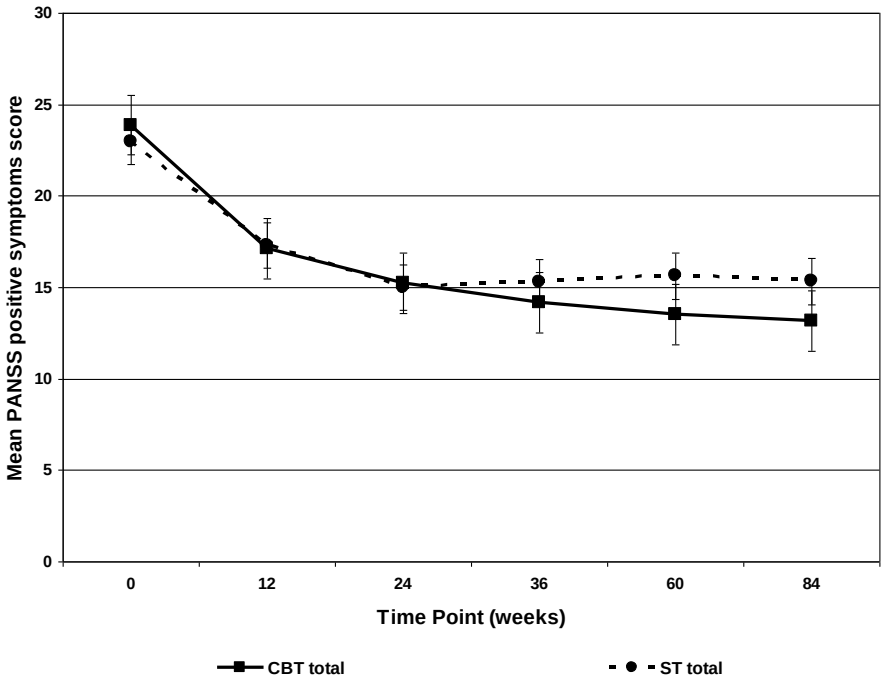

Figure 3: Mean (SE) PANSS positive symptoms score by time point.

Baseline means are raw means, all other means are adjusted to include values from the mixed models

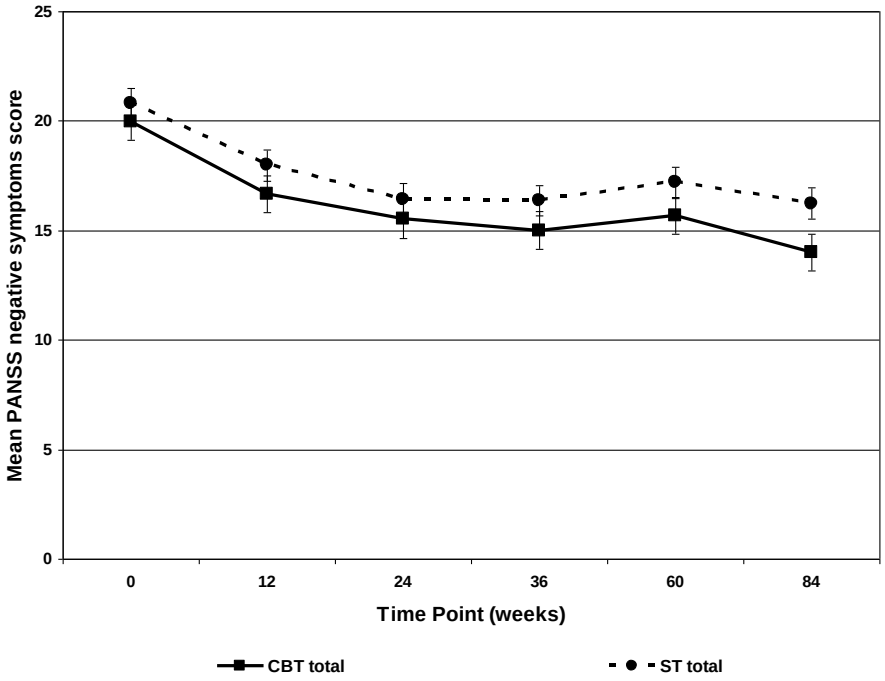

Figure 4: Mean (SE) PANSS negative symptoms score by time point.

Baseline means are raw means, all other means are adjusted to include values from the mixed models

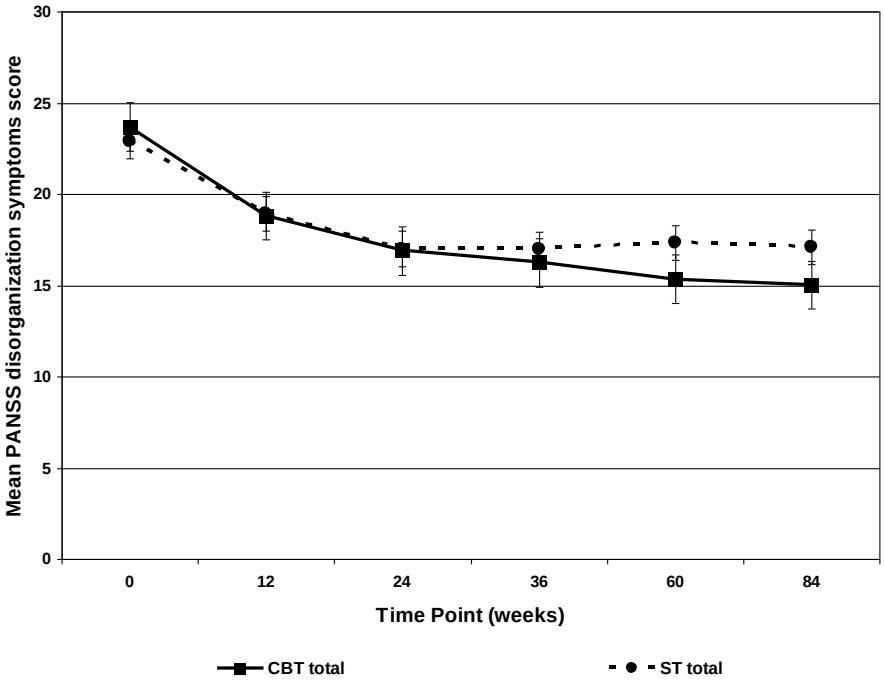

Figure 5: Mean (SE) PANSS disorganization symtoms score by time point.

Baseline means are raw means, all other means are adjusted to include values from the mixed models

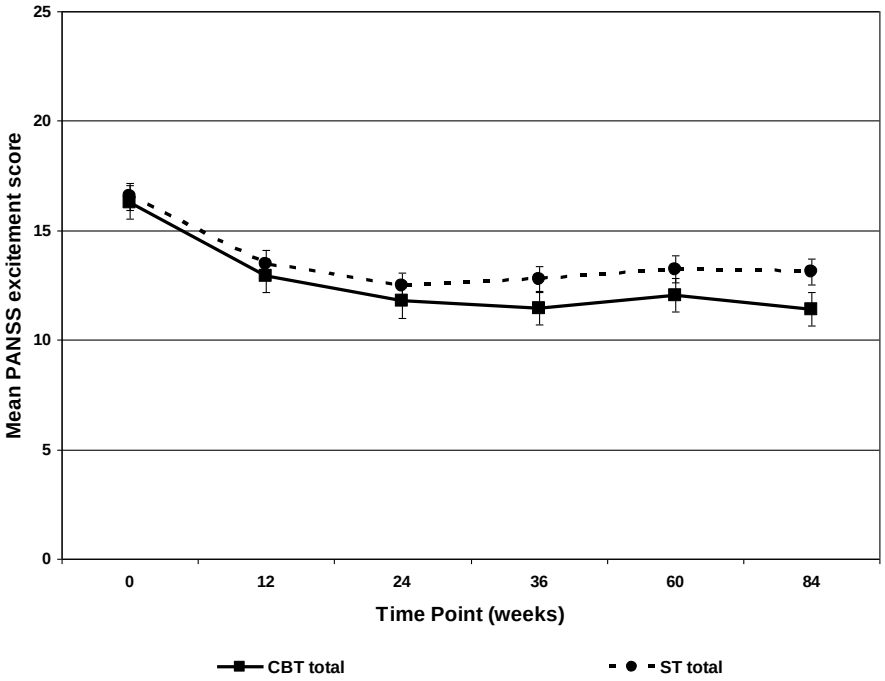

Figure 6: Mean (SE) PANSS excitement score by time point.

Baseline means are raw means, all other means are adjusted to include values from the mixed models

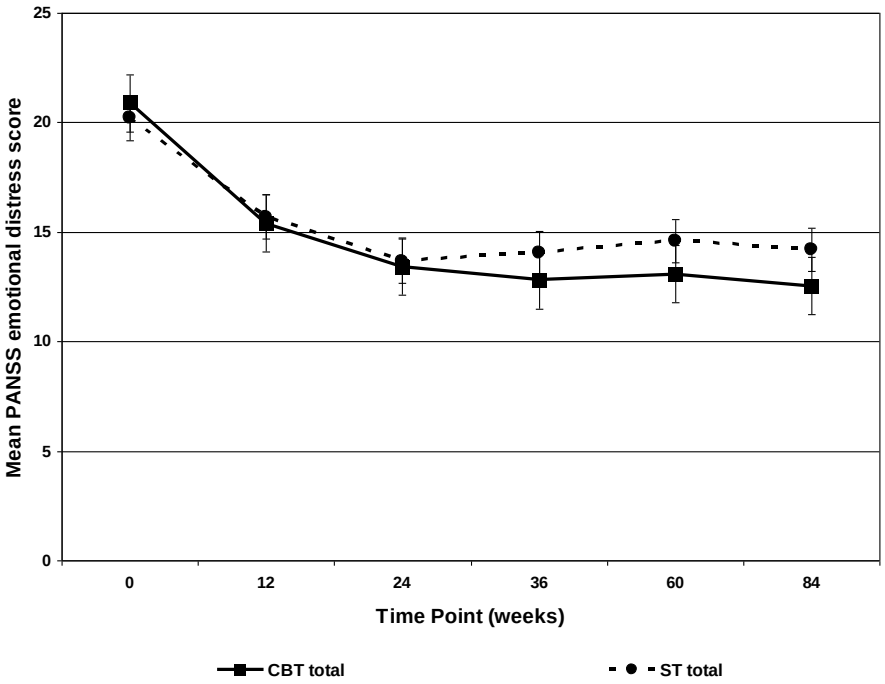

Figure 7: Mean (SE) PANSS emotional distress score by time point.

Baseline means are raw means, all other means are adjusted to include values from the mixed models

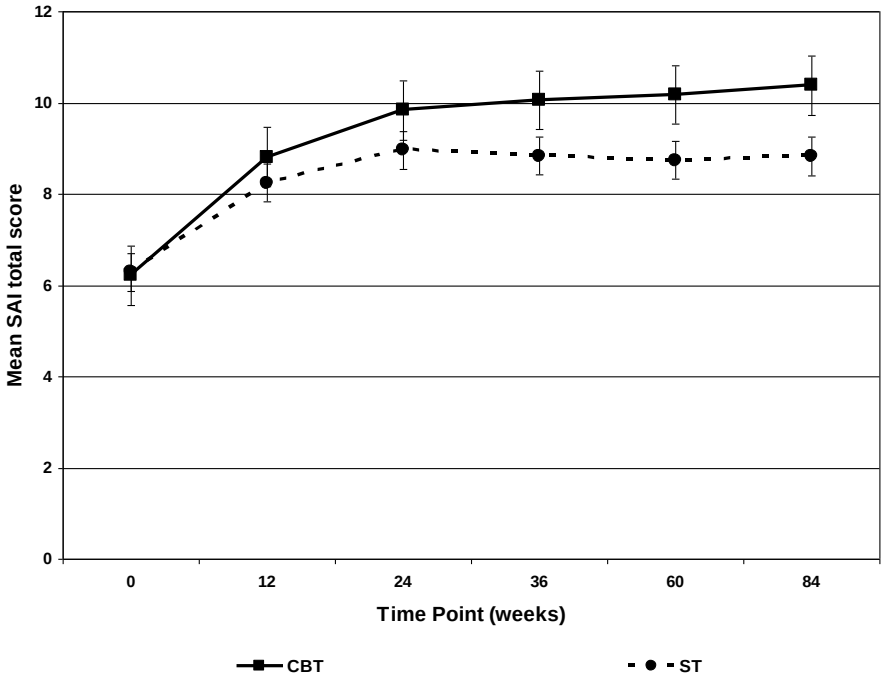

Figure 8: Mean (SE) SAI total score by time point.

Baseline means are raw means, all other means are adjusted to include values from the mixed models

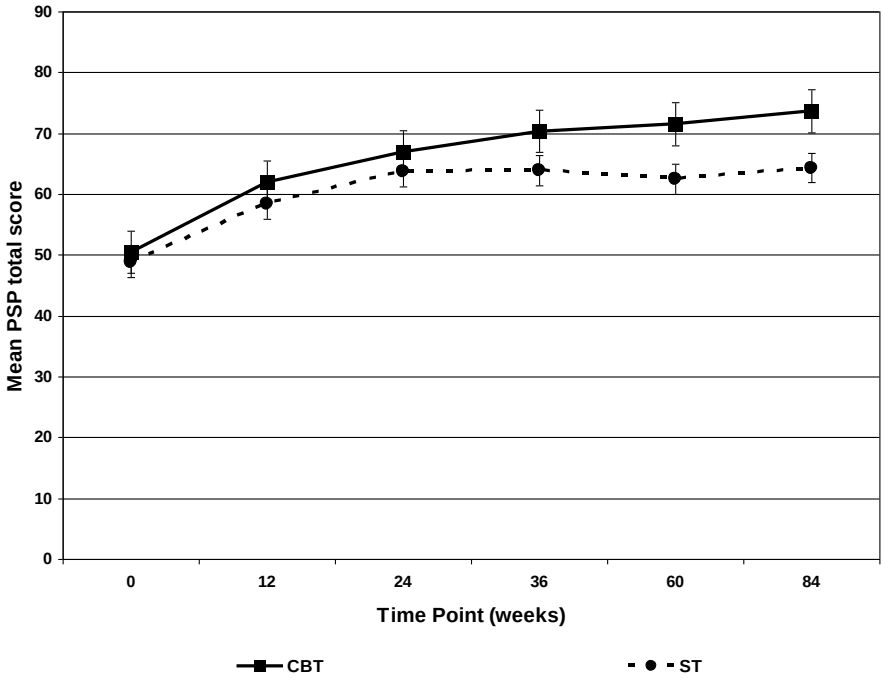

Figure 9: Mean (SE) PSP total score by time point.

Baseline means are raw means, all other means are adjusted to include values from the mixed models