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ORIGINAL ARTICLE

Cognitive–behavioural therapy for patients with schizophrenia: a multicentre randomized controlled trial in Beijing, China

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Background. Meta-analyses support the efficacy of cognitive–behavioural therapy (CBT) for schizophrenia in western cultures. This study aimed to compare the efficacy of CBT and supportive therapy (ST) for patients with schizophrenia in China.

Method. A multicentre 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 an additional 60 weeks. All measures used were standardized instruments with good reliability and validity. The Positive and Negative Syndrome Scale (PANSS) was used to assess symptoms of schizophrenia. The Schedule for Assessing Insight (SAI) was used to assess patients' insight and the Personal and Social Performance Scale (PSP) was used to assess their social functioning.

Results. Effect-size analysis showed that patients made rapid improvements in all symptoms, insight and social functioning as measured by the PANSS, SAI and PSP at 12 and 24 weeks and maintained these improvements over the course of the study to 84 weeks. Patients in the CBT group showed significantly greater and more durable improvement in PANSS total score ($p = 0.045$, between-group $d = 0.48$), positive symptoms ($p = 0.018$, between-group $d = 0.42$) and social functioning ($p = 0.037$, between-group $d = 0.64$), with significant differences emerging after completion of therapy.

Conclusions. Both CBT and ST combined with medication had benefits on psychopathology, insight and social functioning of patients with schizophrenia. CBT was significantly more effective than ST on overall, positive symptoms and social functioning of patients with schizophrenia in the long term.

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Key words: Cognitive–behavioural therapy, randomized controlled trials, schizophrenia, supportive therapy.

Introduction

Schizophrenia is a disabling mental disorder. However, the potential for recovery is increasingly being recognized. Schizophrenia affects approximately 0.7% of people at some point in their lives worldwide (World Health Organization, 2011). This translates to approximately five million people in China, representing over 20% of the total 24 million people suffering from the disorder worldwide (World Health Organization, 2011).

The primary treatment for schizophrenia continues to be pharmacotherapy (National Institute for Clinical Excellence, 2003). However, long-term pharmacotherapy is associated with a range of adverse effects and poor adherence (Velligan *et al.* 2006). It is limited in improving clinical symptoms, personal and social functioning and patients often have a high risk of relapse (Freeman *et al.* 1998; Tarrier *et al.* 2004; Rathod *et al.* 2008; Morrison, 2009; Morrison *et al.* 2011). Certain psychosocial treatments, such as cognitive–behavioural therapy (CBT), have been shown to

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have a beneficial effect on positive and negative symptoms, mood, social functioning and social anxiety and may be effective in reducing readmissions to hospital and duration of admission in Western clinical practice (Lysaker *et al.* 2004; Wykes *et al.* 2008).

CBT has been recommended as a standard treatment for patients with schizophrenia in Western countries (Kreyenbuhl *et al.* 2010; National Institute for Health and Care Excellence, 2014). Guidelines for the use of CBT have been provided by the National Institute for Health and Clinical Excellence (2009) and the Schizophrenia Patient Outcomes Research Team (Kreyenbuhl *et al.* 2010).

When using CBT as a treatment for schizophrenia, studies have focused on addressing positive and negative symptoms, mood and social anxiety (Wykes *et al.* 2008). Emerging evidence indicates that deficits in social functioning are prominent in patients with schizophrenia (Apiquian *et al.* 2009; Brissos *et al.* 2012). Assessing social functioning is therefore important in the antipsychotic (American Psychiatric Association, 2000) and psychosocial treatment of schizophrenia (Burns & Patrick, 2007). Insight is also critical for compliance and engaging patients in a treatment process (Rathod *et al.* 2008).

Previous published studies used supportive therapy (ST) as a comparative group and demonstrated that both CBT and ST have an effect on improving symptoms of schizophrenia due to the non-specific elements such as support and treatment alliance (Tarrier *et al.* 1998; Penn *et al.* 2009). It has also been confirmed that CBT is significantly more efficacious than ST (Turner *et al.* 2014). However, published studies vary in their methodological rigour, either through small sample sizes or inadequate blinding. CBT is not widely accessible to people with schizophrenia in China, although there are a limited number of studies on the effectiveness of CBT for Chinese schizophrenic patients (Wang *et al.* 2004; Jiang *et al.* 2008). All of these studies focused on teaching communication skills, promoting medication compliance and conducting psychoeducation, that is, educating patients to recognize the nature and characteristics of schizophrenia (Jiang *et al.* 2008). A formally developed procedure based on CBT principles that target specific cognitive and behavioural skills for psychosis treatment is lacking and the therapists have not received regular training and supervision in China (Wang *et al.* 2004). There is no robust evidence involving multicentre randomized controlled trials with fully powered clinical samples that CBT is effective to reduce symptoms in Chinese patients with schizophrenia over and above the effects of comparative approaches. This study therefore tested the hypothesis that CBT is effective and has a beneficial effect in Chinese schizophrenia patients in comparison with ST on overall symptoms (primary outcome measure), positive and negative symptoms, disorganization symptoms, excitement and emotional distress, as well as insight and social functioning.

Method

Participants

This study was conducted at three specialized psychiatric hospitals in Beijing, China. Patients were recruited from in-patient units or out-patient 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 (First & Gibbon, 1997) by raters who were well-trained research psychiatrists; a Positive and Negative Syndrome Scale (PANSS) total score greater than 60 indicating at least a mild level of psychiatric symptoms (Zuo *et al.* 2006; Alphs *et al.* 2013); on an adequate dose of an antipsychotic medication for at least the prior 4 weeks; capable of providing written 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 chlorpromazine daily, including a minimum period of at least 2 weeks of treatment with the equivalent of 600 mg chlorpromazine.

Participants were excluded if they met the following exclusion criteria: a co-morbid diagnosis of mental retardation or primary substance dependence; a score of $\geqslant 5$ (worse) of conceptual disorganization according to the PANSS, which included those who could not communicate, had poor rapport, or lack of spontaneity and flow of conversation; had received electroconvulsive therapy within the past 6 months prior to entry into the study; currently receiving other types of systematic psychotherapy. See Fig. 1 for the CONSORT (Consolidated Standards of Reporting Trials) diagram for the trial.

Sample-size calculation

The sample-size calculation was based on a previous randomized controlled trial of a similar design in the UK, which resulted in a recovery rate of 63% in the CBT group compared with 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 α-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.

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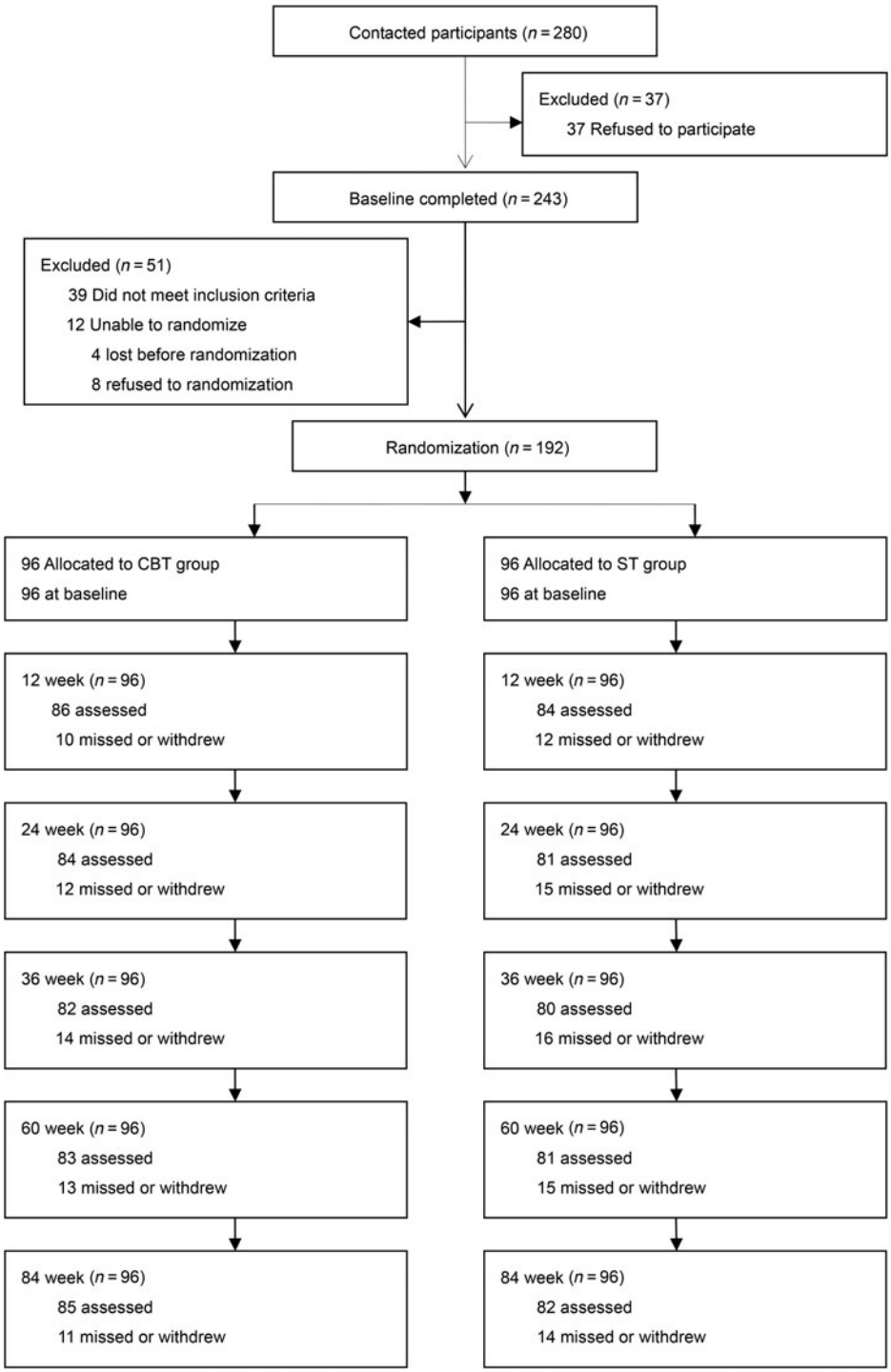

Fig. 1. CONSORT (Consolidated Standards of Reporting Trials) diagram. CBT, Cognitive–behavioural therapy; ST, supportive therapy.

Procedures

Participants deemed eligible for the trial were randomly allocated to the CBT group or the ST group (1:1 randomization). Block randomization 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

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period followed by 60 weeks of follow-up. The trial was registered in the China Clinical Trial Center with reference number ChiCTR-TRC-08000124 (http://www.chictr.org/cn/proj/search.aspx).

Interventions

Medications

Medication prescription was not affected 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 (Sim *et al.* 2004).

CBT

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 booster sessions in the subsequent 12 weeks. Each session lasted for about 40–50 min and flexibility on time was given 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 & 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 were tested on 10 patients with schizophrenia.

The first four sessions were delivered twice a week and focused on the introduction of the treatment, building a therapeutic alliance, psycho-education about the cognitive–behavioural model of psychosis and normalization of the experience of psychosis. The next six sessions in the intermediate stage were offered once a week. These sessions involved cognitive–behavioural work with delusions, hallucinations, negative symptoms and anxiety/depression. Homework was also assigned in a flexible manner after each session to consolidate what was learned in the session. The two sessions in the final phase were delivered once every 2 weeks. They included a discussion of attitudes to medication and relapse prevention work. Finally, three booster sessions were offered once monthly for reviewing patients' progress and consolidating what patients had learned of CBT strategies for coping with future problems related to the recurrence of psychotic symptoms.

ST

ST 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 40–50 min. This intervention is based on supportive models of psychotherapy and has been reported to be the most widely practised 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 psychoeducation to patients. However, ST did not have a therapeutic component and did not have a treatment structure. For example, patients could select session topics such as discussing interests, personal experiences and expressing feelings. Therapists were non-directive but used reflective listening and summarizing 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 5 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 (D. K., D.T. and R.M.K.N.) (Kingdon & Turkington, 2004). The on-site training courses of CBT for schizophrenia lasted more than 100 h throughout the trial period, including didactic teaching, case presentation, *in vivo* demonstration of skills and role play.

Supervision

Psychotherapy was supervised in three ways: peer supervision, expert supervision in CBT, and consultation on culturally related issues. During peer supervision, the therapists 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. 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. Supervision was delivered once every 2 weeks by an expert therapist in CBT for psychosis (D.K.) from the UK via phone, Skype or email. The principal investigator (Z.-J.L.), 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 institutional review boards 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 standardized measures through clinical interviews administered by the clinicians.

Severity of psychopathology

Severity of psychopathology was assessed according to the Chinese version of the PANSS (Kay *et al.* 1987; Si *et al.* 2004). This scale includes 30 items, each of which is scored on a seven-point Likert scale (1=absence of psychopathology; 7=very severe symptom). PANSS scores were calculated using five dimensions: positive symptoms, negative symptoms, disorganization symptoms, excitement and emotional distress validated by Citrome *et al.* (2011). The reliability of the total scale was high, with Cronbach's α of 0.87 and Cronbach α levels of 0.86, 0.89. 0.81, 0.90 and 0.74 for the five dimensions, respectively (Si *et al.* 2004). It also has a good level of construct validity, with the total variances explaining 59% of the variance about the symptoms in Chinese patients with schizophrenia (Si *et al.* 2004). The tool has demonstrated a high level of sensitivity to detect treatment effects in a number of clinical trials (Citrome *et al.* 2011; Jerrell & Hrisko, 2013).

Insight

Insight was assessed using the Schedule for Assessing Insight (SAI; David, 1990). The SAI comprises of questions to assess three dimensions of insight: awareness, relabelling of symptoms, and attitudes to treatment. The 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 score is from 0 to 14. For this study, the internal consistency of the total scale was high, with Cronbach's α of 0.89. The test–retest reliability score was 0.74 and the inter-rater reliability was 0.99 for the total scale. Correlation of the SAI with insight of the PANSS was −0.635 (Xu *et al.* 2013).

Social functioning

Social functioning was rated using the Personal and Social Performance Scale (PSP; Morosini *et al.* 2000). The PSP is reliable and well established, based on the most recent version of the DSM-IV Social and Occupational Functioning Assessment Scale. The Chinese version of the PSP was used for this study (Si *et al.* 2011). The PSP comprised four functioning areas of patients with schizophrenia: (1) participation in socially useful activities; (2) personal and social relationships; (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, with a lower score indicating a lower level of social functioning. Trained mental health professionals assess patients through interviewing patients and the family members or carers who lived with or cared for the patients. The internal consistency (Cronbach's α=0.84) and the inter-rater reliability [intra-class correlation coefficient (ICC) = 0.94] were good. The test–retest reliability was 0.95. The scale showed good construct validity, with statistically significant correlations with the Global Assessment of Functioning Scale (ICC=0.95). The PSP score had a good negative correlation with the PANSS total score (correlation coefficient=−0.79) (Si *et al.* 2011).

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 ICC

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Table 1. *Comparison of demographic and clinical data between treatment groups at baseline*

Characteristics	CBT		ST		
	n	Mean (S.D.)	*n*	Mean (S.D.)	95% CI
					Difference in means
Age, years	96	29.27 (8.36)	96	33.44 (9.51)	1.62–6.72
Education, years	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
Psychotherapy duration, min	85	602.47 (19.77)	82	598.90 (15.60)	−1.89 to 9.02
					Difference 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
Type of schizophrenia					$\chi^2 = 0.64$
Paranoid		70 (72.9)	74 (77.1)		$p = 0.43$
Undifferentiated		26 (27.1)	22 (22.9)		

CBT, Cognitive–behavioural therapy; ST, supportive therapy; CI, confidence interval; S.D., standard deviation.

coefficients of the PANSS, SAI and PSP scales in this study were above 0.85 after training and before commencement of the study. All 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 was CBT and the reference time point was 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. 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 α set at 0.05. A 25% or greater improvement in scores of the PANSS, SAI and PSP between baseline and end-point was identified and used to support a clinically significant change. Within groups, effect sizes were calculated for the first 12 weeks, and it was calculated between groups across six assessment time points in all outcome measures.

Results

Sample characteristics

A total of 96 patients were recruited to each arm of the trial. Table 1 shows comparisons of the demographic characteristics of the two groups. Among the 96 patients in each group, 70 (72.9%) in the CBT group and 74 (77.1%) in the ST group were characterized as paranoid type, and 26 (27.1%) in the CBT group and 22 (22.9%) in the ST group were classed as having undifferentiated schizophrenia. The groups were evenly matched in terms of demographics, with the exception of age. The ST group was significantly older (mean age was 33.44 years) than the CBT group (mean age was 29.27 years). Age was therefore treated as a confounding factor in subsequent analyses.

In all, 85 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%). Of these participants, 12 (six in each group) completed more than six treatment sessions before discontinuing treatment.

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The remaining 10 (four in the CBT group and six in the ST group) participants failed to be engaged in treatment and completed a mean number of three sessions. There was no significant difference in demographic characteristics between the treatment groups among those participants who failed to complete the study.

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 349–360 mg equivalent of chlorpromazine, and the ST group took a 313–321 mg equivalent of chlorpromazine from baseline to 84 weeks. 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 min (S.D. = 1.95, range 37.14–50 min) per session over the course of treatment, while ST group patients spent 40.06 min (S.D. = 0.83, range 37–45 min) per session. There were 80.2% of patients in the CBT group and 79.2% of patients in the ST group attending 15 treatment sessions. There was no significant difference in the total psychotherapy time ($t = 1.64$, $p = 0.17$) or proportion of patients attending the full treatment sessions during the course of the study ($\chi^2 = 0.03$, $p = 0.86$). Reduction in scores over time was observed in both the CBT and ST groups in all of the outcome measures, with the exception of the SAI and PSP in which a score increase over time was observed in both treatment groups (Table 2). The large effect measured by effect size occurred from 12 weeks and after for all measures of the PANSS when a comparison was made between the CBT and ST groups; the statistical significance became apparent from 36 to 84 weeks. However, CBT patients improved to a greater extent than the ST group over time, starting from week 36, and in all measures of the PANSS, PSP and SAI (see Table 3).

The mean PANSS total scores decreased significantly over time in both treatment groups [CBT mean change 25.86 points (36.01%, S.D. = 17.26), within-group Cohen's $d = 1.51$; ST mean change 19.04 points (26.71%, S.D. = 14.89), within-group Cohen's $d = 1.30$]. The mixed-model interaction term for treatment groups and the following times were significant ($p = 0.045$), showing that the CBT group had a significantly lower PANSS total score compared with the ST group in week 84 (adjusted CBT mean of 46.70, S.D. = 12.33; adjusted ST mean of 52.91, S.D. = 13.43, between-groups Cohen's $d = 0.48$). Fig. 2 shows the mean PANSS total scores by treatment group at each time point.

A significant decrease in PANSS positive and negative symptoms was observed in both groups from baseline to 84 weeks. For PANSS positive symptoms, the results were: CBT mean change 10.51 points (44.83%, S.D. = 7.79), within-groups Cohen's $d = 1.36$; ST mean change 7.44 points (33.19%, S.D. = 7.17), Cohen's $d = 1.10$. For PANSS negative symptoms, the results indicated a CBT mean change of 5.85 points (29.91%, S.D. = 6.71), within-groups Cohen's $d = 0.83$, and ST mean change was 4.57 points (21.92%, S.D. = 6.15), Cohen's $d = 0.74$.

The interaction term of 84 weeks for the treatment group was significant for the positive symptoms (whereby $p = 0.018$). This demonstrates that the CBT group had a significantly lower PANSS positive symptoms score after 84 weeks compared with the ST group (adjusted CBT mean of 13.18, S.D. = 5.03; adjusted ST mean of 15.34, S.D. = 5.26, between-groups Cohen's $d = 0.42$; see Fig. 3). 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.

There was also a significant decrease over time in PANSS disorganization symptoms, excitement and emotional distress in both treatment groups (Table 2). There was no evidence of a benefit of CBT over ST at 84 weeks in the above three symptoms.

The mean SAI total score increased significantly over time by an average of 3.98 points (66.14%, S.D. = 4.29) in the CBT group (within-groups Cohen's $d = -0.97$) and by 2.37 points (40.38%, S.D. = 4.86) in the ST group ($d = -0.51$). The interaction term of treatment group and time at 84 weeks approached statistical significance ($p = 0.055$), indicating further improvement in the SAI total score after 84 weeks in the CBT group compared with the ST group.

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

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 ($\chi^2 = 9.35$, $p = 0.002$).

Discussion

This was the first multicentre randomized controlled trial using standardized CBT adapted to suit patients

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Table 2. *Assessment of the CBT and ST groups during the intervention and follow-up periods*

	Baseline	Week 12	Effect size 12 weeks	Week 24	Week 36	Week 60	Week 84	Mean change 0–84 weeks, s.d., % change
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)	1.00	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 (5.43–7.15)	8.22, 3.90 (7.38–9.06)	0.47	8.91, 4.03 (8.02–9.80)	8.78, 4.02 (7.89–9.67)	8.71, 3.99 (7.83–9.59)	8.83, 4.08 (7.93–9.73)	2.37, 4.86, 40.38

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

Data are given as mean, S.D. (95% confidence interval).
CBT, Cognitive–behavioural therapy; ST, supportive therapy; S.D., standard deviation; PANSS, Positive and Negative Syndrome Scale; SAI, Schedule for Assessing Insight; PSP, Personal and Social Performance Scale.

with schizophrenia in China. Compared with ST, CBT showed a significantly greater and more durable effect on PANSS total score and PSP score from week 36.

The significant effect (as measured by effect size in most of the PANSS measures, SAI and PSP) suggested that rapid change occurred in both groups from baseline to weeks 12 and 24, while CBT had no significant advantages compared with ST in the treatment period. This is consistent with findings in a similar study in the UK, in which both CBT and ST led to significant clinical improvement at the end of treatment (Sensky *et al.* 2000). It suggests that the short-term effects may be due to non-specific psychotherapy factors (e.g. therapy alliance, befriending, talking about distressing experience) common to both CBT and ST. During treatment, the lack of significant difference between the two groups may be because cognitive and behavioural skills remain after the end of treatment maintaining the benefits gained.

This study demonstrated the superiority of CBT over ST on overall and positive symptoms in the long term; the positive effects emerged after the completion of therapy in week 36. This is also consistent with Sensky *et al.* (2000) who found that CBT continued to show improvements whereas ST began to lose effectiveness after it was discontinued. The positive effects may be due to the specific techniques of CBT such as normalization, modification of dysfunctional cognitions and behaviours (Warman & Beck, 2003) by examining the evidence, compensating for reasoning biases by using disconfirmation strategies, and developing rational explanations (Kuipers *et al.* 2006). Those skills learned in the sessions could continue to be used by the patients after the end of treatment. Assigning and completing homework is a possible mechanism to lead to the changes (Kazantzis *et al.* 2010). The CBT methods targeting medication compliance and relapse prevention might also have sustained the treatment effects from 36 to 84 weeks.

This study also showed that CBT could significantly improve social functioning in people with schizophrenia. CBT enhances personal coping strategies that allow patients to manage symptoms and daily hassles more effectively and combat dysfunctional 'self-defeating' beliefs or behaviours (Grant *et al.* 2012).

Compared with ST, CBT failed to demonstrate statistical superiority in negative symptoms, disorganization symptoms and excitement. ST has important but non-trivial effects on a variety of clinical outcomes which may have been relevant (Penn *et al.* 2004, 2009).

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

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Table 3. *Difference between CBT and ST group in PANSS, SAI and PSP scores from baseline to 84 weeks assessment*

Variables	CBT ($n = 85$)	ST ($n = 82$)	T	p	Effect size[a]
PANSS baseline	72.92 (13.03)	72.77 (10.90)	0.072	0.943	0.01
PANSS 12 weeks	57.01 (13.15)	58.84 (11.60)	−0.948	0.345	0.15
PANSS 24 weeks	51.30 (13.33)	52.53 (12.79)	−0.6	0.549	0.10
PANSS 36 weeks	48.75 (12.60)	53.09 (13.69)	−2.074	0.04*	0.33
PANSS 60 weeks	49.05 (12.91)	54.86 (14.46)	−2.684	0.008*	0.42
PANSS 84 weeks	46.75 (13.19)	53.00 (14.60)	−2.863	0.005*	0.45
SAI baseline	6.36 (3.83)	6.08 (4.06)	0.464	0.643	0.07
SAI 12 weeks	8.86 (3.73)	8.18 (3.90)	1.137	0.257	0.18
SAI 24 weeks	9.89 (3.64)	8.83 (4.07)	1.741	0.084	0.28
SAI 36 weeks	10.12 (3.61)	8.77 (4.03)	2.232	0.027*	0.35
SAI 60 weeks	10.24 (3.61)	8.65 (3.98)	2.653	0.009*	0.42
SAI 84 weeks	10.44 (3.65)	8.78 (4.07)	−2.735	0.007*	0.43
PSP baseline	51.09 (12.46)	47.40 (13.11)	1.918	0.057	0.29
PSP 12 weeks	62.06 (12.97)	58.01 (13.37)	1.979	0.049*	0.31
PSP 24 weeks	67.05 (11.08)	63.51 (13.87)	1.792	0.075	0.28
PSP 36 weeks	70.48 (13.73)	63.36 (16.11)	3.004	0.003*	0.48
PSP 60 weeks	71.68 (14.00)	62.17 (16.22)	3.979	<0.001*	0.63
PSP 84 weeks	73.85 (14.61)	64.12 (16.72)	3.946	<0.001*	0.62

Data are given as mean (standard deviation).

CBT, Cognitive–behavioural therapy; ST, supportive therapy; PANSS, Positive and Negative Syndrome Scale; SAI, Schedule for Assessing Insight; PSP, Personal and Social Performance Scale.

[a] Effect size: 0.1–0.19, small effect size; 0.20–0.39, moderate level; 0.40 and more, large effect size.

* Statistical significance: $p < 0.05$.

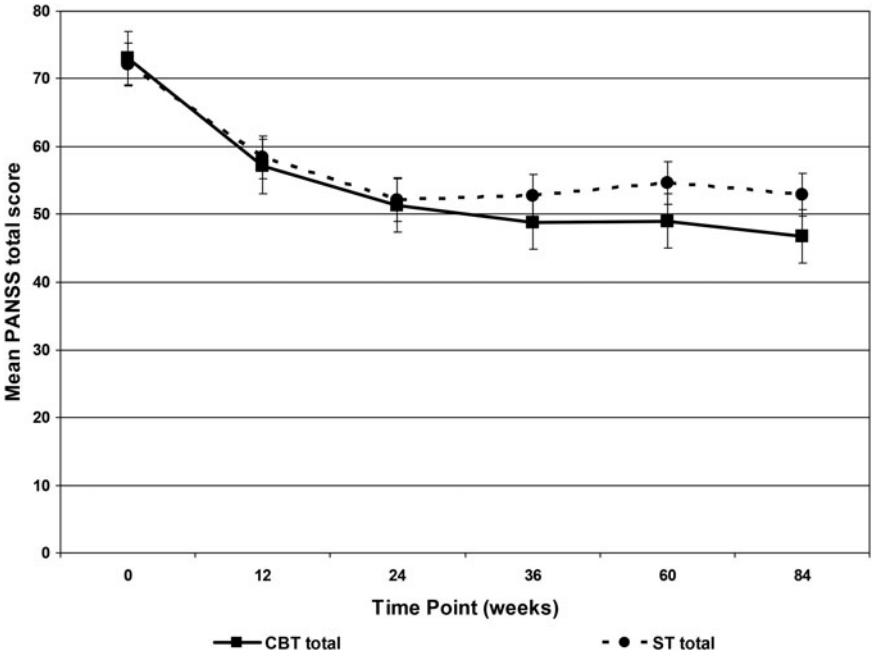

Fig. 2. Mean (standard error) Positive and Negative Syndrome Scale (PANSS) total score by time point. Baseline means are raw means; all other means are adjusted to include values from the mixed models. CBT, Cognitive–behavioural therapy; ST, supportive therapy.

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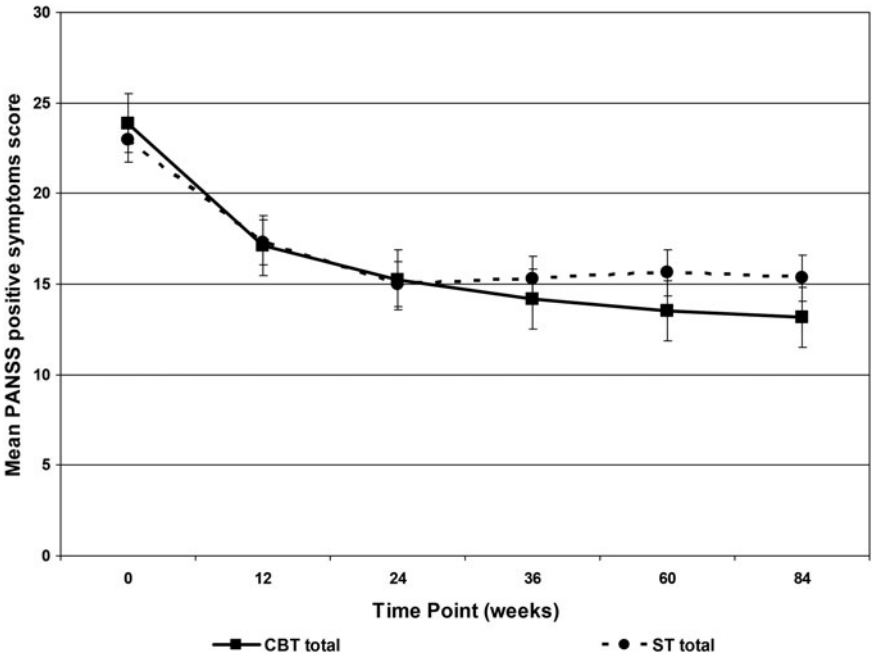

Fig. 3. Mean (standard error) Positive and Negative Syndrome Scale (PANSS) positive symptoms score by time point. Baseline means are raw means; all other means are adjusted to include values from the mixed models. CBT, Cognitive–behavioural therapy; ST, supportive therapy.

emphasis then needed to shift to a more collaborative relationship, with encouragement of the patient contributing to the therapy (Ng, 2006). In Chinese culture, family members play an important role in providing care, and offering support but sometimes pressure for returning to or maintaining employment (Naeem & Kingdon, 2011). 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. 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 had received substantial amounts of training and supervision in CBT by recognized experts in the field and had 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 (Penn *et al.* 2009).

Conclusion

Both CBT and ST combined with medication had benefits on psychopathology, insight and social functioning of schizophrenia patients. CBT had superior effects to ST in positive and overall symptoms of the PANSS, as well as in social functioning as assessed by the PSP at 84 weeks. CBT is a useful adjunctive treatment to medication, with a durable effect at follow-up in people with schizophrenia in China.

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Declaration of Interest

None.

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References

Alphs L, Bossie CA, Sliwa JK, Fu DJ, Ma YW, Hulihan J (2013). Paliperidone palmitate and risperidone long-acting injectable in subjects with schizophrenia recently treated with oral risperidone or other oral antipsychotics. *Neuropsychiatric Disease and Treatment* **9**, 341–350.

American Psychiatric Association (2000). *Diagnostic and Statistical Manual of Mental Disorders DSM-IV-TR (Text Revision)*. American Psychiatric Association: Washington, DC.

Apiquian R, Ulloa RE, Herrera-Estrella M, Moreno-Gómez A, Erosa S, Contreras V, Nicolini H (2009). Validity of the Spanish version of the Personal and Social Performance scale in schizophrenia. *Schizophrenia Research* **112**, 181–186.

Brissos S, Palhavã F, Marques JG, Mexia S, Carmo AL, Carvalho M, Dias C, Franco JD, Mendes R, Zuzarte P, Carita AI, Molodynski A, Figueira ML (2012). The Portuguese version of the Personal and Social Performance Scale (PSP): reliability, validity, and relationship with cognitive measures in hospitalized and community schizophrenia patients. *Social Psychiatry and Psychiatric Epidemiology* **47**, 1077–1086.

Burns T, Patrick D (2007). Social functioning as an outcome measure in schizophrenia studies. *Acta Psychiatrica Scandinavica* **116**, 403–418.

Citrome L, Meng X, Hochfeld M (2011). Efficacy of iloperidone in schizophrenia: a PANSS five-factor analysis. *Schizophrenia Research* **131**, 75–81.

David AS (1990). Insight and psychosis. *British Journal of Psychiatry: The Journal of Mental Science* **156**, 798–808.

First MB, Gibbon M (1997). *User's Guide for the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I): Clinician Version*. American Psychiatric Publishing Incorporated: Washington, DC.

Freeman D, Garety P, Fowler D, Kuipers E, Dunn G, Bebbington P, Hadley C (1998). The London–East Anglia randomized controlled trial of cognitive–behaviour therapy for psychosis IV: Self-esteem and persecutory delusions. *British Journal of Clinical Psychology* **37**, 415–430.

Grant PM, Huh GA, Perivoliotis D, Stolar NM, Beck AT (2012). Randomized trial to evaluate the efficacy of cognitive therapy for low-functioning patients with schizophrenia. *Archives of General Psychiatry* **69**, 121–127.

Jerrell JM, Hrisko S (2013). A comparison of the PANSS Pentagonal and Van der Gaag 5-factor models for assessing change over time. *Psychiatry Research* **207**, 134–139.

Jiang JF, Wei JY, Bia MJ, Xu YF, Gu JY (2008). Effect of cognitive behavioral intervention on recovery of social function of patients with schizophrenic. *Morden Nursing* **14**, 701–702 (in Chinese).

Kay S, Fiszbein A, Opler L (1987). The Positive and Negative Syndrome Scale (PANSS) for schizophrenia. *Schizophrenia Bulletin* **13**, 261–276.

Kazantzis N, Whittington C, Dattilio F (2010). Meta-analysis of homework, effects in cognitive and behavioral therapy: a replication and extension. *Clinical Psychology: Science and Practice* **17**, 144–156.

Kingdon DG, Turkington D (2004). *Cognitive Therapy of Schizophrenia*. Guilford Press: New York.

Kreyenbuhl J, Buchanan RW, Dickerson FB, Dixon LB, Dixon LB (2010). The Schizophrenia Patient Outcomes Research Team (PORT): updated treatment recommendations 2009. *Schizophrenia Bulletin* **36**, 94–103.

Kuipers E, Garety P, Fowler D, Freeman D, Dunn G, Bebbington P (2006). Cognitive, emotional, and social processes in psychosis: refining cognitive behavioral therapy for persistent positive symptoms. *Schizophrenia Bulletin* **32** (Suppl. 1), S24–S31.

Lysaker PH, Lancaster RS, Nees MA, Davis LW (2004). Attributional style and symptoms as predictors of social function in schizophrenia. *Journal of Rehabilitation Research and Development* **41**, 225–232.

Morosini PL, Magliano L, Brambilla L, Ugolini S, Pioli R (2000). Development, reliability and acceptability of a new version of the DSM-IV Social and Occupational Functioning Assessment Scale (SOFAS) to assess routine social functioning. *Acta Psychiatrica Scandinavica* **101**, 323–329.

Morrison AK (2009). Cognitive behavior therapy for people with schizophrenia. *Psychiatry (Edgmont)* **6**, 32.

Morrison AP, Hutton P, Wardle M, Spencer H, Barratt S, Brabban A, Callcott P, Christodoulides T, Dudley R, French P (2011). Cognitive therapy for people with a schizophrenia spectrum diagnosis not taking antipsychotic medication: an exploratory trial. *Psychological Medicine* **42**, 1049.

Naeem F, Kingdon D (2011). *Cognitive Therapy for Psychosis in Beijing, Cognitive Behaviour Therapy in Non Western Cultures*. Nova Science Publishers: New York.

National Institute for Clinical Excellence (ed.) (2003). *Guidelines for Psychological Treatment in Schizophrenia*. Gaskell Press: London.

National Institute for Health and Care Excellence (2014). *Psychosis and Schizophrenia in Adults: Treatment and Management*. Centre for Clinical Practice at NICE: London.

National Institute for Health and Clinical Excellence (2009). *Core Interventions in the Treatment and Management of Schizophrenia in Adults in Primary and Secondary Care*. National Collaborating Centre for Mental Health: London.

Ng R (2006). *Cultural Adaptation of Cognitive Therapy in Hong Kong Chinese, International Handbook of Cultural Psychiatry*. Taylor & Francis: London.

Penn DL, Meyer PS, Evans E, Wirth RJ, Cai K, Burchinal M (2009). A randomized controlled trial of group cognitive–behavioral therapy *vs.* enhanced supportive therapy for auditory hallucinations. *Schizophrenia Research* **109**, 52–59.

Penn DL, Mueser KT, Tarrier N, Gloege A, Cather C, Serrano D, Otto MW (2004). Supportive therapy for schizophrenia. *Schizophrenia Bulletin* **30**, 101–112.

Rathod S, Kingdon D, Weiden P, Turkington D (2008). Cognitive–behavioral therapy for medication-resistant schizophrenia: a review. *Journal of Psychiatric Practice* **14**, 22–33.

Sensky T, Turkington D, Kingdon D, Scott JL, Scott J, Siddle R, O'Carroll M, Barnes TRE (2000). A randomized controlled trial of cognitive–behavioral therapy for persistent symptoms in schizophrenia resistant to medication. *Archives of General Psychiatry* **57**, 165–172.

Si T, Shu L, Su Y, Tian C, Yan J, Cheng J, Li X, Liu Q, Ma Y, Zhang W, Zhang H (2011). The Chinese version of the

Personal and Social Performance Scale (PSP): validity and reliability. *Psychiatry Research* **185**, 275–279.

Si T, Yang J, Shu L, Wang X, Kong Q, Zhou M, Li X, Liu C (2004). The reliability, validity of PANSS and its implication. *Chinese Journal of Mental Health* **18**, 45–47.

Sim K, Su A, Fujii S, Yang S, Chong MY, Ungvari GS, Si T, Chung EK, Tsang HY, Chan YH (2004). Antipsychotic polypharmacy in patients with schizophrenia: a multicentre comparative study in East Asia. *British Journal of Clinical Pharmacology* **58**, 178–183.

Tarrier N, Lewis S, Haddock G, Bentall RP, Drake R, Kinderman P, Kingdon D, Siddle R, Everitt J, Leadley K (2004). Cognitive–behavioural therapy in first-episode and early schizophrenia 18-month follow-up of a randomised controlled trial. *British Journal of Psychiatry* **184**, 231–239.

Tarrier N, Yusupoff L, Kinney C, McCarthy E, Gledhill A, Haddock G, Morris J (1998). Randomised controlled trial of intensive cognitive behaviour therapy for patients with chronic schizophrenia. *British Medical Journal* **317**, 303–307.

Turner DT, Gaag M, Karyotaki E, Cuijpers P (2014). Psychological interventions for psychosis: a meta-analysis of comparative outcome studies. *American Journal of Psychiatry* **171**, 523–538.

Velligan DI, Lam Y, Glahn DC, Barrett JA, Maples NJ, Ereshefsky L, Miller AL (2006). Defining and assessing adherence to oral antipsychotics: a review of the literature. *Schizophrenia Bulletin* **32**, 724–742.

Wang CH, Li Y, Zhao Z, Pan M, Feng JG, Sun FG, Du BG (2004). Controlled study on long -term effect of cognitive behavior intervention on first episode schizophrenia. *Chinese Mental Health Journal* **17**, 200–202.

Warman DM, Beck AT (2003). Cognitive behavioral therapy for schizophrenia: an overview of treatment. *Cognitive and Behavioral Practice* **10**, 248–254.

Winston A, Rosenthal RN, Pinsker H (2004). *Introduction to Supportive Psychotherapy*. American Psychiatric Publishing Incorporated: New York.

World Health Organization (2011). Schizophrenia (http://www.who.int/mental_health/management/schizophrenia/en/). Accessed 19 June 2014.

Wykes T, Steel C, Everitt B, Tarrier N (2008). Cognitive behavior therapy for schizophrenia: effect sizes, clinical models, and methodological rigor. *Schizophrenia Bulletin* **34**, 523–537.

Xu Z, Guo ZH, Fu ZY, Wang N, Zhang Y (2013). Reliability and validity of the Chinese version of the Schedule for Assessment of Insight. *Chinese Journal of Behaviour Medicine and Brain Science* **22**, 752–754.

Zuo XC, Liu SK, Yi ZY, Xie ZH, Li HD (2006). Steady-state pharmacokinetic properties of aripiprazole 10 mg PO q12h in Han Chinese adults with schizophrenia: a prospective, open-label, pilot study. *Current Therapeutic Research, Clinical and Experimental* **67**, 258–269.