

Author's Accepted Manuscript

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PII: S0165-1781(14)00130-9
DOI: <http://dx.doi.org/10.1016/j.psychres.2014.02.012>
Reference: PSY8144

To appear in: *Psychiatry Research*

Received date: 9 January 2013
Revised date: 4 February 2014
Accepted date: 7 February 2014

Cite this article as: Tania M. Lincoln, Winfried Rief, Stefan Westermann, Michael Ziegler, Marie-Luise Kesting, Eva Lüllmann, Stephanie Mehl, Who stays, who benefits? Predicting dropout and change in cognitive behaviour therapy for psychosis, *Psychiatry Research*, <http://dx.doi.org/10.1016/j.psychres.2014.02.012>

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Full title: Who stays, who benefits? Predicting dropout and change in cognitive behaviour
therapy for psychosis.

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Abstract

This study investigates predictors of outcome in a secondary analysis of dropout and completer data from a randomized controlled effectiveness trial comparing CBTp to a wait-list group (Lincoln et al., 2012). Eighty patients with DSM-IV psychotic disorders seeking outpatient treatment were included. Predictors were assessed at baseline. Symptom outcome was assessed at post-treatment and at one-year follow-up. The predictor x group interactions indicate that a longer duration of disorder predicted less improvement in negative symptoms in the CBTp but not in the wait-list group whereas jumping-to-conclusions was associated with poorer outcome only in the wait-list group. There were no CBTp specific predictors of improvement in positive symptoms. However, in the combined sample (immediate CBTp + the delayed CBTp group) baseline variables predicted significant amounts of positive and negative symptom variance at post-therapy and one-year follow-up after controlling for pre-treatment symptoms. Lack of insight and low social functioning were the main predictors of drop-out, contributing to a prediction accuracy of 87%. The findings indicate that higher baseline symptom severity, poorer functioning, neurocognitive deficits, reasoning biases and comorbidity pose no barrier to improvement during CBTp. However, in line with previous predictor-research, the findings imply that patients need to receive treatment earlier.

Keywords: predictors, schizophrenia, psychosis, CBT, dropout, adherence

1. Introduction

Cognitive behavioural therapy for psychosis (CBTp) has been demonstrated to be effective for psychotic disorders (Wykes et al., 2008) and has been incorporated into several national guidelines (Gaebel et al., 2009; NICE, 2009). Nevertheless, a number of patients discontinue therapy (on average 16% according to a meta-analysis by Lincoln et al., 2008) and among those that continue, approximately half do not show reliable symptom improvement (Jones et al., 2004; Wykes et al., 2008). Knowing who is likely to benefit from

CBTp would provide a better basis for an evidence-based allocation of patients to treatment. Furthermore, knowing about who is unlikely to benefit helps us to understand where CBTp needs to be adapted in order to serve specific groups more effectively.

Several studies have attempted to identify baseline predictors of improvement in CBTp. In regard to socio-demographic variables, these studies have found that younger patients benefit more in terms of positive symptoms (Thomas et al., 2011; Morrison et al., 2012) and that women benefit more than men in overall psychopathology (Drury et al., 1996; Brabban et al., 2009). Furthermore, higher level of education was shown to predict better outcome in negative symptoms (Allott et al., 2011).

A clinical baseline variable relevant to outcome is a shorter duration of treated or untreated psychosis, which has been found to be associated with a shorter recovery time (Drury et al., 1996), greater symptom improvement during CBTp (TARRIER et al., 1998; Thomas et al., 2011; Morrison et al., 2012), and less symptomatology at post-assessment (Morrison et al., 2004). Also, lower baseline symptomatology overall was shown to be related to more symptomatic improvement during CBTp (TARRIER et al., 1998), in particular less pronounced negative symptoms were related to greater symptom improvement (Thomas et al., 2011) and outcome (Allott et al., 2011). In contrast, there is some indication that more severe positive symptoms were a positive predictor of symptom improvement (Morrison et al., 2004; Dunn et al., 2006). No study found baseline depression to be related to outcome.

Higher insight into the disorder predicted overall symptom improvement in two studies (Garety et al., 1997; Naem et al., 2008). Interestingly, Garety et al. (1997) also found that among patients with delusions acknowledging the possibility of being mistaken was a predictor of better outcome, although this was strongly associated with insight. Similarly, Brabban et al. (2009) found lower delusion conviction to be associated with overall symptom reduction in a subgroup of patients with delusions who had received CBTp. On a similar note,

cognitive insight, in terms of self-reflectiveness and self-certainty was found to be predictive of favorable outcome (Perivoliotis et al., 2010; Premkumar et al., 2011).

Furthermore, higher baseline occupational functioning predicted lower levels of positive symptoms at one year (Allott et al., 2011). With regard to neurocognitive variables, Penades et al. (2010) found better baseline memory performance to predict symptom improvement following treatment. However, most studies (Garety et al., 1997; DeVille et al., 2011; Premkumar et al., 2011) failed to find predictive value of memory, executive functioning, attention, or verbal fluency on outcome of CBTp.

One problem in drawing valid conclusions from the previous research is that studies have focused on different domains and time-points of outcome. Moreover, most studies are inconsistent in whether they investigate unspecific predictors of change or those specific to CBTp or even merely predict symptom levels at post-therapy without controlling for baseline symptoms. Nevertheless, previous findings highlight the positive predictive value of a shorter duration of psychosis and better insight on outcome. They also indicate that more pronounced negative symptoms at baseline is associated with less favorable outcome, whereas more severe baseline positive symptoms seems to be positively related to symptom improvement. The majority of studies do not find neurocognitive functioning to be a predictor of outcome, while there are singular findings indicating that patients with higher education, younger age, and female gender might benefit more from CBTp.

Surprisingly, some predictors that are likely to be specifically relevant to CBTp have not received sufficient attention. Psychotic symptomatology is associated with a range of reasoning biases, such as jumping-to-conclusions, difficulties in theory of mind and attribution biases and, consequently, CBTp has a strong focus on increasing peoples' ability to question their beliefs and to take more time to weigh the evidence before drawing conclusions (Kuipers et al., 2006). This also involves learning to take peoples' cognitive and

emotional perspective. On a transdiagnostic level, there is some indication that people with stronger cognitive resources (in the sense of fewer dysfunctional attitudes) benefit more from cognitive approaches (e.g. Sotsky et al., 1991). Garety et al.'s (1997) finding that less pronounced delusion-conviction and cognitive flexibility were associated with better outcome seems to support this for psychosis. It would therefore be interesting to test whether lower levels of reasoning biases predict better outcome. Second, psychosis generally goes along with a range of comorbid disorders, in particular anxiety disorders and depression (Fenton, 2001). In clinical practice, CBTp also targets these disorders. Due to the high efficacy of cognitive behavioral interventions for anxiety disorders and depression (Butler et al., 2006), patients with comorbid Axis I disorders might benefit more from therapy than those for whom the sole focus lies on psychotic symptoms. In contrast, Axis II disorders are likely to complicate and prolong therapy and have been found to a negative predictor of outcome in treatment of depression and anxiety (Reich, 2003).

With regard to outcome, most of the studies have focused on global symptomatology, positive symptoms (as the prime target of CBTp) or functioning. To our knowledge, no study has attempted to predict improvement in negative symptoms although it is agreed that negative symptoms constitute a distinct and important therapeutic domain (Kirkpatrick et al., 2006). Finally, although predictors of dropout related to psychosocial treatments for schizophrenia in general have been investigated – finding age, gender, duration of disorder and treatment-related variables to be associated with dropout (Villeneuve et al., 2010), only one study, by Periviolitis et al. (2010), has focused specifically on drop-out during CBTp.

The aim of this study is therefore to extend the research on baseline predictors of short- and long-term improvement in positive and negative symptoms and dropout in a large and clinically heterogeneous sample of patients who received CBTp. The study is a secondary analysis of dropout and completer data from a randomized controlled effectiveness trial of

CBTp for psychosis (Lincoln et al., 2012) that found significant improvement in positive symptoms and overall psychopathology but not in negative symptoms in the CBTp compared to a waitlist group. Over and above the predictors investigated in previous studies, we will analyze the impact of social cognition and reasoning which we expect to have unique relevance to CBTp, as well as the impact of comorbidity.

2. Method

2.1.Design

The study was a single-center stratified (based on the PANSS total scores), single-blind, wait-list controlled, parallel group study comparing a CBTp group ($n=40$) to a wait-list (WL) group ($n=40$) with regard to psychopathology at the end of treatment. As illustrated in Figure 1, the WL group received CBTp after the waiting-period. All patients were re-assessed at a one-year-follow-up. Therefore this design allowed for controlled comparisons at post-therapy, but was limited to pre-post comparisons for the one-year follow-up (Lincoln et al., 2012).

In the CBTp group all predictors were assessed at baseline, prior to treatment (t1), and outcome variables (positive and negative symptoms) were assessed at post-treatment (t2) and at one-year follow-up (t4). In the WL group, predictors were assessed at t1, outcome was assessed at post-waiting time (t2). Furthermore, the predictors that were assumed to be more sensitive to change (depression, delusion conviction, insight, functioning, and reasoning biases) were reassessed for this group at t2. Finally, this group was reassessed on the outcome variables after having received treatment (t3) and at one-year follow-up (t4).

Of the 40 patients randomized to the CBTp group, 34 completed therapy. In the WL group, 39 patients completed the assessments after the waiting-period and 33 completed therapy thereafter. A detailed trial flow is depicted in Lincoln et al (2012).

In this study we investigated 1) differential predictors of CBT versus WL by analyzing the predictive value of variables assessed at baseline (t1) on symptom outcome in participants who had completed CBTp (CBTp group: $n=34$) or treatment-as-usual (WL group: $n=39$); 2) the predictors of change during therapy by combining all treatment completers in the immediate ($n=34$) and the delayed ($n=34$) therapy group and investigating the predictive value of pre-therapy variables assessed at t1 (immediate therapy group) and t1/t2 (delayed therapy group) on outcome at t3 and t4; 3) the predictors of dropout by comparing patients who completed CBTp ($n=68$) or dropped out after the initial rapport and assessment phase during the waiting period ($n=1$) or therapy ($n=11$).

The individualized CBTp was delivered according to a published German-language manual (Lincoln, 2006) and involved assessment, establishment of working alliance and case-formulation, working with auditory hallucinations and other distressing or disabling symptoms, modifying delusional and other dysfunctional beliefs and relapse prevention. The interventions did not follow a specific order or involve a fixed number of sessions.

2.2. Assessments of outcome and predictor variables

Positive and negative symptoms were assessed with the Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987). The PANSS is a semi-structured interview measuring 32 symptoms divided into three groups: positive symptoms (e. g. persecutory delusions, thought disorder, grandiosity), negative symptoms (e. g. blunted affect, emotional withdrawal, poor rapport), and general psychopathology (e. g. anxiety, tension, lack of insight). Symptoms are rated using a seven-point-scale on the basis of detailed descriptions and a semi-structured interview (SCI-PANSS). The interviews were videotaped and rated by independent and treatment-blind raters who were trained and certified by the PANSS Institute (see <http://www.panss.org/>).

Socio-demographic and clinical characteristics (duration of disorder, previous hospitalizations, comorbidity), neurocognitive performance, cognitive biases and social skills were assessed at baseline. Baseline was directly prior to therapy for the CBTp group (t1) and four months prior to therapy for the WL group (t2). Baseline-symptoms, functioning and cognitive biases were assessed directly prior to therapy for all patients.

Clinical variables. Comorbid diagnoses were assessed with the Structured Clinical Interview for DSM-IV (SCID; Wittchen et al., 1997). Depression was assessed with the German version of the Calgary Depression Rating Scale for Schizophrenia (CDSS; Müller et al., 1999), an observer-rated nine-item scale in which symptoms of depression are rated with regard to the previous week. Insight was assessed with the PANSS item G12 “insight and judgment” which takes awareness of symptoms, awareness of need for treatment and awareness of consequences of the disorder into account and is rated on a seven point Likert-scale. The PANSS insight score has been found to be highly correlated with other established measures of insight (for a review of scale correlations see Lincoln et al., 2007) and is frequently used as global measure of insight. Delusion conviction was assessed with the conviction subscale of the German version of the Peters et al. Delusions Inventory (PDI; Lincoln et al., 2009). The PDI consists of 40 items covering a range of delusional beliefs that are rated in regard to presence, distress, conviction and preoccupation.

Functioning. Occupational and social functioning were assessed with an adapted German version of the Role Functioning Scale (Goodman et al., 1993; Lincoln et al., 2012). Higher scores indicate better functioning. Social skills were assessed using the Social Performance Rating Scale (Fydrich & Bürgener, 1999). Scores were transformed inversely so that higher scores indicate more pronounced social skills.

Neurocognition. Verbal memory was assessed with the subtest Logical Memory I of the Wechsler Memory Scale-Revised (WMS-R; Härtling et al., 2000) and cognitive set-shifting with the Trail Making Test, Part B (TMT; Reitan, 1992).

Cognitive biases. The “jumping-to-conclusions-bias” (JTC) was assessed with the beads task (Garety et al., 2005) using a ratio of 80:20. We repeated the task three times, each with a different sequence of beads and counted the number of beads drawn to decide in each task. The score used was the mean number of draws to decision. Attribution biases were assessed using the ‘externalizing bias’ (EB) score from the Internal, Personal and Situational Attributions Questionnaire (IPSAQ; Kinderman & Bentall, 1996) which is calculated by subtracting the number of internal attributions for negative events from the number of internal attributions for positive events. A higher score therefore reflects a stronger self-serving bias. Theory of Mind was assessed by a movie task of social situations (Mehl et al., 2010), a movie version of the Hinting Task (Corcoran et al., 1995). Participants watched four movie sequences presenting complex social situations. In the situations, a character presented a statement that hinted information (e.g. “My birthday is coming soon.” “This necklace is very beautiful.”). Participants were required to answer questions about the protagonists’ hinted intentions and their emotions. For this study we used the combined score of the ‘ability to infer intentions’ and the ‘ability to infer emotions’ (range 0-16). A detailed description of the task was provided in the study by Mehl et al. (2010).

2.3. Analyses

Missing data. There was no missing data for PANSS scores at baseline or post-assessment for the treatment completers, but eleven completers did not provide full data at 1-year follow-up. We used the SPSS EM estimation to test whether missing PANSS data at follow-up was at random and to impute missing data (Lincoln et al., 2012). Missing data in the predictors was not replaced.

The analyses were conducted in several steps. First, based on the sample of patients from the CBTp group who had completed therapy and the patients who had completed the waiting-period ($n=73$) we attempted to identify differential predictors of response to CBTp versus WL by post-assessment. We performed a series of hierarchical multiple regressions, with the post treatment measure (e.g. positive symptoms) as the dependent variable and the baseline for that variable as covariate (hence controlling for initial severity level) included in the first block, followed by the independent variable group (CBTp group versus WL group), the predictor variable (e.g. insight), and the group x predictor interaction in the second block. We evaluated the predictors 1 at a time. The main effect of the predictor variable indicates whether it predicts outcome, controlling for baseline. Main group effects reflect differences in primary outcomes between the two groups (treatment effects). The group x predictor interaction effect indicates whether the predictor predicts outcome differentially (e.g. more for the CBTp group than for the WL group) and is the variable of interest.

Second, we combined the completers in the immediate (CBTp group) versus delayed (WL group) therapy groups ($n=68$) to examine predictors of change from pre-therapy to post-therapy and one-year follow-up in a larger group of people who received CBTp. Again, we conducted a series of regressions in the manner described above. However, for these analyses the post-therapy and 1-year-follow-up assessments for all participants served as dependent variables and the cohort (immediate versus delayed) was the group variable. Thus, main effects of predictors reflect predictors of change during CBTp, controlling for baseline levels, across both cohorts. Main cohort effects reflect differences in primary outcomes between the two cohorts. Significant cohort x predictor interactions were analyzed but will not be reported as they were not a primary focus of the manuscript. However, detailed results and findings can be obtained from the authors upon request. All predictor variables that produced

significant main effects at a probability value of $p \leq .05$ were entered into regression models (method: ENTER) in order to assess their combined impact on outcome.

Finally, in order to predict dropout, we used *t*-tests to compare completers and dropouts on the potential predictors used for the previous analyses (compare Table 1). We did not include reasoning biases or social skills in these analyses due to the lack of a rationale that these variables would predict dropout. However, we added the number of previous hospitalizations as a proxy of previous experience with mental health services. Thus, we conducted 15 single a priori *t*-tests and then entered significant discriminating variables into logistic regression (method: ENTER) to predict their combined effect and prediction accuracy.

The baseline mean values, standard deviations, ranges and possible scores for each of the predictors analyzed are presented in Table 1.

3. Results

3.1. Sample characteristics and therapy delivery

Fifty-nine patients fulfilled DSM-criteria for schizophrenia, twelve for schizoaffective disorder, five for delusional disorder and four for acute psychotic disorder. Comorbid Axis I disorder was diagnosed in 45 patients, comorbid Axis II disorder in 15 patients. Sixteen percent of the sample fulfilled criteria for two or more comorbid disorders. Among the Axis I disorders, anxiety disorders were the most prevalent ($n=25$), followed by affective disorders ($n=18$) and substance abuse or dependency ($n=12$). Among the personality disorders borderline personality disorder was diagnosed the most frequently ($n=4$) followed by avoidant personality disorder ($n=3$).

Eighteen patients were acutely psychotic, 56 were partly remitted and/or episodic, and six patients were classified as fully remitted (DSM-IV single episode, full remission). The

mean age of the sample was 33.1 ($SD=10.6$) and 35 patients were female. The mean duration of psychosis was 10.4 years ($SD=8.5$). The mean number of previous episodes requiring hospital admission was 4.5 ($SD=6.9$). All but four patients were on antipsychotic medication and the majority was reliably taking them as prescribed ($n=48$). The mean GAF score was 45.3 ($SD=12.8$), the mean scores for the PANSS positive, negative and general subscales were 14.9 ($SD=4.5$), 14.2 ($SD=4.6$) and 34.0 ($SD=7.5$) respectively.

Patients who completed therapy received 28.9 ($SD=7.4$) therapy sessions in 38.0 ($SD=15.8$) weeks. The average waiting time was 19.2 weeks ($SD = 7.9$). The mean follow-up period was 53.3 weeks ($SD = 40.2$). Across both groups, patients received additional 7.6 sessions ($SD = 10.7$) between post-therapy and one-year follow-up.

3.2 Differential predictors of improvement in positive and negative symptoms by post-assessment between the CBTp group versus the WL group

PANSS positive symptoms at post-assessment were significantly related to PANSS positive symptoms at baseline ($\beta=0.58, p\leq 0.01$), as was group status ($\beta=0.28, p\leq 0.01$), indicating the significant effect of the treatment on positive symptoms. As can be seen in Table 2 there were no significant interaction effects, indicating that none of the 17 variables investigated predicted improvement in one group more relative to the other. However, there were two trend effects towards significant group x predictor interactions in regard to cognitive set shifting and memory. Post-hoc analyses by group indicated that in the WL group impaired set-shifting ($\beta=0.17, p=0.14$) and impaired memory performance ($\beta=-0.18, p=0.13$) tended to predict higher levels of positive symptoms at outcome while in the CBTp group these variables tended to predict lower levels of positive symptoms at outcome ($\beta=-0.11, p=0.56$ and $\beta=0.18, p=0.35$, respectively).

PANSS negative symptoms at post-assessment were significantly associated with PANSS negative scores at baseline ($\beta=0.56, p\leq 0.01$) while group status was not ($\beta=-0.06, p=0.58$) indicating the absence of a therapy effect on negative symptoms. As can be seen in Table 2 only 2 of the 17 group x predictor interactions were significant. This was the case for duration of disorder and for JTC, with post-hoc analyses by group indicating that a longer duration of disorder tended to predict higher levels of negative symptoms in the CBTp ($\beta=0.28, p=0.07$) and lower levels in the WL group ($\beta=-0.22, p=0.10$) and that a stronger JTC-bias tended to predict negative symptoms in the WL group ($\beta=-0.23, p=0.09$) but not in the CBTp group ($\beta=0.20, p=0.20$). Also, there was a trend interaction for comorbid Axis II disorders with post-hoc analyses by group indicating that comorbidity predicted more negative symptoms in the WL ($\beta=0.33, p\leq 0.01$) but not in the CBTp group ($\beta=0.04, p=0.82$).

3.3. Predictors of improvement from pre-treatment to post-treatment and follow-up in the complete sample

PANSS positive symptoms at post-therapy were significantly related to PANSS positive symptoms at baseline ($\beta=0.33, p\leq 0.01$), but not to cohort ($\beta=0.15, p=0.22$) indicating that there was no difference in outcome between the immediate (previously the CBTp group) and the delayed therapy group (previously the WL group). Over and beyond these variables, higher levels of depression ($\beta=0.40, p\leq 0.01$), more negative symptoms ($\beta=0.51, p\leq 0.01$), poorer social skills ($\beta=-0.39, p\leq 0.01$), poorer role functioning ($\beta=-.48, p\leq 0.01$) and poorer ToM ability ($\beta=-0.25, p\leq 0.05$) significantly predicted positive symptoms at post-treatment. Together, these five variables accounted for a significant amount of variance in post-therapy positive symptoms over and above the variance explained by pre-therapy positive symptoms (change in $R^2=0.40, df=4,53; p\leq 0.01$). PANSS positive symptoms at follow-up were not related to PANSS positive symptoms at baseline ($\beta=0.06, p=0.62$) or to cohort ($\beta=-0.01,$

$p=0.93$). Over and beyond these variables, the predictors age ($\beta=0.28$, $p\leq 0.05$), years of education ($\beta=0.32$, $p\leq 0.05$), depression ($\beta=0.28$, $p\leq 0.05$), negative symptoms ($\beta=0.31$, $p\leq 0.05$) and externalizing bias ($\beta=0.36$, $p\leq 0.01$), were significantly related to positive symptoms at follow-up. Together, these five variables accounted for a significant amount of variance in follow-up positive symptoms over and above the variance explained by pre-therapy positive symptoms (change in $R^2=0.30$; $df=5,48$; $p\leq 0.01$).

PANSS negative symptoms at post-assessment were associated with PANSS negative symptoms at baseline ($\beta = .32$, $p\leq 0.01$) while cohort was not ($\beta=0.13$, $p=0.31$). Over and beyond these variables, lower functioning ($\beta=-0.30$, $p\leq 0.05$), higher delusion conviction ($\beta=0.46$, $p\leq 0.01$) and more positive symptoms ($\beta=0.55$, $p\leq 0.01$) were significantly related to negative symptoms at outcome. Together, these two variables accounted for a significant amount of variance in follow-up negative symptoms over and above the variance explained by pre-therapy negative symptoms (change in $R^2=0.33$; $df=3,63$; $p\leq 0.01$). Negative symptoms at follow-up were associated with PANSS negative symptoms before treatment ($\beta=0.27$, $p\leq 0.05$) while cohort was not ($\beta=-0.13$, $p=0.29$). Over and beyond these variables, the predictors age ($\beta=0.25$, $p\leq 0.05$) and years of education ($\beta=0.29$, $p\leq 0.05$) were significantly related to negative symptoms at follow-up. Together, these two variables accounted for a significant amount of variance in follow-up negative symptoms over and above the variance explained by pre-therapy negative symptoms (change in $R^2=0.14$; $df=2,64$; $p\leq 0.01$).

3.4. Predictors of dropout

Patients who dropped out ($n=12$) had been hospitalized less often (2.8, $SD=1.7$) than completers (4.8, $SD=7.5$; $t(74.3)=2.1$, $p\leq 0.05$), had more lack of insight (2.8, $SD=1.1$ vs 1.8, $SD=1.0$; $t(77)=2.0$, $p\leq 0.01$), lower social functioning (4.5, $SD=3.2$ vs. 7.0, $SD=2.9$; $t(78)=-2.7$, $p\leq 0.01$) and more negative symptoms (16.2, $SD=2.8$ vs. 14.1, $SD=4.7$; $t(24.3)=2.1$,

$p \leq .05$). They also showed a trend towards more positive symptoms (17.4, $SD=5.9$ vs. 13.8, $SD=3.8$; $t(12.7)=1.1$, $p=0.06$) and less Axis II disorders (O versus 15, $\chi^2=3.3$, $p=0.07$). None of the other predictors reached significance.

The results of logistic regression of the four significant predictors on dropout are presented in Table 1. As can be seen, the full model was statistically significant in predicting variance in dropout. However, no variable reached significance as a single predictor within the model. Furthermore, the baseline model already predicted dropout accurately in 85% based on the assumption that no patient would drop out. The regression model predicted seven of the dropouts correctly. However, it also incorrectly predicted three completers to be dropouts resulting in a total prediction accuracy of 87%.

4. Discussion

The study set out to extend on previous findings on predictors of change during CBTp by replicating previous findings and investigating novel predictors with specific relevance to CBTp. To summarize, we found that there were no significant predictors of improvement in positive symptoms in the CBT group compared to wait-list group and only few and weakly significant findings for negative symptoms. The predictor x group interactions for negative symptoms indicated that a longer duration of disorder predicted less improvement in negative symptoms in the CBTp group but not in the WL group, whereas jumping-to-conclusions was positively related to outcome in the WL group but not in the CBTp group. Irrespective of group status there were numerous predictors of change in symptoms over time. As such, we found depression, negative symptoms, impaired social skills, role functioning and theory of mind to predict 40% of positive symptom variance at post-treatment. Negative symptoms at post-therapy were predicted by poorer functioning, delusion conviction and more positive symptoms at baseline that explained 33% of the variance over and above baseline negative

symptoms. Younger age and lower education were significantly related to more improvement in positive and negative symptoms at follow-up. Furthermore, improvement in positive symptoms at FU was predicted by lower levels of depression, negative symptoms and a less pronounced externalizing bias at baseline. Lack of insight and low social functioning were the main predictors of drop-out, contributing to a prediction accuracy of 87%.

In regard to the variables that predict change in general, we were able to confirm a number of the findings from previous predictor studies. For one, we also found younger patients to improve more (compare Thomas et al., 2011; Morrison et al., 2012). In addition, we could also replicate the findings that patients with a shorter duration of disorder show more change during CBTp (Drury et al., 1996; Garety et al., 1997; Tarrrier et al., 1998; Morrison et al., 2004; Allott et al., 2011; Thomas et al., 2011; Morrison et al., 2012) and were able to demonstrate that this predictor was specific to CBTp. Our results also corroborate the findings that negative symptoms at baseline are predictive of less improvement (Allott et al., 2011; Thomas et al., 2011). However, in contrast to previous findings (Morrison et al., 2004; Dunn et al., 2006), we also found higher baseline-levels of positive symptoms to be predictive of less favorable outcome in negative symptoms. This difference in finding is likely to be explicable by differences in methodology and the outcome variables investigated. Finally, by failing to find a significant predictive effect of neurocognitive functioning, our study corroborates the overall pattern of findings from previous CBTp predictor research (Garety et al., 1997; DeVille et al., 2011; Premkumar et al., 2011) indicating that neurocognitive functioning is not particularly relevant to outcome. This is also in line with a review by Kurtz (2011) who did not find neurocognition to be predictive of change in other psychosocial interventions for schizophrenia. In our study, there was a tendency for participants with impaired memory and set-shifting abilities to have worse outcome after the WL period, but

this effect was reversed for the CBTp group. Overall, therefore, concerns that CBT will be less effective for patients with poor neurocognitive functioning seem to be unfounded.

Other findings were not directly in line with previous ones: Our study was the first to identify depression as a negative predictor of improvement in positive symptoms. However, this finding fits in well with the accumulating evidence which indicates that depression and affective processes play a major role in maintaining and predicting positive symptoms (Myin-Germeys & van Os, 2007; Fowler et al., 2012; Freeman, Dunn, et al., 2012; Freeman, Stahl, et al., 2012). In contrast to previous work (Drury et al., 1996; Brabban et al., 2009) we did not find women to improve more. Also, other than Allott et al. (2011) we found lower rather than higher education to predict long-term improvement, which might, however, be due to the fact that Allott et al. focused on functioning at the end of therapy rather than on change. Surprisingly, we did not find that higher insight or lower delusion conviction predict better outcome (compare Garety et al., 1997; Brabban et al., 2009). This divergence could be interpreted as promising in the sense that the working with delusions approach worked sufficiently well for patients with little insight. On the other hand, patients with less insight were more likely to drop out. Also, several relevant aspects of insight, such as need for treatment and recognition of presence of a mental illness were probably generally high as the patients were attending the outpatient treatment on their own free will, presumably out of a felt need for treatment. Possibly, a more detailed assessment of insight that differentiates between insight into need for treatment and insight into the nature of symptoms would have produced different findings. Also, a measure that assesses delusion conviction related to the individuals' specific delusional beliefs as used in the study by Garety et al. (1997) might have been more conclusive than the conviction subscale of the PDI.

With regard to our novel predictors, we found that a stronger JTC-bias tended to predict more negative symptoms after the waiting period but less negative symptoms after

CBTp. The direction of this effect was surprising, perhaps, as we had expected patients with lower reasoning biases to benefit more, based on the resource assumption put forward by Grawe (2002). Our finding is in line with the more classic assumption that the success of therapy is attributable to correcting reasoning biases. In contrast though, more impairment in ToM and a stronger self-serving attribution bias were related to higher levels of positive symptoms at outcome. As these findings were based on the combined treatment sample they are not necessarily specific to CBTp and warrant replication using a more rigorous design. The findings on comorbidity were more straightforward: Although the hypothesis that patients with comorbid Axis I disorders would benefit more was not supported, the expected detrimental effect of comorbid II disorders that has been found in regard to the treatment of other Axis I disorders (Reich, 2003) was also absent. The trend towards an interaction effect indicated that - if present at all - the negative predictive value of comorbid Axis II disorders was restricted to the WL group.

Finally, we found that patients who dropped out during the assessment phase or therapy had been hospitalized less frequently, showed less insight and had lower social functioning and more negative symptoms. This pattern of findings indicates that there might be a more socially isolated and difficult-to-reach subgroup of highly symptomatic patients with low insight, who are more sceptical of services and treatment offers. However, the combination of these variables could hardly improve the overall prediction of drop-out, which is partly explicable by the small numbers of dropout.

We would like to note some methodological aspects that affect the comparability of our findings to previous studies. Overall, despite the absence of exclusion criteria, the sample in our study was comparable to samples from previous CBTp treatment trials in terms of their baseline PANSS scores (e.g. Rector et al., 2003; Bechdolf et al., 2004; Valmaggia et al., 2005), age, gender and length of disorder (Lincoln et al., 2008). Also, the drop-out rates and

pre-post effect sizes for positive symptoms were in the range of those found in the literature (Lincoln et al., 2008). Nevertheless, fewer patients benefited in terms of negative symptoms and this might have led to an underestimation of predictors for negative symptom improvement.

A limitation of this study is the fairly small number of patients on which the CBTp versus WL comparisons are based (34 versus 39). Also, the lack of a control condition for the follow-up analyses makes it impossible to conclude whether variance in follow-up change is related to CBTp. Furthermore, the combined groups differed in the number of assessments and the overall time they spent in the treatment project. We controlled for possible cohort effects by including predictor x cohort interactions in the analyses based on the combined sample. However, there were few significant interactions and these were not straightforward to interpret. Finally, in the light of the numerous single regression analyses that were not adjusted to reduce type I error, the single findings must be interpreted with caution. This applies especially to the few significant specific predictors of change in the CBTp versus wait-list group and to the individual significant predictors in drop-out analyses, of which none reached significance in the logistic regression.

A strength of our study is that the analyses were based on a clinically heterogeneous sample of unselected patients. This might explain why we were able to identify a larger number of predictors than many of the previous studies that were largely based on more selective samples of patients who were more homogenous in terms of symptom severity, comorbidity and functioning.

Although we were able to identify numerous predictors of change in the combined sample, the analyses of CBTp specific predictors based on the controlled design do not provide a sufficient basis to pre-select patients that should or should not be referred to CBTp. Despite the inclusion of numerous potential predictors there was a marked absence of patient

characteristics that significantly predicted whether a patient will improve during CBTp or not. The only noteworthy significant CBTp specific predictor of improvement in negative symptoms was a shorter duration of disorder. On the background of the other studies with similar findings, this indicates that it is important to get patients into treatment at an earlier stage. On a more positive note, the findings indicate that lower education, neurocognitive deficits and comorbid disorders pose no barrier to improvement during CBT. Based on the findings of the predictors of symptom change that took place irrespective of group status, one could speculate that the effect of CBTp might be further enhanced by including a more thorough baseline assessment of comorbid depression, reasoning biases and social cognition and targeting these domains in a more profound way. Possibly the use of more behavioral activation techniques, placing a stronger emphasis on improving self-esteem and using interventions aimed at emotion regulation might prove helpful for patients with comorbid depression. Also, we need to undertake more effort to understand why patients with poor social functioning, lack of insight and negative symptoms discontinue therapy, and reflect on how drop-out in this group might be prevented, for example by doing home visits or adapting the setting (e.g. going for walks with the patient).

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Acknowledgment.

The study was funded in part by the Deutsche Forschungsgemeinschaft (DFG, Grant LI 1298/3-1). We would like to thank Björn Schlier for his assistance with the analyses.

Table 1 Overview of the means and ranges of the potential predictors of outcome at baseline

	CBTp first sample (N = 34)			WL / delayed CBT sample (N = 39)			Possible Range
	M / %	SD	range	M / %	SD	range	
Socio-demographic variables							
Female gender	47.06 %	-	-	43.59 %	-	-	-
Age	33.44	10.06	19 - 52	33.44	10.85	17 - 63	-
Years of education	15.07	4.14	3 - 24	15.77	3.42	10 - 23	-
Clinical variables							
Duration of disorder (in years)	11.26	10.15	1 - 35	9.76	6.92	0.5 - 32	-
Number of hospitalizations ^a	5.56	8.69	0 - 35	3.90	5.65	0 - 25	-
Comorbid Axis I disorder	53.94 %	-	-	49.83 %	-	-	-
Comorbid Axis II disorder	26.47 %	-	-	15.38 %	-	-	-
Symptom severity							
Positive symptoms (PANSS)	14.38	3.58	9 - 24	14.69	4.65	7 - 27	7 - 49
Negative symptoms (PANSS)	14.59	4.86	9 - 26	13.28	4.52	7 - 24	7 - 49
Delusion conviction (PDI)	29.88	26.64	0 - 103	24.64	23.49	0 - 109	0 - 200
Lack of Insight (PANSS G-12)	1.94	1.13	1 - 5	1.87	0.95	1 - 4	1 - 7
Depression (CDSS)	7.15	4.32	1 - 13	5.54	3.22	1 - 13	0 - 27
Social functioning							
Role Functioning Scale	27.35	10.24	2 - 44	30.26	6.73	16 - 43	0 - 48
Social skills	19.29	3.87	7 - 25	20	4.61	7 - 27	5 - 30
Neurocognitive variables							
Cognitive flexibility (TMT-B) ^b	70.26	33.06	19 - 151	56.63	20.22	27 - 96	
Memory (WMS)	23.5	8.33	6 - 41	26.97	8.89	12 - 41	
Reasoning biases							
Jumping-to-conclusions ^c	12.21	4.48	4 - 26	15.69	5.47	3 - 28	3 - 30

Internal attributions of neg. events	7.79	3.62	2 - 13	7.94	3.48	0 - 16	0 - 20
Theory of mind	9.57	3.05	3 - 15	9.95	2.27	4 - 14	0 - 16

Note. PANSS = Positive and Negative Syndrome Scale; PDI = Peters et al. Delusion Inventory; CDSS = Calgary Depression Rating Scale for Schizophrenia; WAIS-Inf = Wechsler Adult Intelligence Scale – Information subscale; TMT = Trail-Making Test; WMS = Wechsler Memory Scale

^a = variable used for prediction of dropout only

^b = higher scores reflect higher completion times

^c = higher scores reflect a larger number of beads drawn, therefore a lower tendency to jump-to-conclusions

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Table 2 Linear Regressions of the Group x Predictor Interaction on Positive and Negative Symptoms
Controlling for Baseline Symptoms

Predictor	Negative Symptoms		Positive Symptoms	
	β	p	β	p
Socio-demographic variables				
Female gender	0.017	0.856	-0.132	.187
Age	0.118	0.906	0.049	.629
Years of education	-0.011	0.901	0.131	.194
Clinical variables				
Duration of disorder	0.050	0.614	0.251	0.015
Comorbid Axis I disorder	0.010	0.914	0.002	0.981
Comorbid Axis II disorder	0.043	0.654	-0.192	0.052
Symptom severity				
Negative/positive symptoms (PANSS) ^a	-0.093	0.289	0.019	0.859
Delusion conviction (PDI)	0.019	0.845	0.072	0.481
Lack of Insight (PANSS G-12)	-0.093	0.326	-0.161	0.108
Depression (CDSS)	0.057	0.554	-0.129	0.176
Social functioning				
Role Functioning Scale	0.069	0.469	0.002	0.988
Social skills	-0.063	0.523	-0.023	0.821
Neurocognitive variables				
Cognitive flexibility (TMT-B)	-0.184	0.075	0.101	0.363
Memory (WMS)	0.187	0.061	-0.129	0.191
Reasoning biases				
Jumping-to-conclusions	-0.054	0.580	0.217	0.039
Internal attributions of neg. events	0.036	0.731	-0.186	0.110
Theory of mind	0.088	0.341	0.087	0.375

Note. Baseline symptoms were entered in block one (with $\beta = 0.59$, $p < 0.001$ for positive symptoms and $\beta = 0.56$, $p < 0.001$ for negative symptoms). Group status was entered in block two along with the predictor and the group x predictor interaction (with β s ranging from 0.27-.36, all $ps < 0.01$, for positive symptoms and from -0.04 - -0.12, all $ps > 0.20$ for negative symptoms).

^a Baseline negative symptoms were entered as a predictor of positive symptoms at outcome and baseline positive symptoms were entered as a predictor of negative symptoms at outcome

Table 3 Results of the logistic regression of predictors on dropout versus non-dropout

Included	B(SE)	95% CI for Odds Ratio		
		Lower	Odds Ratio	Upper
Constant	-.68 (2.1)			
No of previous hospitalisations	-.09 (.09)	.78	.92	1.1
Negative symptoms	-.04 (.10)	.79	.96	1.2
Insight	.57 (.32)	.96	1.8	3.4
Social functioning	-.38 (.16)	.66	.78	1.0

Note. $R^2=.14$ (Cox & Snell), $.25$ (Nagelkerke). Model $\chi^2(4)=12.2, p=.016$.

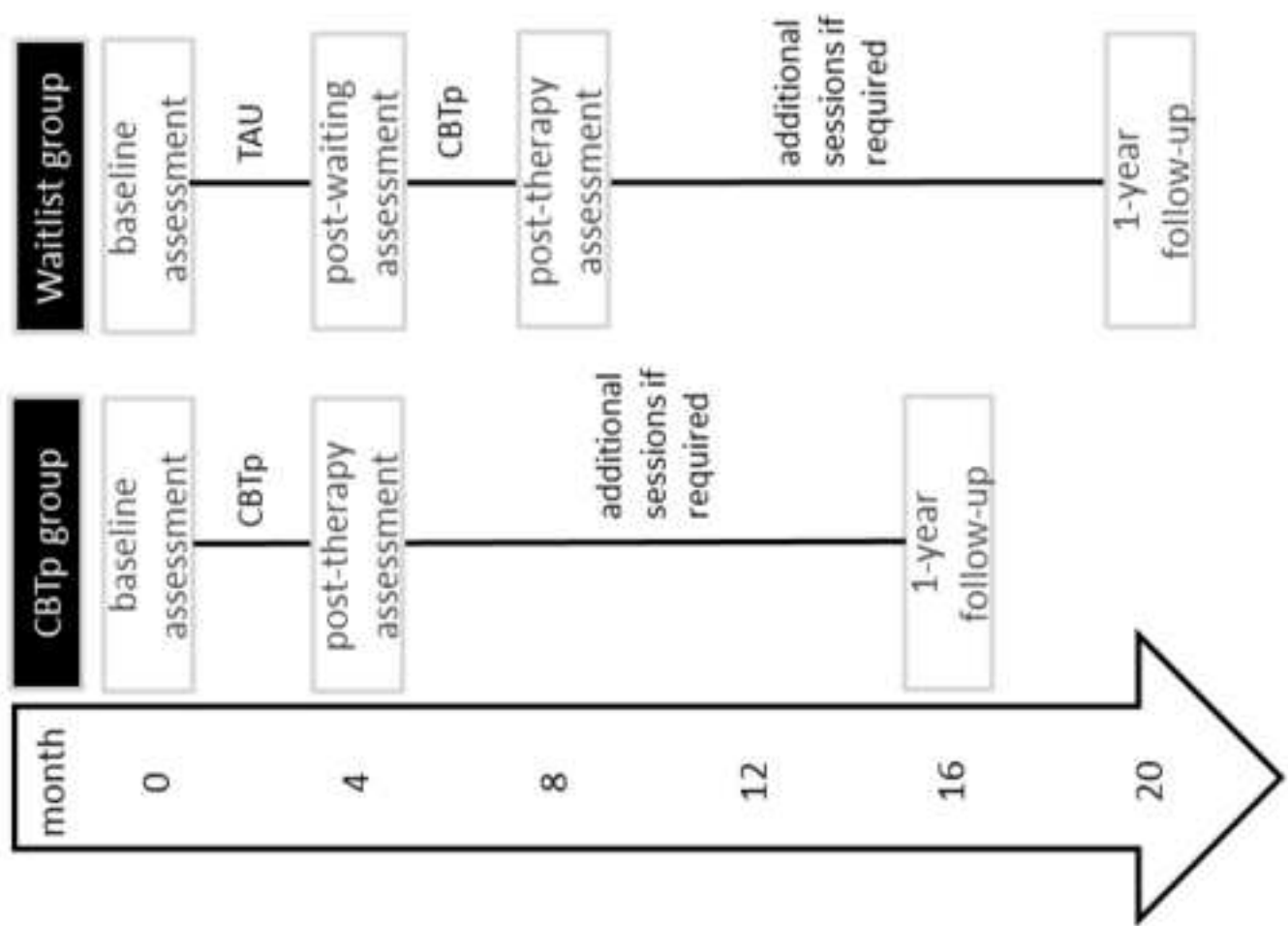


Figure 1 - Timepoints of the Assessments in the CBTp and the Waitlist Group.

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