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Original article

What is the minimal dose of cognitive behavior therapy for psychosis? An approximation using repeated assessments over 45 sessions

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ABSTRACT

Background: The general efficacy of cognitive behavior therapy for psychosis (CBTp) is well established. Although guidelines recommend that CBTp should be offered over a minimum of 16 sessions, the minimal number of sessions required to achieve significant changes in psychopathology has not been systematically investigated. Empirically informed knowledge of the minimal and optimal dose of CBTp is relevant in terms of dissemination and cost-effectiveness.
Methods: We approached the question of what constitutes an appropriate dose by investigating the dose (duration of CBTp) × response (symptomatic improvement) relationship for positive symptoms, negative symptoms and depression. Patients with psychotic disorders ($n = 58$) were assessed over the course of 45 sessions of CBTp in a clinical practice setting. At baseline and after session 5, 15, 25, and 45, general psychopathology, psychotic symptoms, symptom distress and coping were assessed with self-report questionnaires. Additionally, individually defined target symptoms and coping were assessed after each session.
Results: Significant symptom improvement and reduction of symptom distress took place by session 15, and stayed fairly stable thereafter. The frequency of positive and negative symptoms reached a minimum by session 25.
Conclusions: Our findings support recommendations to provide CBTp over a minimum of 16 sessions and indicate that these recommendations are generalizable to clinical practice settings. However, the findings also imply that 25 sessions are the more appropriate dose. This study contributes to an empirically informed discussion on the minimal and optimal dose of CBTp. It also provides a basis for planning randomized trials comparing briefer and longer versions of CBTp.
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1. Introduction

The effectiveness of CBT for psychosis (CBTp) for improving symptoms is well established [1,2] and various international guidelines now recommend to offer CBTp as an adjunct to medical treatment to patients with psychosis [3–5]. Furthermore, there is evidence that CBTp does not increase the likelihood of adverse events and, unlike antipsychotic medication, does not have a range of unpleasant side effects [6]. Finally, it has been shown that the effects found in randomized-controlled trials generalize well to clinical practice settings [7–9].

Despite its evidence base, implementation of CBTp in clinical services is unsatisfactory [10,11]. Even in the United Kingdom, where it has been most intensely studied, only 10% of those who should have been offered CBTp are estimated to have access to it [11,12]. The situation is even less satisfactory for other countries that have included CBTp in their national guidelines, such as Germany [13,14], Canada [15] or the United States [16].

Some researchers have suggested adapting current practices in CBTp both in duration and in complexity in order to make them more applicable in clinical practice [15]. The question of whether CBTp can also be delivered in a shorter format than the minimum of 16 sessions recommended in the NICE guidelines [6] has inspired a heated debate among researchers and practitioners in the area of CBTp. Although shorter interventions might be more likely to be implemented, especially in inpatient settings, opponents of such suggestions are concerned that "watering

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down" the original concept of CBTp will render it less effective or – in the light of the small effect sizes – possibly even utterly ineffective.

This concern is understandable. However, it needs noting that the evidence base for the NICE recommendation that CBTp is to be offered with a minimum of 16 sessions of 60 minutes [5] is primarily driven by studies that included at least 16 planned sessions rather than by research that investigated the question of optimal length. In fact, the authors of the guidelines point out that they were unable to draw any firm conclusions from subgroup analyses assessing the impact of treatment duration. The duration of the randomized-controlled trials was guided by the requirements posed by the health care system, which was, in most cases, the National Health Service in the United Kingdom. Had most of the randomized controlled trials been conducted in Germany, where the typical length of CBT for severe mental disorders is 45 sessions, the guidelines might have recommended a higher number of sessions. In recognition of this problem, the NICE guidelines stress the need to conduct an adequately powered RCT "to investigate the most appropriate duration and number of sessions for CBT in people with schizophrenia" (page 243) [6]. Although we agree that conducting an RCT is the ideal way to investigate the question of appropriate dose, it poses the practical question of which durations should meaningfully be compared with each other. As there is an almost infinite number of potentially interesting comparisons (e.g. 10 sessions versus 40 sessions, 15 sessions versus 30 sessions), it appears to be more efficient to arrive at a first approximation by investigating dose-response relationships within a setting that allows for a comparatively long duration of treatment.

A question that may be added in the face of the complex symptomatology of psychotic disorders is whether the minimal effective dose is equal for all symptom domains or whether different symptoms improve at different rates, and thus require longer or shorter durations of treatment. For example, it can be assumed that negative symptoms, that have been found to have an enduring quality [17] and do not respond well to medical or psychological interventions so far [18,19], and delusions, for which only small effects have been found in CBTp trials [20], take longer to change. In contrast, depression, that has been shown to respond more quickly to therapy than other disorders [21], may change earlier in treatment.

Using longitudinal data that were assessed over the course of 45 treatment sessions, we investigated (1) the timing of symptomatic improvement and (2) whether the symptomatic improvement differs for different symptom clusters (i.e. positive symptoms, negative symptoms, or depression). Furthermore, we aimed to (3) find the exact time-point during therapy, at which improvement in therapy outcome reached its peak. Based on the peak values in symptom improvement (i.e. optimum-response), an optimal dose (i.e., therapy-length) can be estimated.

1.1. Design

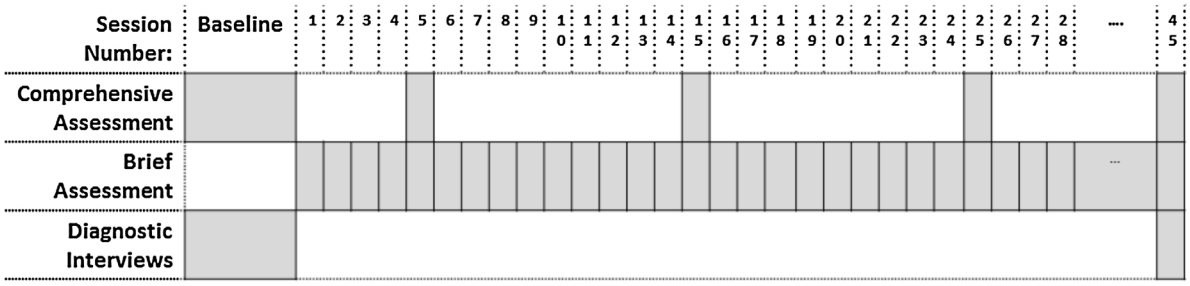
This study is part of a clinical trial on predictors and mechanisms of change in CBTp using an uncontrolled longitudinal design with repeated assessments (compare Fig. 1).

2. Method

2.1. Setting

The study took place at the outpatient clinic of a psychology department in Germany. Treatments were covered by the German insurance companies after application and expert review of indication and rationale. The number of sessions the health insurances generally provide for cognitive behavioral interventions varies between 25 sessions ("short therapy") and 45 sessions ("extensive therapy"). The 45 sessions for extensive therapy were applied for and provided to all patients included in this study.

The trial was approved by the Ethical Committee of the Department of Psychology of the University of Marburg and informed consent was obtained from all participants or their legal guardian.



LEGEND

Comprehensive Assessment: - Symptom Checklist 27plus (SCL-27plus) - Choice of Outcome In CBT for Psychoses (CHOICE) - Community Assessment of Psychic Experiences (CAPE)
Brief Assessment: - Symptom Checklist 9 (SCL-9) - Abbreviated CHOICE (CHOICE-3) - Individualized items from CAPE (CAPE-10)
Diagnostic Interviews: - Positive and Negative Syndrome Scale (PANSS) - SKID-I (in diagnostic phase only)

Fig. 1. Time-points of the assessments.

2.2. Participants

The sample consisted of 58 patients with a diagnosis of a psychotic disorder (62% schizophrenia, 31% schizoaffective disorder, 3% delusional disorder, and 3% brief psychotic disorder). The diagnoses were assessed using the Structured Clinical Interview for DSM-IV (SCID) [22]. Further inclusion criteria were:

- the presence of at least one positive or negative symptom assessed by the Positive and Negative Syndrome Scale (PANSS) [23] with a score ≥ 3;
- age between 18 and 65 years;
- sufficient language skills to communicate in German;
- absence of acute suicidality, and acute substance dependence.

Demographic and baseline clinical variables are summarized in Table 1.

2.3. Procedure

The individualized CBTp was delivered according to a published German-language manual by the first author [24] that was based on the manuals described by the pioneers of CBTp [25–28]. The intervention included the following main components:

- building rapport and gaining a detailed understanding of symptom development. A normalizing approach to psychotic symptoms was used to facilitate engagement and reduce distress;
- case formulation based on cognitive models of positive symptoms;
- working with distressing symptoms, which were conceptualized in the context of their antecedents and consequences. Maintaining factors were targeted using established cognitive behavioral techniques including problem-solving, social-skill training, exposure, socratic questioning, and behavioral experiments;
- modifying delusional beliefs using cognitive interventions such as reviewing the evidence for the beliefs;
- modifying dysfunctional beliefs about self and others;
- relapse prevention, which involved improving patients' ability to identify and react to early warning signs and symptoms.

Table 1
Demographic and clinical data at baseline.

	% or M (SD)
Sex (male/female)	60%/40%
Age	35.67 (12.69)
Years of education	13.92 (3.72)
Level of education: no/low/medium/high	2%/22%/28%/47%
Current working situation: not working/part time/full time	45%/33%/19%
Family status: married or partner/single/divorced/widowed	21%/64%/10%/2%
Years of psychosis	12.07 (7.96)
Number of previous hospitalizations	3.57 (3.71)
Number of previous psychotic episodes	4.82 (3.66)
Patients with comorbid disorders	36%
Patients not on medication	12%
Positive and Negative Syndrome Scale, positive score	15.08 (5.14)
Positive and Negative Syndrome Scale, negative score	16.97 (6.34)
Positive and Negative Syndrome Scale, general psychopathology score	36.05 (8.98)
Global assessment of functioning	42.89 (12.00)

Due to their individualized formulation-based nature, the interventions did not follow a specific order and with the exception of the assessment phase, case formulation and relapse prevention, no single intervention was mandatory. However, therapists were required not to use interventions beyond those described in the manual.

Eleven therapists (eight female; three male) treated 2 to 12 patients, respectively. Therapists had received a minimum of 10 hours of training in CBTp as part of their 3-year clinical training in CBT. All therapists received regular psychosis specific group supervision and participated in monthly self-conducted group supervision without the presence of a formal supervisor.

Prior to therapy, participants were assessed using the SCID [29] and the PANSS [23]. As can be seen in Fig. 1, in the assessment phase and after the fifth, the fifteenth, the twenty-fifth, and the final forty-fifth therapy session, the patients received a comprehensive self-report booklet including the Symptom Checklist 27 plus (SCL-27plus); [30], the Choice of Outcome In CBT for Psychoses (CHOICE) and a modified version of the Community Assessment of Psychic Experiences (CAPE) [31,32] along with other measures that were not part of this study. These comprehensive assessments took between 30 and 60 minutes to complete. Additionally, participants completed a brief inventory after each therapy session, which took about 5 minutes. At the end of therapy, patients were re-assessed with the PANSS (see Fig. 1).

2.4. Measures

2.4.1. Baseline and post-therapy assessment

Psychotic symptoms were assessed with the PANSS [23], a semi-structured interview that measures positive symptoms, negative symptoms, and general psychopathology. Symptoms are observer-rated on a 7-point-scale using detailed anchoring criteria. All patients were rated by their therapist as part of the initial diagnostic session. Two of the therapists (E.J. and M.W.) completed a certified PANSS training by the PANSS Institute and trained the other therapists prior to partaking in this study. Thirty-seven of the video-documented PANSS interviews were rated by a second therapist in order to test for interrater reliability. Rating correlations were high for the positive symptom scale ($r = 0.86$), negative symptoms ($r = 0.81$), and general psychopathology ($r = 0.77$).

2.4.2. Comprehensive assessment at baseline and sessions 5, 15, 25, and 45

The CAPE [31] is a 42-item-questionnaire that measures frequency and distress related to the three psychotic symptom categories positive symptoms (i.e., paranoia, delusions, bizarre experiences, and hallucinations), negative symptoms (i.e., affective flattening, amotivation, and social withdrawal), and depression (i.e., negative mood and hopelessness). Participants indicated on 4-point Likert scales how often they had experienced every symptom during the previous month (0 = "never", 1 = "sometimes", 2 = "often", 3 = "almost always"). For every item rated with 1 or more, participants also answered how distressed they felt due to the experience (from 0 = "not distressed" to 3 = "very distressed").

The SCL-27plus [30] is a screening instrument for mental health problems. It contains 27 items that explore five facets of psychopathology (depressive, vegetative, agoraphobic, symptoms of social phobia, and pain), which are summed up to a global severity index.

The CHOICE [33] is a CBTp and service-user oriented self-report questionnaire assessing therapy outcome. It comprises of 20 items, which deal with CBTp outcome principles (e.g., ways of dealing with distressing experiences) and recovery (e.g. coping or the ability to relax). For each item, patients rate the severity ("How would you rate yourself for this?", 0 = "worst", 10 = "best") and

satisfaction (“How satisfied are you with this?”, 0 = “not at all”, 10 = “very”). The global mean scores of CHOICE severity and CHOICE satisfaction were analyzed in this study.

2.4.3. Brief assessment after every session

Brief versions of the CAPE, SCL-27, and CHOICE were devised to assess weekly change in symptoms and therapy outcome. Psychotic symptoms were measured with an individualized brief 10-item CAPE: For each patient 10 target-symptoms with the highest scores at baseline were selected from the 42 items of the original CAPE. In equivocal cases (e.g. if twelve items had received the highest rating of three) patients were asked to select from among the items in question those that he or she considered to be most relevant. As a measure of general psychopathology, the established 9-item short form of the SCL (SCL-K-9) [34] was included. Finally, as a stand-in for the full CHOICE, the three CHOICE-items assessing “ways of dealing with everyday life stresses”, “ways of dealing with distressing experiences (e.g. beliefs, thoughts, voices)”, and “ways of dealing with unpleasant feelings and emotions (e.g. depression, worry, anger)” were included. For each of the scales the rating referred to the last seven days.

2.5. Strategy of data analysis

All analyses were carried out using R 3.2.2 (R Core Team, 2015). First, in order to estimate the extent of pre- to post-change and the comparability to previous trials on CBTp, the PANSS pre- to post-effect sizes were calculated.

As the main analysis, we tested for the timing of symptom improvement by calculating linear multilevel regression (i.e., five assessment time-points were nested within patients) of CAPE positive symptoms, negative symptoms and depression scores as well as CHOICE and SCL27-scores. Assessment point was treated as a factor. Thus, all assessment points (session 5, 15, 25, and 45) were tested for a difference from baseline (i.e., session 1). This analysis provides both an indicator of approximate time of first symptom improvement (i.e., first significant difference from baseline) as well as an indicator of stability of symptom improvement (i.e. stable significant differences following an initial symptom improvement).

As a secondary outcome, we calculated the number of patients who could be considered as “recovered” on the symptom outcome measures (CAPE and SCL-27plus). This was operationalized by defining the cut-off as the point from which it is more likely that a patient belongs to the “functional” than to the “dysfunctional” population. The recovery criterion was calculated by using the population mean and reliability for each of the respective questionnaires in order to estimate a patient’s individual 95% estimation interval for their score based on the standard error of measurement (SEM, with 95% estimation interval = individual score $\pm$ 1.96*SEM). Patients were considered recovered on the respective dimension, if (a) their score differed from the average score of schizophrenia patients and (b) their score was comparable to the healthy population mean. A 95% estimation interval (i.e., individual score $\pm$ 1.96*SEM) had to include the population mean score, but not the schizophrenia patient mean score. For the CAPE we used the mean scores and standard errors of measurement (SEM) from a healthy population sample and patients with a current diagnosis of schizophrenia (Jaya et al., in prep). Due to a lack of norm data for psychosis samples for the SCL-27plus, patients were considered to be recovered if their score-band included the population mean (M = 0.85) [30].

Finally, in order to test for the specific time-point with peak symptom improvement, we calculated linear multilevel regression models of the brief assessment outcome variables. In all analyses the independent variable session was entered as factor. Thus, the regression weight for factor level x (= session no x) equals the symptom change from baseline to the respective session.

All multilevel regression analyses were random intercept, fixed slope models. For all analyses, all available data from all participants were used, including participants with any amount of missing values and participants who discontinued prior to 45 sessions of therapy.

3. Results

3.1. Pre- to post-changes in the PANSS and attrition rates

Of the 58 patients, 36 completed the full 45 sessions, 5 patients completed therapy at an earlier time-point, while 17 patients discontinued over the duration of the trial. An overview of the reasons for and time of discontinuation is presented in Fig. 2.

Pre- to post-effect sizes of PANSS-subscales at the beginning and end of therapy indicate a medium reduction in positive symptoms (d = 0.552; 95% CI: [0.210; 0.893]), negative symptoms (d = 0.512, 95% CI: [0.148; 0.876]) and general psychopathology (d = 0.505; 95% CI: [0.190; 0.820]) for patients who were interviewed post-therapy (n = 30).

3.2. Improvement in symptoms and coping over the course of treatment

Participants completed 75.5% of the comprehensive self-report booklets at baseline assessment, on the fifth, twenty-fifth and forty-fifth therapy session. Among those who completed the full 45 sessions of therapy the overall completion rate of the questionnaires was 91.2%. Comparatively more data was missing at the later assessment points, with 98.3% completion at baseline, 82.8% at session 5, 74.1% at session 15, 62.1% at session 25 and 60.3% at session 45.

As can be seen in Table 2, the first significant reduction in frequency and distress scores of negative symptoms and depression was found by session 15 and remained stably reduced for the remaining time-points. Logistic regression of recovery rates corroborated this pattern for negative symptom distress and depression distress. However, significant increases in recovery rates for negative symptom frequency were not evident before session 25 and the recovery rates in depression frequency did not increase significantly over the course of the treatment. For positive symptom frequency, significant decrease in terms of absolute change was only found by session 45. Positive symptom distress, by contrast, was decreased by session 15 but this reduction did not remain stable throughout the following assessment time-points. Moreover, the findings for recovery rates diverged: for symptom frequency there were no significant changes, while recovery scores of positive symptom distress indicated stable reduction in distress by session 5.

Akin to negative symptoms, the group average SCL-27plus symptom score had dropped significantly below the starting mean score by 15 sessions of therapy ($b = -0.20$, $t(160.1) = -3.13$, $p = 0.002$) and remained stable after that. Similarly, the logistic multilevel regression showed the number of participants fulfilling the SCL-27plus recovery criterion to increase significantly from baseline to 15 sessions (OR = 4.94, $z = 2.38$, $p = 0.017$, see Table 2 for a complete overview).

Similarly, coping as indicated by the CHOICE subscales increased significantly by session 15 (CHOICE severity: $b = 0.53$, $t(159.3) = 3.95$, $p < 0.001$; CHOICE satisfaction: $b = 0.72$, $t(160.0) = 4.70$, $p < 0.001$) and remained stable after that.

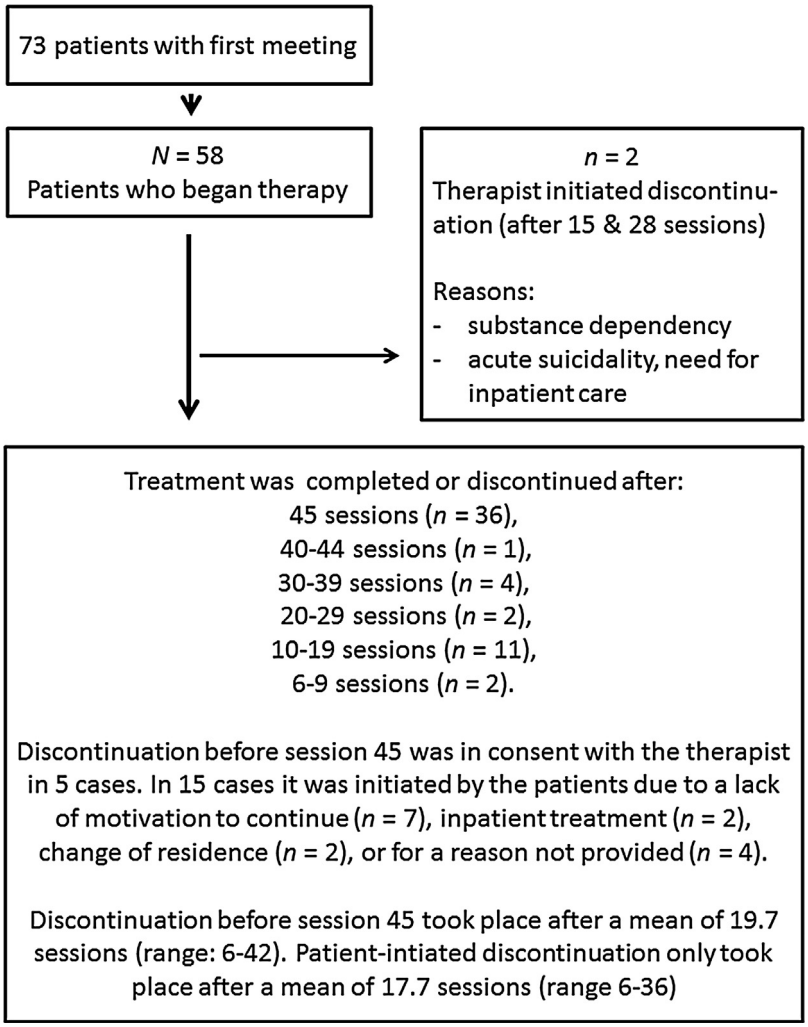


Fig. 2. Flowchart of patient dropout.

3.3. Peaks of symptomatic improvement in the session-by-session assessments

Participants completed 60.2% of all brief self-report sheets after every session. Among the therapy completers the completion rate of brief self-report sheets was 72.5%. Fig. 3 depicts the symptomatic improvement from baseline onwards in the CAPE 10, SCL-K-9, and CHOICE-3, scores. As can be seen, the CAPE negative symptoms showed the most change from baseline at session 27 ($b = -2.09$, $t[1439.4] = -6.461$, $p < 0.001$). Change in CAPE depression scores showed a similar peak at sessions 26 ($b = -1.70$, $t[1344.4] = -4.454$, $p < 0.001$), with the most improvement by session 44 ($b = -1.89$, $t[1343.8] = -3.922$, $p < 0.001$). Changes in CAPE positive symptom scores, by contrast, showed a late, non-significant, maximum peak of symptom improvement at session 36 ($b = -0.55$, $t[1203] = -1.59$, $p = 0.111$). For general pathology in the SCL-K-9 and the CHOICE coping items the peak in improvement was at session 27 (SCL-K-9: $b = -0.56$, $t[1443.6] = -4.22$, $p < 0.001$; CHOICE-3: $b = 5.11$, $t[1432.1] = 5.52$, $p < 0.001$).

4. Discussion

With the exception of positive symptom distress we found no significant changes in global psychopathology, symptom frequency or distress or coping to be evident before session 15. Thus, up to 15 sessions are likely to be required for statistically or clinically significant improvements in psychopathology to occur. This appears to confirm the recommendation in the NICE guidelines to conduct at least 16 sessions [5].

However, before drawing firm conclusions it is worth analyzing the pattern of findings in more detail. If we consider the primary variable of interest, it becomes clear that changes were evident by session 15 for negative symptoms, depression, global psychopathology and the consumer-rated outcome measure CHOICE. For positive symptoms, however, only symptom distress was significantly, albeit transiently, reduced by session 15 while symptom frequency did not change until session 45. Moreover, if we consider the secondary variable of interest, significant increases in the number of patients recovered, the improvement by session 15 is less obvious. Although recovery rates increased significantly for symptom distress in all domains, this was not the case for the frequency of positive and negative symptoms or depression. Thus, it appears that reliably reducing symptom frequency might require longer. It follows that recommendations on the minimal number of sessions also depend on the outcome variable of interest.

Further additional findings are worth noting: The changes achieved in negative symptoms, depression, general psychopathology and in the CHOICE by session 15 generally remained fairly stable thereafter. If we consider the session-by-session ratings in Fig. 3 we see that improvement continued until somewhere between session 20 and session 30 in each of these scales with no obvious trend towards further improvement after this time-period. For positive symptoms the overall picture is less clear, with

Table 2
Response in terms of absolute change in outcome measure scores and change in percentage considered recovered at session 5, 15, 25, and 45.

		Absolute change: b; *t*-value or recovery: odds-ratio; *z*-value			
Outcome measure	Analysis	Session 5	Session 15	Session 25	Session 45
CAPE positive symptoms					
Frequency	Absolute change	−0.06****; −1.72	−0.07****; −1.91	−0.07****; −1.83	**−0.11****; −2.89
	Recovery	1.53; 0.46	2.28; 0.86	7.49****; 1.87	2.22; 0.81
Distress	Absolute change	−0.08****; −1.90	**−0.12****; −2.62	−0.09****; −1.92	−0.08****; −1.69
	Recovery	**10.5****; 2.87	12.2**; 2.85	8.87*; 2.47	17.4**; 2.89
CAPE negative symptoms					
Frequency	Absolute change	−0.04; −0.45	**−0.19***; −2.20	−0.36***; −3.95	−0.19*; −1.98
	Recovery	1.03; 0.05	2.87****; 1.79	**8.65****; 3.13	5.47*; 2.49
Distress	Absolute change	0.14****; −1.73	**−0.27****; −3.08	−0.42***; −4.50	−0.32**; −3.31
	Recovery	1.83; 1.03	**6.86****; 2.97	5.95**; 2.67	3.25****; 1.73
CAPE depression					
Frequency	Absolute change	−0.08; −1.19	**−0.18***; −2.49	−0.21**; −2.65	−0.16****; −1.93
	Recovery	1.32; 0.42	2.24; 1.09	1.82; 0.76	1.90; 0.79
Distress	Absolute change	−0.14****; −1.66	**−0.29*****; −3.39	−0.30***; −3.36	−0.28**; −2.97
	Recovery	2.43; 1.55	**9.19*****; 3.30	9.04**; 3.15	10.5**; 3.10
SCL-27plus	Absolute change	−0.08; −1.33	**−0.20****; −3.13	−0.24***; −3.56	−0.22**; −3.12
	Recovery	2.83****; 1.65	**4.93***; 2.38	6.75*; 2.67	4.85*; 2.10
CHOICE severity	Absolute change	0.18; 1.40	**0.53*****; 3.95	0.69***; 4.90	0.65***; 4.39
CHOICE satisfaction	Absolute change	0.23; 1.58	**0.72*****; 4.70	0.68***; 4.23	0.84***; 4.90

Absolute change: b: absolute change from baseline/session 1; unstandardized coefficient (linear multilevel regression); recovery: recovery rate in comparison to baseline/session 1 (logistic multilevel regression); SCL-27plus: symptom checklist 27plus; CHOICE: CHoice of Outcome In Cbt for psychosEs; CAPE: Community Assessment of Psychic Experiences.
Bold printed figures mark the first significant change from baseline.
P-values (satterwhaite approximation).
* $P < 0.05$.
** $P < 0.01$.
*** $P < 0.001$.
**** $P < 0.1$.

distress improving early in therapy but symptom frequency improving slowly or not at all (depending on the criterion) and no clear indication of an optimal point for discontinuation of therapy before session 45.

Taken together, we argue that 15 sessions as a minimal dose to improve symptom distress, global psychopathology and consumer relevant outcomes is justified by the data. However, 15 sessions seem to constitute the lowest boundary and 25 sessions might be more appropriate if the aim is to reach to stronger improvements and improvements across a wider range of outcomes. With the exception of positive symptom frequency continuing for longer than 25 sessions did not appear to have obvious benefits.

The finding that 15 sessions of CBT for psychosis appear to be a minimal dose corresponds well with what has been shown in regard to psychotherapy in other diagnostic groups. Howard et al. [21] first introduced a dose-effect methodology and also found a negatively accelerated curve indicating that the effect of psychotherapy is greater in earlier sessions and increases more slowly at higher dosage levels. They also reported that 75% of the patients improved by the 25th session and adding another 25 sessions only increased this rate to 85%. Anderson and Lambert [35] found the median time required to attain clinically significant change to be 11 sessions, but patients with high levels of distress to require more sessions.

However, these findings relate to typical research settings. In clinical practice settings, patient and structural issues often require adaptations to interventions [36] that might also affect the minimal number of sessions required. In this study, therapists were recruited for study participation according to their availability and did not receive the intensive trainings and supervision typical of RCTs. Also, therapist treatment adherence was not monitored. Rather, therapists were free to apply the techniques in a manner that they felt comfortable with. Although, we did not control for the techniques used and cannot rule out that therapists strayed from the manual or were one-sided in their use of techniques, the documentation of interventions in a previous clinical practice setting demonstrated a broad and flexible use of the techniques in the manual [7]. Finally, unlike the homogeneous, well-selected patient samples in RCTs, the only exclusion criteria we used were based on safety (exclusion of suicidal or acutely intoxicated patients) or feasibility (language skills). Despite this, the PANSS positive, negative, and general scores were comparable to previous RCTs using the PANSS, as were age, gender distribution, and length of disorder (Lincoln et al., 2008). Although previous clinical practice studies have indicated good transferability of CBTp to outpatient settings [7–9], in this study the uncontrolled pre-post-effect sizes for general psychopathology (d = .51), positive symptoms (d = 0.55), and negative symptoms (d = 0.51) were in the bottom part of the range of those found in the literature. Moreover, the dropout rate of almost 30% exceeded those described in the literature of RCTs [37] but was comparable to those found in effectiveness trials [8,9,38]. In this regard, it needs noting that the inclusion criterion of a PANSS positive or negative item of 3 that indicates only mild or little interference with functioning is a very low threshold for psychosis. This criterion was the result of a compromise between including a help-seeking sample without any further restriction (and thus maximal generalisability to clinical practice settings) and assuring a minimal degree of symptoms. However, this approach is likely to have made it harder to detect change during therapy than using the stricter criteria typical of RCTs of CBT for psychosis would have done.

Thus, the "minimal dose" of 15 sessions and the potentially more "optimal dose" of 25 sessions that are suggested by this study need to be interpreted in the light of clinical practice settings with routinely trained therapists. The effects might have been larger with more intense training, more specialized supervision and treatment monitoring and it is likely that in the case of stronger effects fewer sessions would have been needed altogether. On the other hand, the therapists in this study were nevertheless motivated young therapists who followed a treatment manual.

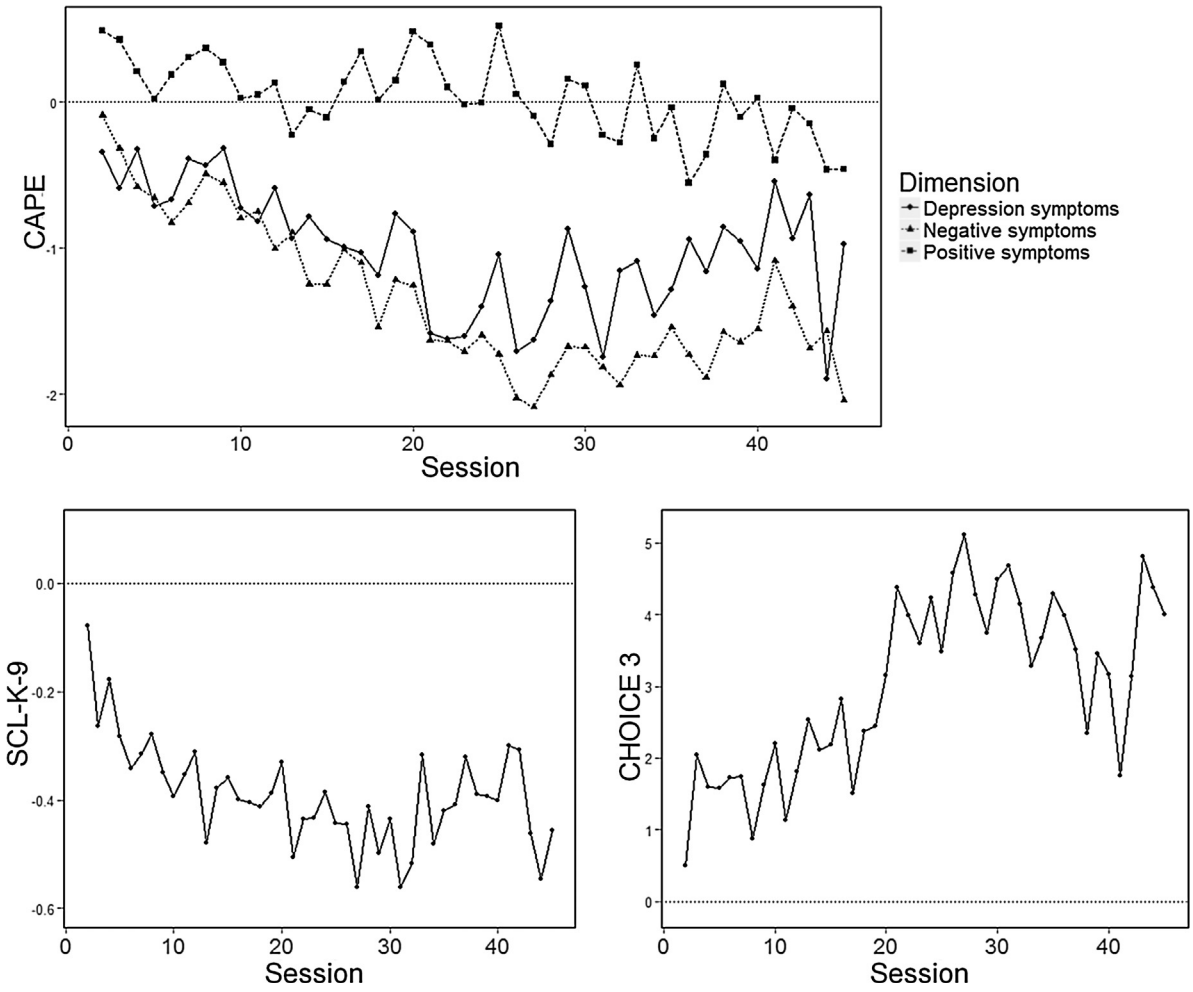


Fig. 3. Estimated difference from session 1 in general psychopathology (SCL-9), therapy outcome (CHOICE- 3) and psychotic symptoms (CAPE). Estimated differences based on random intercept, fixed slope multilevel regression by therapy session (as an ordered factor with 45 levels).

In contrast, many practitioners are reluctant to fully adhere to a manual [39] and thus may need longer to achieve the same level of success. Thus, the boundary of 15 or 25 sessions may even represent the lower end within a clinical practice setting and can only be recommended if treatment is conducted following appropriate treatment manuals.

An interesting finding was that recovery rates for positive symptom distress increased significantly by session 5. This is likely to be the result of using a normalizing approach, which has been found to make patients feel more understood, validated and motivated to continue treatment than psychoeducational approaches, even after just one session [40]. A somewhat surprising finding was that negative symptoms improved at a higher rate than did positive symptoms. Due to the slightly higher baseline-values in negative symptoms, a conservative interpretation could be that this reflects a comparatively stronger regression to the mean. Even so, the assumption that negative symptom change will lag behind change in other domains was not justified by the data.

Another finding worth comment was that 20 patients discontinued therapy before reaching the full 45 sessions. In 5 of these cases, both therapist and patient consented on terminating treatment, agreeing that the main aims had been reached. Among the remaining 15, only 4 discontinued for external reasons (necessity of inpatient treatment, change of residence). It can thus be speculated that in some of the other cases, the decision to terminate was based on patients' estimations that they had already achieved what they wanted to achieve at present. Interestingly, discontinuation before session 45 took place after a mean of 19.7 sessions, which is more than what we have concluded to be a minimal dose. Relatedly, Stiles et al. [41] recently analyzed treatment gains and treatment duration in a cohort of more than 25,000 patients, who had received talking therapies in routine care settings in the UK. They considered their findings to be consistent with the responsive regulation model, which suggests that in routine care participants tend to end therapy when gains reach a good-enough level and suggested to shift attention away from decisions about optimal treatment length to the question of what constitutes good-enough gains for individual patients. Thus, although investigating minimal and optimal doses can inform health care decisions, health care systems should allow for recommended dosage to be used in a flexible manner, taking into account that some patients (e.g. those taking sedative medication or those with chronic symptoms [42]) may take longer to benefit than others.

4.1. Strengths and limitations

The use of the session-by-session ratings combined with full assessments at 5 time-points over the course of therapy that allowed for treatments of up to 45 sessions is a major strength of the study. Furthermore, the inclusion of individualized symptoms and the CHOICE measure is an advantage because they are more suitable to reflect individual changes than are the global symptom measures. The setting chosen reflects clinical reality and is thus

generalizable to other clinical practice settings and unlikely to underestimate the minimal number of sessions needed.

A limitation is the high rate of missing data, which was partly due to difficulties in motivating therapists and patients to comply with the tedious data compilation. Attrition was particularly high in the final treatment phase between session 25 and 45 rendering estimates for this phase less reliable.

The CAPE, rather than observer-rated interview-based assessments was chosen for reasons of practicability based on numerous studies indicating that patients can reliably self-report negative [43,44] and positive symptoms [45]. Nevertheless, more commonly used observer-rating scales, such as the PANSS would have been more comparable to the outcome measures used in other studies that have provided the basis for existing guideline recommendations. Pre- to post-PANSS scores, however, were used to assess the overall treatment effect and compare it with other studies. In this regard, it is a limitation that only the therapist-rated PANSS-ratings were available at post-assessment, which might have led to an overestimation of the effect. Moreover, the selection of the individually most problematic CAPE items for the weekly rating makes it difficult to rule out a regression to the mean phenomenon where they ameliorate. However, the other weekly ratings were not selected on this basis and showed a comparable pattern of change. Finally, it needs noting that – comparable to previous work on dose-response relationships [21,41] – this is an uncontrolled trial. Only a controlled design can identify how the minimal changes (or maintenance) achieved after session 15 relate to an untreated control group and can thus be considered as truly due to the treatment.

5. Conclusion

Based on the absence of significant change before session 15, we argue, however, that it is safe to say that any attempt to reduce the duration of CBT below the number of 16 sessions as recommended in the NICE guidelines is unlikely to be successful in clinical practice. Thus, the 15 sessions identified as minimal present a lower boundary for the randomized controlled trial recommended by NICE that is needed to further elucidate the question of optimal treatment duration.

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Disclosure of interest

The authors declare that they have no competing interest.

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