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Meta-analysis and Meta-regression of Cognitive Behavioral Therapy for Psychosis (CBTp) Across Time: The Effectiveness of CBTp has Improved for Delusions

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Published research shows small-to-medium effects of Cognitive Behavioral Therapy for Psychosis (CBTp) on reducing psychotic symptoms. Given the on-going development of CBTp interventions, the aim of this systematic review is to examine whether the effectiveness of CBTp has changed across time. MEDLINE, EMBASE, PsycINFO, and CENTRAL were searched for randomized controlled trials examining CBTp interventions targeting positive and/or negative symptoms vs treatment as usual. Four meta-analyses were carried out to examine the effectiveness of CBTp for: positive symptoms; delusions; hallucinations; and negative symptoms. Four meta-regressions examined whether the effectiveness of CBTp changed across time for these groups of symptoms. A total of 28 studies (n = 2698) yielded a pooled g of −0.24 (95% confidence interval [CI] −0.32, −0.16, P < .001) favoring CBTp for positive symptoms, with nonsignificant heterogeneity (Q = 26.87, P = .47; I^2 =0%); 13 studies (n = 890) yielded a pooled g of −0.36 (95% CI −0.59, −0.13, P = .002) for delusions, with substantial heterogeneity (Q = 31.99, P = .001; I^2 =62%); 16 studies (n = 849) yielded a pooled g of −0.26 (95% CI −0.42, −0.11, P < .001) for hallucinations, with nonsignificant heterogeneity (Q = 18.10, P = .26; I^2 =17%); 19 studies (n = 1761) yielded a pooled g of −0.22 (95% CI −0.33, −0.12, P < .001) for negative symptoms, with nonsignificant heterogeneity (Q = 20.32, P = .32, I^2 =11%). Meta-regressions indicated a significant effect of year on the effectiveness of CBTp only for delusions (F[1, 11] = 5.99, P = .032; R^2 = 0.594); methodological quality did not effect this finding. Findings indicate small-to-medium effects of CBTp for psychotic symptoms, with increasing effectiveness across time for delusions.

Key words: psychosis/trauma/meta-analysis

Introduction

Over their lifetime, approximately 1% of the UK population will receive a diagnosis of schizophrenia.[1] The complexity of this condition puts pressure on services to provide effective treatments. The National Institute for Care and Health Excellence (NICE) recommends Cognitive Behavior Therapy for Psychosis (CBTp) as one of the psychological treatments for psychosis.[2] A recent meta-analysis reported that CBTp had small effects on psychotic symptoms, and the authors subsequently questioned whether CBTp should continue to be a recommended treatment.[3] McKenna and Kingdon have similarly argued that CBTp has been "oversold" as a treatment for psychosis.[4]

Meta-analyses have consistently reported small-to-moderate effects of CBTp on psychotic symptoms. One meta-analysis reported an effect of 0.25 for positive symptoms when CBTp was compared with a control intervention and an effect size of 0.31 when CBTp was compared with treatment as usual (TAU).[3] When aspects of bias were considered, the effect sizes decreased. Another meta-analysis reported an effect size of 0.37 for positive symptoms, although, when methodological quality was taken into account, the effect size for the high-quality studies reduced and was 0.22 against 0.49 for the low-quality studies.[5] A more recent meta-analysis found a small effect of 0.16 for positive symptoms favoring CBTp vs other psychological interventions.[6]

Bentall proposed that examining individual psychotic symptoms, such as delusions and hallucinations, could be particularly helpful as it could lead to identifying symptom-specific psychological mechanisms that could be targeted in therapy.[7] Steele et al similarly suggest that exploring the positive syndrome could lead to missing out on the multidimensional nature of individual symptoms.[8] When types of positive symptoms were assessed separately, one meta-analysis found an effect size of 0.44

favoring CBTp for hallucinations and an effect size of 0.36 favoring CBTp for delusions when compared with the control group (TAU or an active control or a combination of both).[9] Another meta-analysis found an effect size of 0.27 favoring CBTp for delusions when compared with TAU.[10]

In terms of negative symptoms, one meta-analysis reported an effect size of 0.44 favoring CBTp, although, when the studies were divided by methodological quality, the effect size for the high-quality studies reduced and was 0.21 against 0.61 for the low-quality studies,[5] once again pointing to the importance of considering methodological quality. Another meta-analysis reported particularly low effect sizes for CBTp on negative symptoms: 0.08 when compared with a control intervention and 0.13 when compared with TAU.[3] As with positive symptoms, when aspects of bias were taken into consideration, the effect sizes decreased further. This low effect size may also reflect the focus of the clinical interventions. One meta-analysis, eg, found that most studies assessed negative symptoms as secondary treatment targets rather than primary targets.[11] The authors argued that the clinical focus on positive symptoms, and the measurement of these as primary outcomes limits our understanding of the actual effect of CBTp targeting negative symptoms. Others have made similar claims, suggesting that cognitive-behavioral therapists have devoted more time to understanding and addressing positive symptoms. This focus could lead to a poorer understanding of negative symptoms and explain why they are usually the secondary outcomes in randomized controlled trials (RCTs).[12]

As described above, meta-analytic reviews have shown differing effect sizes for the symptom-based outcomes, and difference in the methodological quality of trials has been shown to be important. Another likely reason for the variation is the difference in clinical focus between trials—some interventions target differing symptoms of psychosis, such as delusions or hallucinations. Another explanation for differences in effect sizes could be that clinical practice has evolved and that the delivery of CBTp has improved over time. Since the early trials of CBTp, the intervention has moved from challenging and disputing the content of delusions and/or hallucinations to focusing on changing service users' relationship with their symptoms. This evolution reflects a theoretical shift: it is not the content of thoughts that need to be addressed but rather the interpretation of the thoughts (ie, meta-cognition).[13] In addition to the evolution of CBTp, there have been advances in the understanding of the psychological mechanisms that could contribute to the formation, maintenance, and experience of psychotic symptoms: such as the role of emotion,[14] arousal,[15] self-esteem,[16] attachment,[17] interpersonal issues,[18] and loss and trauma.[19] Understanding these psychological mechanisms may permit more targeted treatment within the CBTp framework for service users, with their variety of personal histories, views of the world, and psychotic difficulties.[20]

A recent meta-analysis examined whether the effectiveness of CBT for symptoms of depression changed across time.[21] The authors found a decrease in effectiveness over time, where studies with earlier publication dates had larger effect sizes than more recent publications. The authors suggested that the declining treatment outcomes could be a reflection of the quality of the intervention, specifically the degree of clinician experience and the fidelity to the manual.

In psychosis research, there is a need to explore the effectiveness of CBTp across time, at least for positive symptoms. In a recent meta-analysis of negative symptoms, a meta-regression of the effects of CBTp was implemented by dividing the year of publication into four chronological clusters.[11] The findings showed a decreasing effect, with better treatment outcomes for studies with an earlier publication date. The researchers also explored the impact of treatment focus and found that studies with strong behavioral interventions had larger effect sizes (Hedges' $g = 0.25$) compared with studies that had fewer behavioral components (Hedges' $g = 0.02$). They demonstrate a change in treatment over time; a shift away from the behavioral components reduced effect sizes, although they also found that higher quality trials were associated with lower effect sizes. This points to a need to consider trial quality as a factor when exploring change over time.

We carried out a systematic review of the effectiveness of CBTp across time, with separate analyses for positive symptoms, delusions, hallucinations, and negative symptoms; we also explored methodological quality. Our first hypothesis was that we would find an increase in the effectiveness of CBTp across time for positive symptoms and for hallucinations and delusions when these symptoms were assessed individually. Our second hypothesis was that there would not be an increase in the effectiveness of CBTp across time for negative symptoms.

Methods

Electronic searches of MEDLINE, EMBASE, PsycINFO, and CENTRAL were conducted on April 26, 2018 without a date restriction. Bibliographic references from previous meta-analytic reviews[3,9] were manually searched for studies that may not have been identified by the search strategy, which is available in supplementary material S1.

Criteria for Study Inclusion/Exclusion

Studies included were parallel-group RCTs, single-blind RCTs, and open RCTs. Participants were those who experienced positive and/or negative symptoms from all mental health settings, including At-Risk-Mental-State (ARMS) participants. ARMS participants are at a preclinical stage and are considered at a higher risk of developing

psychosis than the general population. The inclusion criterion for the intervention group was individual or group CBTp or cognitive therapy (CT) that targeted positive or negative symptoms. The NICE guidelines[2] and a description of the components of CBTp from a Delphi study[22] were used in evaluating whether studies were delivering CBTp. If a study used other therapeutic elements, eg, family interventions, it was included if the CBTp was the predominant intervention. The inclusion criterion for the control group was TAU, which was conceptualized as the accepted usual treatment that was part of routine practice within the service where the RCT was delivered. Only outcomes that were researcher-rated at the end of treatment for positive or negative symptoms were included. Unless stated, it was assumed that the outcome measures were researcher-rated rather than client self-reported.

Unpublished studies and studies not in the English language were excluded. Studies including only children (under age 18) were excluded. Studies where participants had comorbid difficulties, such as recent history of violent behavior, cognitive impairment, or substance use, were also excluded. Studies were excluded if the intervention was integrative rather than predominantly CBTp. Studies were excluded if CBTp was compared with another intervention that was not considered TAU. Studies that described only self-reported outcomes were also excluded. A summary of the inclusion/exclusion criteria is available in supplementary material S2.

Methodological Quality and Bias

Since methodological quality of RCTs has been proposed as a possible source of funnel plot asymmetry,[23] where lower quality trials may show larger intervention effects compared with higher quality trials,[24] the RCT-Psychotherapy Quality Rating Scale (RCT-PQRS) and the Cochrane Risk of Bias Tool were used to evaluate studies included in the meta-analysis.

The RCT-PQRS[25] is a 25-item scale that assesses the quality of psychotherapies in RCTs. Items 1–24 are rated on a 0–2 Likert scale. A score of "0" reflects a poorly described and executed study design element; a score of "1" reflects a moderately described and executed study design element or a well described but poorly executed study design element or a poorly described but well executed study design element; and a score of "2" reflects a well justified, described, and executed study design element. Item 25, which is the omnibus quality rating of the whole study, is rated on a Likert scale from 1 to 7, where "1" reflects exceptionally poor quality and "7" reflects exceptionally good quality. All 25 items are grouped into six domains: description of subjects, definition and delivery of treatment, outcome measures, data analysis, treatment assignment, and overall quality of the study. To determine the omnibus quality rating (a score of 1–7) for each study, all subscales were averaged, then an overall average of the subscales was scaled on a 7-point rating scale; Cronbach's $\alpha = .87$.

The Cochrane Risk of Bias Tool[26] has five domains: selection bias, performance bias, attrition bias, reporting bias, and other bias. There are two parts to assessment within each domain item. First, the magnitude of risk of bias is judged as low, high, or unclear—using the guidance provided in the assessment tool. Second, text descriptions of the trial characteristics on which the judgments of risk of bias are based can be included to ensure transparency and to show support for the decision.

Stages of the Review and Meta-analysis

Author K.S. devised the search strategy with input from an information specialist. K.S. screened eligible studies twice to ensure that no studies were missed. Interrater reliability from a random selection of studies at the screening stage was calculated using ratings from another reviewer—S.R., a research assistant. Any disagreements between K.S. and S.R. were first discussed between themselves; if consensus was not reached authors, B.B. and C.M. were included in the discussion and a consensus decision was made. Data extraction including methodological quality and bias was carried out by K.S.. Interrater reliability for methodological quality and bias was calculated using S.R.'s ratings from a random selection of studies.

Data Analytic Plan

Effect sizes were computed using Review Manager[27] (RevMan; version 5.3) using the random-effects model. The random-effects model assigns study weights, allowing studies that yield a more precise estimate to carry more importance.[28] To examine whether the effectiveness of CBTp has improved over time for positive symptoms, delusions, hallucinations, and negative symptoms, four meta-regression analyses were carried out using the Statistical Package for the Social Sciences (SPSS; version 24) software.[29] The linear regression analysis was selected using the year of publication as the independent variable and Hedges' *g* effect sizes from RevMan as the dependent variable. Higgins and Thompson proposed that a meta-regression should be weighted to take into account both within-study and between-studies variance.[30] All meta-regressions used weights produced in RevMan, which were inserted into the "WLS weight" option in the linear regression.

Since Pickering et al proposed that co-occurring symptoms may confound predictors,[31] hallucinations were adjusted for when examining delusions and vice versa in the additional analyses. As it can be argued that the methodological quality of RCTs assessing CBTp may have changed across time, additional analyses including methodological quality were implemented where we

found significant effect of year of publication on effect size. The methodological quality scores from the RCT-PQRS were entered into the linear regression to assess whether it confounded the relationship between the year of publication and the observed effect sizes and also to assess for moderation using the interaction term RCT-PQRS × YEAR.

Publication bias was examined using the Begg and Mazumdar's Rank Order Correlation test,[32] Egger's regression intercept test,[33] and Duval and Tweedie's trim-and-fill procedure[34] using the Comprehensive Meta-Analysis software (version 3).[35]

Additional Analyses Undertaken

Additional analyses were computed when examining the effects of CBTp for positive symptoms. The inclusion criteria included RCTs where participants experienced positive or negative symptoms. Trials that examined ARMS were, therefore, included.[36,37] Since this population differs from those who have experienced first episode psychosis or recurrent psychosis, a separate meta-analysis was carried out excluding the two ARMS studies to examine whether this affected the observed pooled effect size. Two studies were self-guided and one was based on virtual reality (VR); another separate analysis was carried out excluding these three studies.[38–40] Finally, in terms of negative symptoms, one study used a scale that was not accessible, and we could, therefore, not be sure that it was measuring negative symptoms.[41] Although we excluded this study from the main analysis, we conducted a separate meta-analysis with it included to examine its impact on the pooled estimate.

Results

The systematic literature search produced 3451 titles. After the initial duplicate copies were removed, 2407 remained and were screened by title and abstract; 218 of these articles were included in the final screening phase yielding 29 studies that were eligible for analysis as shown in figure 1. These studies were published between 1998 and 2018.

Additional Study Exclusions and Considerations

One study was excluded because the outcomes were self-reported at baseline and researcher-rated at the end of treatment.[42] We considered that this lack of consistency could have affected outcomes. Another study reported only state paranoia scores—how the individual felt within the past 15 min.[43] We excluded this study because this method of measurement significantly deviated from the other included studies. In one study, two participants in the CT group and one in the TAU group self-reported at the end of treatment[44]; this was included as the rest of the outcome data were researcher-rated. One study[45] was excluded because it did not report the end-of-treatment data, and we were unable to access those data from the authors. Several studies that focused on prioritizing other service user difficulties, such as anxiety or depression,[46] were excluded as not all participants received the same intervention. RCTs that delivered CBTp but only to service users who exhibited warning signs of potential relapse were also excluded as not all service users received the same intervention.[47]

Several of the studies retrieved were based on the same data set. In cases where data could not be extracted from the original article because, eg, they were missing, incomplete, or presented in change scores, the article with the most complete statistical information was sought, although the original article was cited.[48,49] Characteristics of the included studies are shown in table 1.

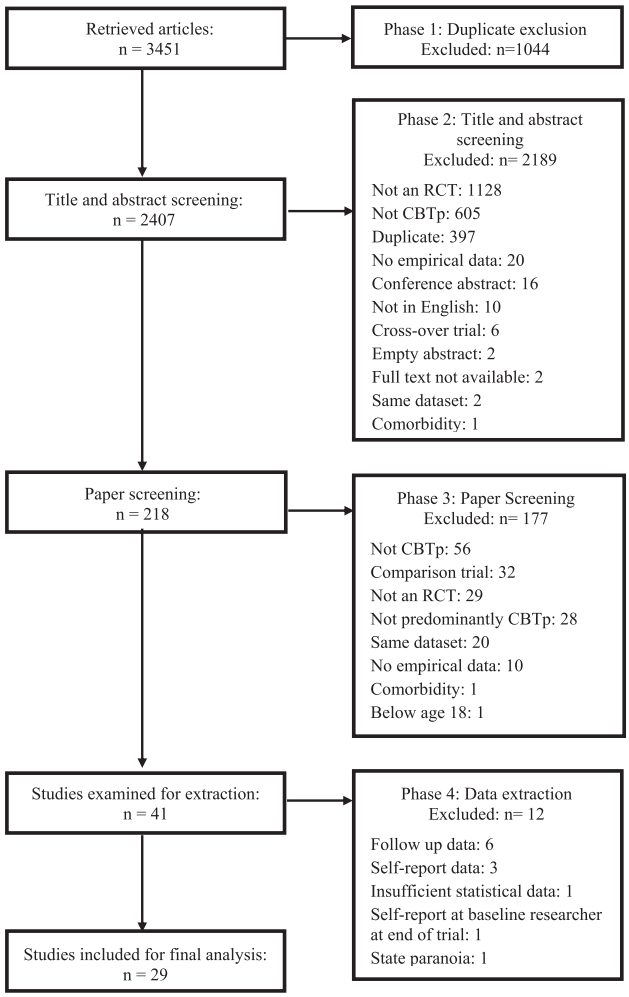

Figure 1. PRISMA diagram of the studies included in the meta-analysis.

Interrater Reliability

From the initial 2407 titles, 406 (17%) were randomly selected for reliability testing. The agreement rate was

Table 1. Study characteristics

Author, year	Intervention group	Control group	Country	Method of delivery	Intervention length	Sessions offered	Sessions received	Targeted symptoms
Tarrier 1998	CBTp + TAU	TAU	United Kingdom	Individual	10 weeks	20 sessions	Not recorded	Positive; negative
Lewis 2002	CBTp + TAU	TAU	United Kingdom	Individual	5 weeks	15–20 h + booster	Mean 16.1; 95% CI (15.2–17.1)	Positive
Rector 2003	CBTp + ETAU	ETAU	Canada	Individual	26 weeks	20 sessions	Not reported	Positive; negative
Durham 2003	CBTp + TAU	TAU	United Kingdom	Individual	39 weeks	20 sessions	Not reported	Positive; negative
Jolley 2003	CT + TAU	TAU	United Kingdom	Individual	26 weeks	18 sessions	Mean 7.5; SD 6.4	Positive (distress)
Trower 2004	CT + TAU	TAU	United Kingdom	Individual	26 weeks	Not reported	Median 16	Hallucinations (distress)
Startup 2004	CBTp + TAU	TAU	United Kingdom	Individual	26 weeks	25 sessions	Mean 12.9; SD 9.4	Positive; negative
Barrowclough 2006	CBTp + TAU	TAU	United Kingdom	Group	26 weeks	18 sessions	Mean 10.4; SD 6.5	Positive
McLeod 2007	CBTp + TAU	TAU	United Kingdom	Group	12 weeks	8 sessions	Not reported	Hallucinations
Lecomte 2008	CBTp + TAU	TAU	Canada	Group	13 weeks	24 sessions	Not reported	Positive; negative
Garety 2008 no carer	CBTp + TAU	TAU	United Kingdom	Individual	52 weeks	12–20 sessions	Mean 14.4; SD 7.8	Positive; negative
Garety 2008 carer	CBTp + TAU	TAU	United Kingdom	Individual	52 weeks	12–20 sessions	Mean 13.9; SD 8.0	Positive; negative
Pinninti 2010	CBTp + TAU(SGA)	TAU(SGA)	United States	Individual	12 weeks	12 sessions	Mean 11.93; SD 0.83	Positive
van Der Gaag 2011	CBTp + TAU	TAU	Netherlands	Individual	26 weeks	26 sessions	Not reported	Positive; negative
Lincoln 2012	CBTp + TAU	TAU	Germany	Individual	38 weeks[a]	Not reported	Mean 28.9; SD 7.4	Positive; negative
Morrison 2012	CBTuhr + TAU + monitoring	TAU + monitoring	United Kingdom	Individual	26 weeks	26 sessions + booster	Mean 9.11; SD 6.69	Positive; negative
van der Gaag 2012	CBTuhr + TAU	TAU	Netherlands	Individual	26 weeks	26 sessions	Mean 10	Positive; negative
Rathod 2013	CaCBT + TAU	TAU	United Kingdom	Individual	16–20 weeks	16 sessions	Mean 13.6; SD 4.9	Positive (distress)
Krakvik 2013	CBTp + TAU	TAU	Norway	Individual	17–26 weeks	20 sessions	Not reported	Positive (distress)
Morrison 2014	CBTp + TAU	TAU	United Kingdom	Individual	39 weeks	26 sessions + booster	Mean 13.3; SD 7.57	Positive; negative
Birchwood 2014	CBTp + TAU	TAU	United Kingdom	Individual	39 weeks	25 sessions	Mean 19; SD 9	Hallucinations (distress)
Naeem 2015	CaCBT + FI + TAU	TAU	Pakistan	Individual	17 weeks	6 sessions	Not reported	Positive; negative
Ruggeri 2015	CBTp + FI + TAU	TAU	Italy	Individual	39 weeks	CBTp: 20–30 sessions; FI 10–15 sessions	Not reported	Positive; negative

Table 1. Continued

Author, year	Intervention group	Control group	Country	Method of delivery	Intervention length	Sessions offered	Sessions received	Targeted symptoms
Velligan 2015	CBT + SS + TAU (MOVE)	TAU	United States	Individual	39 weeks	36 sessions	Not reported	Negative
Naeem 2016	CBTp GSH + TAU	TAU	Canada	Individual	16 weeks	12–16 sessions	Not reported	Positive; negative
Guo 2017	CBTp + TAU	TAU	China	Individual	13 weeks	8 sessions	Mean 6.5; SD 1.7	Positive; negative
Gottileb 2017	Web-based CBTp + TAU	TAU	United States	Individual	Self-paced	10 sessions	Not reported	Hallucinations
Morrison 2018	CBTp + TAU(antipsychotics)	TAU(antipsychotics)	United Kingdom	Individual	26 weeks	26 sessions + booster	Mean 14.39; SD 9.12	Positive; negative
Pot-Kolder 2018	VR-CBT + TAU	TAU	Netherlands	Individual	8–12 weeks	16 sessions	Not reported	Paranoia

Note: Intervention length reflects the maximum number of offered sessions. If studies reported length in months it was multiplied by 4.34 to determine week equivalency. CBTp, cognitive behavior therapy for psychosis; CT, cognitive therapy; FI, family involvement; CaCBT, culturally adapted CBT; SS, social skills; uhr, ultra-high risk; GSH, guided self-help; VR, virtual reality; SGA, second-generation antipsychotic; TAU, treatment as usual; ETAU, enhanced TAU; MOVE, motivation and enhancement training.
[a]Indicates the average number of sessions attended

98%. We agreed to "exclude" 390 studies, "include" 5 studies, and "could not tell" for 2 of the studies. The disagreement rate was 2% with 2 ratings being "include" vs "exclude," and 7 of the ratings being "cannot tell" vs "exclude."

From the 29 studies included, 5 were randomly selected for interrater reliability ratings of the RCT-PQRS and the Cochrane Risk of Bias Tool. For the RCT-PQRS, Cohen's Kappa was (κ) = 0.62 and, for the Cochrane Risk of Bias, Cohen's Kappa was (κ) = 0.73. According to Landis and Koch's criteria, this represents a substantial level of agreement.[50]

Meta-analyses and Meta-regressions

Positive Symptoms. The analysis for positive symptoms included 2698 participants. The pooled effect size for the 28 studies examining positive symptoms was −0.24 (95% CI −0.32, −0.16, $P < .001$) (negative sign favors CBTp). These results indicated nonsignificant heterogeneity ($Q = 26.87$, $P = .47$) with an I^2 =0%. When the two ARMS studies were excluded, the pooled effect size for the 26 studies was −0.26 (95% CI −0.34, −0.18, $P < .001$). These results indicated nonsignificant heterogeneity ($Q = 24.78$, $P = .47$), with an I^2 =0%. Finally, when in addition to the ARMS studies, the one VR and two self-help studies were removed, the pooled effect size for the 23 studies was −0.26 (95% CI −0.34, −0.17, $P < .001$). These findings also indicate nonsignificant heterogeneity ($Q = 20.57$, $P = .55$) with an I^2 =0%. Since excluding the ARMS, VR, and self-help studies made little difference to the overall pooled effect size, all 28 studies were included in the final meta-analysis; the forest plot is shown in figure 2. A weighted meta-regression indicated no effect of year on the effectiveness of CBTp on positive symptoms, $F(1,26) = 0.00$, $P = .996$, with an $R^2 = 0.001$.

Delusions. When 15 out of the 28 studies that report a specific measure of delusions were analyzed, the pooled effect for these studies was −0.33 (95% CI −0.53, −0.14, $P < .001$). These studies were heterogeneous ($Q = 32.80$, $P = .003$) with an I^2 =57%. Within this meta-analysis, there were two studies that reported that they were targeting only hallucinations and not delusions. When these studies were removed, the pooled effect size for the 890 participants was −0.36 (−0.59, −0.13, $P = .002$), with substantial heterogeneity ($Q = 31.99$, $P = .001$) with an I^2 =62%. The forest plot for these studies is shown in figure 2.

A weighted meta-regression indicated a significant effect of year on the effectiveness of CBTp, $F(1,11) = 5.99$, $P = .032$, with an $R^2 = 0.594$. In this model, the year of publication, $t(11) = -2.44$, $P = .032$, was a significant predictor of the effectiveness of CBTp on delusions, indicating that the effectiveness of CBTp increased with increasing year of publication. This finding persisted

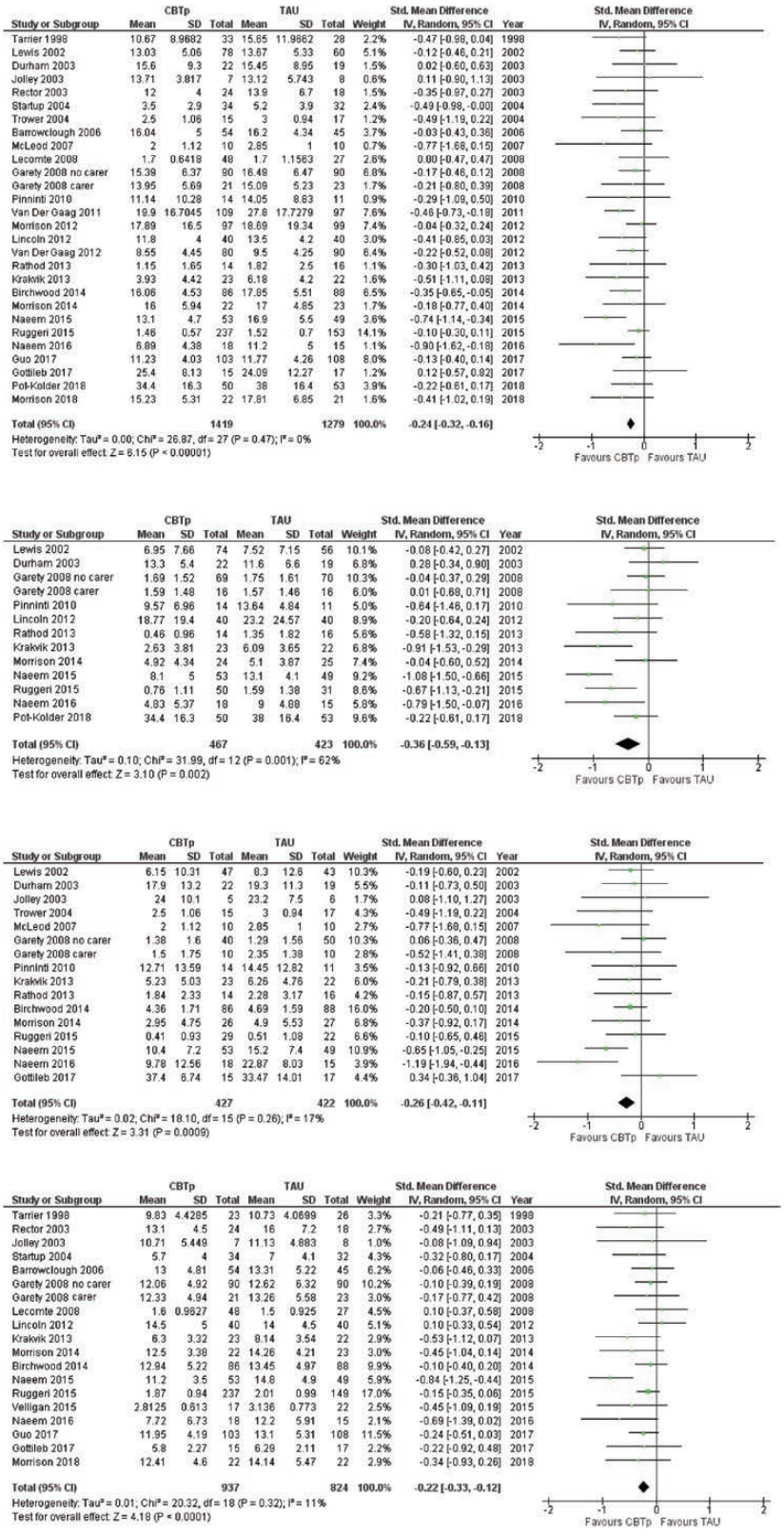

Figure 2. Forest plot of studies in the meta-analysis of positive symptoms, delusions, hallucinations, and negative symptoms, respectively.

when co-occurring hallucinations were controlled for, $F(2,8) = 5.441$, $P = .032$, with an $R^2 = 0.759$, where the year of publication, $t(8) = 2.72$, $P = .026$, still significantly predicted CBTp effectiveness. This finding also persisted when methodological quality (RCT-PQRS) was controlled for as a confounding variable, $F(3,7) = 13.34$,

$P = .003$, with an $R^2 = 0.923$, where the year of publication $t(7) = -4.29$, $P = .004$ continued to predict the effectiveness of CBTp on delusions. This finding suggests that methodological quality did not confound the relationship between year of publication and effectiveness. The interaction term between the methodological quality and year (RCT-PQRS × YEAR) was not significant, $F(1,11) = 3.67$, $P = .082$, with an $R^2 = 0.500$, suggesting that methodological quality did not moderate the relationship between the effectiveness of CBTp on delusions and year of publication.

Hallucinations. When studies that reported a score for hallucinations were taken into account, the pooled effect for the 849 participants in the 16 studies was −0.26 (95% CI −0.42, −0.11), $P < .001$. These studies indicated nonsignificant heterogeneity ($Q = 18.10$, $P = .26$) with an I^2 =17%. The forest plot for these studies is shown in figure 2. A weighted meta-regression indicated a nonsignificant effect of year on the effectiveness of CBTp on hallucinations $F(1,14) = 0.43$, $P = .522$, with an $R^2 = 0.173$. This finding was unchanged when co-occurring delusions were controlled for $F(2,8) = 1.67$, $P = .248$, with an $R^2 = 0.543$.

Negative Symptoms. When all studies that report negative symptoms were taken into account, the pooled effect for the 1761 participants in the 19 studies was −0.22 (95% CI −0.33, −0.12), $P < .001$. These studies were not heterogeneous ($Q = 20.32$, $P = .32$) with an I^2=11%. The forest plot for these studies is shown in figure 2. A weighted meta-regression indicated a nonsignificant effect of year on the impact of CBTp on negative symptoms, $F(1,16) = 0.747$, $P = .400$, with an $R^2 = 0.211$.

Publication Bias

Positive Symptoms. For positive symptoms, Begg and Mazumdar's test generated nonsignificant Kendall's τ of −0.18 ($z = 1.32$; $P = .09$, one tailed). Egger's test generated an intercept of −0.80 (95% CI −1.79, 0.19; $t[26] = 1.65$; $P = .06$, one tailed), which reflects trend-level significance, suggesting that publication bias might well exist. Duval and Tweedie's trim and fill procedure identified five potential missing studies and recomputed the new point estimate at −0.20 (95% CI −0.29, −0.11), which slightly affected the overall magnitude of the effect size.

Delusions and Hallucinations. Tests of publication bias for delusions and hallucinations were nonsignificant, suggesting that bias is not a major problem.

Negative Symptoms. For negative symptoms, Begg and Mazumdar's test generated a significant Kendall's τ of −0.29 ($z = 1.75$; $P = .04$, one tailed). Egger's test generated an intercept of −0.91 (95% CI −2.22, 0.41; $t[17] = 1.45$; $P = .08$, one tailed), which reflects nonsignificance, suggesting that publication bias is not present. Duval and Tweedie's trim and fill procedure, however, identified five potential missing studies and recomputed the new point estimate at −0.14 (95% CI −0.27, −0.02), which affected the overall magnitude of the effect size. All results of tests for publication bias are presented in table 2, with funnel plots in figure 3.

Methodological Quality

Ratings on the six domains of the Cochrane Risk of Bias were mainly low or unclear risk, and only a few studies were rated as high risk on certain domains.

Discussion

The aim of this systematic review and meta-analysis was to examine the effectiveness of CBTp for positive symptoms, delusions, hallucinations, and negative symptoms and to determine whether the effectiveness of CBTp changed across time. The results showed small-to-medium significant effects favoring CBTp for positive symptoms, hallucinations, delusions, and negative symptoms. We had hypothesized an increase in the effectiveness of CBTp over time for positive symptoms, delusions, and hallucinations, but this effect was only observed for delusions. We found that methodological quality did not affect this finding, suggesting that this

Table 2. Results of tests for publication bias for positive symptoms, delusions, hallucinations, and negative symptoms

		Effect size (95% CI)		Egger's test[b]		Begg and Mazumdar's test[b]	
Symptoms	Studies, *n*	Unadjusted	Trim and fill	*t*	*P*	*z*	*P*
Positive	28	−0.24 (−0.32; −0.16)	−0.20 (−0.29; −0.11)[a]	1.65	.06	1.32	.09
Delusions	13	−0.36 (−0.59; −0.13)	None	0.83	.21	0.79	.21
Hallucinations	16	−0.26 (−0.42; −0.11)	None	0.47	.32	0.67	.25
Negative	19	−0.22 (−0.33; −0.12)	−0.14 (−0.27; −0.02)[a]	1.45	.08	1.75	.04

Note: [a]Five studies were imputed.
[b]Tests were one-tailed.

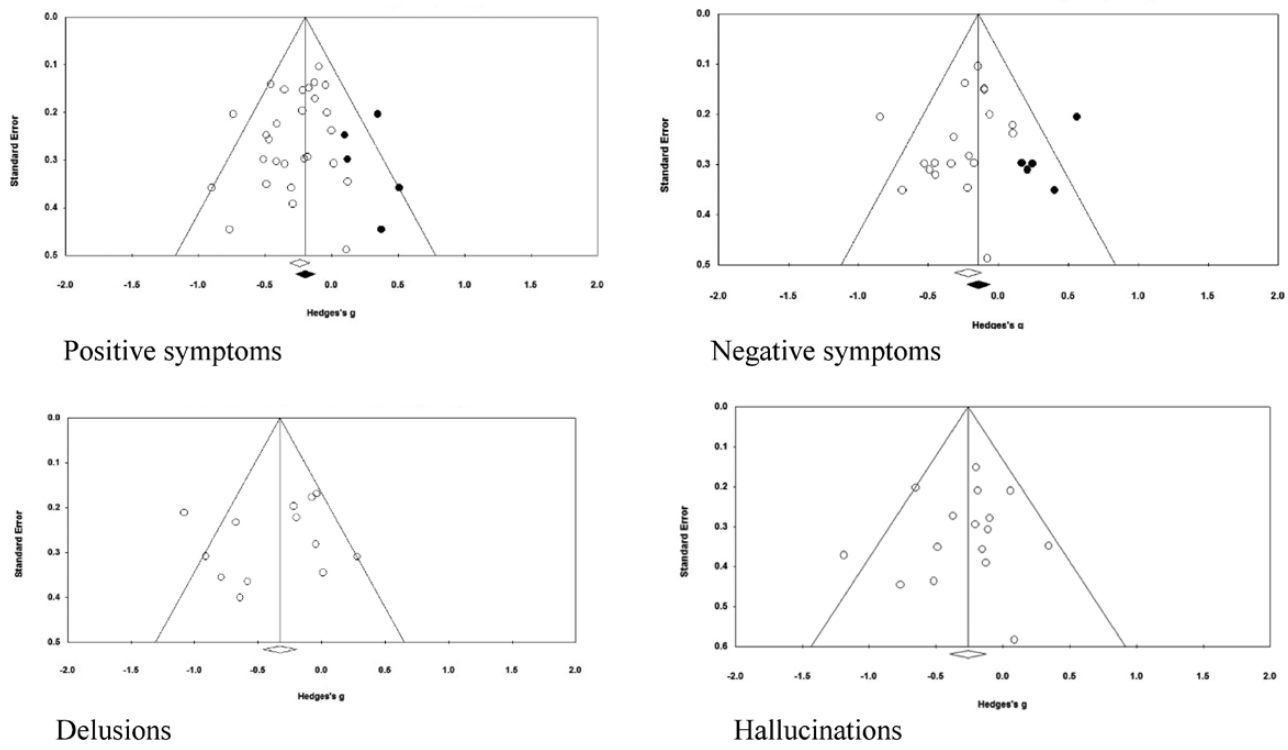

Figure 3. Funnel plot for studies in the meta-analysis examining positive symptoms, delusions, hallucinations, and negative symptoms. Open circles reflect the studies included in the meta-analysis; darkened circles reflect imputed studies; open diamond reflects the unadjusted magnitude of the effect size; darkened diamond reflects the adjusted magnitude of the effect size.

improvement in treatment effectiveness is probably not a result of changes in trial quality.

In terms of positive symptoms, the pooled effect size indicated a small significant effect of 0.24, favoring CBTp over TAU. When publication bias was assessed, the effect reduced to 0.20. Our finding is similar to that of Jauhar et al[3] who found an effect size of 0.24. Wykes et al[5] found a small-to-medium effect size of 0.37 but, as discussed in Jauhar et al, the authors used Glass's approach in calculating effect size, which has been purported to inflate the effect size. When positive symptoms were examined individually, the pooled effect size for delusions indicated a small-to-medium significant effect of 0.36 favoring CBTp and a pooled effect size of 0.26 for hallucinations. This suggests potential differences in the effect of CBTp on reduction of delusions and hallucinations and points to the importance of examining positive symptoms individually in future research.

In their recent meta-analysis assessing the effectiveness of CBTp on delusions, van der Gaag et al[9] reported the same effect size of 0.36 favoring CBTp. In terms of hallucinations, Jauhar et al[3] found an effect size of 0.34, while van der Gaag et al found an effect size of 0.44 favoring CBTp. The effect sizes in these meta-analyses are higher than our finding but an important difference is that these published meta-analyses included any comparison condition (ie, supportive counseling, TAU, and psychoeducation) and pooled data when there was more than one control group. The meaning of this difference is unclear; however, it would suggest that when CBTp is compared with an active comparison group, it appears more effective for hallucination symptoms in some of the studies. Unfortunately, the authors of these meta-analyses did not report the means and SDs; this restricts the making of comparisons between the studies and highlights the importance of future meta-analyses to provide these statistics as they may provide additional information that may be helpful in determining why such differences may exist.

In our systematic review, as in other reviews,[3,5] the hallucination and delusion scores were averaged to generate a positive symptom score in studies that did not report an overall score. Since hallucinations and delusions correlate well with one another[8] (r = .44), there is good justification for such a composite score. However, it has been reported that many people experience only delusions or only hallucinations; averaging these subscales in individuals who experience only one of these symptoms may lead to a deflated score as a result of the loss of important information in terms of severity when the scores are averaged.[8] In this meta-analysis, examining psychotic symptoms individually was shown to be more informative and meaningful than exploring positive symptoms as a syndrome as suggested in previous research.[51–53]

Why has the Effectiveness of CBTp Increased for Delusions but not for Hallucinations?

The main finding in this meta-analysis is that the effectiveness of CBTp increased for delusions but not for hallucinations or negative symptoms. It may be that the evolution in CBTp[13] and developments in the understanding of the psychological mechanisms that contribute to the formation, maintenance, and experience of psychotic symptoms have led to the improved effectiveness of CBTp for delusions.

Some researchers propose that the focus of working with hallucinations is to change the relationship an individual has with their voices (by challenging the power and omnipotence of the voices), leading to a reduction in distress rather than to a reduction in frequency.[54] Although they acknowledge that a reduction in distress might lead to a reduction in the frequency of hallucinations, they assert that this is not the focus of therapy. Since the current meta-analysis examined symptom reduction rather than distress reduction, we were unable to examine the effectiveness of CBTp on distress and whether there was improvement across time.

One of the main limitations of assessing the effectiveness of CBTp for delusions and hallucinations is that we did not always know what symptoms were targeted by the CBTp intervention. For example, only four studies in the hallucinations meta-analysis claimed to be targeting hallucinations only, while one study in the delusions meta-analysis claimed that it was specifically targeting paranoia. The rest of the studies either are not explicit in the symptom focus or they broadly state that they are targeting positive symptoms. Although the two meta-analyses carried out here explored the effectiveness of CBTp on specific symptoms, we do not know what proportion of these symptoms were targeted in each study. As a result, the interpretation of findings is difficult and, although delusions and hallucinations frequently co-occur, there are many people who experience one or the other. One study, eg, reported that delusions and hallucinations co-occurred on the Psychotic Symptom Rating Scale (PSYRATS) in 45% of the sample.[8] The authors found that the mean score for individuals reporting hallucinations only was 27.6 (SD = 6.7) but when combined with the whole group, including those who did not report hallucinations, the mean was smaller 14.4 (SD = 14.6). This difference indicates the loss of important information in terms of severity when the whole group, including those who do not experience hallucinations, is averaged. For people reporting delusions only, the discrepancy in means is smaller: 16.3 (SD = 4.0), with a whole-sample mean of 13.5 (SD = 7.1). Averaging means for the whole sample, in cases where some participants do not experience hallucinations and where hallucinations were not the targeted intervention (even in those experiencing hallucinations), may be another reason why no increase in the effectiveness of CBTp for hallucinations was observed across time. Since we do not know what proportion of the intervention within the studies actually targeted hallucinations, the observed effect of CBTp for hallucinations may not be a true reflection of the actual effect of interventions targeting hallucinations specifically.

One of the main limitations of assessing negative symptoms in the current systematic review was that there was usually no information in the paper as to what proportion of therapy goals were targeting negative symptoms. In the current meta-analysis, there was only one study that focused on targeting negative symptoms.[55] Since it is not certain whether the interventions in the studies included in the present meta-analysis actually targeted negative symptoms, the effect size observed (0.22) may not be a true reflection of the actual effect of targeted treatment. A distinction between primary or secondary negative symptoms would also have been helpful because, if a decrease in negative symptoms were observed, it could have been a result of a reduction in positive symptoms rather than through the direct targeted treatment of negative symptoms. This distinction is important as treatment for negative symptoms poses a major challenge for mental health services, and more effective treatments are needed.[56] Velthorst et al[11] reported similar findings to ours, an effect of 0.09 in favor of CBTp when negative symptoms were examined as secondary outcomes and an effect of 0.16 when negative symptoms were examined as primary outcomes.

Further Research

A closer examination of the studies in the current meta-analysis showed substantial variability in terms of manual use: some studies reported a manualized approach with adherence and fidelity ratings, others reported not using a manualized approach, while yet others reported amalgamating several different manuals. Morrison proposed that, in order to replicate outcomes, RCTs should show adherence and fidelity to the trial's models and manualized protocol.[57] This process might ascertain whether the RCTs are providing the treatment they set out to deliver. It could also help identify which models or manuals are associated with more effective outcomes. Furthermore, an assessment of long-term effectiveness using follow-up data could indicate whether effects persist, increase, or decrease with time.

Limitations

In addition to the limitations above, others need to be considered. First, the current meta-analyses only examined researcher-rated symptom outcomes. Previous research has shown poor correlations between service users' subjective ratings and clinicians' ratings of psychotic symptoms.[58] It would, therefore, have been valuable to examine both ratings; however, since most

of the studies reported researcher-rated outcomes, this would have been a much smaller analysis. Second, the meta-analyses focused on clinical outcomes rather than any other outcome that might have been important to the service users, such as quality of life or subjective recovery. Since recovery in psychosis is a personally defined journey[59] that is not always associated with symptom reduction, it would have been valuable to examine subjective recovery outcomes. Fortunately, there is a growing trend to include service user outcome measures and it may be possible for future reviewers to assimilate data from primary studies that report these items. Third, most studies included in the meta-analysis did not provide adherence ratings and the quality of the intervention, and adherence to the model is unknown. Fourth, length of treatment was not assessed, and the effect of treatment dosage is unknown. Fifth, the current meta-analyses examined data at the end of treatment. This limits our understanding whether the effects persist, increase, or decrease with time. Sixth, the effects of antipsychotic medication were not controlled for. Perhaps it was an evolution in antipsychotic medication that led to an increase in the effectiveness of the observed CBTp rather than the effects of the evolution of CBTp. Although this could be the case, the TAU group usually included medication as one of the treatments, so this does not seem to be a plausible argument. It is plausible that the effect of antipsychotic medication was to help clients engage better in therapy, but this notion would need further examination.

Conclusion

The most recent National Clinical Audit of Psychosis[60] reported that only 26% of service users were offered CBTp. The finding in the current meta-analysis suggests that CBTp can be effective at reducing psychotic symptoms and that the effectiveness of CBTp for delusions has increased over time. This finding is important because it challenges arguments that CBTp has been oversold. Instead, the clinical implications of this systematic review are that CBTp should continue to be offered as a psychological intervention to service users with psychosis, especially those experiencing delusions. On a final note, it is important to note that basing treatment decisions on meta-analytic findings can be difficult as the data rely on "average" outcomes and there are no "average" service users. Evidencing the efficacy of treatment on the outcomes that are important to service users (eg, distress) seems an important next step.

Supplementary Material

Supplementary data are available at *Schizophrenia Bulletin Open* online.

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