Article

Psychological Interventions for Psychosis: A Meta-Analysis of Comparative Outcome Studies

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Objective: Meta-analyses have demonstrated the efficacy of various interventions for psychosis, and a small number of studies have compared such interventions. The aim of this study was to provide further insight into the relative efficacy of psychological interventions for psychosis.

Method: Forty-eight outcome trials comparing psychological interventions for psychosis were identified. The comparisons included 3,295 participants. Categorization of interventions resulted in six interventions being compared against other interventions pooled. Hedges' g was calculated for all comparisons. Risk of bias was assessed using four items of the Cochrane risk of bias tool, and sensitivity analyses were conducted. Researcher allegiance was assessed, and sensitivity analyses were conducted for robust significant findings.

Results: Cognitive-behavioral therapy (CBT) was significantly more efficacious than other interventions pooled in reducing positive symptoms (g=0.16). This finding was robust in all sensitivity analyses for risk of bias but lost significance in sensitivity analyses for researcher allegiance, which suffered from low power. Social skills training was significantly more efficacious in reducing negative symptoms (g=0.27). This finding was robust in sensitivity analyses for risk of bias and researcher allegiance. Significant findings for CBT, social skills training, and cognitive remediation for overall symptoms were not robust after sensitivity analyses. CBT was significantly more efficacious when compared directly with befriending for overall symptoms (g=0.42) and supportive counseling for positive symptoms (g=0.23).

Conclusions: There are small but reliable differences in efficacy between psychological interventions for psychosis, and they occur in a pattern consistent with the specific factors of particular interventions.

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It has been suggested that all psychotherapies are roughly equivalent in efficacy (1–6), although some meta-analyses have suggested differences in relative efficacy between treatments (7). Previous meta-analyses have demonstrated the absolute efficacy of some psychological interventions for psychosis (8–16), while others have been suggested to be unreliable (17). Comparatively little is understood about the relative efficacy of psychological treatments for psychosis. The most extensive meta-analytic evidence was provided by the U.K. National Institute for Clinical Excellence (NICE) (18). However, risk of bias was not assessed, and many comparisons of psychological interventions against other active treatments were underpowered, including subgroup comparisons for positive and negative symptoms (19).

Other comparative meta-analyses have not consistently demonstrated superiority of the intervention of interest. Jones et al. (20) compared cognitive-behavioral therapy (CBT) against other interventions pooled and concluded that CBT was not reliably more efficacious. A limitation of that analysis was that the CBT group also included compliance studies (21). Lynch et al. (22) compared CBT to active control conditions and found a statistically significant benefit (Hedges' g=0.2) of CBT compared with active controls pooled for positive symptoms. However, the authors concluded that CBT was no better than nonspecific comparison treatments and that the significant effect size could be explained by lack of blinding. There were some methodological criticisms of the Lynch et al. study (23–25), and there remains controversy over which psychological interventions are most efficacious for psychosis.

No meta-analysis since NICE (18) has compiled all randomized controlled trials in which two psychological interventions for psychosis are compared and pooled these as comparison conditions (2). Given the limitations of the NICE meta-analyses and of many new studies that have been published since, a further comparative meta-analysis is warranted. Whereas previous meta-analyses

This article is featured in this month's AJP Audio, is an article that provides Clinical Guidance (p. 538), is the subject of a CME course (p. 593), and is discussed in an Editorial by Dr. Strauss (p. 479)

tended to examine only CBT compared with active treatments, in this analysis we considered all intervention types for which sufficient numbers of studies have been conducted. Our aim is to improve our understanding of which therapy is most efficacious, and for which particular symptoms.

Method

Search Strategy

A systematic literature search conducted in May 2013 identified 5,910 articles for potential inclusion. Four databases were included in the search: PubMed (1,539 abstracts), Embase (1,016 abstracts), PsycInfo (2,128 abstracts), and the Cochrane Central Register of Controlled Trials (1,227 abstracts). Abstracts were identified by entering terms indicative of common psychological interventions for psychosis combined with search terms intended to identify all relevant psychotic disorders. MeSH terms, exploded terms, and text words were employed. Reference lists of published meta-analyses were also examined.

Study Selection

We included randomized trials that included a comparison of at least two psychological interventions intended to be therapeutic and to improve psychiatric symptoms in psychosis; included outcome measures intended to assess psychotic or psychiatric symptoms; and included primarily participants with diagnoses of psychotic disorders. Trials that included patients with mood disorders with psychotic features were included only when such patients were in a minority within the sample.

Trials were excluded if the comparison condition could not be deemed an active psychological intervention (e.g., attention controls, treatment as usual, waiting list); if participants were prodromal or ultra-high risk; or if the interventions were primarily aimed at medication adherence or compliance. Only articles in English or German were considered. Interventions were defined as described in Table 1. Two authors (D.T. and M.v.d.G.) categorized interventions into relevant comparisons, and disagreements were resolved by discussion.

Quality Assessment

To assess the methodological quality of the studies included, we used the first four criteria of the Cochrane Collaboration risk of bias tool—sequence generation, allocation concealment, blinding of assessors, and incomplete outcome data (there is no clear indication that the fifth [selective outcome reporting] and sixth [other sources of bias] items influence validity [19]). Because it is impossible for these studies to employ a double-blind design, the third item (blinding of assessors) was adapted to include only outcome assessors in masking procedures. Two authors (D.T. and E.K.) assessed the risk of bias, and disagreements were resolved by discussion.

Data Extraction and Selection of Outcome Measures

Data were extracted by one of the authors (D.T.) and checked for consistency by another (E.K.). A spreadsheet piloted in a previous meta-analysis was used for data collection. Attempts were made to contact authors in cases of missing or unusable data, and calculations of missing values were carried out in accordance with the Cochrane Handbook (35).

Table 2 summarizes the study characteristics. Statistical data were extracted for outcome measures relevant to psychotic or psychiatric symptoms. In studies where multiple relevant outcome measures were used, data from all outcome measures were collected and combined as a mean effect size. Dichotomous outcome data were also considered in cases where symptom measures had been converted to dichotomous outcomes, such as clinical exacerbations.

Meta-Analyses

Psychological interventions for psychosis qualified for inclusion in a separate meta-analysis when there were at least five eligible randomized controlled trials comparing that intervention to another psychological intervention. The comparison group for each separate meta-analysis therefore became the pooled set of comparison interventions from these studies (e.g., CBT compared with other interventions pooled). This resulted in meta-analyses for six intervention types. Separate sub-meta-analyses for positive, negative, or general symptoms were undertaken when there were sufficient studies ($\geq$5) assessing these outcomes.

The Comprehensive Meta-Analysis software package, version 2.2.021, was used for all analyses and calculations. For each individual meta-analysis, aggregated effect sizes indicating the pooled difference between the two groups were calculated at end of treatment using Hedges' g. Hedges' g provides a better effect estimate for small sample sizes than similar measures applied to continuous outcome variables, such as Cohen's d (92). Alpha was set at 0.05, and 95% confidence intervals were computed.

Heterogeneity

A chi-square test provided a Q statistic to determine the presence of heterogeneity alongside an I^2 statistic as a description of the percentage of the variance in each meta-analysis that could be explained by heterogeneity between the studies rather than by chance. A value of 0% indicates no heterogeneity, 25% low heterogeneity, 50% moderate heterogeneity, and 75% high heterogeneity (93).

Additional Analyses

Publication bias was assessed for primary outcomes in each of the six meta-analyses by examining funnel plots produced by the Comprehensive Meta-Analysis program (94) as well as by using the trim-and-fill procedure to estimate the effect size after accounting for publication bias (95). Egger's test of the intercept was conducted to quantify the bias shown by the funnel plots and to determine whether it was significant.

Direct comparisons were made between psychological interventions when there were at least five studies available comparing two specific treatments. Subgroup analyses were conducted for the intervention with the highest number of eligible studies, namely, CBT. This included splitting CBT into two relevant subtypes to determine whether they had similar efficacy. Differential effects of group or individual format were investigated by entering intervention format as a moderator variable.

Researcher allegiance was examined for all studies, using a tool adapted from a previous meta-analysis (96) (see the data supplement that accompanies the online edition of this article). Two researchers independently rated studies and discussed agreement. Subgroup analyses for researcher allegiance were conducted on robust significant findings that survived the sensitivity analyses for high risk of bias, although this was not possible for all such findings because of the limited number of studies available.

Power Calculation

It was expected that a limited number of studies would be available for certain comparisons. Based on the recommendations of Borenstein (97), power calculations were conducted to

TABLE 1. Definitions of Psychological and Psychosocial Treatments of Psychosis[a]

Treatment	Definition	N_{st}	N_p
Befriending	Participants are assigned social support to match therapy hours provided in other conditions. Typically this consists of friendly discussion or social activities, not directly related to symptoms, with a supportive and empathic individual. Discussion instead focuses primarily on neutral topics, such as current affairs or hobbies, and structured group activities may also be provided. Befriending has been suggested as an efficacious intervention in reducing symptoms of psychosis (26, 27).	11	400
Cognitive-behavioral therapy (CBT)	CBT aims to promote awareness of the links between thoughts, behaviors, and feelings to help implement changes in symptoms and functioning. Therapists focus on the modification of dysfunctional thoughts and self-defeating behaviors that perpetuate symptoms or suffering. CBT specifically targeting psychosis has been developed primarily since the 1990s and was originally focused on coping with symptoms (28, 29), whereas more recent approaches have focused on challenging maladaptive cognitions through cognitive restructuring and a formulation-based approach (30–32). We identified these as two main subtypes of CBT for the purposes of this meta-analysis, referring to them as "coping enhancement" and "generic CBT."	22	706
Cognitive remediation	Cognitive deficits have been widely implicated as influential in the development and course of psychosis and have therefore been suggested as worthy treatment targets (33). Cognitive remediation refers to those interventions that target basic cognitive processes, such as working memory, attention, and executive function. This intervention is intended to improve these basic cognitive functions and may also be intended to improve various other aspects of functioning. Computer-based tasks are often the chosen method of implementing cognitive remediation.	11	475
Psychoeducation	Provision of relevant information to participants about their diagnosis with the aim of improving their understanding of and coping with their diagnosis. Various psychoeducation methods have been developed for psychosis that go further than provision of basic information and therefore may involve development of coping strategies and role playing. A group format is often utilized, and there is often considerable diversity in what may be labeled "psychoeducation." This modality is often used as a comparator intervention for more standardized forms of intervention.	8	249
Social skills training	Behavioral intervention based on behavioral and social learning traditions in which participants' social functioning is targeted in order to improve their ability to perform in social situations, manage daily life tasks, and reduce social distress. Importance is typically placed on verbal and nonverbal communication alongside learning appropriate perception and responses to social cues. The intervention may also include training in independent living skills.	16	541
Supportive counseling	Nondirective talking therapy that may be based on the work of Carl Rogers (34) or may simply be described in studies as a nondirective intervention in which participants have an open forum to discuss their difficulties, without being actively led or challenged by the therapist. Supportive counseling was therefore defined as an intervention in which the common factors of psychotherapy were present without the specific techniques applied in other, more directive therapies, such as CBT. The opportunity to discuss problems with an empathic therapist in a healing setting may provide relief for the participant without any focus on acquiring new skills or challenging cognitive distortions. Supportive counseling is often used as a means of comparing other interventions against only the common factors of psychological interventions (1).	17	529

[a] N_{st}=number of studies; N_p=number of participants who received the intervention.

determine how many studies were required for sufficient statistical power to identify relevant effects. Previous meta-analyses identified small effect sizes (g=0.1 or g=0.2) in favor of specific interventions. Conservatively assuming a high level of between-study variance (tau-squared), a statistical power of 0.80, and an alpha of 0.05, we estimated that 22 studies with a mean of 30 participants in each intervention arm would be required to detect an effect size of g=0.2. To detect an effect size of g=0.1, we estimated that 88 studies would be required.

Results

After removal of duplicates, 4,768 titles and abstracts were examined, of which 489 articles were retrieved for possible inclusion. Figure 1 describes the selection process. In the 48 included studies, a total of 3,295 participants were included in relevant comparisons of psychological interventions. Six common psychological intervention modalities were identified.

Twenty-four studies used the group format, 21 used the individual format, and three used a combination of individual and group sessions. CBT had the highest proportion of studies using only the individual format (77%), followed by supportive counseling (47%), befriending (45%), cognitive remediation (36%), psychoeducation (12.5%), and social skills training (6%). The time from baseline to posttreatment assessment ranged from 3 weeks to 104 weeks. Risk of bias varied among studies (0–4) and among intervention types. CBT had the highest proportion of studies assessed as having no bias risk (59%), followed by befriending (45.5%), supportive counseling (41%), cognitive remediation (36%), social skills training (12.5%), and psychoeducation (12.5%).

TABLE 2. Selected Characteristics of Studies Comparing Psychological or Psychosocial Interventions for Psychosis[a]

Study Authors (Reference Number)	Sample Characteristics	Relevant Comparisons	Symptom Outcome Measures	Format	Bias Risk (0–4)	Duration (weeks)	Follow-Up	Allegiance
Barretto et al. (36)	DSM-IV schizophrenia; 6 months clozapine treatment-resistant; outpatients	CBT (N=12) vs. BF (N=10)	CGI, BPRS, PANSS	Individual	2	21	6 months	CBT
Bechdolf et al. (37, 38)	ICD-10 schizophrenia or related disorder; inpatients	CBT (N=40) vs. PE (N=48)	PANSS	Group	0	8	6 and 24 months	None
Bowie et al. (39)	Schizophrenia or schizoaffective disorder; outpatients	SST (N=38) vs. CR (N=38)	PANSS	Group	1	12	24 weeks	None
Cather et al. (40)	Schizophrenia or schizoaffective disorder; outpatients	CBT (N=15) vs. PE (N=13)	PANSS, PSYRATS	Individual	1	16	N/A	CBT
Crawford et al. (41)	Schizophrenia; outpatients	BF (N=140) vs. AT (N=140)	PANSS	Group	0	12	24 months	AT
Dobson et al. (42)	DSM-III schizophrenia; outpatients (severe patients excluded)	SST (N=15) vs. BF (N=13)	PANSS	Group	3	11	3 months	None
Drury et al. (43, 44)	Current functional psychosis, excluding bipolar, hypomania, organic syndrome, confusional states, and drug or alcohol disorders	CBT (N=20) vs. BF (N=20)	PAS	Both	3	12	5 years	CBT
Durham et al. (45)	Schizophrenia, schizoaffective disorder, or delusional disorder with positive symptoms; outpatient and inpatient	CBT (N=22) vs. SC (N=23)	PANSS, PSYRATS, GAS	Individual	0	39	3 months	CBT
Eack et al. (46)	DSM-IV schizophrenia or schizoaffective disorder, in early stages of illness; outpatients	CR (N=31) vs. PE (N=27)	Composite symptoms	Group	2	104	12 months	CR
Falloon et al. (47, 48)	DSM-III schizophrenia from families high in expressed emotion; inpatients	SC (N=18) vs. FI (N=18)	Clinical exacerbation; remission; target symptom ratings	Individual	3	39	24 months	FI
Farreny et al. (49)	DSM-IV-TR schizophrenia or schizoaffective disorder; illness duration >2 years; outpatients	CR (N=34) vs. BF (N=28)	PANSS	Group	2	16	40 weeks	CR
Fries et al. (50)	ICD-10 schizophrenia and schizoaffective disorder; at least two hospitalizations; in at least partial remission at baseline	PE (N=23) vs. SC (N=17)	BPRS, SANS	Group	4	25	12 months	None
Garety et al. (51)	Recently relapsed nonaffective psychosis (ICD-10 F2 or DSM-IV), with positive symptoms; carers included in study	CBT (N=27) vs. FI (N=28)	PANSS, PSYRATS, BDI, BAI	Individual	0	52	24 months	None
Haddock et al. (52)	DSM-IV schizophrenia or schizoaffective disorder (< 5 years); current acute ward admission for positive symptoms	CBT (N=9) vs. SC (N=10)	BPRS	Individual	1	5	N/A	CBT
Haddock et al. (53)	DSM-IV schizophrenia or schizoaffective disorder; with history of violence; current antipsychotic medication and positive symptoms	CBT (N=38) vs. BF (N=39)	PANSS, PSYRATS	Individual	0	26	12 months	CBT

continued

TABLE 2. Selected Characteristics of Studies Comparing Psychological or Psychosocial Interventions for Psychosis[a] (*continued*)

Study Authors (Reference Number)	Sample Characteristics	Relevant Comparisons	Symptom Outcome Measures	Format	Bias Risk (0–4)	Duration (weeks)	Follow-Up	Allegiance
Hayes et al. (54)	DSM-III-R schizophrenia; noncurrent positive symptoms; from a range of services	SST (N=23) vs. SC (N=22)	BPRS, SANS	Group	4	18	6 months	SST
Hogarty et al. (55, 56)	RDC schizophrenia or schizoaffective disorder from families high in expressed emotion; inpatients	SST (N=23) vs. FI (N=23)	Symptom relapse	Individual	4	104	N/A	None
Hogarty et al. (57, 58)	DSM-III-R or DSM-IV schizophrenia or schizoaffective disorder; outpatients	CR (N=67) vs. PE (N=54)	Composite symptoms	Group	3	52	24 months	CR
Horan et al. (59)	DSM-IV schizophrenia or schizoaffective disorder; clinically stable outpatients	SST (N=17) vs. PE (N=17)	BPRS	Group	2	6	N/A	SST
Horan et al. (60)	DSM-IV schizophrenia, schizoaffective disorder, delusional disorder, or psychosis not otherwise specified (not secondary to substance disorder); clinically stable outpatients	SST (N=19) vs. CR (N=24)	BPRS	Group	2	12	N/A	SST
Jackson et al. (61)	First-episode psychosis, including schizophrenia, schizophreniform, schizoaffective, bipolar, delusional disorder, and psychosis not otherwise specified; inpatient and outpatient	CBT (N=31) vs. BF (N=31)	BPRS, SANS	Individual	2	12	12 months	CBT
Keefe et al. (62)	Chronic DSM-IV schizophrenia, moderate severity	CR (N=27) vs. BF (N=26)	PANSS	Group	1	12	N/A	CR
Klingberg et al. (63, 64)	DSM-IV schizophrenia, with at least one negative symptom; positive symptoms excluded; outpatients	CBT (N=99) vs. CR (N=99)	PANSS, SANS, CDSS, CGI, SCL-90	Individual	0	52	N/A	CBT
Lecomte et al. (65, 66)	Early psychosis (< 2 years), with current psychotic symptoms; stabilized outpatients	CBT (N=48) vs. SST (N=54)	BPRS	Group	0	13	6 and 12 months	None
Lewis et al. (30)	DSM-IV schizophrenia, schizophreniform, schizoaffective, or delusional disorder; first or second admission; inpatients and outpatients	CBT (N=101) vs. SC (N=106)	PANSS, PSYRATS	Individual	0	5	18 months	CBT
Liberman et al. (67)	Persistent and unremitting schizophrenia; outpatients	SST (N=42) vs. OT (N=42)	BSI, GAS, BPRS	Both	3	26	24 months	None
Lukoff et al. (68)	DSM-III schizophrenia; inpatients	SST (N=14) vs. PE (N=14)	PAS	Group	2	10	N/A	None
Marder et al. (69)	DSM-III schizophrenia; at least two acute episodes or 2 years of psychotic symptoms; male outpatients	SST (N=13) vs. SC (N=14)	BPRS exacerbations	Group	3	104	N/A	None

continued

TABLE 2. Selected Characteristics of Studies Comparing Psychological or Psychosocial Interventions for Psychosis[a] (*continued*)

Study Authors (Reference Number)	Sample Characteristics	Relevant Comparisons	Symptom Outcome Measures	Format	Bias Risk (0–4)	Duration (weeks)	Follow-Up	Allegiance
Moritz et al. (70)	Broad psychotic inpatients who met criteria for schizophreniform disorder	CBT (N=24) vs. CR (N=24)	PANSS, PSYRATS	Both	0	4	N/A	CBT
Ng and Cheung (71)	DSM-IV schizophrenia; inpatients	SST (N=18) vs. SC (N=18)	BPRS, SANS	Group	0	8	6 months	SST
O'Connor et al. (72)	DSM-IV delusional disorder; stabilized on medication	CBT (N=12) vs. SC (N=12)	MADS, BAI, BDI	Individual	3	24	N/A	CBT
Ojeda et al. (73)	DSM-IV schizophrenia; treatment-resistant; inpatients	CR (N=47) vs. OT (N=46)	PANSS	Individual	2	13	N/A	CR
Patterson et al. (74)	DSM-IV schizophrenia or schizophreniform disorder; older chronic Latino inpatients	SST (N=21) vs. SC (N=8)	PANSS	Group	3	26	12 months	SST
Patterson et al. (75)	DSM-IV schizophrenia or schizophreniform disorder; older chronic inpatients	SST (N=124) vs. SC (N=116)	PANSS, HAM-D	Group	2	26	N/A	SST
Penadés et al. (76, 77)	DSM-IV schizophrenia, chronic, with a prevalence of negative symptoms and cognitive impairment	CBT (N=20) vs. CR (N=20)	PANSS	Individual	0	17	6 months	CR
Penn et al. (78)	Schizophrenia or schizoaffective disorder and current auditory hallucinations; outpatients	CBT (N=32) vs. SC (N=33)	PANSS, BAVQ, PSYRATS	Group	0	12	3 and 12 months	CBT
Pinto et al. (79)	DSM-IV schizophrenia; treatment-refractory; outpatients	CBT (N=19) vs. SC (N=18)	BPRS, SAPS, SANS	Individual	3	26	N/A	CBT
Rodewald et al. (80)	DSM schizophrenia or schizoaffective disorder; inpatients	CR (N=44) vs. PST (N=45)	PANSS	Group	3	3	N/A	PST
Röhricht and Priebe (81)	DSM-IV schizophrenia; at least two episodes; outpatients	SC (N=21) vs. BP (N=24)	PANSS	Group	0	10	4 months	BP
Sensky et al. (26) and Turkington et al. (82)	DSM-IV or ICD-10 schizophrenia; treatment-resistant; outpatients	CBT (N=46) vs. BF (N=44)	CPRS, SANS, MADRS	Individual	0	39	9 months, 5 years	CBT
Shawyer et al. (83)	DSM-IV schizophrenia or related condition; with command hallucinations in previous 6 months; outpatients	CBT (N=21) vs. BF (N=22)	PANSS, PSYRATS, CH	Individual	0	15	6 months	CBT
Tarrier et al. (28)	DSM-III-R schizophrenia; treatment resistant	CBT (N=15) vs. PST (N=12)	BPRS, PSE	Individual	3	6	6 months	CBT
Tarrier et al. (29, 84, 85, 86)	Schizophrenia according to PSE; acute-ward inpatients	CBT (N=19) vs. SC (N=19)	BPRS, SANS	Individual	0	13	12 months	CBT
Tas et al. (87)	DSM-IV schizophrenia; clinically stable outpatients	SST (N=22) vs. BF (N=27)	PANSS	Group	0	16	N/A	SST
Valmaggia et al. (31)	DSM-IV schizophrenia; with residual delusions or auditory hallucinations; medication resistant	CBT (N=36) vs. SC (N=26)	PANSS, PSYRATS	Individual	0	22	6 months	CBT
Wykes et al. (88, 89)	DSM-IV schizophrenia; with >2 years contact with services; outpatients and inpatients	CR (N=20) vs. OT (N=16)	BPRS	Individual	0	13	6 months	CR

continued

TABLE 2. Selected Characteristics of Studies Comparing Psychological or Psychosocial Interventions for Psychosis[a] (*continued*)

Study Authors (Reference Number)	Sample Characteristics	Relevant Comparisons	Symptom Outcome Measures	Format	Bias Risk (0–4)	Duration (weeks)	Follow-Up	Allegiance
Xiang et al. (90)	DSM-IV schizophrenia; clinically stable outpatients	SST (N=48) vs. SC (N=48)	PANSS	Group	1	9	6 months	SST
Xiang et al. (91)	DSM-IV schizophrenia; clinically stable inpatients and outpatients	SST (N=50) vs. PE (N=53)	PANSS	Group	2	4	6 and 12 months	SST

[a] AT=art therapy; BAI=Beck Anxiety Inventory; BAVQ=Beliefs About Voices Questionnaire; BDI=Beck Depression Inventory; BF=befriending; BPRS=Brief Psychiatric Rating Scale; BSI=Brief Symptom Inventory; BP=body psychotherapy; CBT=cognitive-behavioral therapy; CDSS=Calgary Depression Scale for Schizophrenia; CGI=Clinical Global Impressions scale; CH=command hallucinations; CPRS=Comprehensive Psychopathological Rating Scale; CR=cognitive remediation; FI=family intervention; GAS=Global Assessment Scale; HAM-D=Hamilton Depression Rating Scale; MADRS=Montgomery-Åsberg Depression Rating Scale; MADS=Maudsley Assessment of Delusions Schedule; N=number of participants in treatment group; OT=occupational therapy; PANSS=Positive and Negative Syndrome Scale; PAS=Psychiatric Assessment Scale; PE=psychoeducation; PSE=Present State Examination; PSYRATS=Psychotic Symptom Rating Scale; PST=problem-solving therapy; RDC=Research Diagnostic Criteria; SANS=Scale for the Assessment of Negative Symptoms; SAPS=Scale for the Assessment of Positive Symptoms; SC=supportive counseling; SCL-90=Symptom Checklist–90; SST=social skills training.

FIGURE 1. Flowchart of Study Selection

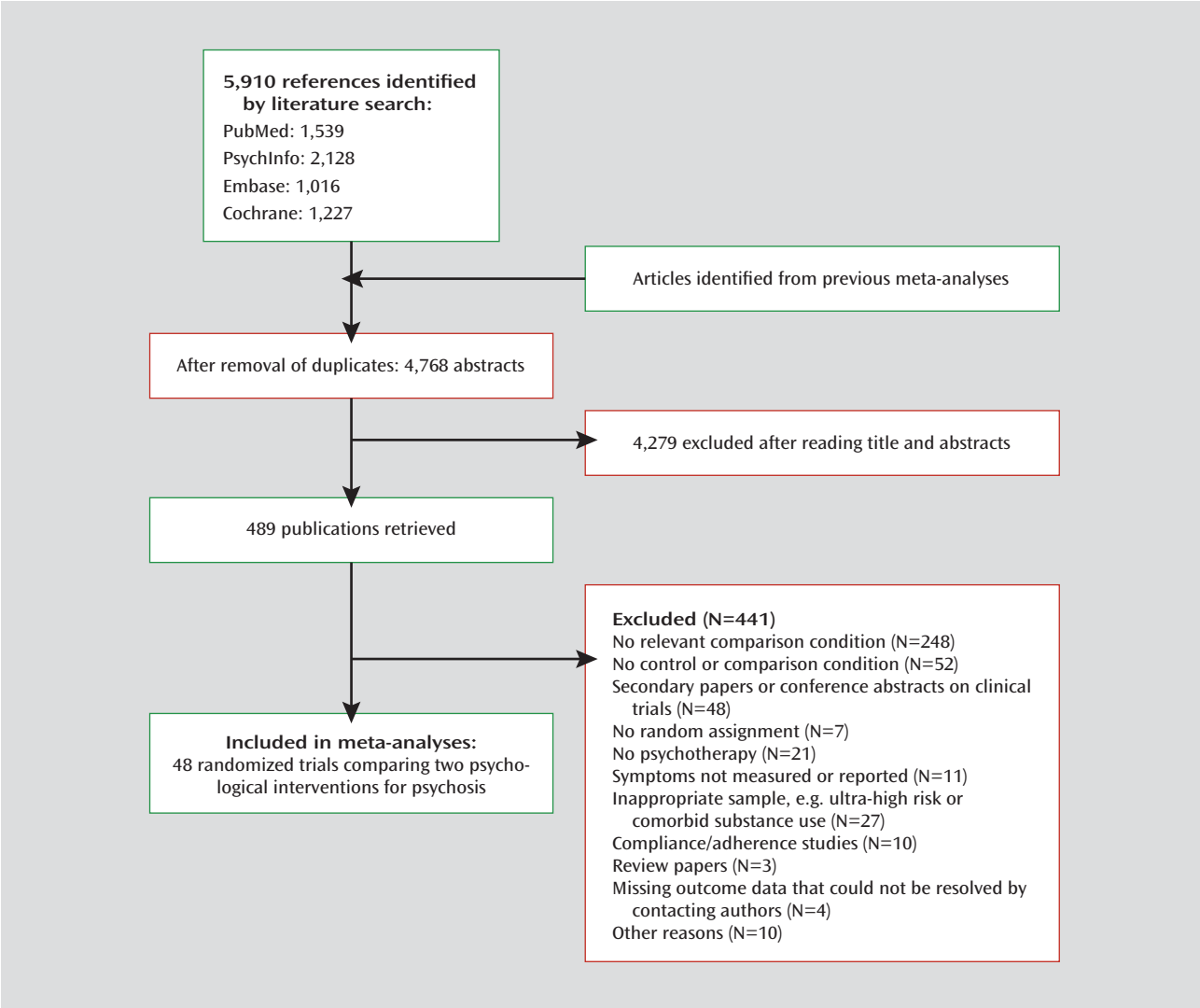


TABLE 3. Effect Sizes for Psychological Interventions Compared With Other Interventions Pooled[a]

Comparison	N	Hedges' g	95% CI	Z-Score	Q	I^2 (%)
Befriending vs. all other therapies						
All symptoms						
All eligible studies	11	–0.37*	–0.60, –0.13	–3.08	21.24*	52.93
Excluding high risk of bias (≥3)	9	–0.28*	–0.51, –0.05	–2.39	14.84	46.08
Excluding low risk of bias (≥2)	6	–0.22	–0.50, 0.06	–1.56	10.78	53.61
Excluding any risk of bias (≥1)	5	–0.20	–0.52, 0.11	–1.27	10.04*	60.17
Positive symptoms						
All eligible studies/excluding high risk (≥3)	6	–0.14	–0.41, 0.13	–0.10	8.81	43.23
Excluding any risk of bias (≥1)	4	–0.17	–0.56, 0.22	–0.86	8.50*	64.72
Negative symptoms						
All eligible studies	9	–0.22	–0.41, 0.04	–1.69	18.12*	55.85
Excluding high risk of bias (≥3)	8	–0.18	–0.45, 0.80	–1.37	15.93*	56.67
Excluding low (≥2) and any risk of bias (≥1)	5	–0.10	–0.44, 0.24	–0.56	11.94*	66.49
General symptoms (PANSS)	5	–0.24	–0.61, 0.13	–1.26	10.42*	61.61
Cognitive behavioral therapy vs. all other therapies						
All symptoms						
All eligible studies	22	0.16*	0.04, 0.28	2.64	23.91	12.18
Excluding high risk of bias (≥3)	18	0.12*	0.00, 0.23	2.01	14.98	0.00
Excluding low risk of bias (≥2)	15	0.10	–0.03, 0.22	1.53	11.30	0.00
Excluding any risk of bias (≥1)	13	0.11	–0.02, 0.24	1.72	9.16	0.00
Positive symptoms						
All eligible studies	17	0.16*	0.04, 0.28	2.67	11.17	0.00
Excluding high risk of bias (≥3)	15	0.14*	0.02, 0.27	2.32	9.42	0.00
Excluding low risk of bias (≥2)	12	0.15*	0.02, 0.28	2.18	9.19	0.00
Excluding any risk of bias (≥1)	11	0.14*	0.00, 0.27	1.97	7.44	0.00
Negative symptoms						
All eligible studies	15	0.04	–0.09, 0.16	0.55	13.94	0.00
Excluding high risk of bias (≥3)	14	0.02	–0.10, 0.15	0.36	13.04	0.34
Excluding low risk of bias (≥2)	11	–0.00	–0.15, 0.14	–0.06	8.13	0.00
Excluding any risk of bias (≥1)	10	–0.01	–0.15, 0.14	–0.06	8.14	0.00
General symptoms (PANSS)						
All eligible studies/low risk of bias (≥2)	8	0.10	–0.13, 0.32	0.86	12.10	42.16
Excluding any risk of bias (≥1)	7	0.05	–0.14, 0.24	0.54	7.60	21.06
Cognitive remediation vs. all other therapies						
All symptoms						
All eligible studies	11	0.13	–0.05, 0.31	1.46	14.63	31.69
Excluding high risk of bias (≥3)	10	0.20*	0.01, 0.39	2.06	11.34	20.65
Excluding low risk of bias (≥2)	6	0.14	–0.05, 0.33	1.41	3.21	0.00
Excluding any risk of bias (≥1)	4	0.12	–0.11, 0.34	1.02	2.49	0.00
Positive symptoms						
All eligible studies	6	0.16	–0.17, 0.49	0.97	14.11*	64.56
Excluding low risk of bias (≥2)	4	0.29	–0.06, 0.64	1.63	6.61	54.59
Negative symptoms						
All eligible studies	6	–0.14	–0.39, 0.06	–1.12	8.47	40.99
Excluding high (≥3) and low (≥2) risk of bias	4	–0.08	–0.38, 0.22	–0.50	5.23	42.59
Psychoeducation vs. all other therapies						
All symptoms						
All eligible studies	8	0.10	–0.27, 0.11	–0.80	8.02	12.66
Excluding high risk of bias (≥3)	6	–0.13	–0.41, 0.14	0.94	7.43	32.67
Positive symptoms						
All eligible studies/excluding high risk (≥3)	4	0.19	–0.06, 0.44	1.50	1.70	0.00
Negative symptoms						
All eligible studies	5	0.02	–0.22, 0.25	0.13	3.06	0.00
Excluding high risk of bias (≥3)	4	0.03	–0.22, 0.28	0.23	2.97	0.00

continued

TABLE 3. Effect Sizes for Psychological Interventions Compared With Other Interventions Pooled[a] (*continued*)

Comparison	N	Hedges' g	95% CI	Z-Score	Q	I^2 (%)
Social skills training vs. all other therapies						
All symptoms						
All eligible studies	16	0.06	–0.17, 0.28	0.49	45.33*	66.91
Excluding high risk of bias (≥3)	10	0.19*	0.02, 0.36	2.15	8.72	0.00
Excluding low risk of bias (≥2)	4	0.34	–0.02, 0.70	1.87	5.47	45.13
Positive symptoms						
All eligible studies	7	0.09	–0.23, 0.41	0.56	16.44*	63.51
Excluding high risk of bias (≥3)	6	0.09	–0.26, 0.45	0.50	16.41*	69.53
Negative symptoms						
All eligible studies	9	0.27*	0.01, 0.53	2.01	17.33*	53.83
Excluding high risk of bias (≥3)	7	0.32*	0.07, 0.56	2.55	10.25	41.47
Excluding low risk of bias (≥2)	4	0.56*	0.31, 0.82	4.29	1.99	0.00
Supportive counseling vs. all other therapies						
All symptoms						
All eligible studies	17	0.00	–0.21, 0.22	0.04	40.31*	60.31
Excluding high risk of bias (≥3)	10	0.01	–0.30, 0.32	0.06	32.97	72.70
Excluding low risk of bias (≥2)	9	–0.12	–0.30, 0.05	–1.37	6.18	0.00
Excluding any risk of bias (≥1)	7	–0.08	–0.28, 0.11	–0.83	1.74	0.00
Positive symptoms						
All eligible studies	8	–0.14	–0.36, 0.09	–1.12	10.28	31.90
Excluding high (≥3) and low (≥2) risk of bias	6	–0.05	–0.25, 0.15	–0.51	5.33	6.27
Excluding any risk of bias (≥1)	5	–0.02	–0.27, 0.23	–0.17	5.00	19.98
Negative symptoms						
All eligible studies	9	–0.12	–0.41, 0.17	–0.83	18.55*	56.87
Excluding high (≥3) and low (≥2) risk of bias	6	–0.21	–0.57, 0.15	–1.13	13.34*	62.52
Excluding any risk of bias (≥1)	5	–0.09	–0.45, 0.27	–0.50	7.74	48.30

[a] All comparisons were made using a random-effects model. Risk-of-bias analyses were included only in instances where at least four studies were available. N=number of comparisons; PANSS=Positive and Negative Syndrome Scale.
* $p<0.05$.

Differences Between Psychological Interventions and Other Interventions Pooled

The results of the six meta-analyses comparing psychological interventions with other interventions pooled are presented in Table 3. Separate meta-analyses were conducted for psychosis symptom groupings. Within each symptom grouping, sensitivity analyses were conducted for varying levels of bias risk. Sensitivity analyses were conducted only when at least four studies were available for that comparison.

Befriending was less efficacious for all symptom outcome measures pooled compared with other therapies pooled (g=−0.366, $p<0.05$). This effect was robust when studies with a high risk of bias were excluded (g=−0.279, $p<0.05$) but lost significance when studies with a low risk and no risk of bias were excluded. Removing the studies with a low risk and no risk of bias also limited the power of this comparison. Seven comparisons of befriending and other interventions pooled showed moderate heterogeneity, and two comparisons showed low heterogeneity.

CBT was more efficacious compared with other interventions pooled for all symptom outcome measures pooled (g=0.161, $p<0.05$). This effect was robust when studies with a high risk of bias were excluded (g=0.118, $p<0.05$) but lost significance when studies with a low risk and no risk of bias were excluded. For positive symptom outcome measures, CBT was more efficacious (g=0.162, $p<0.05$). This effect was robust in all three sensitivity analyses when we sequentially removed studies with a high risk (g=0.144, $p<0.05$), a low risk (g=0.149, $p<0.05$), and no risk of bias (g=0.137, $p<0.05$). All comparisons of CBT with other interventions pooled showed no heterogeneity or low heterogeneity.

Social skills training was more efficacious compared with other interventions pooled for negative symptoms (g=0.267, $p<0.05$). This finding was robust when studies with a high risk of bias (g=0.317, $p<0.05$) and those with a low risk of bias (g=0.563, $p<0.05$) were excluded. Only one social skills training study suggested no risk of bias, so it was not possible to run a sensitivity analysis for no risk of bias. Social skills training was more efficacious for all symptom measures pooled when studies with a high risk of bias were excluded (g=0.187, $p<0.05$), but this comparison lost significance when all studies were included or when studies with a low risk of bias were excluded. Here too, not enough studies were available for a comparison including only studies with no risk of bias. Heterogeneity among comparisons of social skills training and other interventions pooled varied, with four comparisons showing moderate heterogeneity.

Cognitive remediation was more efficacious than other interventions pooled for all symptoms in the sensitivity analysis excluding high risk of bias (g=0.202, $p<0.05$) but was not shown as significantly more efficacious in any other comparisons. Heterogeneity varied among comparisons for cognitive remediation, with two comparisons showing moderate heterogeneity.

Direct Comparisons of Psychological Interventions

The results of direct comparisons between interventions are presented in Table 4. Limited comparisons were possible since few studies were available. CBT was more efficacious than befriending for all symptom measures pooled (g=0.419, $p<0.05$). CBT was also more efficacious than supportive counseling for positive symptoms (g=0.226, $p<0.05$).

Meta-Analyses for CBT Subtypes

To examine whether there were differences between CBT subtypes (coping enhancement and generic CBT), subgroup analyses were conducted. Results included in Table 4 suggest that generic CBT was more efficacious for all symptom measures pooled and for positive symptoms. The between-group comparisons for group versus individual format were not significant, but this comparison was hampered by low power. No subgroup analyses showed significant heterogeneity.

Researcher allegiance. Sensitivity analyses for researcher allegiance were conducted for the robust effects of CBT on positive symptoms and social skills training on negative symptoms. The effect of CBT on positive symptoms became nonsignificant in both sensitivity analyses, although only three studies could be included in the no-allegiance group, resulting in low power. The effect of social skills training on negative symptoms remained significant in the sensitivity analyses, although comparison was not possible for the stricter risk of bias categories because of the limited number of studies available.

Publication bias. Funnel plots and the trim-and-fill procedure suggested the presence of publication bias in some comparisons of the cognitive remediation and social skills training meta-analyses. The funnel plot for all symptoms pooled in the cognitive remediation meta-analysis suggested that three studies with negative findings remained unpublished. Using the trim-and-fill procedure to investigate the significant effect shown for overall symptoms without studies with a high risk of bias (g=0.20), two studies were trimmed, meaning the effect size was reduced to g=0.10 (95% CI=−0.12, 0.32). For the social skills training overall symptoms meta-analyses, the funnel plot suggested that seven studies had not been published when all studies were included. However, when the funnel plot and trim-and-fill procedure were examined for the only significant finding within this meta-analysis, there was no suggestion of publication bias. Similarly, there was no suggestion of publication bias for the significant effects of social skills training found for negative symptoms.

Discussion

This series of meta-analyses comparing psychological interventions for psychosis found significant differences in their relative efficacy for the reduction of psychotic symptoms, as summarized in Figure 2. While some of these differences lost significance when sensitivity analyses were conducted for risk of bias, others were more robust. CBT showed a small but robust superiority in reducing positive symptoms, while social skills training showed a small but relatively robust superiority in reducing negative symptoms. Befriending was shown as less efficacious than other interventions in reducing overall symptoms, although this result was not robust when the more stringent sensitivity analyses for risk of bias were conducted. Similarly, significant effects suggesting benefits of CBT, social skills training, and cognitive remediation for all symptom measures pooled were not significant after sensitivity analyses for risk of bias. It should be noted that the more robust sensitivity analyses resulted in the statistical power dropping well below 0.80. Heterogeneity did not appear as a significant problem in the CBT meta-analyses, whereas some comparisons for the other intervention modalities did show moderate to high heterogeneity, including social skills training. Sensitivity analyses for researcher allegiance resulted in the effect of CBT on positive symptoms losing significance. This was not the case for the effect of social skills training on negative symptoms. Researcher allegiance comparisons were hampered by very low power; it should also be noted that no significant differences in effect sizes were found when comparing studies for CBT and social skills training with allegiance against those with no allegiance.

CBT also showed superiority when compared directly to befriending for all symptoms and when compared with supportive counseling for positive symptoms. The generic CBT subtype appeared more efficacious in reducing overall symptoms and positive symptoms.

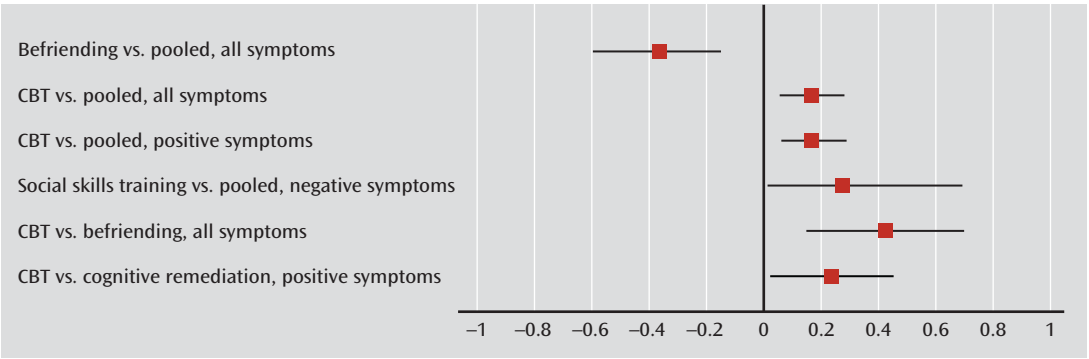
With respect to the much discussed thesis that all psychotherapies produce similar outcomes (1), our results provide evidence that could both support and contradict this proposition. The differences shown between interventions are small in terms of clinical significance. This may suggest that the major therapeutic effects of interventions occur through common factors. However, the pattern of differences in efficacy is consistent with the specific aims of the interventions. CBT appears most successful in reducing positive symptoms, consistent with the rationale of challenging positive symptoms through a formulation-based approach and cognitive restructuring (31, 98). Similarly, social skills training appeared most suitable for reducing negative symptoms (54, 99). These findings provide potential evidence for the role of specific

TABLE 4. Direct Comparisons of Interventions, Segregation of CBT Subtypes, and Subgroup Analyses for Therapy Format, and for Researcher Allegiance in Robust Significant Findings[a]

Comparison	N	Hedges' g	95% CI	Z-Score	Q	I^2 (%)	p
Direct comparisons of two interventions							
CBT vs. befriending							
All symptoms (R)	6	0.42*	0.15, 0.69	3.02	7.00	28.61	
CBT vs. supportive counseling							
All symptoms (F/R)	8	0.10	–0.10, 0.30	0.99	6.09	0.00	
Positive symptoms (F/R)	6	0.23*	0.01, 0.44	2.07	5.00	0.04	
Social skills training vs. supportive counseling							
All symptoms (R)	6	–0.07	–0.54, 0.40	–0.29	26.27	80.96	
CBT subtypes vs. other interventions pooled							
Coping enhancement subtype							
All symptoms (F/R)	6	–0.01	–0.19, 0.18	–0.08	1.83	0.00	
Negative symptoms (F/R)	5	–0.04	–0.23, 0.15	–0.41	2.45	0.00	
Generic subtype							
All symptoms (R)	16	0.22*	0.08, 0.37	2.97	16.96	11.58	
Positive symptoms (F/R)	13	0.17*	0.03, 0.32	2.28	10.66	0.00	
Negative symptoms (R)	10	0.01	–0.08, 0.28	1.07	10.44	13.76	
Subgroup analyses of CBT: group vs. individual format[b]							
All symptoms							
Individual (R)	18	0.18*	0.05, 0.32	2.66	19.93	14.9	
Group (R)	3	0.00	–0.26, 0.27	0.03	1.08	0.00	
Overall (R)	21	0.13	–0.02, 0.29	1.64	22.45	10.93	0.24
Positive symptoms							
Individual (F/R)	13	0.16*	0.02, 0.30	2.17	9.04	0.00	
Group (F/R)	3	0.12	–0.13, 0.36	0.93	0.39	0.00	
Overall (F/R)	16	0.15*	0.01, 0.34	2.04	9.50	0.00	0.80
Negative symptoms							
Individual (F/R)	12	0.09	–0.06, 0.23	1.15	12.05	8.68	
Group (F/R)	3	–0.11	–0.35, 0.14	–0.85	0.16	0.00	
Overall (F/R)	15	0.02	–0.17, 0.20	0.17	13.94	0.00	0.19
Subgroup analyses of researcher allegiance for comparisons with robust significant effects							
CBT vs. all other therapies[c]							
Positive symptoms (F/M)							
Excluding high risk of bias (≥3)							
No allegiance	3	0.10	–0.15, 0.35	0.80	0.24	0.00	0.42
Allegiance for CBT	11	0.17	0.01, 0.32	2.40	5.35	0.00	
Excluding low risk of bias (≥2)							
No allegiance	2	0.08	–0.25, 0.40	0.50	0.21	0.00	0.60
Allegiance for CBT	9	0.18	0.03, 0.33	2.33	5.07	0.00	
Excluding any risk of bias (≥1)							
No allegiance	2	0.08	–0.25, 0.40	0.50	0.21	0.00	0.58
Allegiance for CBT	8	0.19	0.03, 0.34	2.36	4.96	0.00	
Social skills training vs. all other therapies							
Negative symptoms (M)							
All eligible studies							
No allegiance	3	0.37	0.04, 0.7	2.20	2.30	13.27	0.55
Allegiance for social skills training	6	0.21	–0.21, 0.62	0.98	15.50	67.7	
Excluding high risk of bias (≥3)							
No allegiance	2	0.30	–0.10, 0.71	1.48	1.51	33.82	0.83
Allegiance for social skills training	6	0.36	0.04, 0.69	2.19	8.97	44.25	

[a] The p values in the right-hand column refer to the difference between subgroup effect sizes. CBT=cognitive-behavioral therapy; R=random-effects model; M=mixed-effects model; F/M=mixed model and fixed model identical; F/R=fixed and random-effects model identical; N=number of comparisons.
[b] Excluding one study that used both group and individual format.
[c] Excluding one study with allegiance against CBT.

FIGURE 2. Main Results of Comparisons of Psychological Interventions for Psychotic Symptoms[a]



[a] The other main comparisons did not result in significant findings. This figure does not include sensitivity analyses for risk of bias or researcher allegiance; complete results are presented in Tables 3 and 4. CBT=cognitive-behavioral therapy.

factors as at least partially influential in determining treatment outcome. When we consider that the effects of common factors are already accounted for in the treatment comparisons and that a high proportion of the participants also receive pharmacotherapy, findings suggesting that specific factors influence their targeted symptoms are of interest. The design of this study, however, does not allow us to control completely for other potential influences on outcome, which may explain the effect we are attributing to specific factors. An attempt was made to control for researcher allegiance, but only limited comparisons were possible, primarily because few studies showed no allegiance.

We are aware that CBT is uniform in its assumption that negative emotions and behavioral problems are the result of the appraisal and interpretation of antecedent events. By changing appraisal and interpretation of events and stimuli, the emotions and the behavior will change. However, there are variants within CBT that differ in degree of emphasis on cognitions or on behavioral experiments. We have the impression that variations in CBT are not typically reflected in results, although the meta-analysis by Wykes et al. (11) found a trend for larger effect sizes in more behavioral CBT. Comparisons could be made to antipsychotic medication, where almost all agents target dopamine D_2 receptors. Although the compounds are slightly different from each other, they have about the same efficacy (100). A recent development is that CBT using the same general technique is becoming more focused. For example, CBT protocols are being developed to address command hallucinations (101) and negative symptoms (102, 103). Preliminary results show larger effect sizes for more focused applications compared with generic CBT for psychosis.

Our study had several limitations that affect the extent to which robust conclusions can be drawn from the results. The majority of comparisons had low statistical power (<0.80). Without satisfactory power, there is a high risk of type II errors. A limitation of any meta-analysis categorizing randomized controlled trials into groups by intervention type is that such decisions involve a degree of subjectivity. We attempted to address this issue by having two researchers agree on categorization. There was some controversy regarding study selection following the Lynch et al. CBT meta-analysis (22–24, 99). The risk of bias procedure applied in our meta-analysis addresses the issues raised about inclusion since all but one of the studies excluded in the Lynch et al. meta-analysis were excluded in the most stringent sensitivity analysis. For the aims of this meta-analysis, there did not appear to be any reason to exclude this study (75).

Another limitation concerns our focus on positive, negative, and general symptoms. While CBT, supportive counseling, and befriending target symptom reduction, psychoeducation, social skills training, and cognitive remediation only indirectly target symptoms. Psychoeducation is often intended to improve medication adherence, with secondary symptom improvement, and although the effects on symptoms were not significantly different from all other interventions, this does not mean that psychoeducation was not able to improve adherence. Similarly, cognitive remediation targets the improvement of cognitive functioning, and the absence of an effect on symptoms does not mean that there was no improvement in cognitive functioning. Those effects are beyond the scope of the meta-analyses we present and are not reported. It was also beyond the scope of this study to consider the possibility of patients with better prognosis being channeled into a particular treatment, interaction with pharmacotherapies, and diagnostic heterogeneity among samples, since information on these domains was not reliably available across studies.

There was considerable variety in the quality of studies as assessed by the risk of bias procedure, and there were marked differences in quality between specific intervention types. CBT had the highest proportion of studies assessed as having no risk of bias, and social skills training had the lowest. It is important that future studies on the relative efficacy of social skills training address these issues. Research should continue to compare psychological interventions for psychosis in order to improve statistical power in meta-analyses.

It is essential, too, that comparative randomized controlled trials minimize bias risk and that the issue of researcher allegiance be addressed. Meta-analytic studies must also answer related questions about psychosis interventions, such as predictors of treatment outcome and dropout. This includes individual participant data meta-analyses, in which the authors of this study are currently involved. Future research may also focus on dismantling studies, which provide insight into the influence of common and specific factors. Future development of treatment plans may take into account the effects of specific factors on the specific symptom areas and integrate these to optimize both positive and negative symptom reduction.

In conclusion, although the differences observed between interventions for psychosis were small in this meta-analysis, the relatively robust nature of the differences and the pattern by which differences occur have implications for the continued clinical implementation, design, and improvement of psychosocial therapies for psychosis.

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Clinical Guidance: Psychological Interventions for Psychosis

Cognitive-behavioral therapy is superior to other psychological treatments for reducing positive symptoms, and social skills training is more efficacious for negative symptoms, according to a meta-analysis by Turner et al. Befriending is less helpful in ameliorating symptoms than other interventions. In his editorial, Strauss (p. 479) underscores the need to consider the diversity of treatment options in relation to the even greater diversity of patients with severe mental illness. Cognitive training focuses on neural systems rather than symptoms, and Keshavan et al. (p. 510) report that it can benefit patients with schizophrenia and may improve functioning when combined with other forms of rehabilitation and coaching. The editorial by Harvey (p. 482) notes that training in a global cognitive process, such as planning, exercises multiple basic skills, such as sustained attention.